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ISIORT Meeting

1 speaker

FULL-DOSE INTRAOPERATIVE RADIOTHERAPY WITH ELECTRONS IN BREAST SURGERY

R. Orecchia

European Institute of Oncology and University of Milan, *Milan, Italy*

Long-term results of the Milan III trial – a large randomised trial comparing Quadrantectomy, Axillary Dissection and Radiotherapy (QUART) vs. Quadrantectomy, Axillary Dissection without Radiotherapy (QUAD) – showed that about 86% of recurrence in the ipsilateral breast occur in the previously involved quadrant. In addition a very important reduction in local failure has been observed in older patients (over 55 years), also in the group without postquadrantectomy irradiation. These observations encourages the choice, for peri- and postmenopausal patients, of a more limited radiation treatment aimed at the elimination of potentially residual cancer cells in the vicinity of the primary tumour, while irradiation of the whole breast may be avoided.

We have focused our interest on the use of IOERT. The use of IOERT as the sole modality of irradiation in a selected group of patients has the potential for accurately treating the tumour bed since the applicator can safely be placed under the direct visual control into the open surgical field. The skin and the subcutaneous tissue are not irradiated, thus decreasing the potential risk of fibrosis and eventually obtaining a better cosmesis. Furthermore, if a significant dose, equivalent to a full course of fractionated radiation therapy, can safely be delivered with IOERT, in selected patients with the lowest risk of ipsilateral breast tumour recurrence the conventional approach could be replaced by a intraoperative limiting treatment to the surgical bed with obvious advantages in terms of overall treatment time, treatment logistics, cost and patients' comfort and QoL. The biologic equivalent of a single IOERT dose is felt to be 1.5-2.5 higher than the dose delivered with external beam radiotherapy. For example, a total dose of 60 Gy given with a 2 Gy fractionation is equivalent biologically to a single dose of IOERT of 22.3 Gy when alfa/beta ratio = 10 Gy (mammary tumour).

A long period (more than four months) of extensive testing has been necessary for the ELIOT program to be activated. Logistics, organisation and personnel training were provided before the first patients were successfully treated (July, 19th, 1999).

Our subsequent clinical experience was planned and developed in 4 phases:

- A dose-escalation study in order to define the maximum tolerate dose in single fraction and establish an equivalence between the reached value of single IOERT dose and the conventional fractionated schedule of external radiation therapy; this phase was closed in April 2000.
- A phase II study (from May to November 2000) at the maximum tolerated dose level reached (21 Gy), in order to assess in a larger cohort of patients, the acute and intermediate toxicity.
- A prospective randomised study (started in December 2000 and currently ongoing) comparing standard external beam irradiation (50 Gy on the whole breast and 10 Gy boost on tumour bed) with a single dose (21 Gy prescribed at 90% isodose) of intraoperative irradiation on a limited field, in order to evaluate effectiveness of the new approach in terms of local control, regional control, disease-free, distant metastases and overall survival, cosmetic outcome, and cost.
- A nipple-sparing mastectomy study (since March 2002 and to date oingoing) testing a new technique to preserve the nipple and areola complex during mastectomy, which includes the delivery of a 16 Gy single dose to this anatomic area.

2 oral

LINAC-BASED IOERT AS BOOST STRATEGY DURING BREAST CONSERVING THERAPY IN LIMITED-STAGE BREAST CANCER: RESULTS OF AN ISIORT POOLED ANALYSIS

F. Sedlmayer, G. Fastner, F. Merz, R. Reisamer, C. Menzel, A. Ciabattoni, A. Petrucci, E. Hagen, N. Willich, A. Schuck, M. Brinkmann, R. Orecchia, V. Valentini

On behalf of the ISIORT Europe

Purpose/Objectif: Local recurrences after breast conserving therapy (BCT) primarily occur in the vicinity of the former tumor site. The idea of linac- based intraoperative radiotherapy with electrons (IOERT) is the delivery of a single high dose to a zone at highest contamination with subclinical tumor cells. The European Group of the International Socoitey of intraoperative Radiotherapy (ISIORT) performed a pooled outcome analysis among those institutions where intra- and postoperative radiation treatment was comparable in techniques, sequencing and dosage.

Materials/Methods: From 10/98 until 05/05, IOERT was performed in 1104 patients during breast conserving surgery. The median age was 57,3 years (22,5-89,9). Tumor characteristics are summarized in table 1. 670 patients (60%) showed up with at least one adverse prognostic factor in terms of tumor size (T3), Grading (G3), age (‹45a) and/or positive nodes.

The tumor bed was treated predominantly with electron energies of 6 and MeV (4-18 MeV). A median single fractional dose of 9,7 Gy (0,7 SD, range 5-17) was applied to the 90% reference isodose, using round perspex tubes with 5-8 cm diameter. Whole-breast irradiation with 50- 51 Gy (ductal carcinoma) to 54 Gy (lobular carcinoma) was performed after wound healing. Over 95% of the patients received additional adjuvant systemic therapy.

Results: (state of analysis 2/07): For 60 Patients no follow-up data were available at the time of analysis. In the remaining 1044 patients, 5 in-breast recurrences have been observed during a median follow-up period of 52,6 months (3,5-101), yielding a local tumor control rate of 99,4%. 42 patients have developed metastases, 32 of them died from cancer. At 7 years, disease free survival, disease specific survival and overall survival amount to 89,5%, 96,8% and 94,3%, respectively. 964 patients are alive without disease breast. A cosmetic evaluation was performed in 358 patients following a 5 – point scoring system (double evaluation).

Conclusions: IOERT as anticipating boost strategy can be performed without excess morbidity and allows for small treatment volumes and complete skin sparing. Direct visualisation of the tumor bed guarantees highest accuracy in dose delivery. So far, excellent local tumor control rates could be achieved.

Table 1. Tumor characteristics

	T		N		Grade
Data	10	N0	641		
T0	5	N1	367	G1	137
T1	734	N2	35	G2	551
T2	313	N3	8	G3	309
T3/T4	8	Nx	9	Gx	3
Not stated	24		44		309

3 oral

IN VIVO DOSIMETRY DEVELOPMENTS USING RADIOCHROMIC FILMS DURING IOERT IN EARLY-STAGE BREAST CANCER

M. Ciocca[1], S. Comi[1], F. Cattani[1], G. Gatto[2], R. Lazzari[2], A. Luini[3], P. Veronesi[3], V. Galimberti[3], M. Intra[3], U. Veronesi[3], R. Orecchia[2]
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Purpose/Objectif: In two previous papers (Radiother Oncol 2003;69:285-9 and 2006;78:213-6), we published the results of in vivo measurements using respectively radiochromic films and real-time micro-MOSFET detectors in electron beam IORT. In the present study, a further improvement was made, aiming at checking not only the dose delivered to the patient, but also the "exit" dose, i.e. the dose to the deep margin of the target volume.
Materials/Methods*:* In vivo dosimetry was addressed to patients affected by early-stage breast cancer, who underwent IOERT, exclusive or as a boost to the tumour bed (12 or 21 Gy, at 90% isodose), after quadrantectomy. IOERT was delivered using electron beams (4 to 10 MeV) at very high dose per pulse, produced by either a Novac7 or a Liac mobile linac, located in two operating rooms. In vivo dosimetry consisted of combined entrance and pseudo-exit dose determination. The former was derived from the measurement of the surface dose, while the latter was directly measured below the target, both using thin and calibrated MD-55 radiochromic films, wrapped in small and sterile envelopes. In particular, to determine the minimum absorbed dose to the tumour bed, films were put on top of the shielding disc used to protect the underlying normal tissues (muscle, lung, heart). Films were analysed 24-72 hours after the irradiation, using an EPSON scanner and a commercial dedicated software (Picodose TA).
Results*:* In January 2007, in vivo dosimetry was performed on 7 patients. Concerning the entrance dose, the mean ratio between measured and expected doses was 0.982, with one SD equal to 2.6%. Two cases were excluded due to observed displacement of the films inside the treatment field. As regards exit dosimetry, in 4 patients inhomogeneous blackening of the films was found, while in the remaining 3 cases the mean dose was 85% of the prescribed dose. Measured doses were 10-15% lower than the expected values based on the measurement of target thickness acquired by the surgeon. The overall uncertainty of in vivo dosimetry was estimated around 3.5% (1 SD).
Conclusions: Preliminary results showed nice agreement between expected and measured entrance doses, while suggesting the need to slightly modify the exit dosimetry procedure. The observed poor results could be due to a displacement of the internal shielding disc during IOERT: wider films, covering most of the disc surface, will be used for next cases to investigate this issue.

4 oral

DOSIMETRIC PLANNING SYSTEM FOR ELECTRON IORT WORK IN PROGRESS

F. Calvo, M. Desco, J. Lopez, JA. Santos, A. Santos, PG. Barreno
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Purpose: Changes in the patient geometry-anatomy during the surgical pre-radiation procedure requires IORT dosimetric adaptation. Pre-or post-operative CT or MR images do not reflect the anatomical status when the radiation in applied. Dosimetric planning for IORT procedures is a pending need.
Materials and method: A simulation program has been developed in the IDL image processing environment (a high level programming language for image management). The program can be used (1) as a pre-treatment tool to better plan the surgical intervention or (2) to elaborate dosimetry representation and registration.
1. The program allows to interactively modify the preoperative CT or MR images in order to match the final geometry of the area when the radiation is applied (surgery simulation). The whole data set is displayed in the three small orthogonal views, initially representing the axial, saggital and coronal planes. The views can manually be edited, simulating the surgical removal of objects. Once the images adequately resemble the surgical approach and status, the user can overlay isodose curves (standard curves previously measured in a water phantom for all the collimator sizes, angles and available energies). Results may be used to redefine the original tentative planning (collimator type, energy, surgical approach).
2. Besides, an accurate dosimetry can be provided by generating a new modified data set and exporting it into a standard planning equipment for isodose curves calculation.
Results: Initial tests have reported the present dosimetry tool (1) as a useful feature for initial planning. Exact dosimetry (2) was considered relatively, but slow valuable for post-surgical precise dose control.
Conclusions: The system may substantially improve the quality, reliability, and safety of IORT treatment by allowing a more precise dosimetry estimation and registration.

5 oral

HIGH LOCAL CONTROL AND LIMB PRESERVATION RATE IN PATIENTS WITH MARGINALLY RESECTED SOFT TISSUE SARCOMA (STS) OF THE EXTREMITIES FOLLOWING INTRAOPERATIVE (IORT) AND EXTERNAL-BEAM RADIOTHERAPY (EBRT)

B. Röper[1], EM. Kächler[1], E-M. Schottdorf[1], H. Rechl[2], A. Kretzler[3], F. Würschmidt[4], F. Still[5], D. Hölzel[6], M. Molls[1], R. Gradinger[2]
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Purpose/Objectif*:* Soft tissue sarcomas of the extremities are a rare tumour entity, and the role of IORT for limb preservation is not clearly defined, as availability is restricted to specialized centres and randomized data is lacking. We evaluated the data of our institutional series with focus on overall survival (OS), metastatic-free survival (MFS) and local control (LC) after radiotherapy (RT) with and without IORT.
Materials/Methods: 97 pts with STS of the extremities (new primaries/recurrences 70/27, upper/lower limb 16/81, UICC-stage I:13, II:20, III:56, IV:8) presented in 1995-2005 for limb-sparing resection and local RT. Individual treatment decisions led to EBRT alone (group 1, n=47, median dose 60Gy), IORT + EBRT (group 2, n=41, median doses 15 Gy IORT plus 54 Gy EBRT) or IORT alone (group 3, n=9, median dose 15Gy). Adverse prognostic factors did not differ significantly between group 1 and 2–except for larger tumour size in group 2 (68% ›=10cm vs. 30% in group 1, p‹0.01, X^2-test)–and accumulated in group 3. Resection margin was close (0.1-2mm) in 42 pts and positive in 36 pts (incl. 8 R2-resections). Median follow-up was 40.7 months (range 5-130; 47 mts for 57 pts alive). Survivors were invited for functional evaluation according to Enneking [perfect function: 100%].
Results*:* At last follow-up 18, 16 and 6 patients had died in group 1, 2 and 3, respectively (30/40 due to distant disease) with a median OS of 85mts (95%-CI 72-97) and actuarial 5yr-OS of 66%. OS did not differ significantly between group 1 and 2 (70.5% vs. 60.3%, p=0.15 logrank), but was poor in group 3 (21%). Likewise, actuarial 5yr-MFS was similar between group 1 and 2 (66% vs. 56%, p=0.40) and limited in group 3 (25%).

11, 5 and 3 recurrences in group 1, 2 and 3 led to an actuarial 5yr-LC of 66.0%, 85.4% and 58.3%, respectively (p=0.052, logrank). Recurrence required amputation in 5 and 3pts of group 1 and 2, thus limb preservation was possible in 89/97 pts (92%). 39/57 living pts could be scored for overall limb function with a median score of 70% in group 1 and 83% in group 2.
Conclusions*:* In spite of adverse tumour characteristics and marginal resection, RT enabled long-term limb preservation in ›90% of our pts. Even though tumours were larger in group 2, LC and overall limb function tended to be superior with combined treatment (IORT+EBRT) compared to EBRT alone. IORT can be recommended for limb preservation in STS. OS is determined by rate of metastases.

6 oral

INTRAOPERATIVE ELECTRON RADIOTHERAPY FOR ADVANCED ANTERIOR SKULL BASE TUMOURS: SIX YEARS EXPERIENCE

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Purpose/Objectif: Advanced (T3-4) malignant skull base tumours establish a therapeutic challenge, yet surgical capabilities enable accomplishing free histological margins (R0-resection). However, because of anatomical characteristics, achieved free margins are very narrow. Despite postoperative radiotherapy, local recurrence is the most frequent treatment failure and fatality cause. In order to improve treatment results, an additional radiation dose may be delivered by intraoperative electron radiotherapy (IOERT) to the volume of narrow histological margins. We report our six years experience with IOERT in conjunction to surgery.
Materials/Methods: Since January 2001, 30 patients with advanced anterior skull base tumours were treated with IOERT using single doses between 8 and 10 Gy. IOERT to the skull base with its irregular surface was only possible with a special technique developed at Salzburg University, which allows the evaluation and compensation of the irregular surface for dosimetry. In addition, sensitive structures have been spared from irradiation by individually shaped perspex shields.
Results: After a median follow-up time of 20.4 months (2-70 months), seventeen patients are alive. Thirteen patients have died. The overall 5 year survival rate is 48%. No patient with primary tumour suffered from or died because of recurrent tumour at the sie of IOERT. There were no side effects attributable to the use of IOERT.
Conclusions: IOERT is possible and in our opinion successful in the treatment of advanced anterior skull base tumours. Prerequisites are surgical techniques which allow electron tube placement and optimized radiotherapy with surface dosimetry and field blocking.

7 oral

CLINICAL RESULTS AND ISODOSE PLANNING OF NEURONAVIGATION-GUIDED INTRAOPERATIVE RADIOTHERAPY (IORT) IN 77 BRAIN TUMOR PATIENTS: ADEQUATE TARGET VOLUME COVERAGE IMPROVES RESULTS

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Purpose/Objectif*:* Even after resection and radiotherapy, malignant gliomas still have a bad prognosis. Many new treatment methods have been tried with little success. We report on our experience with neuronavigation-guided IORT and postoperative isodose calculation.
Materials/Methods*:* From 1992 to 2006, 77 pts. with malignant gliomas were treated with IORT. 26/77 pts. had grade III gliomas, 51/77 pts. had glioblastomas (GBM). 53/72 primarily treated pts. received 20 Gy IORT + 60 Gy external RT, 19/72 pts. with recurrences received 20-25 Gy IORT alone. The beam angle was selected using neuronavigational guidance according to the preoperative CT images. To preserve this angle during transportation, we constructed a special device known as 'beam direction indicator' (BDI). Gantry and couch angles were adjusted to the intended direction by directing a central beam laser to the tip of the BDI. The electron energy was chosen so that the 90% isodose surrounded the tumor bed by 1 cm. In the last 11 patients, the beam parameters were calculated from the neuronavigation data by coordinate transformation and entered into the treatment planning system, enabling postoperative isodose planning. PTV coverage and dose at organs at risk were assessed by quality parameters such as D90, D100, and V90. The influence of prognostic factors (including adequate target colume coverage) on survival was studied using uni- and multivariate analysis. Adequate target volume coverage was defined as follows: 1. EBRT dose ›= 56 Gy. 2. IORT dose ›= 20 Gy. 3. a) Therapeutic range of electrons ›= tumor size AND tube size ›= tumor size (clinical setup) OR 3. b) D90 ›= 80% AND V90 ›= 80% (isodose plan).
Results: The complication rates were 1.5% for wound infections and 4.5% for bleeding. For grade III gliomas, the median specific survival time amounted to 14.9 months, that of GBM was 14.2 months. The 2-year survival rates amounted to 26.9% (gliomas III) and 7.0% (GBM). Significant prognostic factors included histology (p=0.0346) and target volume coverage (p=0.0428). Resection status reached borderline significance (p=0.077). KPI (p=0.6520), primary or recurrence (p=0.2977) and temozolomide application (p=0.8955) were not significant. Multivariate analysis showed histology (p=0.033) and target volume coverage (p=0.011) as remaining prognostic factors. Recurrences and glioblastoma patients showed significantly better results than a historical control with EBRT only. Initial symptoms improved in 59% (hemiparesis), 50% (aphasia), 50% (hemianopsia), and 60% (convulsions). The evaluation of the target volume coverage showed a characteristic "learning curve" with 2 early pts. who received a significant underdosage because of low electron energy.
Conclusions: IORT was shown to be feasible. In most cases, symptoms could be improved. Survival rates were improved for recurrences and glioblastomas. The dose reconstruction method developed by us allows the calculation of a 3-D dose distribution for IORT and enables postoperative quality control. The learning curve indicates that quality assurance can improve treatment by facilitating the correct choice of electron energy. An adequate target volume coverage significantly improves treatment results.

8 speaker

INTRAOPERATIVE RADIATION THERAPY IN PANCREATIC CARCINOMA: A MULTI-INSTITUTIONAL POOLED ANALYSIS

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Background: Local recurrence is one of the most common sites of failure after resection of pancreatic adenocarcinoma. Intraoperative

radiotherapy (IORT), which involves delivery of high doses of irradiation to the surgical bed after resection, seems to safely improve local control in these patients (pts).
The purpose of the current report was to evaluate efficacy of IORT using pooled data on 185 patients with pancreatic cancer treated at 5 European Institutions from 1985 to 2005.
Materials and methods: 185 patients affected by pancreatic carcinoma underwent surgical resection. A potentially curative resection with negative margins was achieved in 110 pts (60%). Microscopic positive margins and macroscopic residuals of disease were found in 44 pts (23%) and 31 pts (17%) respectively.
IORT was delivered to all 185 pts (median dose 20 Gy, range 9-25 Gy). Twenty-four of these pts also received neoadjuvant chemoradiation (median dose 45 Gy, range 30-50 Gy) and 66 pts adiuvant radiotherapy (median dose 45 Gy, range 36-61 Gy).
Results: The perioperative morbidity was 33 % and the perioperative mortality was 3 %. With a median follow-up of 120 months, the overall rate of local recurrence the patients was 32 %. Actuarial one and three-year local control was 64% and 32% (median 15 months), metastases free survival was 43% and 18% (median 9 months) and overall survival was 67% and 17 % (median 16 months).
Patients treated with neoadjuvant chemoradiation and IORT, IORT plus adjuvant radiotherapy and IORT alone, had a rate of local recurrence of 19%, 25% and 46 % respectively (p=0.0001).
At the univariate analysis tumor diameter ‹ 2 cm, negative margins of resections and neoadjuvant radiotherapy combined with IORT showed a significantly improvement in local control, metastases free survival and overall survival.
Conclusions: Intraoperative radiation therapy seems to not increase the morbidity or mortality of potentially curative surgical resection for pancreatic cancer. IORT when associated with neoadiuvant chemoradiation rather than in the other settings, appears to improve local control and overall survival.

9 speaker

THE TREATMENT OF LOCALLY ADVANCED RECTAL CANCER BY INTRAOPERATIVE ELECTRONBEAM RADIOTHERAPY (IOERT) CONTAINING MULTIMODALITY TREATMENT: RESULTS OF AN EUROPEAN POOLED ANALYSIS

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Purpose/Objectif*:* External beam doses necessary to achieve control in case of microscopically residue in rectal cancer are in excess of 60 Gy. However dose limitation to surrounding healthy tissues restrict external irradiation to 50-50,4 Gy. The gap between the maximal external beam dose and the theoretically most optimal tumoricidal dose can be overcome by means of IOERT boosting of the area at risk. The penetration depth of electrons can be controlled within a millimeters marge. The benefits of a local high dose to may outweigh the complications resulting from this irradiation of a very limited volume at risk. One of the most successful areas for the use of IORT boosting is in patients with locally recurrent or locally advanced rectal cancer. In the pelvis, even extended surgery is confined to natural boundaries that restrain surgical possibilities.
Materials/Methods: Four major referral centers for locally advanced rectal cancer have been involved in IOERT since more than 10 years. Despite the fact that parts of the multidisciplinary treatment differed among these institutes and also changed in time, the protocol for the use of IOERT remained unchanged: 10 Gy boost at the area of risk in completely resected patients. From these institutes 651 patients were pooled. Follow-up ranged from 0-179 months. The 50% overall survival rate was observed at 102 months.
Results: At 5 yrs OS was 67% and at 10 Yrs 46%› The local control rate was 88% and 86% at 5 yrs and 10 yrs respectively. Circumferential margin positivity was a strong (p‹0.0001) predictor of survival, as well as local recurrence (p‹0.01). The use of neoadjuvant radiochemotherapy seems to improve overall survival (70% versus 64 % at 5 yrs, p‹0.05), but had no impact on local recurrence rate. Patients who responded well to neoadjuvant treatment survived significantly better than those who had not (p‹0.0001). This was also true for the development of local recurrence. Level of the tumor (below or above 5 cm from the anal verge) had neither impact on local recurrence rate or overall survival rate.
Conclusions*:*The use of IOERT containing multimodality treatment resulted in a selected group of patients with locally advanced rectal cancer, not likely resectable with curative intent, in an excellent overall survival and local control. Hence, this treatment modality merits intensified evaluation.

10 oral

INTRAOPERATIVE RADIATION THERAPY IN LOCALLY ADVANCED RECTAL CANCER

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Purpose/Objectif: To assess effectiveness and tolerance of IntraOperative Radiation Therapy (IORT) in patients suffering from locally advanced rectal cancer, treated with preoperative radiotherapy followed by surgical resection.
Materials/Methods: In this French, multicentre, comparative, open-label, 2-parallel group, phase III study, 142 included patients with locally advanced rectal cancer (T3 or T4 or N+, and M0), having received a 4-week preoperative radiotherapy (for a total of 40 grays) were randomly assigned to either surgical resection alone (Control group : n=69) or combined to a 18-gray intraoperative radiation therapy (IORT group : n=73).
Results*:* The 5-year cumulative incidence of local control was 91.8 % with IORT and 92.8 % with surgery alone (p=0.6018) ; the mean duration without local relapse (Kaplan-Meier method) was of 107 versus 126 months, respectively. No statistically significant difference was demonstrated for overall surgical (p=0.2578) disease free survival (p=0.7808) and probability of metastatic relapse (p=0.6037) with 5-year cumulative incidences of 69.8% versus 74.8%, 63.7% versus 63.1% and 26.1% versus 30.2%, respectively.
Seventeen patients per group developped at least one local and/or metastatic relapse. Two patients of the IORT group were lost to follow-up at 2 and 39 months, respectively. In all, 48 patients f the IORT group and 53 patients of the Control group were alive with a median follow-up of 60.1 and 61.2 months, respectively. No patient died during either the surgical intervention or the intraoperative radiation therapy. Complications tended to be more frequently observed in the IORT group (21 patients, 29.6%) than in the Control group (13 patients, 19.1%) (p=0.15); however, a single perioperative death occured in one patient of the Control group due to cardiac disorders on D10.
Conclusions*:* In our study, no statistically significant difference was demonstrated between intraoperative radiation therapy and surgical resection alone in term of efficacy for the treatment of advanced rectal cancer in patients having received preoperative radiotherapy ; however the actuarial 5-year local control was more than 90% in each group. Tolerance profile was acceptable.

11 oral

MULTIORGAN RESECTION AND INTRAOPERATIVE IRRADIATION IN RECURRENT PELVIC CANCER: LONG-TERM RESULTS

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Purpose: To evaluate feasibility and results of extensive pelvic surgery plus intraoperative electron irradiation as rescue treatment in localized cancer recurrence.
Methods & Material: From 10/95 to 2/07 48 recurrent patients were explored and treated with IORT. There were 28 female and 20 males. Age range from 21 to 84 years old (median 53.8). 54% of pts were symptomatic. Dominant histology was adenocarcinoma 73%. Primary sites included gynaecologic 32%, colo-rectal (63%) and urologic. Topography of recurrence were: centro-pelvic (56%), presacral (25%), and lateral walls (19%). Size of recurrence was a superior to 5 cm in maximal dimension in 30% of cases. 65% had previous pelvic radiotherapy (RT).
Results: Surgery required sacropelvic resection in 27% of procedures, multiorgan in 39% and atypical debulking or tumor exposures in 33%. IORT dose were 10 Gy (38%), 12,5 Gy (50%), 15 Gy (12%). Additional RT was given to 25% and CT to 33%. Surgical resection margins were cancer positive in 37% of the specimens. 72% of recurrences involved 4 or more pelvic structures. With a median follow-up time of 62 months, patterns of disease recurrence showed pelvic alone in 17%, distant in 27% and mixed in 8%. 14 pts are alive NED (+5 to +144 months; 7 pts are over 4 years follow-up).
Conclusions: A significant number of patients are alive NED long-term after extensive surgery and IORT in individually designed combined rescue treatment for localized pelvic cancer recurrence.

12 oral

MULTIMODALITY TREATMENT CONTAINING IORT FOR RECURRENT RECTAL CANCER

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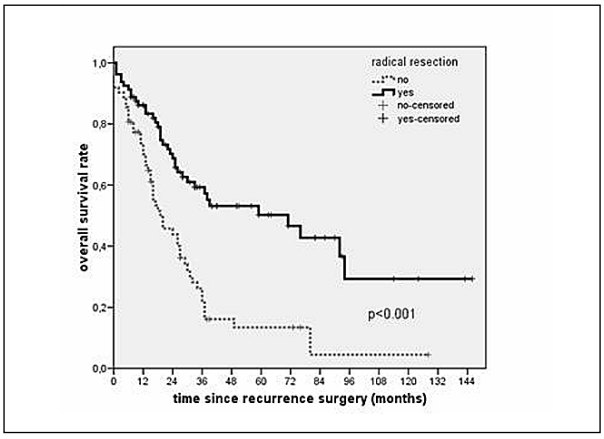
Purpose/Objectif: Recurrent rectal cancer is a highly lethal disease. Since standard treatment of primary rectal cancer includes radio(chemo)therapy, the treatment options for a local recurrence and subsequent options for cure are limited due to dose accumulation toxicity. It is of great importance to know which factors are of influence on the prognosis and what is the best treatment option. We assessed the outcome of a large series of patients who underwent multimodality treatment for locally recurrent rectal cancer.
Materials/Methods: A retrospective review was performed on 142 consecutive patients who underwent neoadjuvant (chemo)radiation followed by resection and IORT for locally recurrent rectal cancer between March 1994 and July 2006. Eighty-two men and 60 women were included. Median age was 62 (range 39-87). Overall, disease-free and cancer-specific survival (OS, DFS, CSS) curves were constructed by the Kaplan-Meier method and compared by log-rank analysis.
Results: Mean follow-up time for survivors was 45 months (range 6-146). Median time interval between resection of primary and recurrent disease was 27 months (range 3-200). Five-year OS, DFS and CSS were 33.3, 36.4 and 39.1% respectively. Radical resection was obtained in 80 patients (56.3%), R1 resection in 42 patients (29.6%) and R2 resection in 20 patients (14.1%). Radical resection was significantly correlated with improved OS, DFS and CSS and local recurrence free interval (p‹0.001). Primary TNM stage, type of neoadjuvant treatment (no vs. reirradiation vs. full course), type of surgery for recurrence (LAR vs. more extensive surgery) and IORT dose were significantly correlated with OS (p=0.006, p=0.038, p=0.016 and p=0.001 respectively). When only the radically resected patients were analysed, primary TNM stage remained the only significant factor for OS (p=0.019). Five-year OS, DFS and CSS for radically resected patients were 50.2, 52.4 and 56.1% respectively. Patients who underwent irradiation as part of the primary treatment benefit from reirradiation. After reirradiation significantly more radical resections could be realised compared to no irradiation (61% vs. 27%, p=0.01).
Conclusions*:* Radical resection is the most significant predictor of improved survival. Despite aggravating consequences, multimodality treatment is the best option in order to realise radical resection in patients with locally recurrent rectal cancer.



13 oral

LONG-TERM RESULTS OF INTRAOPERATIVE RADIOTHERAPY (IORT) IN ADVANCED AND RECURRENT RECTAL CARCINOMA

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Purpose/Objectif: About a third of rectal cancer patients develop logoregional recurrences. Long-term local control is the main challenge in these patients. Surgical treatment with IORT can achieve 5-year survival rates of up to 31%. We present long-term results from a non-dedicated facility.
Materials/Methods: From 1997 to 2005, 33 patients (pts.) (21 male, 12 female, age range: 39 to 77 years) with advanced primary (5/33 pts.) or recurrent rectal carcinoma (1 residual tumor, 22 first recurrences, 4 second recurrences, 1 secondary tumor) were treated with electron beam IORT alone or in combination with external beam radiotherapy (EBRT). 12/33 pts. had been previously irradiated with a median dose of 50.2 Gy (9/12 with simultaneous chemotherapy). 24/32 pts. were treated with curative, 8/32 with palliative intent (M1). 14/32 pts. received IORT alone (1 with adjuvant chemotherapy), 2/32 IORT+adjuvant EBRT, 16/32 neoadjuvant radiochemotherapy+IORT (1 with adjuvant chemotherapy). IORT dose amounted to 9-10 Gy (3 pts.), 15 Gy (19 pts.), and 20 Gy (11 pts.). Patient data were retrospectively collected from surgical and radiooncological files and updated by further inquiries to general practitioners and registration offices. Survival data were analysed using the Kaplan-Meier method and compared using the log rank test.
Results: Median overall survival (OS) amounted to 34.8 months (3-year OS: 48.8%, 5-year OS: 37.5%). There was no significant difference between primary and recurrent tumors (p=0.55). The difference between curative and palliative treatment was highly significant (p=0.0006). Median OS for curative pts. amounted to 65.5 months

(3-year OS: 62.5%, 5-year OS: 52.1%). Median freedom from recurrence (FFR) for all pts. amounted to 22.0 months (3-year FFR: 28.4%). The most frequent radiotherapy side effects or complications were fistulae (15%), anastomotic leakage (12%), obstruction of the ureter (6%), stool incontinence (6%), chronic diarrhea (6%), urinary incontinence (6%), rectal stenosis (6%), chronic proctitis (3%), and intestinal necrosis (3%). Prior to (re-)operation and IORT, continence had not been preserved in 25% of patients (19% rectum amputation, 6% complications of initial therapy). After surgery+IORT, the percentage of pts. with enterostomy increased to 69% (56% rectum amputation, 6.5% complications of initial therapy, 6.5% complications of IORT).

Conclusions

Long-term overall survival and local control were in the upper range of the results of IORT reported in the literature, even for patients with recurrent tumors and especially when no distant metastases were present. The combined treatment was feasible with tolerable late radiation side effects and complication rates.

14 speaker

OVERVIEW OF IORT ACTIVITIES IN EUROPE

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Background and Purpose: New indications such as intraoperative radiotherapy (IORT) during breast-conserving treatment and new technology such as mobile linear accelerators appear to be increasing the interest in IORT. However, although a large number of patients have been treated with IORT worldwide, it has so far not been possible to scientifically prove the effectiveness of the method in randomized multicentre trials. The aim of this work was mainly to achieve a better conception of the present IORT activities in Europe.

Material and Methods: A questionnaire was formulated and distributed to all European institutions which had contributed to IORT meetings since 1992. Items of the questionnaire included indication of therapy modality, use of dedicated or multi-purpose facilities, treatment sites, participation in clinical studies, applicators, methods of beam energy selection, dose prescription and normalisation, planning methods and tools, dosimetry and quality assurance.

Results: The questionnaire was answered by 72.8% of the addressed institutions, and the data shows that between 1984 and 2005 more than 10,845 patients have been treated with IORT in Europe. Average annual IORT numbers lie around 1300 to 1500 patients. The survey indicates that the main indications for IORT are cancers of breast and rectum. Distributions of treatment frequencies for all examined indications will be presented.

Conclusions: The results of the survey may serve as part of a data base to plan future IORT studies and collaborations. Furthermore, the large number of patients treated annually should provide sufficient data for the initiative of ISIORT/Europe to perform pooled analysis for certain indications with the aim of proving the favourable therapeutic effect of IORT.

WORKSHOP ON: 3D IMAGE-BASED BRACHYTHERAPY IN CERVIX CANCER

Gyn GEC ESTRO recommendations I/II

15 speaker

GYNE GEC-ESTRO RECOMMENDATIONS I/II FOR 3D-TARGET AND ORGANS AT RISK DELINEATION IN CERVICAL CANCER BRACHYTHERAPY

E. Van Limbergen, C. Kirisits
On behalf of the GYNE GEC ESTRO Working Group

The Gyne GEC-ESTRO protocol aims at reaching a consensus on how to delineate the GTV,CTV and OAR in cervix cancer brachytherapy and to use a common language for reporting this procedure based on common terms and concepts. Delineation of GTV and CTV is performed at the time of each brachytherapy application (GTV 2/CTV 2, GTV 3/CTV 3 etc.) at the Brachytherapy Treatment Planning System based on a set of sectional images (preferably MRI T2 weighted images) with the applicator in place and on the actual clinical examination. The topography and pathology as they present during these examinations form the frame for the delineation process. The GTV 1 includes the macroscopic tumour extension at diagnosis as detected by clinical examination and as visualised on MRI: high signal intensity mass(es) at FSE T2 in the cervix/corpus, parametria, vagina, bladder and rectum. The GTV 2 Brachytherapy (after external beam radiotherapy) includes the macroscopic tumour extension at the time of brachytherapy as detected by clinical examination and as visualised on MRI: High signal intensity mass(es) in the cervix/corpus, parametria, vagina, bladder and rectum. The high risk CTV for brachytherapy carrying a high tumour load includes the GTV 2, the cervix and the presumed extracervical tumour extension at the time of brachytherapy. The presumed tumor extension is defined by means of clinical examination and by MRI findings at the time of brachytherapy (GTV2) taking into account the tumour spread at diagnosis as indicated on clinical examination and initial MRI for staging (GTV1). Pathologic residual tissue(s) as defined by palpable induration and/or residual grey zones in the parametria, the uterine corpus, the vagina or rectum and bladder organs are included in the CTV of brachytherapy. This high tumour load CTV is to receive a radiation dose as high as possible. Another target definition aims at including the area with a medium tumour load: intermediate risk CTV for brachytherapy. It is based on the macroscopic tumour extension at diagnosis (GTV 1), which is superimposed on the anatomical area as it presents at the time of brachytherapy taking the original anatomical tumour spread as reference, e.g. distal parametrium, distal vaginal extension, proximal uterine extension. External organ wall contouring of Bladder, Rectum, Sigmoid and adjacent small bowel is recommended to delineate OAR It is assumed that no extra margins are needed neither for patient related uncertainties (e.g. organ movement) nor for set up uncertainties. Therefore, the PTV is identical to the CTV. In addition to the ICRU 38 concepts and point A dosimetry the Gyne GEC-ESTRO recommendations part II introduce a DVH based parameter set. Dose to target volumes should be reported in terms of D90 and D100, the dose received by at least 90% and by the whole volume (minimum target dose), respectively. For organs at risk the minimum dose received by the most exposed $2cm^3$ (D2cc), $1cm^2$ (D1cc) and $0.1cm^3$ (D0.1cc) are of major importance. These values can be analyzed directly from cumulative dose volume histograms. In order to have a direct comparison to other treatment schedules and to allow a dose constraint based treatment planning, each dose per fraction is normalized to a 2 Gy fractionation (EQD2) and added to the dose from external beam.

* C. Haie-Meder, R. Pötter, E. Van Limbergen et al. Radiotherapy and Oncology, 74: 235-245, 2005. # Pötter R, Haie-Meder C, Van Limbergen E, et al. Radiother Oncol, 78:67-77, 2006

Contouring of GTV, CTV and OAR

16 speaker

CT AND MR IMAGING, GYN GEC ESTRO RECOMMENDATIONS

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Purpose/Objectif: Brachytherapy of locally advanced cervix is increasingly performed with the assistance of 3D sectional imaging (CT, MRI). If these imaging modalities are appropriately integrated into the procedure of medical/physical brachytherapy treatment planning, including adaptation of application technique, applicator reconstruction, delineation of the target and organs at risk and dose adaptation, there is an increase in treatment conformity and subsequently an improvement in clinical outcome. The recommendations for this approach, developed and promoted by the GYN GEC ESTRO group, describe how to implement this method to enhance accuracy of treatment planning and performance.

Materials/Methods: Direct comparison between CT and MRI in regard to the needs of cervix cancer brachytherapy reveals the superiority of MRI. When using MRI, soft tissue depiction quality is highly increased and direct multiplanar imaging is performed with high resolution. Accurate delineation of organ borders, organ walls, target and patho-anatomic structures is enabled. An interobserver study for contouring with dosimetric evaluation, showed that CT provides a good estimate for organs at risk, while on the other hand, major deviations resulted for the target (Viswanathan et al. IJROBP 2007-Article in Press). In terms of applicator reconstruction CT seems to be beneficial. The applicator channels can be marked and directly visualised. These markers are metallic and therefore not suitable for MRI. Oil or water containing MR markers could be alternatives. Depending on the applicator type and the method used, either T2-weighted sequences alone, or both T2- and T1-weighted sequences are needed for reconstruction.It is crucial to tailor the CT or MR image acquisition technique to the needs of brachytherapy and to directly integrate these imaging modalities into the process of applicator implantation ("image-guided") and of medical-physical treatment planning. The information provided from MRI at diagnosis, as well as from the clinical examination at diagnosis and at the time of brachytherapy has been proven to be sufficient to decide upon the application technique. MRI is therefore usually performed after the clinical insertion of the applicator has been finished. The MR image acquisition protocol includes the following: bowel preparation, MR-compatible applicators (intracavitary and interstitial), vaginal packing (with contrast medium, e.g. impregnated with gadolinium), bladder balloon filled with a contrast medium (e.g. diluted gadolinium) and a plastic rectal probe (optional). Applicator, vaginal packing, bladder balloon and rectal probe are then displayed with low-signal intensity on T2-weighted images. T2-weighted sequences in axial, para-axial, para-sagittal and para-coronal orientations are considered as standard for the visualisation of the tumour, targets, organs at risk and patho-anatomical structures. The complementary use of thin-section axial oblique T2-weighted may add to the depiction of parametrial invasion and of tumour spread in complex anatomical regions (e.g. fornices, lower cervical area, cranial part of parametrium) and moreover, to reduce misinterpretation due to partial volume effects. On T2-weighted images, the tumour is depicted with intermediate to high signal intensity, the organ walls with low-signal intensity. Image reading has to be carried out by taking into account direct and indirect signs of tumour-persistence and –regression: macroscopic tumor mass(es), high signal intensity zones surrounding the cervical canal, grey zones within the uterus/parametria/vagina, reconstitution of the cervical stroma. The uniform GTV at time of diagnosis (GTVD) converts into the inhomogeneous HR-CTV (GTV at time of brachytherapy (GTVBT)

+ grey zones at time of brachytherapy). The overall ability to visualize the GTVBT and the "grey zones", the cervix rim, the uterine corpus and three out of the four borders of the parametrial space on MRI at time of brachytherapy has been shown to be 98% (Dimopoulos et al. IJROBP 2006;64(5):1380-8). The overall discrimination quality factors were 1.2, 2.9 and 1.2-2.9, respectively, when a scoring system (0-4) was applied. There were no significant differences for most of the structures examined compared to the respective findings at time of diagnosis.

Conclusions: To integrate sectional imaging (CT, MRI), into the procedure of cervical cancer brachytherapy, image acquisition has to be tailored to the needs of this procedure. Image reading has to be carried out by taking into account the signs of direct and those of indirect tumour-persistence and -regression. MRI, compared to CT, provides more accurate 3D information for appropriate definition in particular of the CTV, but also of OAR and the relevant patho-anatomic structures. Some restrictions for MRI are given for applicator reconstruction, where merging with other imaging modalities is needed in many cases at present. MRI, when utilized appropriately, has proved to be an essential tool for accurate 3D assisted medical/physical treatment planning, enabling a significant enhancement of treatment accuracy and improvement of clinical outcome. Appropriate use of MRI within this MRI based treatment approach needs comprehensive education and training of radiologists, radiation oncologists and medical physicists.

17 speaker

INTEROBSERVER VARIATION

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Introduction: During the past decade, sectional imaging has been integrated into brachytherapy (BT) treatment planning at increasing number of institutions. Using individual optimisation of dwell-times and positions of 192Ir high- and pulse-dose rate stepping sources, this approach enables dose escalation to the target volume without exceeding tolerance limits of organs at risk (OAR). To establish a common language in this evolving field, the gynaecological (GYN) GEC-ESTRO working group (WG) issued recommendations for contouring in 3D image based BT of cervix cancer. With increasing conformity of dose delivery, the influence of contouring uncertainties on the ability to achieve uncomplicated cure becomes more and more important. Delineation uncertainties can be expressed in terms of three error components: (1) random observer variations, (2) systematic observer variations and (3) systematic deviations associated with imaging modality.

Material and Methods:

Majority of published interobserver studies deal with contouring variability in external beam radiation therapy (EBRT). Most commonly utilized methodological approaches are based on volumetric and DVH-parameters analysis. The concept of conformity index (CI- ratio of common to encompassing volume) provides a measure of differences in volume size and position. Poor agreement is indicated by a low CI. As the agreement increases, CI approaches 1. Being normalized to the union of volumes, CI is sensitive to small variations in overlap. Consequently, it is more sensitive when small volumes are evaluated compared to the evaluation of conformity in large volumes. CI provides no information on topography of regions of disagreement in relation to patient anatomy. Different methods for evaluation of topographic differences in outlines have been proposed by some authors.

There is an ongoing effort within the GYN GEC-ESTRO WG to assess feasibility of recommendations, to analyze and quantify interobserver uncertainties in 3D image based cervix cancer BT and to propose strategies to minimize such uncertainties. Several studies have been performed within the WG to adress some of these issues.

Results: When contouring is performed in accordance to GEC ESTRO recommendations by experienced observers, analysis of interobserver variation reveals good agreement in terms of high CI, comparable DVH-parameters and small topographic variation of contour extent. This could be shown both in intra- as well as in inter-institutional studies, involving experienced centers, despite differences in treatment concepts applied.

Two multi-institutional intercomparison studies, involving three centers, have shown good volumetric and DVH-parameters agreement (Lang et al. Radiother Oncol 2006;78:185-193, Nulens et al. Abstract presentation, GEC-ESTRO, Budapest, 2005).

In another study, involving two institutions, CI for target volumes was arround 0.6. DVH parameters were comparable (Dimopoulos et al. Abstract presentation, GEC-ESTRO, Montpellier, 2007).

A comparison of MRI and CT as imaging modalities for delineation revealed no significant differences in volume sizes and DVH parameters for the OAR. However, for target volumes, CT-based contouring overestimated the contour-width as compared to MRI. This was reflected by significant variations in D90, D100 and V100 values for the HR-CTV (Viswanathan et al. Article in press. IJROBP, 2007).

In a study estimating the agreement between HR-CTV outlines as delineated by two observers on transverse (T) and para-transverse (PT) MR images, interobserver and interplane CI were high (0.71–0.79). Topographic interobserver variation and interplane variation in DVH parameters were non-significant. Contouring difficulty was lower in PT plane (Petric et al. Article submitted to IJROBP, 2007).

At two contouring workshops with favourable teaching conditions and experienced observers, analysis of delineations revealed a high level of agreement (Washington, Milwaukee, 2006). Results from another workshop, attended by observers with less experience, were unfavourable (CI: 0.1-0.3) (Dublin, 2005).

Conclusion: Results of presented studies, involving experienced observers, are favourable when compared with the published data from similar analyses in EBRT. This indicates feasibility of the GEC-ESTRO recommendations. Unfavourable results obtained when comparing unexperienced observers, underscore the importance of education in achieving high conformity. Interobserver inconsistencies can be minimized through standardized formal training. CT appears to be valid for contouring of normal tissues, while MRI remains the gold standard for target volumes. Contouring in PT, as compared to T plane, allows for a »circumferential view of the cervix« and facilitates a comprehensive understanding of spatial relations between the applicator and the patho-anatomical structures. It is marked by a lower contouring difficulty and leads to comparable outcome in terms of DVH parameters.

A satellite study of clinical EMBRACE trial with a large number of trained observers and systematic application of contouring recommendations will be initiated to quantify even more precisely the delineation variability in cervix cancer BT. In addition to basic volumetric, DVH and qualitative methods of assessment, an elaborate analysis of topographical inconsistencies between delineations will be implemented.

Applicator Reconstruction

18 speaker

APPLICATOR RECONSTRUCTION: IMPORTANT CONSIDERATIONS AND PITFALLS USING SECTIONAL IMAGING. GUIDANCE FROM GYN GEC-ESTRO NETWORK

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Traditionally, evaluation of a brachytherapy implant has been based on a pair of X-ray images whereas dose calculations based

upon sectional imaging have played a minor role in brachytherapy, as opposed to external beam radiotherapy. For calculating dose to anatomical structures, the geometry of the applicator and the source dwell positions have to be transferred from the images to the treatment planning system (TPS); a process often referred to as applicator reconstruction. Inaccuracy in this process could lead to geometrical uncertainties and thus uncertainties in definition of source positions. These uncertainties could affect the calculated dose distribution to both target volumes and organs at risk. Thus, it is important to include considerations on the reconstruction process when evaluating uncertainties in 3D based treatment planning for brachytherapy.

A survey that was conducted within Gyn GEC-ESTRO network showed that the process of applicator reconstruction is closely related to image modality used and to available functionalities in the treatment planning system. The survey showed further that the method used for applicator reconstruction was either "direct reconstruction" (DR) or "library plan" (LP). The latter method is only possible with rigid applicators. Using the DR method the applicator is reconstructed directly in the acquired images, while the LP method utilises a predefined applicator geometry which is imported into the acquired 3D study. Both methods are encumbered by uncertainties.

The DR method is especially challenging when an applicator curves through several sectional images (e.g. the ring applicator). In such situations it is often difficult to reconstruct the correct applicator geometry and this could in turn alter the source positions. Most treatment planning systems do now days facilitate multiplanar reconstructed (MPR) images. Using DR method these images could be very useful if the relevant part of the applicator could be visualised in one image.

Using the LP method minimum three well defined points are usually required to merge the pre-defined applicator with the acquired 3D study. In one of the systems used within the Gyn GEC-ESTRO network, these points could only be recognised in the original images and not in the MPR images. If a coronal view from the CT shows that some of the points are located in between the CT-slices, the merge will not be entirely correct. The system should therefore facilitate the possibility of rotating and translating the pre-defined applicator until it fits the 3D study. When using several rigid applicators each applicator should be imported separately, since there is a risk that the position of the applicator in relation to each other could change inside the patient.

If the applicator reconstruction is performed using CT images, a markerstring is often used to define the source or dwell positions. However, the Gyn GEC-ESTRO working group recommends T2-weighted MR images for target and OAR delineation. Ideally the reconstruction process should also be performed in this image set, therefore the lumen of the applicator should be visualised in these images. At present there are no commercially available markerstring for T2 MR images, but several tests have been performed in different hospitals with small plastic tubes filled with oil or gadelinium. The key issue is of course the diameter of the inserted plastic tubes (i.e. the volume of the contrast medium). In many applicators the entrance hole is very narrow. Hence it is very difficult to visualise the lumen. Alternatively, a larger reference structure could be used as long as the location related to the sources or dwell positions is known.

A solution to the above mentioned problem with T2 MR images is to perform the reconstruction of the applicator in another image set (e.g. CT or T1 MRI) and then merge these two studies. However, uncertainties could occur due to patient movement between the two acquisitions.

Recently, titanium applicators are commercially available. One should be aware that the applicator geometry appears incorrectly in MR images due to interference between the titanium and the magnetic field. This could in turn lead to incorrect applicator reconstruction and thus affecting the dose distribution.

To quantify the impact of applicator reconstruction uncertainties on the dose distribution, incorrect reconstruction was simulated by shifting the dose distribution cran/caud (± 3, ± 5 mm), ant/post (± 3 mm) and lateral (± 3 mm) for 10 cervical cancer patients treated with a ring and tandem applicator. Changes in DVH parameters were evaluated for tumour (D90, HR-CTV) and organs at risk (D2cc for bladder, rectum and sigmoid). Uncertainties of DVH parameters depended on both organ and direction of applicator displacement. The most sensitive organs were rectum and bladder where mean DVH shift in ant-post direction was 5% per mm applicator displacement. Otherwise, shifts were between 1% and 3% per mm.

Treatment Planning

19 speaker

3D IMAGE BASED BRACHYTHERAPY IN CERVIX CANCER–TREATMENT PLANNING–BIOLOGICAL ASPECTS

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Sectional image based treatment planning and optimisation for brachytherapy of cervical carcinoma has to include dose constraints for target volumes and organs at risk. Dose constraints have to be based on total doses, applied by external beam therapy and brachytherapy. As the biological effect of a certain dose depends on the applied time dose schedule (dose rate, treatment time, fractionation, etc), radiobiological model calculations are necessary to respect biologically weighted total dose constraints.The applied algorithm is based on the linear-quadratic model for monoexponential sublethal cell damage repair and includes dose, dose rate and fractionation of the whole radiotherapy setting, consisting of external beam therapy plus HDR-, LDR- or PDR-brachytherapy. Physical dose values are converted to Biologically Effective Doses (BED) and subsequently to more familiar isoeffective (equivalent) doses in 2 Gy fractions (EQD2 or DIsoE). Biological model parameters that are used in the calculation are $\alpha/\beta = 10$ Gy for the tumour and CTV, $\alpha/\beta = 3$ Gy for late effects of organs at risk (bladder, rectum, sigmoid, intestines) and repair half time $T1/2 = 1.5$ h for all involved tissues. EQD2 is biologically equivalent to classical LDR brachytherapy at 50 cGy/h.DVH analyses are performed to evaluate the dose that covers 90% of High Risk CTV (HR CTV) (D90) and minimum doses to most exposed 2 cm3 of organs at risk (D2cc). Dose from external beal therapy is integrated (dose to ICRU point) to respect dose constraints for the whole treatment. Dose constraints currently applied in the centres within the GEC-ESTRO Network of 3D GYN Brachytherapy are: D2cc (bladder) ‹ 70-90 Gy$\alpha\beta$3, D2cc (rectum, sigmoid) ‹ 70-75 Gy$\alpha\beta$3, D90 (HR CTV) › 75-90 Gy$\alpha\beta$10 (depending on the tumour width). Treatment plan optimisation (loading pattern and dwell time optimisation) for each brachytherapy fraction is then based on DVH constraints of physical dose values per fraction reconverted from total EQD2 doses. Achieved target dose and sparing of organs at risk of already delivered brachytherapy fractions are incorporated in the algorithm. For practicability the whole calculation is integrated into a Microsoft Excel spread sheet that allows frast and straightforward application. Tissue parameters, dose constraints and treatment parameters are easily modified and the result, the corresponding physical dose for the remaining brachytherapy fractions, is automatically updated. The program will be presented at the workshop and can be made available to those requesting it. An upcoming publication will provide more detailed information on this procedure with its potential and its limitations (Lang et al. IJROBP 2007 in press).The presented method to respect total dose constraints is reliable and efficient, and an essential tool when aiming at increasing local control and minimising side effects for 3D image-based brachytherapy in cervix cancer.

20 speaker

MEDICAL ASPECTS: GTV, CTV, DOSE VOLUME RELATIONS, UNCERTAINTIES

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In contrast to the situation for external beam radiotherapy (EBRT) image based 3D treatment planning of brachytherapy (BT) in cervical cancer is a new feature. Thus today, most departments are still relying on orthogonal X-rays and point related dose prescription, with the BT dose most often prescribed to point-A and not to a clinical target volume (CTV). Also the dose to organs at risk (OAR) is represented by specific reference points such as ICRU bladder and rectum points. For locally advanced cervical cancer approximately 80-85 GyEQ2 is frequently prescribed to point-A combining EBRT and BT, with approximately 35-50% of the dose given by BT. Depending on tumor size, FIGO stage and overall treatment time pelvic control rates of 50-90% are usually obtained applying 2D BT. However, in retrospect it has been difficult to demonstrate a formal dose–response curve, with the point-A dose being superseded by stronger prognostic parameters. This indicates that dose to point-A is only a weak surrogate marker for the actual dose to the BT target, which is supported by experience with 3D image guided BT where point-A very often is situated in the target periphery. Based on the available experience it is anticipated that D90 for the high-risk clinical target volume (HR-CTV) will be a strong prognostic factor in the future with an expected local control of 95% if a dose of up to 88 Gy EQ2 is obtained in the HR-CTV. New technologies such as DCE MRI and PET-CT using specific tracers such as FAZA may even enable us to identify radio resistant subvolumes within the GTV, which may permit us to further optimize the dose distribution within the HR-CTV. For OAR, a relationship between dose to the ICRU rectum point and rectal complications has been established. At doses below 85 GyEQ2 the risk for severe complications has been found to be ‹ 10% but rising steeply with higher doses. Comparison of 2D and 3D volumetric calculations has shown that the ICRU rectum point is a reasonable surrogate for the minimum dose to the most irradiated 2cc of the rectum wall. The 2cc volume is being considered to be a good and clinically relevant parameter to correlate with complications, but should be used together with the the 1 and 0.1 cc volume to assess the dose inhomogeneity within this volume. Concern was raised for the introduction of both HDR and concomitant Cisplatin after a study showing an alarmingly high complication rate even before 1-year follow-up. In this study the dose to the ICRU rectum point was very high (median value of 139 GyEQ2). In a recent study with MRI based HDR BT and concomitant Cisplatin, grade 3-4 rectal complications was completely absent even at longer follow-up, underlining the importance of "putting the dose where the tumor is". A specific uncertainty with 2D BT is the dose to upper rectum and sigmoid, which is very difficult to estimate and where significant morbidity may arise. Essentially the dose contribution to these parts of the GI tract can only be assessed by 3D DVH analysis. For rectum and sigmoid it has been shown that a limit of 70-75 GyEQ2 to 2cc is safe. Regarding the bladder, the ICRU bladder point has been shown to be an uncertain predictor of the minimum dose to the most irradiated 2cc and uncertainty exist as to the true dose volume constrain to apply for this organ. Currently 90 GyEQ2 to 2cc is being advocated as an appropriate dose volume constraint. A prerequisite for both 2D and 3D dose planning is the possibility to add doses from EBRT and BT which inevitably requires some biological assumptions of both repair capacity and repair half times of the involved tissue. Repair capacity in the form a/b ratios are well established, apart from some data suggesting that higher than expected a/b ratio may influence the rectal response due to consequential late damage. Regarding repair half times these are not very well known, which may have inadvertent consequences especially if a therapeutic gain is expected on the basis of an assumed difference in repair halftimes between tumor and normal tissue. Ideally deformable registration of the involved normal and tumor tissue should also be possible to account for distortion of the anatomy caused by the applicator compared to the relaxed position of the organs during EBRT. Such software is currently being developed. For EBRT the shift from 2D to 3D treatment planning involved a considerable intellectual challenge in splitting the radiation treatment into its individual components of target contouring and treatment planning. With 2D BT the techniques and systems in a similar manner describe both the target and the treatment planning with a resulting dose from BT to target and OAR dictated by a more or less static standard loading pattern. This also means that the possibility for taking tumor topography and position of OAR at time of brachytherapy into considerations is very limited. However, with the introduction MRI based image-guided brachytherapy we now face the challenge of creating a true "BT plan of the day" with dynamic contouring and an individualized optimisation based on active treatment planning.

21 speaker

PHYSICS ASPECTS: STANDARDS AND OPTIMIZATION (INVERSE PLANNING), UNCERTAINTIES

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The primary goal of 3D image guided dose optimisation in intracavitary brachytherapy is to shape the inhomogenous dose distribution according to the individual patient anatomy in order to obtain an optimal coverage of the tumour and target while keeping the dose to organs at risk at an acceptable level. Treatment planning involves optimisation of dwell times and dwell positions. The procedure is mainly guided by 3D dose volume histogram (DVH) parameters that describe dose coverage of tumour, the tumour dose, and "hot spots" in organs at risk: V100, D100, D90 for target volumes and D2cc for bladder, rectum and sigmoid. However, because of the large dose inhomogeneity also parameters indicating the high dose volumes (V150/V200 or D70/D50) should be considered for the target and smaller volumes like 1 cm3 and 0.1 cm3 for the OAR. In order not to deviate more than necessary from the traditional pear shaped dose distribution the starting point for optimisation should always be a standard loading pattern. For modulation of dwell times and dwell positions different tools can be used: manual, graphical (also called drag and drop of isodoses) and inverse optimisation. With manual optimisation, dwell times and positions are adjusted manually in an iterative way until DVH constraints are fulfilled as closely as possible. This procedure is depending on the dose planner and may be time consuming, but the advantage is that the dwell time pattern is continuously under observation during the dose planning procedure. With graphical optimisation, isodose lines are pushed or pulled by the dose planner, while the system calculates corresponding dwell times. By nature, the graphical optimisation technique has the focus on isodose lines, and the planner is advised to keep track of the dwell time pattern to avoid large inhomogeneities in dwell time distribution. Inverse planning is still a quite unexplored way of optimisation, and a clear documentation of advantages and disadvantages is still awaited. Since this method is guided exclusively by DVH constraints, the pitfalls are large deviations from standard loading patterns and blowing up/reducing high dose volumes. Visual inspection of the isodose curves is always essential for all optimisation techniques, since DVH parameters do not contain any spatial information about where the dose is delivered. It is necessary to add doses from all BT fractions since the goal of treatment planning is to respect certain dose volume constraints in terms of biologically weighted equivalent dose EQD2 for the whole radiotherapy treatment in a given

patient. Such addition also allows for describing a certain patient population on the department level and to compare treatment effects between different departments as necessary for communication of results. The accuracy of DVH calculation is essential for treatment planning, since the dose optimisation procedure is guided by DVH parameters. There has been and there is a large activity in the field to evaluate uncertainties due to different factors, for instance: inter-fraction deformation of organs, contouring uncertainties, and reconstruction uncertainties. It is in principle recommended to use MR for each fraction, but due to limitations in MR capacity in many departments this may be difficult to achieve. When MRI based treatment planning is not available for every fraction, and the treatment is delivered according to the optimised treatment plan of the first fraction, the delivered dose to the tumour/CTV (because of shrinkage) will generally be higher than what was calculated from the first fraction. This may also be true for OAR, although here the situation is more complex. In the absence of MR imaging, the use of CT and X-ray findings may contribute to reduce such uncertainties and potential over-dosage. Even with MR for each fraction, addition of dose from succeeding BT fractions is complicated by inter-fraction deformation. A crude addition of D2cc for subsequent BT fractions will lead to an overestimation of dose when different parts of the organ are exposed to a high dose in different fractions as e.g. for a moving sigmoid or a bladder with a different filling status. On the other hand one should be careful when it is obvious from the images that the same part of an organ is in the high dose region in every fraction as e.g. for the anterior rectal wall. Highly conformal dose distributions can be vulnerable to contouring and reconstruction uncertainties due to the steep dose gradients. In the cranial direction the dose gradient can be kept less steep at the border of the target when the loading in the tandem is extended above the target (when this is possible without compromising OAR's). It has already been shown in several studies that dose optimisation can significantly improve DVH parameters for both tumour and organs at risk. The potential amount of increase in target coverage and radiation dose is in the range of 10-20%. The potential amount of change in dose volume parameters for OAR is even more pronounced, depending on the individual topography. The clinical potential of dose optimisation is that this change in dose and volume will lead to improved local control and/or decreased morbidity.

22 speaker

3D IMAGE BASED TREATMENT PLANNING IN CERVIX CANCER BRACHYTHERAPY: DIFFERENT APPROACHES WITHIN THE GYN GEC ESTRO NETWORK

C. Kirisits

On behalf of the Centres Particpating in the 3D Gyn GEC ESTRO Network

The centres participating in the Gyn GEC ESTRO network perform the currently most sophisticated treatment planning approach based on MRI at time of brachytherapy.

The majority of centres start with a standard dose distribution as a starting point. After 3D reconstruction and structure delineation a standard loading pattern for a given applicator geometry is taken with a fixed dose to a certain point, located at the same coordinates as point A. Two centres include additional points at 5 mm from the ovoid/ring surface. The following optimization process includes a careful look on the isodose lines projected on the MRI anatomy and in a more systematic manner the analysis of dose volume histograms (DVH) using certain parameters as the D90 for the target and the 2 ccm volume for Organs at risk. 3D optimisation is performed if target coverage is not sufficient or dose reduction is required for organs at risk (OAR). In clinical routine this is done by iterative forward planning: shift of the normalization points, change of dose normalization points, manual adjustment of loading pattern and dwell weight. "Drag and drop" of isodose lines is used in some centres, but this procedure always includes a careful check of the resulting loading pattern and the evaluation parameters. The individual steps in treatment planning depend significantly on the treatment planning system.

Centres with point A tradition prescribe to the HR-CTV, while those who are used to the 60 Gy reference volume prescribe to the IR-CTV. The dose for certain dose-volume parameters is combined from each fraction and external beam therapy by biological normalization. The accepted method is the LQ-model to calculate the dose equivalent to a 2 Gy fractionation using α/β=10 Gy for target and α/β=3 Gy for OAR structures (EQD2). The prescribed dose varies between 75 to 85 Gy for the HR-CTV or 60 Gy to the IR-CTV. The dose constraint for the rectum is similar among the different centres with a maximum limit for the D2cc of 70-75 Gy. For the bladder the situation varies considerably among the centres with clinical constraints between 70 to 90 Gy for the D2cc. For HDR brachytherapy the optimization process is changing the dose distribution only. In case of PDR brachytherapy the number of pulses and the pulse size are additional parameters to meet dose volume constraints, in particular for organs at risk.

The success in achieving all dose constraints is limited by the application geometry and the topographic situation. In general the insertion of intracavitary applicators alone is not sufficient for clinical target volumes larger then 5 cm in width at time of brachytherapy and for unfavourable topography of target and/or OARs. One possible solution is the insertion of additional needles, e.g. using a combined intracavitary/interstitial approach. Such an approach is increasingly used by individual centres while the industry develops commercially available applicators of this type.

Looking at numeric values for the parameter set provided by the Gyn GEC ESTRO recommendations (D90 for target, D2cc for organs at risk), treatment planning within the European network seems to become similar. However, loading patterns and dose distributions used in clinical practice have to be analysed in more detail. When correlating clinical outcome to treatment parameters DVH values for target structures, bladder, rectum, and sigmoid should be considered. In addition, size and location of high dose volumes and the spatial dose distribution in general is recommended for consideration. Existing treatment planning tools should be compared and evaluated. Their improvement may help to follow planning guidelines in daily clinical practice.

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Outcome: 3D related evaluation

23 speaker

MRI-BASED BRACHYTHERAPY (BT) IN THE TREATMENT OF CERVICAL CANCER : EXPERIENCE OF THE INSTITUT GUSTAVE-ROUSSY.

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Background: BT in gynaecological tumours has recently evolved with the integration of 3D images into treatment planning systems. Accurate delineation of tumour and critical organs enables individual adaptation of dose distribution to CTV. This procedure is more easily possible with implementation of stepping source technology. This individual dose adaptation is also possible with low dose-rate

brachytherapy even in a less extended procedure.
Material and methods: Since 2000 in our institution, patients with cervical cancer have undergone MRI at the time of BT, whenever possible, i.e. depending on the availability of MRI. Generally one to two patients per week could undergo this procedure, performing MRI with the vaginal mould in place. The intermediate-risk CTV (IR-CTV) was systematically delineated as well as the organs at risk (bladder, rectum and sigmoid). ICRU points were also checked : rectum, bladder plus one bladder point located 1.5 cm above the ICRU point. The high-risk CTV was retrospectively delineated to perform DVH analysis. The dose was prescribed to the IR-CTV with a total dose of at least 60Gy, integrating the external irradiation of 45Gy when performed. Low dose-rate BT using cesium sources was performed. Optimization was limited with this technique, modifying the pear-shape isodose essentially by adapting the time duration and/or the length of each radioactive source.
Results: Between October 2000 and April 2004, 123 patients (pts) were treated using 3-D based BT. Median age was 46 (25-82). Pts were treated either with pre-operative BT followed 6 weeks later by a colpohysterectomy and lymphadenectomy: 39 pts (Group 1) or with concomitant chemoradiation 45 Gy plus weekly Cisplatinum 40mg/m2 followed by BT: 84 pts (Group 2). FIGO classification in Group 1 was : 36 IB1, 1 IB2, 1 IIA and 1 IIB, Group 2: 3 IB1, 17 IB2, 5 IIA, 37 IIB, 2 IIIA, 20 IIIB, 4 IVA (bladder) and I IVB (supra-clavicular node). The initial tumour volume was 5cc (0.5-23) in Group 1 and 48cc (1-468) in Group 2. In Group 1, median D90 IR-CTV was 75 Gy (29-129 Gy), median D90 HR-CTV was 109 Gy (37-198 Gy), median ICRU bladder dose was 33 Gy (12-64 Gy), median bladder point 1.5 cm above the ICRU point was 63 Gy (20-120 Gy), median 2cc bladder was 65 Gy (30-128 Gy), median ICRU rectal point was 41 Gy (23-170 Gy), median 2 cc rectum was 35 Gy (20-77 Gy). In Group 2, median D90 IR-CTV was 69 Gy (52-103 Gy), median D90 HR-CTV was 79 Gy (53-132 Gy), median ICRU bladder dose was 63 Gy (51-80 Gy), median bladder point 1.5 cm above the ICRU point was 70 Gy (55-88 Gy), median 2cc bladder was 77 Gy (59-132 Gy), median ICRU rectal point was 70 Gy (50-108 Gy), median 2 cc rectum was 63 Gy (52-108 Gy).
In Group 1, the 3-year overall survival, disease-free survival and local recurrence-free survival were respectively 94%, 91% and 91%. In Group 2, the 3-year overall survival, disease-free survival and local recurrence-free survival were respectively 67%, 63% and 65%. In Group 1, 4 pts presented a local and/or regional recurrence and/or distant metastasis. One pt presented a latero-pelvic recurrence, 2 pts presented pelvic node recurrence and 3 pts presented metastasis. Among them, 2 had both pelvic node recurrence and metastasis. In Group 2, 31 pts presented a local and/or regional recurrence and/or distant metastasis. 10 pts presented a local recurrence, 2 pts presented pelvic node recurrence, 10 pts a paraaortic recurrence and 21 presented metastasis. Among them, 8 presented both local recurrence and metastasis. Local recurrences according to FIGO Stage distribution occurred in: 3 IIB, 1 IIIA, 4 IIIB and 2 IVA.
Complications were observed in 13 pts in Group 1, and 28 pts in Group 2. No grade 3 complication was seen in Group 1 while 4 grade 3 complications were observed in Group 2 : 2 digestive (1 small bowel, and 1 rectum) and 2 urinary complications (1 ureter and 1 bladder).
Conclusion: Good local control was achieved with low dose-rate 3-D MRI based BT, even in pts with advanced cervical cancer. These results can probably be improved with the help of pulsed dose-rate allowing a more sophisticated optimisation procedure

24 speaker

3D IMAGE BASED BRACHYTHERAPY IN CERVIX CANCER. OUTCOME: 3D RELATED EVALUATION. DISEASE CONTROL: DEFINITIVE RADIO(-CHEMO)THERAPY IN ADVANCED DISEASE: RESULTS FROM LARGE SERIES. VIENNA UNIVERSITY

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Introduction: In cervix cancer the major parameters for assessing outcome in regard to the course of disease are local control, regional control, overall and cancer specific survival. Local control is recognized as having major impact on overall outcome. Large series and comprehensive overviews based on traditional dose planning have indicated a strong correlation between dose at point A and local control. Different dose levels have been related to high control rates in limited and extensive locally advanced disease: 75-80 Gy and 85-90 Gy. A significant improvement has been reported through radiochemotherapy with regard to overall survival, cancer specific survival and local control. With the development of 3D image based cervix cancer brachytherapy a response adapted 3D target approach (HR CTV and IR CTV) for prescribing and reporting has been proven to be technically and clinically feasible. First clinical series have implemented this approach. Outcome and disease control can now in principle be related to 3D dose volume parameters.
Data on the first Vienna clinical experience are reported in the following (1): The clinical impact of systematic MRI based cervix cancer brachytherapy combined with external beam radio-chemotherapy has been investigated applying dose volume adaptation and dose escalation in a consecutive group of patients with locally advanced cervix cancer.
Methods: In the period 1998-2003, 145 patients with cervix cancer stages IB to IVA were treated with definitive radiotherapy +/- cisplatin chemotherapy. Median age was 60 years. In 67 patients, the tumour size was 2-5 cm, in 78 patients it was ›5 cm. In 29 cases the standard intracavitary technique was combined with interstitial brachytherapy. Total prescribed dose was 80-85 Gy (total biologically equivalent dose in 2 Gy fractions). Since 2001, MRI based treatment planning integrated systematic concepts for High Risk Clinical Target Volume (HR CTV) and organs at risk (OAR), Dose-Volume-Histogram analysis, biological modelling, dose-volume-adaptation (D 90, D 2cm3), and dose escalation, if appropriate and feasible.
Results: Dose volume adaptation was performed in 130/145 patients. The mean D90 during the whole period was 86 Gy, with a mean D90 of 81 Gy and 90 Gy during the first and second period, respectively ($p \ll 0.01$). Median follow-up was 51 months. Complete remission at 3 months was achieved in 138/145 patients (95%). Actuarial continuous complete remission for true pelvis (CCRtp) was 88% at 3 years. For tumours 2-5 cm, CCRtp was 96% both in 98-00 and 01-03. For tumours ›5 cm it was 71% in 98-00 and 90% in 01-03 ($p=0.05$).
Progression free survival (PFS) for true pelvis (local control) was 85%, PFS for distant metastases was 80 %, both at 3 years. Local control for tumours › 5 cm was 64% in 98-00 and 82% in 01-03 ($p=0.09$) and 100% and 96%, respectively, for tumours 2-5 cm. PFS for distant metastases remained the same during the two treatment periods with 79% and 80%.
Overall survival (OS) was 58 %, and cause-specific survival (CSS) was 68% at 3 years. In the two different periods improvement in OS was from 53% to 64% ($p=0.03$) and in CSS from 62% to 74% ($p=0.13$). Improvement occurred only in tumours › 5 cm: OS 28% versus 58% ($p=0.003$); CSS 40% versus 62% ($p=0.07$).
Gastrointestinal+urinary actuarial late morbidity (G3, G4) was total 6%, 10% in 98-00, 2% in 01-03.
Conclusion: The results of this series indicate that outcome can be actually related to 3D dose volume parameters. In locally advanced extensive cervix cancer, local control of ≥85% can be achieved with low treatment related morbidity (G3/4), when exploiting the poten-

tial of MRI based 3D treatment planning including dose volume adaptation, dose escalation and a combined intracavitary/interstitial brachytherapy, if appropriate. A significant impact of this improvement of local control on survival is to be expected. For locally advanced limited disease the MRI based approach will likely result in assuring excellent local control (≥95%) and in minimizing treatment related morbidity. More prospective clinical 3D based trial research is necessary to further elaborate this approach in a multi-centre setting and to validate these findings.

1. Pötter R, Dimopoulos J, Georg P, et al. Clinical impact of MRI assisted dose volume adaptation and dose escalation in brachytherapy of locally advanced cervix cancer. Radiotherapy and Oncology, submitted.

25 speaker

OUTCOME: 3D RELATED EVALUATION. MORBIDITY: RECTUM, SIGMOID

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Introduction: When analyzing treatment outcome for patients with cervix cancer, it is important to assess the incidence of late adverse side effects. The overall actuarial 5-year rate of severe late adverse side effects ranges in many studies with moderate doses from 3 to 10%.If high radiation doses are applied and late effects are carefully evaluated the rate of adverse late side effects reported is even higher. Late sequelae in rectum and sigmoid mainly occur during the first 2 years following treatment, with a decrease later on. Factors responsible for radiotherapy-induced toxicity are divided into two categories: the major factors are directly linked to the radio- and brachytherapeutic techniques and doses, other factors are independent of radiotherapy, and include patient and treatment related factors (e.g. diabetes, concomitant chemotherapy)

2D radiotherapy: dose at points and morbidity

It is known from classical series based on 2D radiotherapy in cervix cancer, that the most significant factor affecting the incidence of late adverse side effects is the total radiation dose to the pelvic organs by both whole pelvic irradiation and intracavitary insertions. The incidence of complications increases significantly when the dose to point A exceeds 80 Gy (Perez et al. 1984) An analysis with a large number of patients (n=1456) confirmed the role of total dose (Perez et al. 1999). In the rectosigmoid, the incidence of morbidity significantly raised when the total dose at point A exceeded 75 Gy: 4% with doses below 75Gy versus 9% with higher doses. The dose to the latero-pelvic wall was also a significant factor influencing small intestinal complications: the complication rate was less than 1% with a total dose of 50 Gy or less, 2% with 50 to 60 Gy, and 5% with higher doses. Using the ICRU reference point for the rectum (reproducible and reliable, not necessarily representing the maximum dose) the majority of groups reporting in literature could show a strong correlation between dose at this point and late side effects for the rectum. According to the experience of the "group de neuf" (Pourquier et al.1982) the amount of late morbidity applying LDR brachytherapy increased significantly when the cumulative dose was above 75 Gy. In addition the size of the 60 Gy volume and the dose rate had a significant impact (Barillot et al. 2000). Similar dose values were demonstrated for fractionated HDR brachytherapy. In this experience the linear quadratic model was applied and BED threshold value of 125 Gy3 were reported. Above these values corresponding to 75 Gy EQD2 a significant increase in major side effects was reported (Clark et al. 1997, Pötter et al. 2000)

3D radiotherapy: dose volume parameters and morbidity

For the combined external irradiation and brachytherapy, typical adverse effects from brachytherapy are local inflammation, fibrosis, teleangiectasia, ulceration, necrosis and fistulas. These occur mainly in limited volumes close to the applicator, that are irradiated with high doses (›70-80 Gy), whereas whole organ side effects (e.g. overall organ inflammation, fibrosis, stenosis and overall teleangiectasia) occur mainly after whole organ irradiation with intermediate and/or high doses (60-70 Gy). When assessing late adverse side effects from brachytherapy, small organ (wall) volumes irradiated to a high dose seem to be of major interest. Applying the Gyn GEC ESTRO recommendations for dose volume parameters for the rectum with D2cc, D1cc and D0.1cc it has been demonstrated that average dose values for D2cc and at the ICRU point have a strong correlation (0.92, Kirisits et al. 2005). Due to the inhomogeneous dose distribution in these volumes, dose values for D1cc and D0.1cc are significantly higher, usually in the range of 105-130%. For the sigmoid no correlation can be given as there has been no appropriate point dose assessment for the sigmoid reported in literature. Due to the sharp dose fall off of brachytherapy, doses in larger volumes (e.g., 20, 30 ccm) seem to be negligible, if the dose from external beam therapy is 45 Gy. The dose contribution from brachytherapy in these larger volumes adds then up to be around 5-10 Gy with a total dose in these volumes of about 50-55 Gy. However, if larger doses from external beam therapy are applied (e.g. 60 Gy), also larger volumes have to be taken into account to assess the overall effects of brachytherapy and external beam therapy. In the Vienna clinical experience in 141 patients treated from 1998-2003 with a MRI based brachytherapy approach, the 3-year actuarial rates for G3 and G4 late toxicity after a median follow-up of 40 months were 2% for the rectum and 2% for the sigmoid. Patients with a rectum D2cc ›75 Gy (EQD2) had a significantly higher incidence of late toxicity: G1-G4 was 20% above 75 Gy and 4% below (PÖtter et al. 2007). For the sigmoid the corresponding values were 9% and 1% using the same cut-off level. However, for the sigmoid the cut-off level is more unclear due to uncertainties in dose volume assessment (moving organ) and morbidity assessment. The clinical experience from this first 3D series compares well with what has been reported for 2D radiotherapy applying point doses for correlation to late rectal morbidity. Based on these data from this first 3D clinical experience, it can be expected that a 3D based approach for cervix cancer brachytherapy can keep the rate of severe adverse side effects for the rectum and sigmoid below 5%, taking into account a dose volume constraint of 75 Gy EQD2 (normalized dose to 2Gy per fraction) as minimum dose in 2 ccm.

Conclusion: Several centres in Europe and worldwide are implementing and evaluating 3D based gynaecologic brachytherapy at present. Since this is a new approach, only limited clinical data are available so far to evaluate late morbidity thoroughly. According to first clinical experience, D2cc seems to represent a good predictive value for late rectal morbidity. However, D1cc and D0.1cc should also be prospectively assessed. For sigmoid a clear dose volume relationship is still missing although it seems practical to use the same values as for the rectum. Prospective clinical research is warranted for further clarification dose volume parameters and their correlation with both rectum and sigmoid late morbidity.

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26 speaker

3D RELATED EVALUATION: MORBIDITY OF BLADDER AND VAGINA

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Urinary complications after irradiation of cervix carcinoma are usually less frequent and less severe than the lower intestinal tract complications. According to the major series, bladder complications occur in about 10% to 15% of cases, but severe sequelae represent only 1% to 4%. It is quite difficult to accurately assess the vaginal morbidity, as widely used toxicity scoring systems are not always appropriate for registering vaginal complications. The lower third of the vagina is rarely the site of severe complications, whereas in the upper third the rate of stenosis or fistulae can reach 20% in stage III treated by definitive radiotherapy. 2D based dose constraints The morbidity induced by radiation therapy obviously depends on technical factors related to brachytherapy. However until now, we failed to establish from orthogonal films technique, non ambiguous dose-volume constraints for bladder and vagina. ICRU reference point definition seems not to be adequate for bladder dosimetry, as this dose point does not correlate well with complication rate or severity. The various methods proposed to try to locate the true bladder maximum dose point showed that it is usually located 1.5 to 3 cm cranially and laterally than the ICRU point and that the maximum bladder dose is 2 to 3 times higher than the ICRU reference dose. However, there is no clinical proof that this alternative reference dose is relevant regarding the complication probability. Conversely, in LDR dose rate recorded at the bladder reference point seems to significantly correlate with complications, thus suggesting that the bladder base may tolerate very high dose providing the dose rate at the bladder neck can be kept below a reasonable dose rate around 0.6 Gy/h. Vaginal dose surface is usually calculated by placing on orthogonal films dose points on the lateral surface of the vaginal applicator at a given distance from cesium source or each activated dwell position. There is little data on the tolerance of the vagina. The vaginal-to-Point A dose ratio seems an important one to define and document. In LDR, the vaginal surface dose rate usually varies based on applicator diameter and available source strengths, and should be in the range of 140% to 200% of the Point A dose. In HDR, vaginal surface doses reported range from 140% up to more 600% of the Point A dose for tandem and ring applicator and from 50% to 175% for tandem and ovoids applicator. 3D based dose constraints The GYN-GEC-ESTRO group has proposed to record dose-volume parameters in 0.1cc (D0.1cc), 1cc (D1cc) and 2cc (D2cc) of organs at risk. Although these recommendations have been published recently, some data are available. The largest experience comes from Vienna where 141 patients received MRI based HDR brachytherapy from 1998 to 2003. In that population, the overall incidence of bladder complication was 20% (4% of severe complications). Regarding to the defined dose-volume parameters, no clear cut off point for bladder side effects could be demonstrated. Nevertheless, in a clinical approach a D2cc ≤ 90 Gy normalized to conventional 2 Gy per fraction (EQD2) might be taken as dose volume constraints. Dose-volume parameters have not been introduced so far for the vagina. In order to assess the dose received by the vagina, organ wall contours were delineated retrospectively on axial MRI slices in 40 out of the 141 patients previously treated. Additionally, two sets of dose points defined at the ring surface and at 5 mm tissue depth were observed. No significant correlation was found between dose from points and dose from volume parameters. Moreover results were obviously influenced by large inaccuracies due to contouring and geometrical positioning. Conclusions It is too early to draw some conclusions from this preliminary experience of the routine use of MRI regarding the prediction of bladder complication, more data are awaited. Although no clear relationship between dose volume-parameters and complication become apparent, MRI based dosimetry may help us to accurately analyse the mechanisms of bladder side effects. Currently, we could not recommend using any type of dose-volume constraints for dose planning in the vagina, but 3D based brachytherapy planning will increase our expertise in contouring and could serve to compare vaginal dose volume relations between different applicator types and treatment schedules.

Ongoing activities in research and development

27 speaker

3D IMAGE-BASED BRACHYTHERAPY IN CERVIX CANCER: ONGOING ACTIVITIES IN EDUCATION, RESEARCH AND DEVELOPMENT

R. Pötter
Gyn GEC ESTRO network: Work packages and task groups

Gyn GEC ESTRO network: Work packages and Task groups
After set up and publication of the Recommendations for 3D Gynaecological Brachytherapy the GYN GEC ESTRO working group decided to build up a network for 3D Gynaecologic Brachytherapy.
This network is to promote the field of 3D Gyn Brachytherapy in general and in particular
• to create a platform for education,
• to support research and development
• to spread and test the Gyn GEC ESTRO Recommendations for cervix cancer.
Different areas of interest were defined and Work Packages (WP) formed:
• 3D image based Contouring of GTV, CTV and OAR (WP 1);
• Applicator reconstruction (WP 2);
• Treatment Planning (WP 3);
• Applicator Development (WP 4).
Task groups have been set up for each Work Package (2-5 members) with persons at different centres of the network responsible for coordination of the work programme in the Work Package. Participation is linked to a practical interest at the specific centre in setting up a programme with MRI based gynaecological brachytherapy. Altogether 12 centres from 10 European countries have joint the network so far (12/2006): Aarhus, Dublin, Erlangen, Leeds, Leuven, Lubljana, Mount Vernon London, Nancy, Oslo, Paris IGR, Utrecht, Vienna. The programme was initiated in May 2005 at the GEC ESTRO meeting in Budapest. Method of work has been specific tasks taken over by certain persons and centres, respectively, and cooperation of work within the Work Package groups. Workshops were organized for contouring in Dublin (European centres, WP1, 12/2005), for applicator reconstruction and contouring in Utrecht (WP 1, 2, 4/2006), for treatment planning in Ljubljana (2/2007). Various publications are in preparation on 3D imaging, on inter-observer variation, on applicator reconstruction, and on treatment planning. The major "sponsors of the network" are the participating academic institutions. Sponsoring of meetings has been partly also by Varian and Nucletron with increasing interest. Sponsoring through public money (grant application) has not been established yet, but is planned for future activities.
Joint transatlantic group for image based gynaecologic brachytherapy
A joint transatlantic group for image based gynaecological brachy-

therapy has been set up combining activities in Europe and North America (US) with continuous exchange of information and with joint meetings (e.g. workshops). GEC ESTRO Recommendations form the basis for these activities. Two workshops on contouring have been performed in cooperation with the American colleagues (ABS/ASTRO/RTOG/AAPM/ACR), one in Washington (3/2006), one in Milwaukee (9/2006). Aims are similar to those of the Gyn GEC ESTRO network.

Prospective Clinical Trials on 3D Image-Based Gyn Brachytherapy: STIC, EMBRACE

STIC (Soutient aux thÉrapeutiques innovantes et couteuses): National French prospective multicentre comparative trial.

Aim of the study is to compare two treatments:

"classic": 2D LDR brachytherapy with treatment planning based on radiography

"innovative": 3D PDR brachytherapy with 3D sectional image based treatment planning (CT or MRI)

Primary objective: 50% reduction of late adverse side effects (G3/G4 from 7% to 3.5%); secondary objective: local control (equivalent). Aims are: homogenisation of techniques, imaging, target definition, and dose optimisation; constitution of a data base; Medico-economic data and evaluation, quality assurance programme (EQUAL), application of Gyn GEC ESTRO recommendations for evaluating dose volume parameters for CTV and OAR. 425 patients are foreseen in each treatment arm. Accrual was for 2005 and 2006. 5 year follow-up is planned. The study is supported by the French Ministry of Health.

EMBRACE (European study on MRI based 3D brachytherapy in locally advanced cervical cancer):

Within the 3D Gyn GEC ESTRO network a study protocol has been drafted for a prospective observational multi-centre trial on the feasibility and the clinical impact of MRI based 3D brachytherapy (phase II) in definitive treatment of cervix cancer (external beam therapy ± chemotherapy and brachythetrapy): Study aim is to establish and to investigate the clinical impact of 3D MRI based brachytherapy for cervix cancer:

• To investigate response adapted dose volume prescription for High Risk CTV stratified for different tumour volumes at diagnosis and at brachytherapy

• To investigate dose volume response for rectum, sigmoid, and bladder

• To apply the GEC ESTRO Recommendations for recording and reporting.

There is no general prescription in this trial for a certain dose in a given volume for brachytherapy. Each centre can treat according to its treatment policy, but has to apply MRI based 3D brachytherapy and has to apply the Gyn GEC ESTRO recommendations for reporting. There are some prescriptions for external beam therapy with regard to dose and technique. The aim is to investigate the clinical impact using certain dose levels for HR CTV and for OAR. Local control and morbidity for the different dose levels used in the trial by the different centres are the primary endpoint. Doses are given as EQD2 (equivalent doses to 2 Gy per fraction) applying the linear quadratic model with an alpha-beta value of 10 vor tumours and 3 for OAR. A prospective Quality Assurance Programme will be included in the trial including a dummy run before start of the trial. The start of this trial is projected to be at the end of 2007. The study will be open for participation to everybody fulfilling the criteria for MRI based treatment planning as mentioned above.

Are cancers avoidable ?

Pr Hélène SANCHO-GARNIER

To prevent the apparition of a disease it is necessary to know the causes of such disease. What do we know for cancers? Risks for cancer are determined by both exogenous and endogenous factors. The exogenous factors are either environmental or behavioural and interact with biological characteristics like age, metabolism, genetic polymorphism…

Data on cancer causing external agents accumulated via epidemiological surveys and animal experiments. Presently the major risk factors are tobacco, alcohol, obesity, sedentarity, infections, professional exposures and radiations… Such known external risk factors, acting alone or combined, may explain 60 to 80 % of cancer incidence.

However, not all identified causes are equally modifiable therefore a distinction is now made between identified causes of cancer and avoidable causes of cancer. Estimates of the proportion of avoidable cancers were made by different authors for different countries. This estimation varies depending upon the incidence (or mortality) rates and the prevalence of exposures to cancer risk factors. These figures provide the baseline of maximum achievable benefit relative to the total burden, in a country.

At an individual level the most important difference is between smokers and non smokers. For example in the US 75 % of cancer deaths could be avoided in smokers and 50 % only in non smokers by successively removing the effects of smoking, known infections, alcohol sunlight, current occupational pollution, inactivity and obesity, (J. Peto 2001).

However the likely impact in most cases would be smaller than this, since it depends on whether the intervention is really reducing the prevalence of exposure. While information related to the possible benefits of prevention is available, the preventive actions are widely uncontrolled and, as a consequence, not strongly efficient.

First, an amount of confusing information is widely spread by exposure producers using mediatic power. Second, the major cancer risk factors concern individual behaviour upon which few clearly effective actions are developed. Third, preventive interventions are rarely evaluated, thus many ineffective actions are permanently reproduced everywhere.

Therefore to be more effective evidence-based preventive actions are required. Prevention must also use an integrated and global approach, emphasizing partnership; inter sectoral collaboration and community participation. Such an approach means:

- Developing healthy public policies, legislation and economic and fiscal controls,
- Creating environments which are protective and supportive,
- Strengthening community action through social mobilisation,
- Increasing knowledge and skills using education and communication,
- Reorienting health services more towards prevention and population needs.

Teaching Lecture

How to analyse DVH in Clinical Brachytherapy

28 speaker

HOW TO ANALYSE DVH CLINICAL BRACHYTHERAPY: ENDOCAVITARY BRACHYTHERAPY

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In recent years endocavitary brachytherapy (BT) for cervical cancer has shown significant development in the field of 3D image based treatment planning. The possibility to tailor dose to target and organs at risk has obvious advantages compared to the limited possibilities within treatment planning based on 2D radiography. Dose volume histogram (DVH) parameters are crucial in 3D treatment planning both for guiding the treatment optimisation procedure and for reporting. In 2006 the GYN GEC ESTRO working group published a recommendation paper with emphasis on the use of 3D dose volume parameters [1].
For target structures (GTV, HR CTV, IR CTV) it is recommended to evaluate the minimum delivered dose to 90% and 100% of the target (D90, D100) as well as the target coverage (V100). D90 and D100 are isodoses surrounding the outer part of the target. Due to the large dose gradients, the central part of the target will receive a much higher dose which may be essential with regard to tumour control probability. In order to quantify the high dose regions, parameters like D70 and D50 are relevant.
For organs at risk (OAR) – rectum, bladder and sigmoid – minimum dose to the most irradiated volume should be evaluated for 0.1, 1 and 2 cm3 (D0.1cc, D1cc, D2cc) to assess typical BT related morbidity. The clinical relevance of these OAR parameters (correlation to morbidity) is still to be validated, but the rationale is that they represent both focal hot spots (0.1 cm3) and somewhat larger contiguous high dose regions in the organ wall: e.g. 20 mm x 20 mm x 5 mm ~ 2 cm3. As for the target there are significant dose gradients over the organs at risk, which makes the dose distribution totally different from what is typical with external beam radiotherapy. Large parts of the OAR receive a low dose.
It is important to pay attention to the accuracy of DVH calculations since relatively small geometric errors can translate into problematic errors in dose evaluation. Uncertainties on DVH parameters depend mainly on contouring, applicator reconstruction and organ movement. Reports so far (seem to) indicate that D90 and D100 for HR CTV and IR CTV are rather robust to target delineation, when contouring is done by experienced physicians. Uncertainties correlated to reconstruction of applicators should be minimised by avoiding systematic errors and by keeping a small slice thickness for imaging. For fractionated treatments, calculation of total BT dose is complicated by inter-fraction organ deformations. Simple addition of DVH's for succeeding BT fractions is based on the assumption that volumes irradiated to a high dose stay in the high dose region. It should be kept in mind that this leads to a conservative estimation of dose based on this "worst case assumption". This will likely apply mainly for fixed structures, as the GTV, CTV (fixed by the applicator) and OAR like anterior rectum wall and bottom-posterior bladder wall.
The steep dose gradients of brachytherapy carry great advantages but also true challenges. Evaluation and reporting of a highly heterogeneous dose distribution cannot be considered as straightforward. DVH parameters will always be a reduction of the inhomogeneous 3D dose map, and it should be kept in mind that DVH analysis should always be supplemented by direct visualisation of the 3D dose distribution and related to 3D topography. Reliability of DVH parameters depends on the whole dose planning procedure being carefully optimised: imaging, contouring, applicator reconstruction and dose calculation.

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29 speaker

HOW TO ANALYSE DVH IN CLINICAL BRACHYTHERAPY: INTERSTITIAL BRACHYTHERAPY

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Dose volume histograms (DVH) are graphical representation of volumes receiving a specified dose, and since they summarize lots of information provided in three-dimensional treatment planning they play an important role in modern brachytherapy (BT). Moreover, anatomy based optimization is also based on DVH-s. In clinical practice they can be used for quantitative evaluation of treatment plans and comparing rival dose plans. Though the ICRU Report 58 recommends using volume parameters (low dose and high dose volumes), the use of histograms are only partially discussed in the report.
DVH-s used in interstitial BT can be categorized as implant or organ related. In classical BT implant related DVH-s were calculated only, and they were used to quantify the dose homogeneity in the implanted volume with the dose-nonuniformity ratio (DNR) and dose homogeneity index (DHI). Another classification of DVH-s is: cumulative, differential and natural. Cumulative histograms represent the summation of volume elements over dose, and if calculated for organs they provide a fraction of an organ receiving a defined dose. Differential histograms present a graphic view of how volume is distributed with respect to dose. In natural DVH the effect of inverse square law is suppressed, and a high dose uniformity is represented by a high, narrow peak.
Integration of cross-sectional imaging into interstitial BT has made possible to calculate DVH-s for defined structures, such as target volume and organs at risk. From these histograms coverage index (CI), external volume index (EI), relative dose homogeneity index (HI), fractional target volume receiving a defined dose (V90, V100, V150, V200), relative dose irradiating 90% of the target (D90), minimum dose (D100) and conformal index (COIN) can be calculated. The COIN takes into account the coverage of target by the reference dose, as well as the unnecessary irradiation of normal tissues around the target. The higher the COIN more conformal the dose distribution is. For temporary prostate implants the GEC/ESTRO-EAU recommends reporting dose to organs at risk with fixed points or fixed volumes. Indication of the dose to the most exposed 2 cm3 of rectum or bladder (D2ccm), and for the most exposed 0.1 cm3 of the urethra (D0.1ccm) or for 1% of the contoured prostatic urethra (D1%) is suggested. For target D90, D100, V100, V150 and V200 should be reported. For permanent seed implantation of prostate cancer the ESTRO/EAU/EORTC recommends the use of D90, V100 and V150 for the target in postimplant dosimetry, but no guidelines are given to describe the dose received by urethra or rectum. For breast implants there are no recommendations to characterize the dose to target, lung and heart, but similar evaluation indices could be used as for the prostate.
In the presentation clinical examples on the use of different DVH-s and quality parameters will be shown for breast and prostate interstitial BT. Correlations between different quantifiers will be presented. Although there are some guidelines on the use of DVH-s and the related parameters for reporting dose distributions in interstitial BT, the clinical significance of implant quantifiers is not well known yet. Therefore further clinical investigations are required to find a correlation between dose-volume parameters and clinical outcome.
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Boost Advanced Head and Neck: BT vs IMRT

30 speaker

BRACHYTHERAPY AS BOOST IN HEAD AND NECK CANCER–USEFUL OR NECESSARY? TECHNIQUES, VALUE OF IMAGING, EFFICACY, SIDE EFFECTS

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The most often technique using for brachytherapy of head neck cancer is the multicatheter interstitial technique with exception of nasopharyngeal cancer, who the intracavitary technique is more appropriate. The detailed description of these techniques is available in each textbook, but very little is written about the value of modern imaging techniques for implantation of head and neck tumours. Currently simultaneously to clinical investigation it is possible to use as furthermore information's the X-ray imaging, CT-, or MR-imaging. The X-ray imaging allows very good catheter reconstruction, but no information's are available about tumor. In contrast to it the CT imaging make sometimes possible to distinguish the tumor bulk but in case of small tumors and particularly in postoperative cases (only surgical scare is present!) no or very limited information's about the tumor size and region are available. Often also the metal artifacts' (teeth-fillings) hamper to distinguish the correct size and form of tumor bulk. Nearly the same limitations presents the MR-imaging (the teeth-fillings leads to effacements of MR-signal), but the diversity of soft tissue imaging is among all imaging methods the best. In summary: The finger and eye of the surgeon is by nothing to replace; but the support of the CT- or MR-imaging is useful.
The efficacy and side effects of LDR- and PDR-brachytherapy as boost for head and neck tumors are very good documented in a lot of clinical studies: The local control rates are mostly between 80-90% or better also in cases of locally advanced tumors and the probability of serious side effects such soft tissue necrosis or osteoradionecrosis is nowadays below 5%.
In summary: Interstitial brachytherapy as boost for head and neck tumours' is a treatment option with excellent efficacy for carefully selected patients. The morbidity associated with brachytherapy is in experienced hands low and acceptable but can be significant and, therefore, should be performed at hospitals with adequate experience in planning and implementing this treatment. If done properly, the interstitial brachytherapy as boost is safe and delivers a dose that is higher and more conformal than what can be achieved by external beam radiation alone with the expected biologic advantages.

31 speaker

SIMULTANEOUS INTEGRATED BOOST TECHNIQUE WITH INTENSITY MODULATED RADIOTHERAPY (IMRT) IN HEAD AND NECK CANCER

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Background: Radiotherapy often comprises two phases, in which irradiation of a volume at risk for microscopic disease is followed by a sequential dose escalation to a smaller volume either at a higher risk for microscopic disease or containing only gross disease. This technique is difficult to implement with intensity modulated radiotherapy, as the tolerance doses of critical structures must be respected over the sum of the two plans. Techniques that include a simultanuous integrated boost (SIB) have been proposed to address this problem. The purpose of this study was to compare IMRT and 3D conformal radiotherapy (3D-CRT) with regard to radiation-induced (RTOG acute toxicity(XERRTOG)) and patient-rated xerostomia (EORTC QLQ-H&N35(XERpat)) among patients with HNSCC.
Material and methods: We included 248 patients with HNSCC treated with bilateral irradiation ± chemotherapy. Since 2000, all patients treated with HNSCC were included in a study program, in which acute and late morbidity according to the RTOG and QoL were prospectively assessed on a routine basis at regular intervals. Before October 2004, all patients were treated with 3D-CRT (n=144). After clinical implementation in October 2004, 104 patients received IMRT. In this study, the differences regarding XERRTOG and XERpat up to 12 months after radiotherapy were analysed. Dose-volume histograms (DVH) of the salivary glands were made in all patients.
Results: The use of IMRT resulted in a significant reduction of the mean dose of the parotid glands (26.2 Gy versus 44.2 Gy($p<0.001$). During radiation, grade 2 or higher XERRTOG was significantly less with IMRT as with 3D-CRT in the first 4 weeks. At 6 weeks after completion of radiation, the rate of XERRTOG d2 was 45% after 3D-CRT versus 29% after IMRT (p=0.041). Significantly less XERRTOG d2 was observed after IMRT upto 12 months after therapy. At 6 months the rate of XERRTOG d2 was 56% vs 30% with 3D-CRT and IMRT, respectively (p=0.006). At 12 months these rates were 52% vs 30% respectively (p=0.003). In addition, the incidence of moderate or severe XERpat at 6 weeks was 63% after 3D-CRT versus 39% after IMRT (p=0.005). At 6 months, moderate or severe XERpat scores were observed significantly less after IMRT (46%) compared to 3D-CRT (67%)(p=0.02).
Conclusion: IMRT with a SIB technique is feasible and results in a significant sparing of salivary glands and subsequent reduction of xerostomia. Important advantages of the SIB is that the number of fractions remains the same and allows for a integrated interpretation of dose distributions in organs at risk. Furthemore, SIB-IMRT gan be given without any unplannend treatment gaps or prolongation of the overall treatment time.

Gynaecology

32 oral

INTEROBSERVER COMPARISON OF TARGET DELINEATION IN MRI ASSISTED CERVIX CANCER BRACHYTHERAPY ACCORDING TO THE GYN GEC-ESTRO RECOMMENDATIONS

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Purpose/Objectif: To investigate the interobserver variation after implementation of the GYN GEC ESTRO contouring recommendations for MRI assisted brachytherapy of cervix cancer in two different institutions representing two different traditions for CTV assessment: HR CTV and IR CTV.
Materials/Methods: 19 patients, with biopsy proven cervical cancer, treated by radiotherapy in IGR-Paris (n=9 pts) and AKH-Vienna (n=10 pts.) were included for analysis. FIGO stage distribution was: IB1=1, IIA=1, IIB=9, IIIB=6, IVA=2. Treatment planning was performed according to institutional practice for 3 D image based brachytherapy (MRI). Dose prescription at IGR was to IR CTV and in Vienna to HR

CTV. Two radiation oncologists contoured the targets according to the GYN GEC ESTRO recommendations. To perform quantitative volumetric analysis, MRI scans containing the delineations of both observers were transferred to the Oncentra TPS (Nucletron®). For each scan, absolute volumes were registered for the GTV, HR CTV and IR CTV. For each volume, a common volume and an encompassing volume was calculated and their conformity index (CI). For dosimetric comparison DVH parameters for GTV, HR CTV and IR-CTV (D90, D100, V100) were evaluated. Doses were normalised to 2 Gy per fraction using the LQ-model (EQD2, α/β=10 Gy). Statistical significance was analyzed by the Wilcoxon-test.

Results: The absolute values are listed in table 1 for volumes and for DVH parameters.

Conformity indices for the delineated pairs of GTV, HR-CTV and IR-CTV contours were 0.5, 0.6 and 0.6 for Paris and 0.6, 0.7 and 0.7 for Vienna, respectively. There were no significant differences except for the absolute volumes of the IR CTV in Vienna (p=0.005) and the D100 of GTV in Vienna (p=0.015).

Conclusions*:* The application of the GYN GEC ESTRO recommendations for contouring in MRI based brachytherapy in two different clinical settings is feasible and associated altogether with minor inter-observer variation.

	IGR Paris volume [cm³ (mean (range))]		Vienna volume [cm³ (mean (range))]	
	Observer 1	Observer 2	Observer 1	Observer 2
GTV	5 (2.1 – 11.1)	4.9 (1.8 – 10.2)	18.1 (2.6 – 43.4)	16.7 (1.2 – 41.3)
HR CTV	25.7 (15.0 – 59.2)	29.4 (13.4 – 50.8)	53.1 (13.2 – 95.6)	49.7 (12.0 – 96.6)
IR CTV	85.6 (50.6 – 182.1)	102.2 (63.3 – 178.2)	118.2 (42.9 – 199.2)	141.9 (53.1 – 221.5)
	D90 [Gy_{eq10} (mean (range))]		D100 [Gy_{eq10} (mean (range))]	
PARIS	Observer 1	Observer 2	Observer 1	Observer 2
GTV	96.0 (52.1 – 123.1)	102.4 (54.5 – 144.2)	77.2 (41.5 – 98.6)	80.4 (42.6 – 107.6)
HR CTV	70.1 (34.8 – 98.6)	68.3 (42.6 – 96.5)	57.6 (26.2 – 78.7)	57.3 (32.6 – 78.7)
IR CTV	57.7 (28.3 – 77.6)	54.0 (30.4 – 66.3)	49.0 (21.1 – 64.1)	47.7 (21.1 – 57.7)
	D90 [Gy per fraction (mean (range))]		D100 [Gy per fraction (mean (range))]	
VIENNA	Observer 1	Observer 2	Observer 1	Observer 2
GTV	10.5 (6.7 – 14.6)	11.8 (6.4 – 17.8)	7.1 (3.7 – 12.2)	8.5 (3.1 – 15.3)
HR CTV	7.2 (4.2 – 9.4)	7.4 (4.6 – 10.0)	4.5 (2.5 -6.9)	4.4 (2.3 – 6.3)
IR CTV	4.4 (2.9 – 6.3)	4.5 (3.1 – 6.0)	2.5 (1.2 – 3.7)	2.6 (1.3 – 4.1)

33 oral

INTER- AND INTRAOBSERVER VARIATION IN HR-CTV CONTOURING: INTERCOMPARISON OF TRANSVERSE AND PARATRANSVERSE IMAGE ORIENTATION IN 3D–MRI ASSISTED CERVIX CANCER BRACHYTHERAPY

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Purpose/Objectif: Till recently, a majority of treatment planning systems (TPS) allowed for contouring in transverse (perpendicular to body axis–T) plane only. With introduction of new functionalities in the TPS, contouring in different image orientations became possible. The following investigation was performed to analyze agreement between the target volumes, as delineated by two observers on transverse and para-transverse (perpendicular to the tandem–PT) MR images for cervix cancer brachytherapy.

Materials/Methods: In thirteen patients, High Risk-CTV (HR-CTV) was outlined by two observers in T and PT image orientation, respecting the GYN GEC-ESTRO recommendations for 3D image based cervix cancer brachytherapy. Degree of difficulty of the two contouring approaches was evaluated, utilizing a three-tiered scoring system. To estimate interobserver and interplane agreement, HR-CTV sizes were compared and the ratio of common and encompassing volume (conformity index–CI) was assessed. Scalar and vector interobserver variations in contour-extent along cranio-caudal and eight radial directions were measured and compared between delineation planes. In addition, a qualitative estimation of topographic differences was performed. After applying a standard treatment plan, an intercomparison of DVH-parameters V100, D90, and D100 for the HR-CTV was carried out.

Results: Overall contouring difficulty score was higher in T than PT orientation (1.7 vs. 1.4, p=0.01). Interplane CI did not differ significantly between observers (0.72 vs. 0.71), nor did the interobserver CI between planes (0.79 vs. 0.78). Interobserver comparison of scalar and vector variations in contour-extent demonstrated no significant deviations between different radial directions. The Interobserver differences in DVH parameters were more pronounced in in PT than T plane. Interplane variations in DVH parameters were non-significant.

Conclusions: Although contouring in PT, as compared to T orientation, is feasible and allows for a good HR-CTV depiction, no clear clinical benefit of this approach could be shown. Interobserver inconsistencies can be minimized by systematic training and following the published recommendations.

34 oral

UNCERTAINTIES OF DVH PARAMETERS ASSOCIATED WITH SYSTEMATIC AND RANDOM ERRORS OF APPLICATOR RECONSTRUCTION IN 3D IMAGE BASED GYNAECOLOGICAL BRACHYTHERAPY

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Purpose/Objectif*:* 3D MRI based dose planning is increasingly used for brachytherapy (BT) of cervical cancer. DVH parameters for tumour and organs at risk are used for guidance of dose planning and for reporting. Poor visibility of applicator source channels and potential distortions in MRI can lead to both random and systematic errors in applicator reconstruction. Reliability of DVH parameters is essential, and the purpose of this study was to evaluate the impact of applicator reconstruction on uncertainties of DVH parameters.

Materials/Methods: Dose plans were analysed for 10 cervical cancer patients with intracavitary (ring applicator) MRI based BT. Uncertainty of applicator reconstruction was modelled by displacing the applicator in cranio-caudal (±3, ±5mm), lateral (±3mm) and ant-post (±3mm) directions, and rotating the ring by ±15mm dgr. Changes in DVH parameters per mm of reconstruction uncertainty were evaluated for tumour (D90, HR-CTV) and organs at risk (D2cc, bladder, rectum, sigmoid). These data were used to model DVH uncertainties for different numbers of BT fractions and for varying random and systematic uncertainties, by assuming that random reconstruction uncertainties are normally distributed.

Results*:* Uncertainties of DVH parameters depended on organ type and on direction of applicator displacement. The most sensitive organs were rectum and bladder where mean DVH shift in ant-post direction was 5% per mm applicator displacement. Otherwise, shifts were between 1% and 3% per mm. DVH deviations of less than 10% for at least 90% of a patient population can be obtained by keeping random and systematic errors under certain levels. An example of tolerances is shown in the figure below for cranio-caudal direction (4 fractions BT). Light grey indicates a region of acceptable reconstruction uncertainty whereas uncertainties in the dark area are unacceptable for a significant amount of patients. Systematic errors have much larger impact on DVH uncertainties than random errors. Tolerances are tighter for schedules with few BT fractions.

Conclusions*:* Comprehensive quality control of applicators and imaging procedures should be used to prevent systematic uncertainties in applicator reconstruction. Furthermore, random errors should be minimised by using small slice thickness and by having clear guidelines for reconstruction. With careful applicator reconstruction procedures, reliable DVH parameters for tumour and organs at risk can be obtained.

35 oral

WORK IN PROGRESS: TREATMENT PLANNING IN MRI BASED CERVIX CANCER BRACHYTHERAPY IN 11 CENTRES. RESULTS FROM THE GYN GEC ESTRO TREATMENT PLANNING WORKSHOP 02/2007 IN LJUBLJANA

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Purpose/Objectif: Background: To perform a qualitative and quantitative comparison of different treatment planning methods for MRI based intracavitary brachytherapy (BT) of cervix cancer.

Materials/Methods*:* The workshop was attended by 10 European and 1 American Centre that are performing 3D image based gynaecological BT. 6 cases were discussed in total, 3 of them are included in this sub-analysis. Clinical features at time of diagnosis and at BT were systematically presented for patients treated with a tandem-ring (patient 1), a tandem-ovoid (patient 2) and a tandem-mould applicator (patient 3), respectively. Tumours had a width › 4 cm at time of diagnosis and major remission after external beam therapy (EBRT) to a width ‹ 4 cm at time of BT. High Risk (HR) CTV, Intermediate Risk (IR) CTV and organs at risk (OAR) bladder, rectum and sigmoid were contoured, and the applicators were reconstructed prior to the workshop. The centres performed MRI based treatment planning with the applicator, fractionation schedule (HDR, PDR, number of fractions, pulses) and optimisation method they use in clinical routine. In order to quantitatively compare the final treatment plans, common dose volume constraints were defined. Dose reporting is based on total (EBRT + BT) biologically equivalent doses in 2 Gy fractions (EQD2, LQ-model, α/β=10Gy for CTV and reference volume, α/β=3Gy for OAR, T1/2=1.5h for all tissues). EBRT dose was 24 x 1.8 Gy. The goal was to achieve a total D90 (HRCTV) › 85Gy, while keeping the D2cc (bladder)‹90Gy and D2cc (rectum, sigmoid) ‹70Gy.

Results*:* All centres use their standard plans as a starting point for optimisation where the dose is normalised to Point A: loading pattern, dwell times and shap of the isodose line going through Point A originate from different traditions of intracavitary BT and vary considerably between different applicators and also between identical applicators. Optimisation was performed by manual loading pattern and dwell time modification (man) or by drag and drop of isodose lines (d&d). One centre that does not routinely modify the dose distribution had to be excluded from evaluation. In this preliminary descriptive evaluation a table is shown giving the following parameters: fractionation schedule, optimisation method, absolute volumes of the 60Gy isodose (ICRU Report 38 Reference Volume), 85Gy isodose (Treated Volume), 120Gy isodose (High Dose Volume), Point A doses and DVH-parameters for CTV and OAR.

Conclusions: The variation of the spatial dose distributions and DVH-parameters seemed to be smaller in the optimised plans compared to the standard plans. A comprehensive analysis will include the parameters mentioned above and in addition loading pattern, dwell time optimisation, spatial distribution of high dose regions, and biological effects: (1) comparison between standard and optimised dose plans for each centre, and (2) variation between centres before and after optimisation.

Centre	A	B	C	D	E	F	G	H	I	J
Pt	1	1	1	1	1	1	2	2	3	3
Applic.	ring	ring	ring	ring	ring	ring	ovoids	ovoids	mould	mould
Fraction.	PDR	PDR	HDR	HDR	HDR	HDR	HDR	PDR	PDR	PDR
Fractionsx-pulses	3x18	2x43	3	4	5	6	4	1x73	1x30	1x37
Opt.method	man	man	man	man	man	d&d	d&d	man	d&d-man	d&d-man
V(60Gy) (cm^3)	168	196	118	128	115	178	196	228	209	259
V(85Gy) (cm^3)	50	56	41	43	39	54	66	60	68	82
V(120Gy) (cm^3)	23	23	19	20	19	25	33	25	33	39
D(PointA) (Gy)	67	69	64	65	66	66	71	76	8	83
HR CTV D90(Gy)	87	88	82	83	84	84	68	76	79	86
IR CTV D90(Gy)	64	67	58	60	57	63	56	60	66	71
Bladder $D2_{cc}$(Gy)	55	55	51	51	51	53	94	90	65	68
Rectum $D2_{cc}$(Gy)	54	54	53	54	52	54	66	69	59	61
Sigmoid $D2_{cc}$(Gy)	70	70	76	75	78	73	52	58	65	69

36 oral

CLINICAL APPLICATION OF MR BASED 3D DOSE PLANNING FOR BRACHYTHERAPY OF CERVICAL CANCER

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Purpose/Objectif: Introduction of 3D dose planning based on MR imaging for Fletcher type applications according to the GEC-ESTRO guidelines

Materials/Methods*:* 1) Two applicator reconstruction methods were tested: For each application MR scans with applicator in situ were made, three T2 weighted scans (4.5 mm slice thickness) and a Balanced Fast Field Echo (BFFE) scan (1.5 mm slice thickness). The applicator was reconstructed in Plato BPS directly on the BFFE scan (reconstruction method A), and on a resampled combination of the three T2 scans to an image set with resolution of 1x1x1 mm3 (method B). Targets and OAR's were delineated on the T2 scans and imported into Plato. Three observers made reconstructions A and B for 5 applications. Reconstruction accuracy was analyzed by comparing the dose parameters D90 for GTV, High Risk-CTV and Intermediate Risk-CTV, and D2cc for bladder, rectum, sigmoid and small bowel.2) Ten patients received 2 PDR applications, for which reconstruction method A and 3D optimization was applied. For all 20 applications a standard plan was made using conventional film reconstruction, according to ICRU guidelines, based on 29 pulses of 60 cGy and the above-mentioned dose parameters were calculated for target and OAR. If necessary the dose distribution was optimized according to GEC-ESTRO guidelines, by adjusting dwell positions and dwell times and the same dose parameters were analyzed for the optimized plan.

Results: 1) For both applicator reconstruction methods the interobserver variation for the dose parameters was comparable (avg 1.2%, ‹ 1cGy/pulse). Differences between the two methods were larger (avg 3.4%, up to 9% for D2bladder) and could be related to positioning differences between the 4 MR scans.The easier and faster reconstruction method A based on the 1.5 mm slice BFFE scans is thereafter used in clinical practice. 2) For 20 PDR applications, tak-

ing into account the OAR constraints, the average doses to the High Risk-CTV amounted for the standard plans and the optimized plans D90HR-CTV=74.8 (SD 11) Gy EQD2 and 79 (SD 11) Gy EQD2, respectively. The average doses to the bladder were: D2bladder =83.2 and 83.9 Gy EQD2, respectively. Average D2bladder was higher than ICRU point dose, while D2rectum was lower than the ICRU point dose (table 1).For 18/20 applications an optimized plan was calculated and 15 times applied after 2/29 or 3/29 pulses with standard plan.
Conclusions*:* Applicator reconstruction based on MR data is feasible in clinical practice, and optimization improves both dose distribution and insight. However, optimization results stay limited for the tandem/ovoid combination. An additional interstitial approach seems to be necessary.

	Standard plans		Optimized plans	
in cGy/pulse	D2cc	ICRU point dose	D2cc	ICRU point dose
Bladder	73 (19)	68 (33)	63 (8)	56 (21)
Rectum	35 (10)	53 (6)	36 (10)	56 (9)

table 1 Pulse doses to rectum and bladder for 20 applications, average (SD)

37 oral

ON BEHALF OF THE « STIC PDR » GROUP. PRELIMINARY RESULTS OF A PROSPECTIVE MULTICENTRIC FRENCH STUDY OF PDR 3D BRACHYTHERAPY FOR CERVIX CARCINOMA : PATIENTS TREATED BY EXTERNAL BEAM THERAPY AND BRACHYTHERAPY

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Purpose/Objectif: In 2005 a French multicentric non randomized prospective study ("STIC PDR*") was initiated to compare 2 groups of patients treated for cervix carcinoma according to brachytherapy method. For the first group of patients (2D group), dosimetry was performed on orthogonal X Rays; for the second group (3D group) dosimetry was planned on 3D imaging and performed with Pulsed Dose Rate Brachytherapy. The study will end after 2,5 years accrual and the enrollment of 850 patients, half in each group. This study will describe the first 96 patients treated by external beam therapy (EBT) and brachytherapy.
Materials/Methods
Data are available for 96 patients: 47 in the 2D classical group, 49 in the 3D conformal group. The 2 groups were comparable in terms of clinical presentation: 92% were squamous cell carcinoma, 6% adenocarcinomas; 17 and 14% of patients presented with stage I disease, 40 and 57% with stage II disease, 38 and 29% with stage III respectively in the 2D and 3D group. 43 and 49% had pelvic adenopathies on CT scan.
20% of the patients had a pelvic lymphadenectomy performed at time of diagnosis; 30 and 40% positive nodes were found among them in the 2 groups. EBT (plus chemotherapy) was performed as first treatment, followed by brachytherapy. In both groups, ICRU bladder and rectal points were drawned; "isodose 60 Gy" corresponded to 60–EBT dose; the volume of isodose 60 Gy was measured ; in the 3D group, CTV volumes were delineated according to GEC ESTRO recommendations (High Risk CTV (HR CTV) and Intermediate Risk CTV (IR CTV)), as were the external wall of the organs at risk (bladder, rectum and sigmoid); cumulative DVH were performed on CTV and organs at risk. The dose to 100% (D100) and 90% (D90) of CTV was analysed.
Results: 77 and 84% of patients received pelvic irradiation in 2D and 3D groups respectively (21 and 16% pelvic and para aortic EBT); the median dose delivered was 45 Gy in 25 fractions. Respectively 74 and 84% of the patients received concomitant chemotherapy consisting in weekly cisplatyl most of the time.
Brachytherapy
Data are available for 83 patients (44 in the 2D and 39 in the 3D group).
Results are comparable between the 2 groups in terms of isodose 60 Gy volume (121 and 143 cc respectively), dose to ICRU bladder point (16,5 and 17 Gy respectively) and rectal point (16 and 18 Gy), and TRAK (138 vs 145 Gy.cm2).
In the 3D group, for a median prescription of 15 Gy, median D100 and D90 for HR CTV were 14 and 21 Gy respectively; median D100 and D90 for IR CTV were 8 and 15 Gy respectively. Median dose delivered by bT to 2cc of bladder was 21 Gy (8-91 Gy), and to 2cc of rectum 16 Gy (5-36 Gy).
Conclusions: In this series of patients there appears to be no difference in treated volumes between 2D and 3D groups. This preliminary experience may correspond to a learning curve during which physicians didn't modify to a large extent their mode of prescription while evolving towards 3D brachytherapy. In the 3D group, low doses to CTV were delivered compared to GYN GEC ESTRO recommendations. Longer follow up is needed to know more about local control and complications.
*Grant from the French Ministry of Health

Prostate Monotherapy: Seeds vs HDR

38 speaker

PERMANENT SEED IMPLANTATION FOR LOW RISK PROSTATE CANCER

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Early stage prostate cancer is now an epidemiological phenomenon. Adequate management should consider clinical and radiobiological as well as logistic and organizational issues.
We present permanent seed implantation as a way to streamlined patient workflow in early stage prostate cancer. In our opinion, permanent seed implantation is superior to high-dose-rate due to several reasons:
1. Radiobiology of ultra-low-dose-rate is beneficial to improve therapeutic ratio. Increased benefit for HDR due to estimated low α/β ratios is controversial.
2. Developments in software for 3D-US reconstruction, real-time navigation and treatment planning permit WYSWYG ("what you see is what you get"), getting dose distributions very similar to those planned.
3. Patient workflow can be improved using seed implantation. It is possible to have implant and immediate post-implant dosimetry in one operation slot.
4. Predictive models can be built based upon a combination of clinical and dosimetric parameters. Useful clinical decision can be derived from those models.
We will present video material and simulations illustrating the concepts shown here.

39 speaker

HDR MONOTHERAPY

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HDR prostate brachytherapy offers practical advantages, physical advantages and biological advantages over seed brachytherapy and external beam treatment.
In practical terms it uses an existing HDR source and therefore no

extra cost is involved. There are no radio protection issues related to the use of free live sources and no risk of source loss. It can be given as an outpatient procedure.
The physical advantages relate to the ability to implant a wider area than with seed brachytherapy and with greater accuracy than is possible with external beam radiotherapy. Thus HDR brachytherapy implants can treat the peri-prostatic tissues and the seminal vesicals and even include the bladder base. There is no associated organ movement from the time of implant to the time of radiation delivery and therefore no problems relating to set-up error or internal movement.
The biological advantage is related to the low alpha beta ratio for prostate cancer. The implication of this is that it is relatively more sensitive to large fraction sizes and the only means of delivering large individual doses per fraction to the prostate within normal tissue tolerance is by using HDR brachytherapy. When used as monotherapy doses which are equivalent to over 100Gy in 2Gy fractions can be delivered with confidence.
The physical, biological and practical advantages of HDR mean that it is now being explored in several centres as monotherapy. Early results from these phase II studies confirm high tumour control rates despite the inclusion of patients with advanced local disease. One of the striking observations compared with seed brachytherapy is a marked reduction in both the severity and duration of urinary symptoms after implantation and a suggestion that there are much lower rates of late urinary and bowel damage and erectile impotence. Bowel toxicity is rare similar to that seen with seed brachytherapy and far less than with even the most sophisticated external beam techniques.
Overall therefore it can be seen that HDR monotherapy is the optimal means of delivering high conformal doses to levels that cannot be achieved with external beam treatment to the prostate gland exploiting the low alpha beta ratio whilst being able to address locally advanced disease by the ability to implant widely around the prostate gland to cover regional disease.

Clinical Miscellaneous

40 oral

IS THERE A DIFFERENCE IN THE CLINICAL OUTCOME AFTER VARIOUS BOOST TYPES IN BREAST CONSERVING THERAPY (BCT): RETROSPECTIVE CONSIDERATIONS ON 1635 PATIENTS.

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Purpose/Objectif: The results of BCT using breast irradiation and a boost to the tumor bed with either electron beam or interstitial 192-Ir implant or no boost are reviewed retrospectively.
Materials/Methods*:* A total of 1635 patients with stage pT1-2 underwent whole breast irradiation +/- boost (45-50 Gy, 1.8 Gy daily, 5 fr./week). Group A: electrons in 702 patients, group B: 192-Ir implants 784 pat., group C: no boost in 149 patients. For A, patients with superficial tumors only were selected. Group B presents with both, superficial and predominantly deep seated locations, and has the highest rate of negative prognostic factors. Group C are patients with pT1 stage, low risk parameters only and tamoxifen medication. Local control, survival and cosmetic results are reviewed. Median FU is 97 months (53-191).
Results: The 5-yr local recurrence rates were 2.0% in the T1, and 4.4% in the T2 groups (5.8% and 8.2% respectively after 10 years). There was no significant difference in the breast relapse rate and in survival parameters between the groups. Cosmetic results were rated as excellent/good in 83% of patients with T1 tumors in group A, 78.6% of patients in group B, and 87% in group C, and 67.0% (A) and 78.3% (B) respectively in patients with T2 tumors. In a 4-grade scoring cosmetic results changed by a factor of 1.08 in group A, 1.19 in group B and by 1.02 in group C after 5 years (n.s.).
Conclusions: Concerning the selection bias in A, B and C there is no significant difference in local tumor control and in survival parameters. The cosmetic results of the external beam boosts and the HDR-192-Iridium boosts are similar (no significant difference).

41 oral

THE ROLE OF HIGH-DOSE-RATE (HDR) BRACHYTHERAPY (BT) BOOST IN BREAST-CONSERVING THERAPY (BCT): TEN-YEAR HUNGARIAN EXPERIENCE

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Purpose/Objectif: To report the 10-year experience of the Hungarian National Institute of Oncology with fractionated HDR BT boost for high-risk breast cancer patients treated with BCT.
Materials/Methods: Between 1995 and 2006, 98 early-stage (pTis: 6; pT1: 55; pT2: 37; pN0: 68; pN1-2: 26; pNx: 4) breast cancer patients received an HDR BT boost after breast-conserving surgery and whole-breast irradiation (median dose: 50 Gy). Surgical margin status was clear (› 2mm), close, positive, and unknown in 67 (68.3%), 13 (13.3%), 5 (5.1%), and 13 (13.3%) cases, respectively. Nineteen patients (19.4%) had EIC+, 31 (31.6%) LVI+, and 25 (25.5%) HG 3 tumours. Ten patients (10.2%) received a single-fraction HDR boost of 8-10.35 Gy using rigid needles, while 88 (89.8%) were treated with fractionated multi-catheter HDR BT boost. The latter consisted of 3 x 4 Gy (n = 19), 3 x 4.75 Gy (n = 68), and 2 x 6.4 Gy (n = 1). Breast cancer related events, cosmetic results and side-effects were assessed.
Results: At a median follow-up time of 75 months (range: 7 to 133) only 5 (5.1%) local (2 true recurrences, and 3 elsewhere failures), 2 (2.0%) regional recurrences, and 3 (3.1%) contralateral breast cancers were observed. The 5- and 10-year actuarial rate of ipsilateral breast failure was 4.5% and 8.7%, respectively. The 5- and 10-year disease-free, overall, and cancer-specific survival was 80.3% and 73.8%; 86.6% and 71.7%; and 87.7% and 78.6%, respectively. Cosmetic outcome was rated excellent in 16%, good in 41%, fair in 32%, and poor in 11%. Data on late radiation side-effects were available at 86 patients (87.8%). Grade 3 fibrosis and grade 3 teleangiectasia occured in 6 (7.0%) and 2 (2.3%) patients, respectively. In univariate Cox regression analysis only positive margin status had a significant negative effect on local control (5-y LR rate: 20.0% vs. 3.7%; p = 0.0006). Close or unknown margin status, tumour size (pT1 vs. pT2), nodal staus (pN0 vs. pN1-2), EIC, LVI, HG, ER- and PgR-status had no significant impact on local tumour control.
Conclusions: Fractionated HDR BT boost using multi-catheter implants produce excellent long-term local tumour control, with acceptable cosmetic outcome, and low rate of grade 3 late radiation side-effects. Our results confirm that high-dose HDR BT boost can mask classical risk factors for local recurrence (with the exception of positive margins).

42 oral

INTERSTITIAL HIGH DOSE RATE (HDR) BRACHYTHERAPY FOR EARLY STAGE BREAST CANCER : A REPORT OF 124 CASES

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Purpose/Objectif: External Beam Radiation Therapy (EBRT) given over 5-6 weeks has been the standard of care for breast conservation radiation therapy. Recent data indicates that Interstitial Implant and High Dose Rate (HDR) radiation afterloading delivered over 5 days, compares very favorably to EBRT in selected patients. We report our results in 124 patients treated with HDR.

Materials/Methods*:* Patients with Tis, T1, and T2 tumors measuring ‹ 3 cm, negative surgical margins, and negative axillary lymph nodes were judged to be candidates for Interstitial Implant, followed by HDR radiation afterloading. Subsequently, patients who had, or were scheduled to receive anthracycline based Chemotherapy were excluded.

Results*:* Between 2000 and 2007, 124 patients underwent Interstitial Implant under Stereotactic Mammographic guidance with conscious sedation and local anesthetic. The implants were placed using a custom designed Anderson-Nair template using from 3 to 8 planes, and 8 to 57 needles. Catheters were subequently threaded thru the needles, and the needles removed. Catheter spacing was 1.0 to 1.5 cm. Radiation Treatment planning was performed using CT Scanning and the Plato System. Treatment volumes ranged from 25 cc to 359 cc. HDR radiation treatment was given using the Nucletron afterloading system. The breast implant volume received 3400 cGy in 10 fractions prescribed to the Planning Target Volume, given BID over 5 days. The procedure was well tolerated. No patient required hospital admission. With a median follow-up of 48 months, (range 6-84 months), local recurrence occurred in 4.0% (5/124) of patients. Cosmetic results were good to excellent in 86.3% (107/124) of the patients. Wound healing complications developed in 5.6% (8/124). Three of these patients had received anthracycline based Chemotherapy. The other five had large (› 200 cc) implant volumes, catheter spacing of 1.5 cm, and D-150% of › 30%. Two patients healed after 6 months of conservative treatment. Surgery was required in six patients who developed fat necrosis.

Conclusions: With median 48 month follow-up, breast conservation radiation therapy utilizing Interstitial HDR Implant has yielded local recurrence rates and cosmetic results which compare favorably to EBRT in selected patients. Treatment with anthracycline based chemotherapy, large (› 200 cc) implant volumes, and D-150% › 30%, appear to be relative contraindications to Interstitial HDR Implant. Finally, catheter spacing of 1 cm yielded optimal dosimetry and mininized complications.

43 oral

LONG TERM RESULTS OF PULSE DOSE RATE BRACHYTHERAPY FOR REPEAT IRRADIATION IN LOCALLY RECURRENT BREAST CANCER

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Purpose/Objectif: To assess the effectiveness and tolerability of PDR-brachytherapy as a second radiotherapy treatment regime for locally recurrent breast tumours. To evaluate the feasibility of interstitial partial breast irradiation after local excision as an alternative to mastectomy in patient with recurrent breast cancer.

Materials/Methods: 32 patients with small local recurrent breast cancer initially undergoing breast conserving therapy, which included postoperative radiotherapy, were prospectively treated with local tumour excision and PDR-brachytherapy from 11/1996 to 09/2005. Recurrences have occurred after a median interval of 119 months (range, 13-310 months) after primary treatment. All patients received local excision for their recurrence followed by radiation therapy with median 50.4 Gy (range, 48-60.2 Gy) PDR-brachytherapy. The prescribed dose was 0.6-1 Gy per pulse. 32 patients were examined for local tumour control, in 18 patients late side effects and global cosmetic outcome have been evaluated. QoL was evaluated using QLQ-C30 and QLQ-BR23 and compared to a standardised, healthy control group (Schwarz et al. 2001)

Results: Thirty (93.8%) of 32 patients are still alive after a median follow up of 41 months (range 6-117) after recurrent breast cancer. Local control has been observed in 30 patients. Two women had a second local tumour recurrence 12 months after PDR-brachytherapy and had to undergo mastectomy. Four different patients showed signs of having distant disease (2) or axillar lymph node metastasis (2). Three women had contralateral breast cancer (before the appearance of ipsilateral recurrent breast cancer) and one patient had an ipsilateral tumour with a different histology to the primary tumour. One woman died due to distance metastasis (156 months after primary tumour), the other due to cardiac problems. Global cosmetic result, classified by radiooncologists, was excellent to fair in 64.7% of patients. From the patients view, 88.2% had an excellent to fair cosmetic outcome. Concerning late side effects, scored using LENT-soma, no telangiectasis was found in 66.7% of patients. 16.7% of women developed telangiectasia grade 1 and 16.7% of women grade 2. Fibrosis grade 1 was found in 16.7%, grade 2 in 61.1% and grade 3 in only one patient (5.6%). Atrophy was found in 55.6% of women, mostly grade 1. Concerning QoL our collective was only significant worse concerning dyspnoea compared to a healthy female control group.

Conclusions: PDR-brachytherapy following surgical intervention for locally recurrent breast cancer after primary BCT gives encouraging results in patient's local tumour control and recurrence free survival. Furthermore it is a well tolerated therapy with moderate late side effects, good cosmetic outcome and satisfying QoL. It seems to represent an attractive opportunity to mastectomy.

44 oral

PULSED DOSE-BRACHYTHERAPY: RE-IRRADIATION OF HEAD AND NECK CANCERS.

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Purpose/Objectif: The aim of this study was to investigate the feasibility and efficacy of a PDR-brachytherapy re-irridiadiation as a treatment option of local recurrent tumours of the oral cavity, base of tongue, lips and buccal mucosa after previous curative radiotherapy.

Materials/Methods: Between 1997 and 2004 in our department 83 patients with recurrent head and neck tumours underwent an interstitial PDR-brachytherapy irradiation as boost or as exclusive therapy with or without a concurrent chemotherapy after a sufficient previous external radiotherapy. The implant geometry and treatment planning were done analogous to the Paris system. The dose were delivered with pulse doses of 0.55 (0.40-0.70) Gy/hour and a mean total dose of 24 Gy as boost or 57 Gy as single radiation therapy. All patients received a platinum-based chemotherapy with or without 5-FU. 45 of all had a surgery before radiotherapy and 41 (49.4 %) of all a macroscopic tumour. Brachytherapy exclusive were given in 77.1 % (64) of the cases. After the IBT 22 patients got an interstitial hyperthermia.

Results: After the follow-up of 7 years maximum 24 patients (28.9 %) had a local relapse, 11 (13.3 %) distant metastases and 46 (55,4%) were dead. The Kaplan-Meier curve (after 24 months) shows a overall

survival rate of 66.7 %, a recurrence free survival rate of 45.9 % and a metastases free survival rate of 39.0 %. As late side effects necrosis of the lower jaw bone was found in 10.6 % (9 pats.) and soft tissue necrosis in 14.5 % (11 pts.) of all cases–surgical treatment here was necessary in 2 (2.4 %) cases respectively 1 (1.2 %) case.
Conclusions: The interstitial pulsed dose brachytherapy in patients with head and neck cancers after a previous curative radio-/chemotherapy is in case of local recurrence a effective treatment option and shows a high local control rate with low side effects. It offers for selected cases a curative treatment option.

45 oral

CONSERVATIVE MANAGEMENT OF SQUAMOUS CELL ANAL CARCINOMA WITH EXTERNAL BEAM RADIATION THERAPY AND LOW DOSE 192IR INTERSTITIAL BRACHYTHERAPY.

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Purpose/Objectif*:* To evaluate carcinologic results and late toxicity of low dose rate 192Ir interstitial brachytherapy (BT) and external beam radiotherapy (EBRT) combination in a series of 83 patients (pts) treated for a non metastatic primary anal squamous cell carcinoma.
Materials/Methods: From 1986 to 2001, 83 pts were treated by BT for anal squamous cell. In all 83 pts, BT was used as a complementary boost after EBRT . Median age was 62.1 years [37.8-87.9] with a sex ratio of 1M/5F. TNM classification was: 15 T1, 42 T2, 21 T3, 5 T4, 68 N0, 8 N1, 6 N2, 1 N3. Mean dose of EBRT was 43,4 Gy [20-48]. As primary treatment 24 pts received EBRT only, and for 59 pts EBRT was associated with a cisplatinum based chemotherapy regimen (neo-adjuvant (2 pts), concomitant (40 pts), both (17 pts)). BT was delivered with a mean delay of 40 days [4-128] after the end of EBRT. According to Paris'system, mean delivered BT boost dose was 20 Gy [15-30]. Late toxicity was evaluated using RTOG scale.
Results: With a median follow-up of 62 months, the 5-year actuarial disease free and overall specific survival rate were respectively of 88.4 % (+ 3.9 %; CI [81.1-96.3]), and 84.5 % (+ 4.1 %; CI [76.8-93]). Thirteen pts developed further recurrence: local (n=6), local with lymph node involvement (n=4), distant metastasis (n=1), and both loco-regional and distant relapse (n=2). Salvage abdomino-perineal excision was performed for 5 pts. Seven pts developed a grade 3-4 late toxicity, 5 of them requiring abdomino-perineal excision. Severe grade 3-4 toxicity were mainly: rectitis (n=5); diarrhea (n=1); anal incontinence (n=1).
Conclusions*:* Brachytherapy and EBRT combination is an efficient loco-regional treatment for management of anal carcinomas with an acceptable rate of late severe toxicity and a high rate of conservative sphincter function.

46 oral

EVALUATION BY PATIENTS OF BRACHYTHERAPY FOR PENIS CARCINOMA

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Purpose/Objectif: In case of penis carcinoma limited to the glans, brachytherapy (BT) is one of the reference treatments. Local excision combined with reconstructive surgery may also be proposed. The side effects of the treatments are reported by physicians who are mainly focused on local control. The goal of the study was to analyze the opinion of the patients (pts) after BT for carcinoma of the penis.
Materials/Methods: A questionnaire was sent to all the patients treated by BT for penis carcinoma and without disease at the last news. The questionnaire evaluated in intensity and duration different symptoms/items potentially related to BT, at the present time: penis pain, sexual activity, urinary symptoms and cosmetic aspect of the penis. Finally, pts gave their opinion on BT.
A total of 83 questionnaires were sent, 50 of them could be analyzed. The median age at BT was 62 years (33-87) and the questionnaire were received at a median time of 67 months (7-326) after BT. In the follow-up after BT, 1 pt had a local relapse treated by excision, 12 pts had urethral stricture and 9 had pain (requiring medicine), 2 of these complications requiring surgery.
Results: The pts had no pain in 66% or very moderate and rare pain in 24%, only 1 pt taking medicine. The impact of BT on sexuality couldn't be evaluated in 30% of the pts because having no sexual activity any more (not related to BT). Quality of sexuality was decreased significantly in 20% of pts and 8% couldn't have any sexual activity because of BT. Sexual desire, erection and sexual satisfaction were decreased in 20%, 30% and 28% of the pts, respectively. No impact or very moderate impact of BT on urinary function was expressed by 58% and 18% of the pts, 2% of the pts having urethral stricture requiring dilatation. The aspect of the penis was considered to be significantly modified by BT and circumcision for 38% of the pts, but without any consequence for 30% of pts and very limited consequences for 32%. The pts formulated to be very satisfied or satisfied by BT in 58% and 30% of cases.
Conclusions*:* Although this study has been realized retrospectively and represents a snapshot at various time after BT, pts appear to be generally satisfied by BT. Pain is rare. BT has an impact on sexuality in one third of the pts and a moderately impact on urinary function. The combination of BT and circumcision modifies the aspect of the penis without any consequences for most of the pts.

47 oral

TREATMENT OUTCOMES AFTER I-125 EPISCLERAL PLAQUE BRACHYTHERAPY FOR UVEAL MELANOMA

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Purpose/Objectif: To determine the long-term outcomes of I-125 plaque brachytherapy for uveal melanoma. To identify dosimetric factors associated with ocular complications and tumor control.
Materials/Methods
Medical records were reviewed for 249 patients treated with I-125 plaque brachytherapy for uveal melanoma from 1997 to 2005. Brachytherapy records were reviewed in order to analyze radiation doses at specific points (i.e. prescription point, tumor apex, tumor base, fovea, optic disk, lens, center of the eye, and opposite retina). Medical records detailing ophthalmologic follow-up appointments were analyzed to assess the incidence of ocular complications after therapy. Statistical analysis was used to assess outcomes in relation to dose delivered.
Results: Mean tumor thickness and long basal diameter were 4.85 mm and 11.3 mm, respectively. The mean dose to the tumor apex was 100.66 Gy, to the tumor base was 261.56 Gy, and to the prescription point was 85.57 Gy. The mean follow-up was 38 months (4 to 114 months.). The estimated 5-year overall and cause-specific survivals were 78% and 91%, respectively. Fifteen patients (6%) developed metastatic disease. Local control was 97.6% with 6 local failures. The radiation dose to the tumor base was greater in those with local control compared to those with local failures (263 Gy versus 186 Gy; $p = 0.078$). There was no correlation of local control to the apical tumor dose (100 Gy versus 101 Gy; $p = 0.95$). Twenty patients (8%) underwent enucleation. The reasons for enucleation were local recurrence (4 patients), second primary tumor (1 patient), infectious scleritis (1 patient), and severe radiation toxicity (14 patients; 5.6% of treated patients). Tumor doses in patients with radiation toxicity leading to enucleation were significantly greater than those in pa-

tients without enucleation. The mean dose to the tumor apex was 101 Gy in those with enucleation compared to 88 Gy for those without enucleation (p = 0.0078). The corresponding radiation doses to the tumor base were 453 Gy and 250 Gy (p ‹ 0.0001).
Conclusions*:* I-125 episcleral plaque brachytherapy leads to excellent local control and globe preservation. Radiation toxicity leading to enucleation correlates with higher radiation doses. Local control was more closely correlated to dose to the tumor base than dose to the tumor apex.

Physics: Reconstruction techniques and Miscellaneous

48 oral

INVERSE PLANNING FOR 3-D MRI-BASED PULSE DOSE-RATE INTRACAVITARY BRACHYTHERAPY IN PATIENTS WITH CERVIX CANCER.
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Purpose/Objectif: To evaluate the use of the inverse planning simulated annealing (IPSA) sofware for dose distribution optimization in patients with cervix carcinoma treated with magnetic resonance imaging (MRI)-based pulsed-dose rate (PDR) intracavitary brachytherapy (ICBT).
Materials/Methods: A group of 30 patients treated with MRI-based PDR ICBT with a technique using customized vaginal mould was selected to test the IPSA algorithm. Dose-volume parameters obtained by the IPSA method were compared with the manual "classical" method of optimization (MMO). Target volumes (high risk CTV and intermediate risk CTV) and organs at risk (OAR) were delineated according to the GEC-ESTRO recommendations. A quantitative analysis of dose-volume histograms (DVH) for the target (the minimal target dose [D100], the dose received by at least 90% of volume [D90], and the volume treated with at least the prescribed dose [V100]) was performed. ICRU reference points and the minimum dose received by the maximally irradiated 2cc volume of the OAR were calculated. The treated volume (VPD) encompassed by the prescribed dose derived from the MMO and from the IPSA method was also calculated. In addition, the conformal index (COIN) was used to compare both treatment plans.
Results*:* The first dose distribution calculation by the IPSA algorithm proposed a very heterogeneous dose distribution related to dwell time position and distribution. Some dwell time positions were activated with very high values, while other positions were inactivated. With two additional constraints, one on a maximal stopping time and the second on a 5 mm delineation around each dwell time position catheters and applying a minimal volume dose constraint to these dummy structures, heterogeneity was corrected. The constraints applied, the means D90, D100 and V100 calculated for both methods did not differ significantly. For the bladder, doses calculated at the ICRU reference point derived from the MMO differed significantly from the doses calculated by the IPSA method (means, 58.4 Gy vs 55 Gy respectively; p=0.0001). For the rectum, the doses calculated at the ICRU reference point were also significatly lower with the IPSA method (means, 63.8 Gy vs 61 Gy; p=0.004). The DVH calculated for OAR showed a statistically significant decrease of the D2cc to the rectum (mean, 58.2 Gy [IPSA] vs 59.7 Gy [MMO]; p=0.009), bladder (mean, 68.6 Gy [IPSA] vs 70.7 Gy [MMO]; p=0.016) and vagina (mean, 95.6 Gy [IPSA] vs 100.2 Gy [MMO]; p=0.012) with the IPSA method. This difference was not significant for the sigmoid. The VPD value for the IPSA method was lower in comparison with the VPD measured by the MMO (227cc vs 238cc, respectively; p=0.03). The global assessment of implantation quality measured by the COIN showed a significant difference between both methods (mean, 0.44 [IPSA] vs 0.41 [MMO]; p=0.007).
Conclusions: Inverse planning method provided fast and automatic solutions for dose distribution optimization. However, rules of equivalence between linear and puntual sources were disrupted creating large heterogeneity in dwell time positions. Two additional constraints were therefore defined to have control of dwell time values and dwell time positions activation. With these additional constraints, treatment plans generated by the IPSA method were more conformal than plans optimized manually. With this regards, as the impact of such heterogeneity on clinical results is unknown, software tools allowing automatic optimization should be used with caution.

49 oral

QC OF BT WITH LOW ENERGY PHOTON SOURCES: CURRENT PRACTICE IN BELGIUM AND THE NETHERLANDS
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Purpose/Objectif: In February 2004, a working party of the Dutch Commission on Radiation Dosimetry (NCS) started to study the clinical practice of QA aspects related to the use of low energy photon sources. The final goal is to publish a report with recommendations on QC regarding their use for permanent prostate brachytherapy (PPBT). This work should also stimulate the development of a standard in Belgium and The Netherlands and make calibration methods at each center traceable to (inter)national measurement standards.
Materials/Methods: To gain insight in the current practice of QA of seed implantations, a questionnaire was distributed to all radiotherapy centers in Belgium and The Netherlands. The questions were related to prostate implantation procedures and techniques, treatment planning and source calibration. Based on these results, it was decided to develop a test procedure for the TPS and to validate the seed calibration procedure in all institutions. A visiting team performed air kerma measurements using two commercially available measurement systems, both calibrated at the Dutch Standards Laboratory (NMi). The results were compared to the measurements performed with the local equipment (if available) and to the source strength specified on the manufacturer's certificate. A NIST traceable calibration factor for each seed model/brand was available.
Results: 19 centers in Belgium and 12 centers in The Netherlands participated to the study. Only the use of I-125 sources was reported, most often for PPBT, but also for eye and mamma treatments (1 institute). About 100 individual seeds were measured during the visits, and some strands and Mick cartridges. No significant deviation from the source certificate beyond the stated uncertainty was detected. Regarding the verification of the source strength by the institute a large variability was observed in procedures, timing and measurement equipment. The majority of the instruments are not calibrated in a traceable manner and 7 centers had no own measuring equipment. In the 4 different TPS's encountered, AAPM TG 43-like dose formalism is implemented, but some centers use obsolete data, others a non-correct implementation of the data. The results of the TPS checks and the on-site measurements will be discussed in more detail.
Conclusions: With respect to source strength verification the lack of (international) recommendations, unawareness on how to maintain sterility during measurement and difficulty to obtain a traceable calibration factor seem to be the major drawbacks for the physicists. Most users were found to apply the TG43-data supplied by the TPS manufacturer, but these data are not always up-to-date. The NCS sub-commission aims at publishing later this year a report with rec-

ommendations for QC of low-energy-photon sources, thus making a contribution to improve and harmonize the QC efforts in all hospitals in Belgium and The Netherlands.

50 oral

IMPACT OF SEED POSITION EVALUATION ON PROSTATE CT BASED POST-IMPLANT DOSIMETRY

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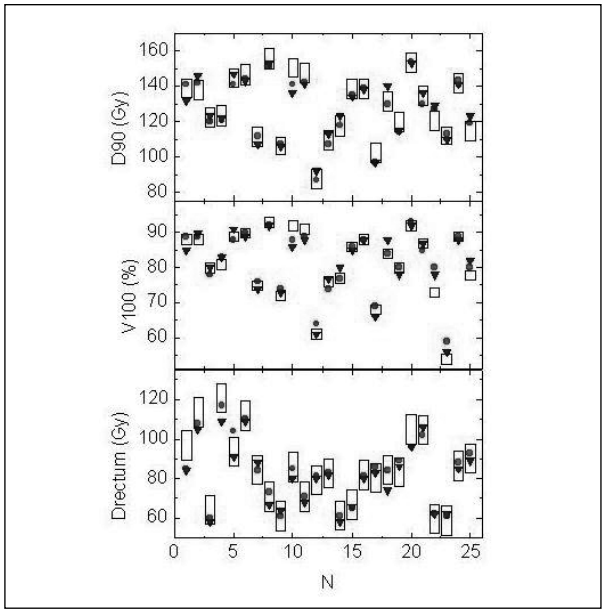
Purpose/Objectif: In this study we propose to quantify the deviation obtained in quality indices when post-implant dosimetry is made by two different approaches: by two physicists independentely and by a commercially available post-implant planning software tool which automatically localizes the implanted seeds.In 125I permanent prostate brachytherapy implants, post-implant analysis is recommended due to its importance as a tool to correlate dosimetric indices, tumor control and morbidity. The precision of seed location is a major factor. Without this information it is impossible to confirm the dose delivered to the patient or to identify any variation from the treatment plan.

Materials/Methods

We use TRUS real-time intra-operative dosimetry. Loose and strands seeds are used. The treatment planning system was Variseed 7.1. A CT was performed four weeks after the implant for post-implant dosimetric analysis.The 25 patients were randomly chosen from all patients treated since June 2004, and three post-implant CT based-dosimetries were made: two done by physicists (at the same institution with similar experience) and another one using an automatic seed finder tool (ASFT) within the TPS, being the reproducibility studied by doing 25 simulations for the same patient.Seed detection by the physicists was done prior to prostate and rectum delineation by the radiologist. Post-implant dosimetries were compared using DVHs.The Bland and Altman statistical method was used to analyse the repeatability of a single measurement method and to compare measurements by two observers.

Results : Table 1 summarises the results when ASFT was used, and those obtained with two operators dosimetries.Analysing the reproducibility, V100 has very close values and the limits of agreement are very small, D90 and D10rectum shows an higher deviation and a 95% confidence interval very high.The observed differences for two operators dosimetries for V100 are somehow big, but not significant. Instead for D90 are significant with very wide limits of agreement. For D10rectum very open values were found.These results show that V100 has a slight dependence but not significant, D90 and D10rectum show an higher dependence, being more significant for D90.Figure 1 illustrates the results obtained for the two approaches in terms of V100, D90 and Drectum. The dots and triangles refering to operators 1 and 2, and the rectangles are the confidence interval for quality indices obtained with ASFT.

Conclusions*:* When seeds location is done repeatedly by ASFT, the observed differences of V100 were not significant, but for D90 and D10rectum the differences are significant. We recommend that at least five repetitions should be made and median values should be taken to converge to those values.The differences observed change significantly when seeds arrangement is performed by two physicists. When we compare both methods, the results clearly show an operator dependence.The major uncertainty with this application is the correct determination of prostate volume and its variation within CT, US and MR images, but this variability is beyond the scope of the present study.



	TPS analysis					Two Physicists dosimetries			
	Max. var.	Median	Mean difference (SD)	Limits of agreement	Limits of agreement (95%)	Max. Var.	Mean dif. (SD)	Limits of agreement	Limits of agreement (95%)
V100	3.1 %	97.1	0.1 (0.7)	-1.3 1.5	± 0.1 ± 0.1	3.9 %	0.4 (2.1)	-3.9 4.7	± 0.5 ± 0.6
D90	10.9 Gy	133.1	1.1 (2.7)	-4.4 6.5	± 0.4 ± 0.4	9.5 Gy	1.0 (4.2)	-9.5 7.5	± 1.3 ± 1.0
D_{max}	13.9 Gy	112.1	-0.3 (3.9)	-8.2 7.5	± 0.5 ± 0.5	12.6 Gy	2.3 (3.9)	-5.6 10.1	± 0.8 ± 1.4

51 oral

INTRA-OPERATIVE OPTIMISATION OF I-125 PROSTATE IMPLANTS WITH C-ARM CONE-BEAM CT BASED DOSIMETRY

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Purpose/Objectif*:* To assess the feasibility of a routine for performing C-Arm Cone-Beam CT (CA-CBCT)-based post-planning and subsequent correction of critical underdosed areas during transrectal ultrasound (TRUS) guided implant procedures.

Materials/Methods*:* The initial study of the method involved 20 patients with cancer of the prostate. After realising the I-125 implant, three gold markers are implanted at anatomically relevant positions using TRUS guidance. The contours of the prostate, urethra and rectal wall are delineated on a post-implant TRUS-study with 2.5 mm thick slices. A 3D C-arm fluoroscopic unit with isocentric design is used to generate CA-CBCT images without the probe in the rectum and with the legs lowered. With the implanted gold markers as a reference, post-implant TRUS and CA-CBCT are co-registered. Following registration the implant is examined for dose-deficiencies. Should the radiation-oncologist consider an underdosage to exist at a clinically relevant area, a correction-plan is made in which seeds are added to optimise the dosimetry. The implant procedure is completed by adding the extra sources using TRUS guidance. A second CA-CBCT is performed and registered with the post-implant TRUS-study to document the final day-0 dosimetry.

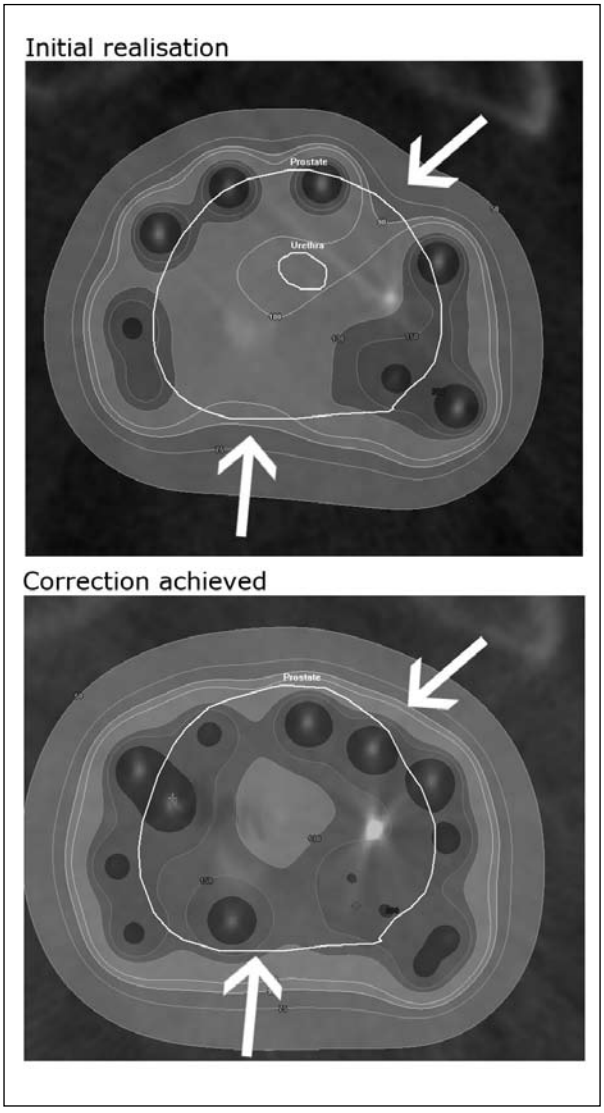
Results: The results obtained with 20 patients to be treated by this method have been analysed to afford assessment of the new procedure. In nine of the 20 patients studied there was evidence of underdosage in critical areas. On average, 4 (2 – 8) additional seeds were implanted resulting in an average increase in D90 of 11 % (2 – 28 %) (see example in figure). A mean increase in V100 of 9 % (1 – 22 %) was observed. The additional time required to carry out CA-CBCT based day-0 dosimetry in the operation theatre and perform the re-

implant procedure was 25 minutes per patient.

Conclusions

In a number of implants, we improved considerably the dosimetry of critical underdosed areas by adding extra seeds intra-operatively. Most of the implants studied did provide adequate dose-coverage, thus rendering intra-operative correction unnecessary.

CA-CBCT-based intra-operative dosimetry during ultrasound guided brachytherapy for prostate cancer is both feasible and time-efficient.



52 oral

PHANTOM INVESTIGATIONS OF SEED IMPLANTS: SYSTEMATIC CT STUDIES

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Purpose/Objectif: One objective of Braphyqs (the physics task group in GEC-ESTRO) is to develop and investigate phantoms for QA of seed implants. The study describes a systematic investigation of the influence of different CT parameters on seed reconstruction in the post-planning procedure using a solid phantom.

Materials/Methods: A Perspex phantom (Kiel-Phantom) was equipped with different test patterns of dummy seeds. CT scans were carried out using a Philips Picker PQ2000 scanner. A commercial treatment planning system (VariSeed 7.1) was applied to detect the seeds in the CT slice set and to reconstruct their positions. For this study, the automatic seed finding option of the software was used without manual interaction. To investigate the quality of seed reconstruction CT measurements with varying parameters and nine different seed models were carried out. In particular the influences of the surrounding medium, the seed model, field of view, tube current, scan type (axial or spiral), slice thickness, and index were analysed. The reconstructed seed positions were compared with the well-known seed coordinates in the phantom. The number of correctly identified seeds and the mean deviation between the reconstructed and the real positions was computed for the longitudinal and transversal direction.

Results*:* In this study it was observed that the peak CT value can differ for diverse seed types in various media that surrounds the seeds (Perspex, water, patient). The reconstruction quality is dependent on the seed model. Standard deviations between 0.2 and 0.6 mm were found for the differences between reconstructed and real positions. Mismatching of one or more seeds could be observed for three seed types. CT scanning parameters for this test were identical. Influences of field of view or tube current on reconstruction quality could not be detected. It was found that when the slice thickness or the table index (respectively an appropriate pitch for helical scans) reaches 4 or 5 mm the accuracy of the CT seed reconstruction decreases in longitudinal direction. Problems with mismatched seeds can occur if two or more seeds are positioned at a close distance.

Conclusions: The impact of slice thickness, index and seed model on seed reconstruction accuracy was determined. Smaller spacing and slice thickness reduces displacements in z direction. Investigations like this may help to optimize seed post-planning techniques and furthermore to improve automatically seed finding algorithms and visualization of seed models.

53 oral

EFFECT OF CATHETER ORIENTATION ON RECONSTRUCTION ACCURACY AND DOSIMETRY IN CT-BASED BREAST BRACHYTHERAPY

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Purpose/Objectif*:* To investigate the effect of catheter orientation related to CT scanning plane on catheter reconstruction and dosimetry in interstitial high-dose-rate breast brachytherapy.
Materials/Methods: A: Five catheters arranged in triangular configuration were CT scanned with 3 mm slice thickness in different positions related to the plane of CT scanning. The catheters perpendicular to CT slices was selected as reference position. Catheters were reconstructed and different dose plans with no optimization (Paris dosimetry system, PDS), geometrical (GO) and dose point optimization (DPO) were created. Treatment time (ttreat) and volume irradiated by the reference dose (Vref) were calculated and compared. B: After that, ten catheters implanted in a special phantom simulating a target volume were used. The phantom setup was rotated in different angles on the CT couch. First, the catheters were parallel to CT scanning plane, and then they were angled in 2, 10, 30, 60 and 90 degrees. 3 and 5 mm CT slice thickness were used. The catheters were reconstructed and the target volume was outlined in each slice. Using three optimization methods (PDS, GO, DPO) treatment plans were created, dose-volume parameters (Vref, V1.5xref, V1.5xMCD, VPTV, V100, V150, D90 and Dmin) and doses in marker points (D1, D2, D3) were calculated and compared.
Results*:* A: The largest deviation in ttreat and Vref were observed when the catheters were rotated by only 1-2 degrees from the parallel position. For ttreat 2.9%, 2.5% and 1.3% and for Vref 4.3%, 3% and 2.3% was found at PDS, GO and DPO method, respectively. At all other orientations the deviation was less than 2% for ttreat and 3% for Vref. B: The values of VPTV were in agreement within 1% for all cases, but mean volume at 5 mm slice thickness was 5% less. At 3 mm slice thickness the maximum deviations related to the perpendicular orientation were 12%, 4%, 6% (Vref), 4%, 5%, 9% (V100), 3%, 2%, 9% (D90), 13%, 15%, 16% (Dmin) for PDS, GO and DPO methods, and at 5 mm they were 7%, 5%, 6% (Vref), 3%, 2%, 9% (V100), 3%, 3%, 11% (D90), 5%, 7%, 35% (Dmin).
Conclusions: The best orientation would be the perpendicular or parallel catheter positions, which is rarely realised in clinical practice. More accurate catheter reconstruction can be achieved with larger angle between the catheters and CT scanning plane and with smaller slice thickness (‹=3mm). The method of dose optimization has also effect on accuracy of dosimetry.

54 speaker

DOSIMETRY OF SEALED BETA SOURCES USED IN BRACHYTHERAPY WITH REFERENCE TO ICRU REPORT 72

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In several benign and malignant diseases, the clinical target volume has a thickness of only a few millimeters and can be reached with an applicator with a sealed radioactive source. In these cases, a beta emitter has important advantages, like a very steep dose gradient, a high dose rate, and ease of shielding. Applicators with Sr-90/Y-90, P-32, Ru-106/Rh-106 are in clinical use, treating diseases like pterygium and eye malignancies with planar or concave sources, and vascular restenosis with line sources.
Thanks to the large interest in beta source application for treatment of coronary (re)stenosis between 1995-2006, many organisations recognized the importance of guidelines for dosimetry and quality assurance. The Dutch Committee on Radiation Dosimetry (NCS, report nr 14, 2004) made an inventory of current practices in 2001 in the Netherlands and Belgium. Among the 23 institutions using sealed beta sources, they found a large variation in equipment, tolerance levels, frequencies, etc. varying from exclusively relying on vendor supplied data up to extensive and frequent in-hospital checks. Minimal and optional requirements were given for equipment, tolerances, procedures and frequencies.
Also AAPM (TG-60, 1999), DGMP (report nr 16, 2001), IAEA (TECDOC 1274, 2002) published guidelines and recommendations on this subject.
Finally, the ICRU (report 72, 2004) published detailed recommendations on specification and measurement of source strength (to be specified as reference absorbed dose rate), and dose distribution. Because of the experimental difficulties the importance of calculations for dose distribution determination is underlined by the ICRU and extensive data for this are given.
From the ICRU and other reports some general practical conclusions can be drawn: Although the same measuring techniques as for photon sources can be used (ionisation, scintillation, film), the typical properties of beta rays require some special equipment and procedures: the steep dose gradient ask for small detector dimensions, typically < 1 mm for the same reason, the positioning accuracy of source and detector should be typically better than 0.1 mm because of the dominant influence of scatter, the measurements are very sensitive for inhomogeneities (metal, airgaps) in phantoms, source holder, detector holders, etc.
For these reasons, source strength and source uniformity determination for beta sources can't be as accurate as for photon sources. Roughly, uncertainties smaller than 10% both in source strength and in source homogeneity are achievable with readily available equipment. This can be considered adequate because the clinical application itself often generates much larger uncertainties (motion, positioning, inhomogeneities) and because of the wide therapeutic windows of the current applications.

Teaching Lecture

55 speaker

IMAGE-GUIDED INTRAPELVIC RT: HIGH-TECH EXTERNAL BEAM VS HIGH-TECH BT

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Various technological developments have been evaluated in a clinical setting in order to improve external beam therapy (EBT) and brachytherapy (BT) during the past years. The most important are imaging tools, immobilization and tracking devices, treatment plan optimization, and the use of new beam qualities. Stimulated by their new technological possibilities, EBT has tried to challenge BT and vice versa. Within this context several studies have been published, mostly treatment planning studies, but also small series clinical studies. The conclusions drawn were rather biased because advanced EBT was predominantly compared with conventional BT. In addition, important concepts such as whether a margin is needed in EBT to account for set-up (SM) and internal motion (IM) were not discussed in depth. Image guided and highly individualized BT has been developed and successfully implemented in clinics and cannot be neglected in such a comparison of (rival) treatment techniques. The aim of this study was to discuss and investigate a comparison of high-tech EBT vs. high-tech BT for cervix cancer patients.
When performing such a comparative treatment planning study a number of items need to be addressed and overcome. E.g. which PTV-CTV margin is appropriate for EBT based on latest technology? When considering recommendations to separate the margin in two components should they be combined geometrically or arithmetically? What kind of DVH parameters are important for EBT? As doses to larger amounts of the bladder (wall) or rectum (wall) are much smaller in BT only high dose values are considered there. More specifically, clinical practice in image guided BT is based on D0.1cc and D2cc which is representative for high dose regions in an organ or organ wall. Although correlations with clinical outcome are available for these DVH parameters, they cannot be simply transferred to EBT because of the very different overall dose gradient of the respective treatment techniques and resulting dose distribution in an organ at risk (OAR). It might therefore not be sufficient to compare D2cc or ICRU point doses but also doses to larger volumes, e.g. D30, D50, or D10cc. In general, when analyzing these larger volume dose parameters the organ walls have to contoured, as the outer contour alone is not sufficient which has been already outlined in GEC ESTRO recommendations I and II. Independent of contouring specific organs the total amount of irradiated volume has to be considered in addition as it has been demonstrated to correlate with morbidity.
Another class of open questions is related to target doses. What dose is needed to control the GTV? If using intracavitary brachytherapy, the dose to the GTV is automatically high due to the vicinity of the sources. D90 values of much more than 100 Gy (EQD2) are observed. Such a high dose to the tumor is considered as one of the major reasons for the success of cervix brachytherapy. However, at the moment it remains unclear how high this dose has to be and if there is a certain dose limit which might be sufficient for EBT. Inverse planning algorithms for advanced EBT are designed to fulfill common ICRU standards for EBT, i.e. a homogeneous target dose. The finding that an inhomogenous dose prescription is more difficult to tackle with inverse planning is in agreement with previous studies in stereotactic body radiotherapy.
From regular cervix patients undergoing combined EBT and BT at the Department of Radiotherapy, three different groups were defined and from each group 2-3 patients were selected. Group a) consisted of FIGO stage IIB patients treated with intracavitary applicators only while group b) consisted of stage IIB patients treated with a combined intracavitary/interstitial approach. Group c) was defined as stage IIIB with complex interstitial implantations. For image guided BT the following target and organs at risk structures were used for individual treatment plan optimization: GTV, HR-CTV, IR-CTV, bladder, rectum and sigmoid. BT treatment planning was performed on a Plato system (Nucletron). For each patient MR image datasets and contours of one single brachytherapy fraction were transferred to the treatment planning system for EBT (XiO, CMS). If needed, additional contours were drawn or defined through Boolean algebra on the XiO system. The underlying EBT technique was based on seven to eleven intensity modulated fields. For EBT the same fractionation scheme as for BT was assumed but the BT CTV were expanded (3mm and 5mm) in order to account for set-up uncertainties and internal motion. As a starting point for inversely planned EBT, available DVH information in absolute volumes, i.e. cm^3, was utilized for OAR. Keeping maximum doses for D2cc at a tolerable level, IMRT was challenged to deliver the highest possible target dose.

Brachytherapy for Re-Irradiation

56 speaker

SALVAGE BRACHYTHERAPY AFTER EXTERNAL BEAM THERAPY FAILURE FOR LOCALIZED PROSTATE CANCER

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Therapeutic options available for recurrent prostate cancer previously treated by external beam radiation are limited. Hormonal therapy, with different modalities and timings is generally admitted as the reference treatment as well as simple observation. The salvage prostatectomy series are reported to have potential significant morbidities.
To focus on patients, having a rising PSA linked to a presumed isolated local recurrence biopsy proven leads to specific conclusions. In such cases, when optimally identified, systemic hormonal treatments can appear to be illogical, regarding a local disease occurring in previously irradiated volumes, the constant occurrence of hormonal therapy resistance, just as significant late effects induced with a continuous treatment regimen.
Recently, salvage re-irradiation therapeutic modalities have been reported in retrospective studies. Ultrasound guided permanent brachytherapy with iodine-125 or palladium-103 appears to be a good approach. The analysis of the different studies underline the importance of patients selection criteria. The results of the main series will be exposed in terms of biological disease free survival and complications rate. The incidence of major complications after salvage brachytherapy appears to be lower than other salvage procedures such as prostatectomy or cryoablation. Due to the short time of follow up, salvage brachytherapy requires further investigations.

57 speaker

BRACHYTHERAPY FOR RE-IRRADIATION IN HEAD AND NECK MALIGNANCIES

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Brachytherapy can be used for re-irradiation in Head and Neck malignancies (H&N Ca) either alone or combined with surgery, external beam radiotherapy, chemotherapy, or hyperthermia. The indications are: 1. Salvage of recurrence, either locally or in the neck, 2. Salvage for secondary new H&N Ca in previously irradiated patients, 3. Salvage therapy for persistent disease shortly after a radical course of radiotherapy with or without chemotherapy. Patient selection in salvage strategy for H&N Ca is highly individualized and preferably the result of a multi-disciplinary consultation with a multidisciplinary

team. The sites, prior treatments, extent of disease, and the patient's conditions influence the decision in order to select the more appropriate risk-benefit strategy, including short and long-term morbidity in the risk-benefit analysis. The literature is difficult to interpret due to the usual culprits (retrospective series, short follow-up, variable modalities, inconsistent morbidity reporting, inconsistent selection of patients, etc.) and, to add to the confusion, better results from most salvage series are more likely related to selection of patients rather than better care. The literature will be presented and the techniques, results, and limitations of brachytherapy either alone or combined will be summarized.
As a general rule, brachytherapy alone is preferable over brachytherapy as a boost with external beam radiotherapy. Peri-operative brachytherapy associated with neck dissection can be quite rewarding, especially in order to avoid carotid resection. In the latter indication, flap resurfacing is required to avoid carotid exposure. Isolated neck and isolated primaries have a much higher chance of salvage than either one in isolation. The results between neck sites and primary sites for salvage are the same. Brachytherapy for secondary new H&N Ca yields better results than from H&N Ca recurrences. The expected results from salvage brachytherapy are 50%-70% complete response, treatment related mortality of 5%-10%, significant long-term morbidity (radionecrosis, dysphagia) in 10%-20% of survivors, death form isolated metastases in 30%- 50% of salvaged neck recurrences, and a salvage rate of 30%-50%.
Conclusion. Highly conformal dose delivery, short overall treatment time, dose for dose radiobiological advantages of low dose rate or pulse dose rate for re-irradiated tissues, acceptable morbidity, and the "last chance factor" for salvage, all contribute to make brachytherapy an essential player in any salvage strategy for H&N Ca.

58 speaker

BRACHYTHERAPY FOR REIRRADIATION IN GYNAECOLOGICAL CANCERS.

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Local recurrences in gynaecological cancer represent a challenging issue as the majority of the patients have already received a high dose of irradiation, usually including both external irradiation and brachytherapy, nowadays combined with concomitant chemotherapy. The risk of complications has to be balanced with the potential for cure-rate. The majority of the patients with recurrences limited to the pelvis therefore receive salvage surgery generally consisting of ultraradical operation frequently sacrificing the bladder and/or the rectum. Brachytherapy however may be considered as an option to treat these patients and avoid mutilating consequences.
Indications for salvaged brachytherapy.
Indications for brachytherapy have never been clearly stated in this situation. The majority of the reported series deal with isolated vaginal recurrences in previously unirradiated areas, in patients with endometrial cancer. Lateral pelvic recurrences have also been reported using interstitial brachytherapy as a salvaged therapeutic approach in either cervical cancer or endometrial cancer.
Patients with extrapelvic disease assessed with clinical and radiological exam represent contra-indications to brachytherapy, unless a palliative approach is considered, for instance to treat continuous bleeding.
Vaginal recurrences require careful tumour extension evaluation. It is generally stated that patients with a maximum tumour diameter of 4 cm should be treated with brachytherapy alone. This size limitation can be reconsidered in some specific sites, such as suburethral metastases where no major organ at risk, except the urethra, limits the dose. The situation is different when the recurrence is located at the vaginal vault with the digestive structures close to the tumour. The tumoral thickness is also very important to assess as it will have an impact on the brachytherapy technique.
Pelvic recurrences are more rarely treated with salvaged brachytherapy. Nor the tumoral volume or the maximal dimensions have been clearly reported to precise brachytherapy indications. Tumours reaching the pelvic wall represent classical contra-indications to brachytherapy.
Brachytherapy techniques and doses.
Low dose-rate, pulsed dose-rate, high dose-rate or permanent implants represent the different treatment modalities, with radiobiological concepts being more in favour of pulsed or low dose-rates in previously irradiated areas.
Superficial vaginal tumours of ‹ 5 mm infiltration can be treated with intracavitary brachytherapy with vaginal cylinders or vaginal moulds.
More infiltrative tumours are approached with interstitial brachytherapy. Different techniques are available, from plastic tube or needle freehand application to various transperineal templates. Guidance methods include fluoroscopy, CT-scan, MRI, or transrectal ultrasound. More recently, laparoscopic guidance has been reported.
A total dose of at least 60-65 Gy is prescribed, generally using the Paris system when interstitial brachytherapy is applied. When intracavitary brachytherapy is performed, the 60-65 Gy dose is usually prescribed at 5mm depth from the surface applicator.
Results/complications.
A local control as high as 80-100% has been reported when patients have been properly selected for brachytherapy. Prognostic factors for local control include time to relapse, tumour volume and total dose. Severe complications range from 2% to 20%. More recent series report a low severe complication-rate, with a better tumour assessment, with the use of modern imaging modalities.

Physics: Advances in Brachytherapy Treatment Planning

59 speaker

AUTOMATIC CATHETER RECONSTRUCTION IN IMAGING BASED BRACHYTHERAPY

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Introduction: Modern brachytherapy (interventional radiation oncology) is imaging based for (a) localisation (CTV, GTV and OARs), (b) guidance of needles/applicators during implantation and (c) treatment planning. Beside the widely established CT imaging there is a continuous increase in using MR imaging especially for gynaecological tumours where for prostate cancer 2D and 3D Ultrasound (US) can be considered as the standard imaging modality. Clinicians require often the implementation of multimodality imaging (MR and US or CT and MR, etc) for combining the advantages of the individual modalities. The catheter reconstruction process, that is the precondition of being able to realise a treatment plan becomes thus a more complex process.
Material and Methods: Focusing on the cases of multi-catheter implants (plastic or metallic catheters) and different imaging modalities, the basic methodologies for automatic catheter reconstruction are summarized. The presentation will focus on CT and 2D and 3D US imaging which represent the majority of applications. The accuracy limitations and the performance of advance methods will be demonstrated. The role of imaging techniques on the accuracy of reconstruction methods will be demonstrated and discusses. 3D US techniques commonly used for HDR and LDR prostate implants will be especially analysed with regard to catheter reconstruction.

60 speaker

ADVANCES IN OPTIMIZATION STRATEGIES

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Due to the rapid adoption of 3D image-based planning, the volumetric information provided to the team performing the dose planning has dramatically changed, both in nature and in quality. This has lead to the development of anatomy-based inverse planning optimization tools such as IPSA. The inverse planning approach can be defined as a method of radiation treatment planning where one starts with the desired dose distribution, or clinical objectives, and then determines the treatment parameters that will achieve it. This is opposed to the conventional forward planning approach where the treatment parameters (MLC shapes and beam weights in external beam, or source loading pattern in brachytherapy) are first chosen and then the resulting dose distribution is calculated, evaluated and iteratively modified. The control of the dose distribution with inverse planning requires the explicit description of the clinical objectives before the optimization is performed. But if the inverse planning approach is different, the required dose distributions established over the years have not changed; e.g. for prostate, dose coverage, conformity and urethra protection are key; for interstitial breast, dose homogeneity and hot spot avoidance are paramount; for a vaginal cylinder, only the surface dose matters, not the dose in the cylinder, etc. Through those clinical examples and others, we will demonstrate how dose constraints parameters are used with IPSA to impact on the dose distributions. Beyond the better control to shape the dose distribution and the significant time saving, we will also illustrate how IPSA can be used to exploit the avalanche of new information from emerging molecular or functional imaging.

Gynaecology/Prostate Clinical

61 oral

VULVAL AND VAGINAL RHABDOMYOSARCOMA IN CHILDREN : AN UP DATE AND A REAPPRAISAL INSTITUT GUSTAVE ROUSSY BRACHYTHERAPY EXPERIENCE WITH A PARTICULAR ATTENTION ON LONG TERM OUTCOME

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Purpose/Objectif*:* The aim of the present study is to report the Institut Gustave Roussy brachytherapy experience in the management of vulval and vaginal rhabdomyosarcoma (RMS) with a special focus on long term outcome.
Materials/Methods: From 1971 to 2005, data from 39 patients treated with brachytherapy as a part of treatment are retrospectively analysed. Among them, 20 patients treated before 1990, where the initial tumoral extension is included in the brachytherapy (BT) volume. Acute and late side effects are classified using the Common Terminology Criteria for Adverse Events v3.0 (CTCAE).
Results*:* Eighty five % of patients recruitment was out of the hospital environment. The median follow up was 8.4 years ranging from 10 months to 30 years. The median age was 16.3 months at diagnosis. Twenty six patients and 6 others presented a strictly located vaginal and vulva RMS, respectively. Botryoid histological form was present in more than ¾ of cases. A multidisciplinary approach including surgery, chemotherapy and BT was discussed in all cases. The 5-year overall survival rate was 91%. Six of the 39 patients presented local or metastasis relapse. Acute side effects were well manageable and 6 patients presented grade 1-2 renal/genitourinary function symptoms. Among the 20 patients treated before the 90's, 75 % presented sequelae in terms of vaginal or urethral sclerosis and stenosis. Four patients had also a follow up treatment for psychological disturbance. After 1990, 2 of 19 remaining patients presented acute side effects with maximal grade 1-2 renal/genitourinary function symptoms and 20 % had vaginal or urethral sclerosis and stenosis. Two cases of psychological disturbance were also reported.
Conclusions: Improvement in terms of volume reduction coverage by BT, better indications of surgery and more efficacious drugs, all combined by a multidisciplinary approach trends to ameliorate results on survival as well as long term sequelae.

62 oral

FDG PET IN PLANNING OF BRACHYTHERAPY AND EXTERNAL BEAM THERAPY IN GYNAECOLOGICAL TUMOURS: MEANINGFUL OR MEANINGLESS?

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Purpose/Objectif*:* To evaluate the value of FDG PET in planning of brachytherapy and external beam therapy by patients with gynaecological tumours without surgery.
Materials/Methods: From 11/2005–1/2007 12 patients (9 with cervical cancer, 2 with carcinoma of the vagina and 1 with vulvar cancer) were examined with FDG PET before external beam therapy and before brachytherapy. At the same time patients underwent a clinical examination and a MRI of the pelvis.
Results: All 12 female patients received the FDG PET before external beam therapy started. In all cases FDG PET showed the primary tumour region as active glucose-storing tumour region. The clinical examination and the MRI presented a tumour with volume in median of 69.3 cm^3 and 49.0 cm^3, respectively. In two cases the treatment plan for external beam therapy was changed because of new FDG PET findings. FDG PET was repeated in 11 patients before brachytherapy, in median after 50,7 Gy (ranging 45.8 Gy–53.9 Gy). 9 of the 11 patients showed none or only a non-specific signal at the primary tumour region in the FDG PET. In two cases the FDG PET could identify tumour tissue but by a very discrete remainder signal, only. However in contrast to it, as well in clinical examination as in MRI significant tumour bulk was clear present in all 11 patients.
Conclusions: FDG PET investigation is suitable for the evaluation of the local and systemic tumour expansion in gynaecological tumours before therapy. For the better target definition in brachytherapy planning FDG PET after external beam therapy isn't applicable, because it shows no signal or only a very discrete signal despite tumour bulk is present.

63 oral

PREDICTIVE VALUE OF FDG-PET UPTAKE FOR LOCAL CONTROL IN PET ASSISTED BRACHYTHERAPY OF CERVICAL CANCER

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Purpose/Objectif*:* To evaluate FDG uptake and response in primary cervical tumors during FDG-PET guided brachytherapy.
Materials/Methods: Thirty-eight patients with cervical cancer participated in this prospective study. The clinical stage of the tumor was Ib1 in 5, Ib2 in 5, IIa in 1, IIb in 16, and IIIb in 11. The mean patient age at diagnosis was 49 years. Patients underwent diagnostic FDG-PET before treatment. FDG-PET metabolic tumor volume at diagnosis ranged from 7 to 536 cc (mean, 111 cc). Patients were treated with concurrent chemoradiation. Chemotherapy was with weekly

Cisplatin given for 6 weeks at 40 mg/m2. External radiation was 20 Gy to the cervix and 50 Gy to the pelvic lymph nodes. Six patients were treated with two fractions of LDR brachytherapy (65 Gy to point A) and 32 underwent 6 weekly fractions of HDR brachytherapy (39 Gy to point A). Patients underwent either FDG-PET or FDG-PET/CT imaging with their tandem and ovoid applicators in place.
Results: The mean follow-up for surviving patients was 39 months. The 5-year overall and progression-free survivals were 75 and 63%, respectively. At the time of last follow-up, 24 patients were alive and free of disease, 4 were alive with disease present, 2 died of intercurrent disease, and 8 were dead due to cervical cancer. Metabolic tumor volumes determined from the FDG-PET brachytherapy at the ends of weeks 1, 3, 5, and three months after therapy completion demonstrated that the mean metabolic tumor volume decreased to 58, 32, 24, and 5% of the pre-treatment metabolic tumor volume. FDG-PET brachytherapy, targeting the metabolically active FDG-avid tumor demonstrated a complete metabolic response in the cervix in 34/38 (89%). Three of the four patients with an incomplete metabolic response subsequently recurred in the cervix. Cox Proportional Hazards Modeling was performed and demonstrated that the only significant prognostic factor for pelvic recurrence was an incomplete FDG metabolic response in the cervix tumor at the completion of therapy ($p = 0.0069$). Metabolic tumor volume at diagnosis and radiation dose were not significantly correlated to primary cervical tumor control ($p = 0.77$ and $p = 0.27$).
Conclusions*:* FDG-PET brachytherapy is a feasible method to evaluate tumor response during therapy. An incomplete FDG metabolic response predicts for pelvic failure, independent of tumor dose and tumor volume.

64 oral

OPTIMIZED PROSTATE BRACHYTHERAPY AMELIORATES THE POOR PROGNOSTIC IMPACT OF A HIGH PERCENTAGE OF BIOPSY CORES INVOLVED WITH ADENOCARCINOMA

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Purpose/Objectif: A higher percentage of positive cores (PPC), obtained at the time of pre-treatment transrectal biopsy, predicts a poor biochemical failure free survival (bFFS) in patients with adenocarcinoma of the prostate (CaP). The likelihood of extra-capsular extension increases with higher PPC. The highest dose covering at least ninety percent of the prostate (D90) is a standard method of measuring implant quality, and is correlated with enhanced coverage of the extra-prostatic space. We tested the hypothesis that PPC loses its adverse prognostic impact in patients who receive implants with D90 Values › 100% of the prescription dose.
Materials/Methods*:* PPC was determined from original pathology reports of 566 patients with clinical stage T1c-T2a, Gleason grade 7-10 and/or PSA 10-20 CaP. These patients had previously been treated on a prospective study that randomized them between 44 or 20 Gy of supplemental beam radiation therapy followed by Pd-103 brachytherapy to respective doses of 90 and 115 Gy. The D90 was determined as a part of the prospective study using a post-implant CT scan obtained on the day of the implant. bFFS was defined as having a serum PSA ‹0.5 ng/ml at last follow-up.
Results: D90 and PPC were quantifiable in 303 patients. With a median follow-up time of 49 months, 5 Year biochemical Failure Free Survival (5-bFFS) was 87% for the entire group and 92% vs. 81% (log rank $p = 0.009$) for those with ‹50% vs. › 50% PPC respectively. On univariate Cox regression analysis, Gleason Score, Absolute PSA, PPC and D90 were statistically significant predictors of time to biochemical failure. On multivariate analysis, only PSA, PPC and D90 maintained significance.
Mean D90 was 114.4% with a standard deviation 21.9%. Amongst patients with › 50% PPC (155), failing patients had a statistically lower D90 than non-failing patients (Student's T Test $p = 0.03$). When the analysis was restricted to the 237 patients who received high quality implants (D90 › 100%), PPC lost its predictive value, but PSA and Gleason score remained independent prognostic factors for time to biochemical failure using a multivariate regression model.
Conclusions: PPC › 50% is an independent predictor for poor biochemical Failure Free Survival in patients treated with brachytherapy. High quality prostate brachytherapy, defined by D90 › 100%, negates the adverse effect of PPC › 50%.

65 oral

ERECTILE FUNCTION AFTER EXCLUSIVE 125I BRACHYTHERAPY FOR PROSTATE CANCER

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Purpose/Objectif: Radiation treatment can affect potency, which is generally considered to be 'the capacity to penetrate the partner'. This criterion alone is however not sufficient to report sexual dissatisfaction linked to erectile disease. We wanted to evaluate a simple scoring system to report progressive erectile troubles specifically linked to radiation treatments.
Materials/Methods*:* 174 patients aged 67.3 ± 7.7 years were consecutively treated with exclusive 125I brachytherapy from 05/99 to 12/2004. 132 of them did not present any pejorative initial prognostic factor (PSA ›10ng/ml, Gleason Score ›6, T›2a). 38 were diagnosed with only one pejorative factor and 4 patients with two of them. Erectile function was scored as follows: ability for intercourse with penetration for at least 15 minutes (5), while requiring phosphodiesterase inhibitors (PDI) (4), ability for at least 5 but less than 15 minutes without or with PDI (3 and 2 respectively), erection not firm enough to penetrate or very short penetration (1).
Results: With a follow up of 46.9 ± 21.7 months, 17 recurrences occurred (9.8%) as well as 3 severe grade 3 but reversible late side effects (1.7%).
60 patients were impotent (score 1) at diagnosis. Out of the 84 patients reporting initial score 5, 45 maintained the initial score while 20 requiring PDI shifted to score 4. 3 of 9 patients with initial score 4 shifted to score 1 while erectile function was maintained for the others. 13 patients reported a borderline initial function (score 2-3), 3 of whom shifted to score 1.
Among the 34 patients aged ≤60 years, 30 were fully potent. 19/30 remained fully potent while 6 were downscored to 4 and 5 of them to score 2.
Conclusions: 77 % and 83 % respectively of all the initially fully potent patients, or those only aged 60 years or less, maintained their erectile function, even though 24 % and 20 % of them required PDI medication. Younger age (≤60 years) favoured erectile function preservation ($p‹0.0001$). These results compare favourably with the impotency rates induced by radical prostatectomy.

66 oral

INTERMEDIATE RISK PROSTATE CANCER PATIENT (IRPC) OUTCOME APPEARS EQUIVALENT WHETHER TREATED BY I-125 BRACHYTHERAPY (BT) OR DOSE ESCALATED EXTERNAL BEAM RADIOTHERAPY (EBRT)

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Purpose/Objectif: To report Intermediate risk prostate cancer patients outcome treated in the same institution .
Materials/Methods*:* Between 1996 and 2003, 318 patients with IRPC (according to D'amico classification) were treated at Institut PAOLI CALMETTES; 162 received transperineal I-125 brachytherapy and 156 conformal EBRT. Patients characteristics were: Median age 68 years (65 for BT and 70 for EBRT), median PSA at diagnosis 11 ng/ml (10.8 for BT and 12 for EBRT). T stage was defined according to biopsy (for298 patients) and TURP (for 20 EBRT patients) results: T1b: 20 pts, T2a: 151 pts, T2b: 147 pts. Gleason score was ‹6 in 90pts, 6 in 133 pts and 7 in 95 pts. One hundred and sixty five pts received androgen deprivation for a median duration of 3 months (1-11 months). EBRT was delivered with high energy photons using a conformal technique to the prostate and pelvic nodes; median dose to the prostate was 78 Gy and to the nodes 46 Gy to ICRU point. BT used stranded iodine-125 seeds (Rapid Strand, Oncura) using a preplanning technique and prescribed dose was 145 Gy. Relapse was defined according to the ASTRO nadir+2 definition.
Results: Median follow-up was 62 months ranging from 24 to 125 months. 8 pts were lost to follow-up. EBRT pts had significantly more Gleason 7 tumors (71 vs 24 pts) received significantly more often neoadjuvant androgen deprivation (99 vs 68 pts) and had shorter follow-up (54 vs 66 months). Sixty one pts experimented relapse (32 in BT treated pts and 29 EBRT treated pts). Median time to relapse was 27 months. Fifty five patients died of these 9 died from prostate cancer metastases and all others from intercurrent disease. Five year relapse free survival was 75% identical in both treatment group. In brachytherapy treated patients PSA nadir was significantly lower 0.2 ng/ml vs 0.5 ng/ml in EBRT pts. Multivariate analysis results will be presented.
Conclusions: In this retrospective study, intermediate risk group patients treated with iodine-125 brachytherapy showed equivalent relapse free survival to those treated during the same period in the same institution with dose escalated conformal EBRT.

PHYSICS : Invited Lecture

67 speaker

DOSE CALCULATIONS AND MONTE CARLO BEYOND THE TG43 FORMALISM

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Current developments in brachytherapy include introduction of 3D imaging, anatomy-based dwell-time optimization and use of low energy sources, e.g. 169Yb and electronic x-ray sources. The dose calculation methods used in treatment planning today are based on superposition of dose distributions for single-sources in homogeneous water. Several studies have shown that this simplistic approach is inaccurate for many heterogeneous geometries, especially for sources in the low and intermediate energy range (~20-150 keV) and in conjunction with finite patient extensions and shields of high atomic numbers. Accurate dosimetry is important for utilizing gained experiences in new situations and for relating treatment outcome with relevant dosimetric parameters.
The primary dose is affected very differently by heterogeneous geometries than is the scatter dose. Effective algorithms for increased accuracy of dose calculations therefore require separate calculation of the dose from primary and scattered photons. The primary dose can be derived as the collision kerma using simple 1D raytracing methods, while the scatter dose requires use of a 3D integration algorithm. The importance of 3D scatter-dose calculations is highest at low and intermediate energies due to closer to elastic scattering, shorter mean-free-paths and high scatter-to-primary ratios causing dose from scattered photons to be significant at short distances.
The TG43 formalism assures accuracy of single-source water-data, much thanks to the detailed modelling of the source geometry in the underlying Monte Carlo simulations. The full potential of the Monte Carlo source-characterization would be better utilized if the dose were scored separated into its primary and scatter constituents. The data could then not only be used for fast calculations based on tabulation or parameterization (as today), but also serve as input for 3D algorithms. Among such methods are the brachytherapy-adapted version of the collapsed cone superposition algorithm, the discrete ordinates method, and direct use of Monte Carlo simulations. Collapsed cone-superposition makes use of point spread kernels derived from Monte Carlo while discrete ordinate is a deterministic approach for solving the transport equation. Efficiency in Monte Carlo can be improved by use of track-length estimators, however the close-to-elastic photon scattering at these energies and the rapid fluence fall-off due to the inverse square law still makes brachytherapy one of the most time-demanding modalities for Monte Carlo simulations and use of additional variance reduction techniques are investigated. Monte Carlo simulations will play an important role in future development of dose calculations, both for pre-processing of source characterization data, benchmarking of fast algorithms dedicated for brachy applications and increasingly also for direct calculations.

Physics: Dose Calculation and Dosimetry

68 oral

COMPARISON OF VOLUMETRIC CALCULATIONS BETWEEN EXTERNAL AND WALL DELINEATION OF ORGANS AT RISK FOR MRI-BASED INTRACAVITARY BRACHYTHERAPY IN CERVIX CANCER

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Purpose/Objectif: During intacavitary brachytherapy in cervix cancer, the real doses and volumes of normal tissues registered for each particular dose distribution may have important variations depending on where and how they are measured. A great variation may be found if calculations are made in the whole organ volume or in the organ wall. The present study provides additional DVH information about correlation between two different modalities to delineate OAR (rectum, bladder, sigmoid and vagina) contours based on MRI.
Materials/Methods*:* Thirty patients with invasive cervix cancer treated by MRI-based pulse dose rate ICBT were considered for this study. After the implantation of the utero-vagina device insertion, the patients were transferred to the MRI-scanner and were scanned on a General Electric Signa Excite 1.5T MRI machine and fast spin echo T2-weighted images (TE 120s, TR 4100s) were generated. After the MRI imaging, orthogonal X-rays were taken and reference points were identified on X-ray films.The axial images were imported to the Plato BPS treatment planning system, (Nucletron, The Netherlands) and a 3D set was reconstructed. All reference points were digitized and transferred from the X-ray images into the treatment planning system. Then, the entire bladder and vagina were delineated. The rectum was contoured 3 cm from the anal margin to the sigmoid flexure and the sigmoid was contoured from the sigmoid flexure to the last MRI slide where the fondus of the uterus was visualized. In

all cases, external contour and wall contour were delineated. Real wall contours were identified as low-signal intensity structures on T2-weighted images and were delineated. A quantitative analysis of DVH for the OAR was performed for external contours and organ wall delineations. The minimal dose delivered to the 1 cm^3, 2 cm^3, 5 cm^3, and 10 cm^3 (D1cc, D2cc, D5cc and D10cc) of the volume receiving the highest dose of each OAR was calculated.

Results: Differences between doses delivered to the OAR defined by the external contour and by the wall contour only were calculated by the Wilcoxon test. For the rectum, significantly differences were detected in doses calculated in each volume analyzed (D1cc [p=0.0003], D2cc [p=0.0004], D5cc [p=0.00001] and D10cc [p=0.000006]). When these differences were correlated to the volume of the structure, no significantly influence of structure volume was noted for calculations done in D1cc and D2cc. Contrarily, this influence was significantly and progressive in D5cc and D10cc calculations. This influence was not longer observed when dose was calculated in the organ wall only. The same phenomenon was noted when dose in external organ and wall organ contours of bladder, sigmoid and vagina were analyzed.

Conclusions: As previously reported, we observed a good correlation between organ wall and external organ contour up to 2cc when correlated to the volume of the structure including vagina, bladder, rectum and sigmoid. When absolute values were compared, the differences were significant even for lower volumes (1 and 2cc). These differences might be related to the real measurement of the organ wall and not to pre-determined fixed thickness assumption.

69 oral

DOSIMETRIC ASPECTS WHEN CHANGING FROM X-RAY TO CT/MRI BASED BREAST BRACHYTHERAPY

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Purpose/Objectif: To check the differences for treatment parameters when changing from X-ray based to CT based treatment planning for definitive PDR breast brachytherapy.

Materials/Methods*:* A tissue equivalent breast phantom containing 5 flexible plastic tubes fixed with skin buttons was scanned with CT (2mm slice thickness) and MRI (Open device, 0.2T, 6mm + 0.5mm gap) in 3 different orientations (0°, 45° 90°) to investigate the influence of imaging parameters.

Each CT/MRI reconstructed implant geometry was compared to the (reference) X-ray plan by using the same set of dwell times.

Volumes of prescribed dose (VPD), 1.5 times the PD (V1.5PD), 1.5 times the Mean Central Dose (V1.5MCD), the distance between digitized skin button points (determining the reconstruction length), and the dose to these points were determined. The same comparisons were made using the X-ray and CT information obtained during 20 clinical cases by retrospective treatment planning. In order to have a first analysis for the dose to the skin DVH parameters were evaluated for a virtual structure positioned on the skin surface around the whole breast for 6 patients. The skin area receiving at least these dose values was measured with the isodose distribution on the CT image.

Results: Comparing VPd, V1.5PD and V1.5MCD results for each scan orientation to the X-ray reference plan showed a mean difference of 0±3% (1SD). The reconstructed lengths between entry and exit point of the catheters (skin buttons) differed on average by 0.07±0.6 mm for all CT scan. Dose to skin buttons was on average within 3±16%. When comparing X-ray to MRI based reconstructions there were differences of 3±7% for the three volume parameters, 2.7±1.6 mm for the catheter length and dose deviations of 5.3±15% for skin points.

For the 20 analyzed patient cases the mean differences were 0.4±3% for VPD, 5.9±11% for V1.5PD and 3.8±8% for V1.5MCD. When comparing the catheter length between reference and CT reconstruction a difference of 2.4±2.2 mm was observed. The dose to the skin button points differed on average by 3±8% between X-ray and CT plan. DVH analysis showed always higher maximum dose values as determined by the skin button points. On average the D0.1cc, D1cc and D10cc was 170%, 110%, and 70% of the maximum skin button dose. These dose values corresponded to areas on the skin of 0.1 to 25 cm^2.

Conclusions: While dose parameters of CT based treatment plans are equivalent to conventional X-ray plans, the use of MRI scans with limited accuracy at the outer body surface has to be investigated in more detail. As dose surface histograms are not available in most treatment planning system the use of help structures and DVH parameters has the potential to obtain reproducible and representative dose values for the skin.

70 oral

INTRA-TUMORAL DOSIMETRY PERFORMED ON LINE DURING BRACHYTHERAPY BY USE OF SMALL ALUMINIUM OXIDE CRYSTALS

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Purpose/Objectif: Until recently brachytherapy has mostly been based on standard 2D loading patterns and the delivered dose monitored using relative large diameter diodes such as rectal probes. However, with the implementation of 3D-dose planning, a demand for more sophisticated dosimetry has emerged. Smaller probes are of special interest to get access to the steep gradient field close to or even inside a tumour. In addition minute instruments are required to perform patient friendly measurements in the organs at risk.

Materials/Methods*:* To address these issues a new dosimetry system for in-vivo measurements during brachytherapy was developed based on radioluminescence (RL) and optically stimulated luminescence (OSL) from small (0.5 by 2 mm2) carbon-doped aluminium oxide crystals (Al2O3:C) attached to 15 m long optical fibre cables. Each cable has one crystal, small enough to fit inside a brachytherapy applicator. The crystals can be read out remotely during the treatment, and the RL signal provides a real-time measurement of the dose rate at the position of the crystal. Immediately after the treatment, the OSL signal then gives the absorbed dose. We use an Ir-192 source from the GammaMed Plus afterloader unit.

Results: Feasibility of the system for patient in-vivo dosimetry was tested in a patient treated interstitially with pulsed dose rate brachytherapy (PDR-BT) for a supra vaginal recurrence of cervical cancer. By use of a needle template, 17 steel needles were inserted into the tumour. Of these only 15 were used for the treatment leaving two needles for the crystals. The prescribed dose of 30 Gy was delivered to the tumour target over 50 pulses, 1 pulse per hour. For each pulse both the dose rate and the total dose were measured. The measured dose rate was compared with calculations of the expected signal and good agreement was found. Both the RL signature for each pulse (see figure) and the total dose per pulse obtained from the OSL signal remained constant throughout the treatment. This shows that the position of the needles remain constant over 50 hours. Also note that the RL/OSL system worked automatically during the entire treatment.

Conclusions: In conclusion we have developed a new system that allows for intra-tumoral on line dosimetry and monitoring of brachytherapy by minute patient friendly equipment. The perspective is to integrate this system in the clinic, enabling surveillance of the progression of PDR-BT with automated interrupts if measured dose rate differs unacceptably from the expected.

71 oral

DISCREPANCY BETWEEN THE RESULTS OF TWO CALIBRATION METHODS IN MRI BRACHYTHERAPY POLYMER GEL DOSIMETRY

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Purpose/Objectif: Gel dosimetry which is the only true 3D dosimetry method is dependent on the ability to calibrate gel response against radiation dose. When surveying the applicability of a normoxic polymer gel dosimeter for our clinical brachytherapy studies, a notable discrepancy was observed between absolute values resulted from two different calibration methods in our measurements.

Materials/Methods: In brief, experiments were carried out in four major steps: First, in order to be able to insert brachytherapy (BT) sources inside the gel, 5 proper gel containers were designed and constructed from PMMA. A normoxic polymer gel (abbreviated as MAGICA) was then fabricated and poured into the containers and a series of plastic calibration test tubes. Second, 3 dosimeters were differently irradiated with a Nucletron Selectron LDR unit with Cs137; one was irradiated with a GZP6 NPIC HDR afterloader with Co60 (non-stepping mode) and one was irradiated with manually afterloaded Ir192 wires. Three different radioactive sources were utilized to assess whether response of the gel depends on energy of radiation and whether the gel can be used as a dosimeter for different clinical applications. The test tubes were uniformly irradiated with a teletherapy cobalt unit to a range of known doses. Third, the dosimeters and test tubes were transferred into a 1.5T MRI Scanner (Siemens, Symphony, Germany) and several images were acquired according to a previously optimized multi-spin echo protocol. Fourth, all MRI images were transferred into a personal computer and after image processing in MATLAB7® 2D dose maps of the dosimeters were obtained. The relation between mean R2 (=1/T2) values of the calibration test tubes with dose was used as the first calibration method; as the second method, R2 values of the first dosimeter which was irradiated with a single Cs source were correlated to TPS dose data along a profile through the source for calibrating other dosimeters. Comparisons were made with dose-vs-distane diagrams along certain profiles on the dose maps.

Results: When compared to the treatment planning anticipations (or manual calculations in the case of Ir wires), results of the first calibration with test tubes show a dose difference (DD) up to 6Gy in plateaus and a "distance to agreement" (DTA) of more than 2mm in steep dose gradients in all dosimeters. However the second calibration improves these results to less than 0.35Gy DD and less than 2mm DTA for all dosimeters.

Conclusions: This discrepancy between absolute values resulted from the two calibration methods might be related to effect of container size as test tubes and original dosimeters have different volumes. It could be either different effect of environmental factors on the test tubes and the original dosimeters or more possibly different propagation of heat inside them during irradiation due to exothermic polymerization reactions that causes such a considerable discrepancy. It can be inferred that it would be best to use a calibration phantom with the same size as original dosimeters to bypass this effect.

Breast: Interstitial BT vs Intracavitary Balloon vs IORT

72 speaker

TECHNICAL AND CLINICAL ADVANTAGES OF IMAGE-BASED MULTICATHETER BREAST BRACHYTHERAPY

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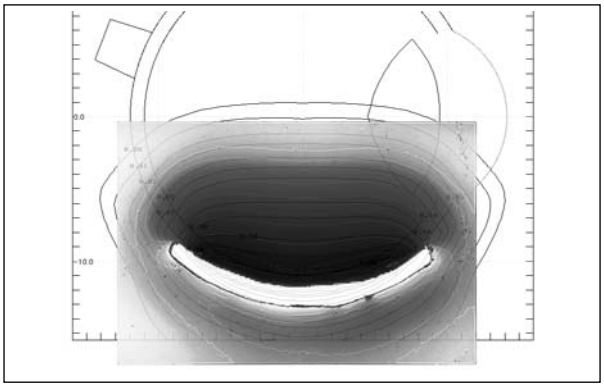
In the last two decades accelerated partial breast irradiation (APBI) using multicatheter interstitial brachytherapy (BT) has been intensively evaluated in Phase I and II studies as a possible alternative to conventional whole breast irradiation. Majority of these trials – using strict patient selection criteria and proper treatment technique – were successful in yielding an annual local recurrence rate in the range of 0 to 1.2%. As the forerunner of competing APBI techniques (e.g. MammoSite BT and intraoperative radiotherapy) by a decade, multicatheter BT has the paramount clinical advantage that its safety and efficacy is supported by long term (up to 8 years) follow-up data obtained from several Phase I and II studies. Oncological and cosmetic results beyond 5 years of other APBI techniques are pending.

The results of earlier studies using partial breast BT have to be viewed critically. In traditional BT series the use of a two-film localization technique did not allow the definition of actual three-dimensional (3D) extensions of the target volume. Furthermore, using traditional dosimetry systems the dose report was related to the geometry of the implant and not to the target volume itself. In modern BT both treatment planning and plan evaluation have to be based on real 3D volume of the target and critical structures. Recently, there are a few publications in which results of CT image-based target-oriented dose-volume assessments are published (Table 1).

These dosimetric results reinforce that in breast BT preimplant CT image-based target volume definition and implant simulation can be effectively used to improve dose delivery regarding both target coverage and dose homogeneity, which may turn into improved clinical results.

Technical advantage of multicatheter BT includes its feasibility in most cases, as inadequate target volume coverage or dose inhomogeneity can be greatly minimized with the integration of experience, image guidance and dose optimization. Spherical APBI devices (including MammoSite and Intrabeam applicators) have limitations to treat lumpectomy cavities that are large, irregular or eccentrically located. MammoSite BT requires a minimum balloon-skin distance of 12 mm to avoid high rate of teleangiectasia observed in some early studies. The rapid dose fall-off from 50 kV photons used in the Intrabeam device does not allow adequate target coverage up to 1 to 2 cm around the lumpectomy cavity. Documentation of 3D dose-volume parameters of APBI using intraoperative electrons (ELIOT) is problematic. Furthermore, ELIOT can deliver adequate dose only to a part of the excision cavity wall (mainly to the pectoral base), while coverage of other dimensions of the target volume (e.g. anterior cavity wall below the skin surface) is at least questionable.

Therefore, until results of alternative APBI techniques are pending multicatheter BT remains the well-established standard option for partial breast irradiation.



73 speaker

INTRACAVITARY BRACHYTHERAPY WITH THE MAMMOSITE (R)– MORE THAN A SIMPLE BALLOON

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The MammoSite® applicator was developed for accelerated partial breast irradiation. The advantage for surgeons is obvious: One dual lumen closed ended catheter with a small inflatable balloon and a port for connecting a remote afterloader. The advantage for the patients is also obvious: In an optimal situation one catheter implanted during primary surgery or as a second procedure later in an additional session. The advantage for treatment planning is one dwell position in the middle of the balloon.
But thinks looking easy, must be not always simple. Especially radiotherapists must know something about the MammoSite tricks. If the balloon has not the optimal round shaped form there might be under and over dosage of surrounding tissue. In case of air gaps and seroma underdosage will occur. Before each radiotherapy fraction delivery the applicator has to be controlled in order of balloon geometry by x-ray or ultrasound because of potential balloon leakage could not be detected by clinical examination. The reference isodose is defined 1 cm from the balloon surface. If the balloon skin distance is less than 1.5 cm the late skin toxicity could increase. The teleangiectasia rate is nearly 30% within two years in the European phase two trial. In 39% the patients suffers from serious seroma. Same things remain in matter for chest wall and lung.
Comparing MammoSite® with interstitial multicatheter breast implantation the target volume coverage is better for MammoSite® compared to conventional interstitial brachytherapy. Dose homogeneity is also better for MammoSite®. But using the MammoSite® you have only limited possibilities to conform your isodose depending on the resection margin compared to multicatheter interstitial brachytherapy.
Patients love the MammoSite applicator, one catheter and less impaired of life quality. The surgeons love the MammoSite applicator, one catheter in the wound cavity and that's it. Radiotherapist could like the MammoSite in some situations. Patients with large breast volumes and deep sited tumours with wide resection margins in all directions will be optimal patients. If the costs for the applicator will decrease it might be attractive as an alternative for interstitial implantation with 10 or more applicators.

74 speaker

INTRA-OPERATIVE RADIATION THERAPY (IORT) IN BREAST CANCER.

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Purpose/Objectif: After tumour resection, IORT is one of the available means of partial breast radiotherapy : either in the form of a boost on the tumour bed after irradiation of the whole breast, or as sole irradiation treatment of one of the quadrants of the breast.
Materials/Methods: Our experience with IORT in the breast started 20 years ago. We evaluated 110 patients with over half having a minimum life expectancy of 10 years.
After local surgery, the edges of the resection in the tumour bed were joined together by sutures to bring them into the target volume. The tumour beds were completely covered in flat circular applicators of 4 to 6 cm. The dose was set at the half-value thickness of the 90% isodose with a focus distance at 100cm. For the 68 patients treated by IORT as a boost, the median delivered dose was 10 Gy, and for the 42 patients treated by IORT as sole treatment, the delivered dose was 21 Gy, using electron-beams with an energy range of 6 to 13 MeV (Median=9 MeV). Late toxicities and cosmetic results were assessed by 2 different physicians according to the CT C 3.0 grading system. European Organization for Research and Treatment of Cancer (EORTC), quality of life (QOL, QLQC 30) and EORTC breast cancer module (QLQBR 23) questionnaires were completed by each patient on their latest medical visit
42 patients of over 65 years old (pN-,Pt1) were included in this Phase II study on the feasibility and reproducibility of using a focused and concentrated electron-beam as sole radiotherapy treatment after tumour resection. For this group, one of the criteria we studied was the in vivo reproducibility of dosimetric comparison of the reference isodoses to the theoretical calculations by use of thermoluminescent dosimeters and ionisation chambers.
Results: After a median follow-up of 12.7 years (range: 0,5-20 years), three local recurrences were observed within the primary tumour bed (one early recurrence at 4 months and 2 late recurrences : 8 years and 14 years after initial treatment). At the time of analysis : 96 patients were still alive (2 at a metastatic stage and 94 without disease), 9 had died from metastases and 5 had died from other causes. Among the 94 disease free remaining patients, no grade 3 or greater toxicities were observed ; 6 patients had experienced grade 2 late subcutaneous fibrosis within the irradiated area. Overall, the scores indicated a very good QOL. In general, the scores for the body image functional scale of the QLQ-BR 23 were good to excellent in 95% of the evaluated patients.
Feasibility and reproducibility were also demonstrated ih this Phase II study, for 42 of the patients, by comparing the theoretical calculations to,the doses measured in vivo.
Conclusions: Our results confirm that IORT is a reliable technique either as a boost after whole breast irradiation, or as a sole treatment. This study demonstrates this technique's physical feasibility as well as its clinical reliability in view of the cosmetic and oncological resultats and confirms the possible role of IORT as a sole radiotherapeutic treatment in combination with tumorectomy for patients over 65 years.

Prostate Cancer

75 oral

COMPARISON OF DIFFERENT DOSE VOLUME PARAMETER CONCEPTS FOR THE RECTUM IN LDR PROSTATE BRACHYTHERAPY

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Purpose/Objectif*:* To compare dose volume parameters obtained for the rectum versus the rectum wall and to check correlations between the various parameters proposed in literature.
Materials/Methods*:* 38 post-implant CT scans obtained 4 weeks after implantation were included. The outer contour of the rectum and the visible rectum wall were contoured. DVH analysis included the dose to certain absolute and relative volumes of the contoured structures (D0.1cc-D10cc and D5-D30, respectively). In addition the volumes of certain dose levels are reported (V100, V150, V200). The impact of the number of slices with the rectum contoured was studied in detail. Statistical difference was tested using the paired T-test.
Results: The difference for D0.1cc was statistically not different between the rectum and the rectum wall contour, the ratio was 0.997 ± 0.03 (1SD). Dose values for larger volumes (D1cc, D2cc, D5cc, D10cc) were statistically different ($p<0.01$). However, the ratio between rectum to rectum wall values is small with 1.01 ± 0.02 for D1cc and 1.02 ± 0.03 for the D2cc. It was essential to take care that slices above and below the prostate were included for contouring, in order to have the D2cc isodose totally within the analyzed structure. For D5cc and D10cc the ratio between rectum and wall was 1.11 ± 0.13 and 1.32 ± 0.37. When comparing the dose to relative volumes these ratios were 0.95 ± 0.05, 0.91 ± 0.06, 0.88 ± 0.07 and 0.89 ± 0.07 for D1, D5,

D10 and D30, respectively. The maximum dose to the rectum was very sensitive for cases with seeds close to the rectum wall, resulting in a wide range of 1SD= ± 0.4. The V100 reported in cc has a ratio of 1.08 ± 0.13 between rectum and rectum wall. When expressing V100 relatively in % the difference increased to 0.75 ± 0.17. However, when reporting rectum doses the V100 can be translated to D2cc using a linear correlation with R^2=0.92. The very often recommended constraint of V100 (145Gy) = 1.5 cc is similar to limiting D2cc to 130 Gy.
Conclusions: When reporting dose values for volumes equal or smaller than 2cc the outer rectum wall contour is sufficient for a reproducible parameter. Relative volumes (e.g. D5, D10) and larger volume parameters (e.g. D5cc, D10cc) have limited accuracy. As different DVH parameters are reported in literature and even in guidelines it might become essential to find correlations between the various concepts in order to compare and recalculate reported dosimetric parameters for rectum morbidity analyses.

76 oral

HDR MONOTHERAPY BRACHYTHERAPY FOR LOCALISED PROSTATE CANCER

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Purpose/Objectif: A phase II dose escalation study has been undertaken to evaluate high dose rate brachytherapy (HDRBT) monotherapy for prostate cancer.As this is a tumour with a low alpha beta ratio large fractions of radiotherapy given to smaller total doses are likely to be more biologically effective. HDRBT can deliver single high dose treatments to the prostate volume with relative sparing of the surrounding normal tissues.
Materials/Methods: 109 patients have been entered, all with locally advanced or high grade prostate cancer. Three dose levels have been used; 34Gy in 4 fractions, 36Gy in 4 fractions and 31.5Gy in 3 fractions. These equate to 226Gy(1.5), 252Gy(1.5) and 252Gy(1.5) respectively. 30 patients have received 34Gy, 25 received 36Gy and 54 patients received 31.5Gy. All patients have been analysed for acute toxicity. Late toxicity has been evaluated in all patients at 6 months and 6 monthly thereafter.
Results: The three groups are well balanced for presenting PSA, Gleason score and T stage. Acute urinary toxicity was assessed by mean IPSS scores and RTOG scores. Mean IPSS scores rise in week 2 to 12.2 (34Gy), 13.1 (36Gy) and 9.6 (31.5Gy), falling to baseline at 12 weeks. Seven patients required catheterisation at 2 weeks; 3 receiving 34Gy, 1 receiving 36Gy and 3 receiving 31.5Gy. Only 3 patients remained catheterised at 12 weeks. Mild GI toxicity (RTOG 1,2) at 2 weeks was seen in 61%, 68%, and 77% across the three arms falling to 25%, 54% and 27% at 12 weeks. Late bladder toxicity (RTOG 1,2) at 6 months was seen in 25%, 28% and 22% respectively.Grade 3 bladder toxicity was seen in only 2 patients at 6 months from the 34Gy and 36Gy arms. Only 1 patient from the 31.5 Gy cohort reported grade 2 bowel toxicity at 6 months. Mean presenting PSA (ug/L) for each cohort was 17.2, 18.2 and 15.5 respectively. At 6 months the mean PSA had fallen to 1.01, 1.32 and 0.6 across the three arms, however 51% of patients are receiving adjuvant antiandrogens. Further PSA response data is awaited. No PSA relapses have yet been seen with a median follow up of 19 months (range 6 – 36 months).
Conclusions: HDR brachytherapy montherapy is well tolerated with low rates of late toxicity. Early results suggest an excellent biochemical response with no differences seen in acute and late toxicity between doses of 34Gy/4f, 36Gy/6f or 31.5Gy/3f.

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INTERSTITIAL HIGH DOSE RATE (HDR) BRACHYTHERAPY AS MONOTHERAPY FOR EARLY STAGE PROSTATE CANCER

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Purpose/Objectif: Transrectal Ultrasound (TRUS) guided interstitial implant for prostate cancer using Low Dose Rate (LDR) and High Dose Rate (HDR) technique has been reported with results comparing favorably to surgery and External Beam Radiation Therapy (EBRT). Often, HDR and LDR interstitial implant is combined with EBRT. There is little published data on HDR alone. We report our results with HDR monotherapy.
Materials/Methods: Between 1997 and 2007, 201 patients with T1 and T2 localized prostate cancer, underwent TRUS guided interstitial implant, under spinal or local anesthetic. There were no Gleason Score or PSA exclusions. No patient received EBRT or Hormonal Blockade. Median Gleason Score was 7 (range : 4 to 10). Median PSA was 9.3 (2.7 to 39.8). Treatment volumes ranged from 41 cc to 196 cc. Treatment volume included the prostate and seminal vesicles in all cases. Radiation treatment planning was performed using CT Scanning and the Nucletron Plato Treatment Planning System. Our IRB protocol for HDR alone, has called for two HDR Implants spaced 4 weeks apart. The treatment volume received 2,250 cGy in 3 fractions prescribed to the 100% Isodose line, given over 24 hours. A 2nd implant was performed 4 weeks later, delivering a further 2,250 cGy in 3 fractions, bringing the final dose to the implant volume to 4,500 cGy in 6 fractions. Urethral dose points (10-16) were followed, and limited to ‹ 105% of the prescription dose.
Results*:* With a median follow-up of 78 months, (range : 6 months to 132 months), PSA disease free survival was 89.1% (179/201). Acute and chronic complications were uncommon. Urethral stricture requiring dilatation has developed in 5.4% (11/201) of patients. Urinary stress incontinence has occurred in 4.0% (8/201). RTOG late bladder toxicities were : 0% Grade 4, 0% Grade 3, and 4.0% (8/201) Grade 2. RTOG late rectal toxicities were : 0.5% (1/201) Grade 4, 0% Grade 3, 1.5% (3/201) Grade 2, and 2.0% (4/201) Grade 1.
Conclusions*:* With a median follow-up of 78 months, results with HDR monotherapy compare favorably to surgery, EBRT, LDR +/- EBRT, and HDR + EBRT, both with regard to PSA disease free survival, and complications. HDR offers other advantages over LDR, such as no radiation exposure to hospital personnel, no seed migration, no seed emboli, greater dose flexibility, and precision dose delivery. Larger volumes can be treated with HDR. By omitting EBRT, bladder and rectal complications may be significantly reduced.

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INTERSTITIAL HIGH DOSE RATE (HDR) BRACHYTHERAPY + INTENSITY MODULATED RADIATION THERAPY (IMRT) VS. HDR MONOTHERAPY FOR EARLY STAGE PROSTATE CANCER

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Purpose/Objectif: Transrectal Ultrasound (TRUS) guided interstitial implant for prostate cancer using High Dose Rate (HDR) + External Beam Radiation Therapy (EBRT) technique has been reported with results comparing favorably to surgery, Low Dose Rate (LDR) brachytherapy +/- EBRT, EBRT, and Intensity Modulated Radiation Therapy (IMRT). The role of supplemental EBRT in brachytherapy is controversial. We compare our results of HDR + IMRT vs. HDR monotherapy.

Materials/Methods: Between 1997 and 2007, 310 patients with T1 and T2 localized prostate underwent TRUS guided interstitial implant. There were no Gleason Score or PSA exclusions. After discussion of treatment options, 109 patients elected HDR Implant + IMRT and 201 patients underwent HDR monotherapy. No patient received Hormonal Blockade. Median Gleason Score was 7 (range : 4 to 10). Median PSA was 9.8 (0.60 to 39.8). In patients who received IMRT + HDR, 4500 cGy in 25 fractions was given via IMRT and 1650 cGy to 2000 cGy in 3 fractions via HDR. Our protocol for HDR alone, has called for two HDR Implants. The treatment volume received 2,250 cGy in 3 fractions prescribed to the 100% Isodose line, given over 24 hours. A 2nd implant was performed 4 weeks later, delivering a further 2,250 cGy in 3 fractions, bringing the final dose to the prostate to 4,500 cGy in 6 fractions.
Results: There was no significant difference between the treatment groups with respect to T- Stage, Gleason Score, and PSA. With a median follow-up of 78 months (range : 6 months to 132 months), the overall PSA Disease Free Survival (DFS) was 88.7% (275/310). In patients undergoing IMRT + HDR Implant, PSA DFS was 88.1% (96/109) vs. 89.0% (179/201) for patients undergoing HDR alone (p=0.6). RTOG late bladder toxicities were : 0% Grade 4, 0% Grade 3, and 3.9% (12/310) Grade 2. RTOG late rectal toxicities were : 0.3% (1/310) Grade 4, 0% Grade 3, 3.5% (11/310) Grade 2, and 4.2% (13/310) Grade 1. RTOG late rectal toxicity was higher in patients undergoing HDR + IMRT with 15.6% (17/109) of patients experiencing Grade 2 and 1 symptoms, vs. 3.5% (7/201) receiving HDR alone ($p < 0.01$).
Conclusions*:* We have observed no significant difference in PSA DFS in patients undergoing HDR monotherapy vs. HDR + IMRT. Complications were similar, though RTOG Grade 1 and 2 late toxicity was higher in patients receiving HDR + IMRT.

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HOW TO MANAGE LOCAL RELAPSES AFTER PERMANENT PROSTATE BRACHYTHERAPY FOR LOCALISED PROSTATE CANCER

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Purpose/Objectif: To determine the feasibility and results of salvage treatment modalities after permanent prostate brachytherapy (PPB) for localised prostate cancer in terms of tumour controle and side effects.
Materials/Methods: At the UMC-Utrecht over 1400 patients were treated with curative intend for localised prostate cancer by PPB. In this group of patients 34 local recurrences were proven by histology. One other patient had a recurrence after retropubic implantation.
Salvage treatment included radical prostatectomy (5 patients), second permanent implant (9 patients), external beam radiotherapy (5 patients), androgen deprivation therapy (8 patients) and deferred treatment (8 patients). We looked to initial and secundary tumour factors in relation to the final outcome and to the complications of salvage treatment.
The mean follow-up from initial treatment was 77 months, range 24-250 months, and from salvage 51 months, range 3-108 months.
Results: After prostatectomy results are available for 4 of 5 patients, one patient was operated in Belgium and lost to follow-up. One patient is alive and bNED at 60 months, two patients are alive with PSA progression, follow-up 21 and 66 months, and one patient died of progressive cancer at 54 months. One patient had such severe problems after surgery that a urine deviation was performed, another patient has urethral stenosis.
After a second implant 6 patients are alive, 2 are bNED, 4 with PSA progression and 3 patients died with prostate cancer. One patient developed a fistula (interval between the two treatments was only 22 months), one patient needs a suprapubic catheter and one patient developed rectal cancer 7 years after his salvage treatment, most likely due to the irradiation. Mean follow-up after this salvage procedure is 75 months, range 25-108 months.
Three of 5 patients after external beam therapy as salvage are alive with PSA progression, 2 died with cancer. No serious toxicity was encountered in this group. One patient had cystoprostatectomy for bladder cancer and again recurrent prostate cancer. Mean follow-up in this group was 77 months, range 59-87 months.
Hormonal treatment in 8 patients resulted in DOD in 5 and biochemical progression in 3. Apart from hormonal side effects there were no complications. In this group the mean follow-up is 27 months, range 5-56 months.
Of 8 patients with deferred therapy 2 patients died of disease, 6 are alive with disease and short follow-up in one. Mean follow-up is 36 months, range 3-64 months.
Conclusions: Salvage therapy is certainly possible in local recurrence after PPB. All modalities are open, including surgery and second implantation. For all patients best results are obtained in patients with a late recurrence, both in relation to PSA control and complications. In general the life expectancy after second treatment is relatively long with a mean follow-up of 69 months. In patients with androgen deprivation or deferred therapy the follow-up is 31 months.

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HDR OR LDR IN THE RADIATION TREATMENT OF PROSTATE CANCER: IDENTICAL RESULTS OR TOXICITY RATES ?

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Purpose/Objectif*:* To analyse results after shifting from LDR brachytherapy (BT) to HDR treatment as a boost to external beam radiotherapy (EBRT).
Materials/Methods*:* From 1997 to 2005, 328 patients with locally advanced prostatic adenocarcinoma were consecutively treated with BT as a boost to 3D conformal EBRT. All over the study, BT techniques remained unchanged except for dose delivery. Until 07/2002, 201 patients received 40 Gy EBRT with a BT boost of 42 Gy by LDR with 192Ir wires. After that date we shifted for the last 127 consecutive patients to a HDR BT boost, as a way to introduce stepping source technology. To shorten BT procedures we decided to give only one fraction of 10 Gy after an increased EBRT dose of 60 Gy to maintain a similar Extrapolated Response Dose (ERD) of 143 Gy3 in the CTV. We also wanted to better cover the seminal vesicles with a higher EBRT dose. The total expected anterior 1/5 rectal ERD were 126 Gy3 and 117 G3 respectively for the HDR and LDR groups.
Results: The median follow up is 60 months for the LDR group and 31 months for the HDR group. Recurrence rates of respectively 23 % and 27 % at 33 months are not significantly different ($p = 0.88$). However, late severe grade 3 rectal toxicity at 2 and 3 years is respectively 2.36 % and 3.15 % for the HDR arm but 0% for the LDR arm ($p = 0.01$).
Conclusions*:* With unchanged EBRT and BT technics and equal 143 Gy3 in the CTV, the control rate of the disease at 31 months was similar in the two different groups. Our experience confirms thus the low α/β ratio of prostatic cancer. Reducing the rectal toxicity rates in the HDR arm requires to lower the anterior rectal ERD to 117 G3 ERD like in the present LDR arm. However, severe rectal toxicity rates will never be better than the 0% described in the initial LDR arm. The observation that HDR and LDR are probably equivalent can have an impact on designing future protocols.

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DOSE ESCALATION BY COMBINED TREATMENT 3D-CONFORMAL RADIOTHERAPY PLUS HDR BRACHYTHERAPY AS TREATMENT FOR INTERMEDIATE–OR HIGH-RISK CANCER: EARLY TOXICITY AND BIOCHEMICAL OUTCOME OF A PROSPECTIVE RANDOMIZED TRIAL

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Purpose/Objectif*:* To report early and late toxicity and preliminar biochemical outcome in 445 patients with intermediate- or high-risk clinically localized prostate cancer treated with either high-dose 3D Conformal Radiotherapy (3D-CRT) or with low-dose 3D-CRT followed by and HDR brachtytherapy implant

Materials/Methods*:* Between 12/1999 and 10/2005, 445 patients with PSA›10, Gleason score›6 and/or T2b-T3 N0 M0 prostate cancer were treated with IMRT followed by HDR brachytherapy implant to the prostate. Patients were randomly assigned to one of the two treatment groups: 76 Gy 3D-conformal radiotherapy (3D-CRT) to the prostate in 38 fractions (group 1; 223 patients) or 46 Gy 3D-CRT to the prostate followed by a boost to the prostate by a 16 Gy HDR brachytherapy implant given in 2 fractions of 8 Gy 6 hours apart (group 2, 222 patients). Both groups were well balanced taking into account patient's as well as tumors' characteristics. Acute and late toxicities were scored by the EORTC/RTOG morbidity grading scales. Special attention to local, regional or distant recurrence, survival, late effects, PSA and testosterone levels and quality of life was done.

Results*:* All patients completed treatment. One patient included in the group 1 and none of the group 2 experienced grade 3 rectal toxicity (rectal ulcer). Twenty eight patients of group 1 (12.5%) and 20 patients of group 2 (9,1%) developed grade 2 rectal toxicity. Nineteen patients in each group (8.6%) developed acute Grade 2 urinary symptoms (mainly dysuria), and none experienced urinary retention. No patient (0%) developed Grade 4 rectal complications or grade 3 or 4 urinary complications. The 5-year actuarial PSA relapse-free survival rates for intermediate- and high-risk group 1 patients were 92 and 91 % respectively and 97 and 96 % for group 2 patients

Conclusions: The data presented demonstrate the feasibility of high-dose 3D-EBRT+HDR brachytherapy as a safe and effective method of escalating the dose to the prostate without increasing the risk of late effects. Acute as well as late rectal and urinary complications were significantly reduced, compared with what has been observed with high-dose conventional, 3D-conformal radiotherapy. Short-term PSA control rates seem to be better with in the HDR-boosted patients, but longer follow-up is needed.

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HIGH DOSE RATE BRACHYTHERAPY IN COMBINATION WITH EXTERNAL BEAM RADIOTHERAPY IN THE RADICAL TREATMENT OF PROSTATE CANCER: INITIAL RESULTS OF A RANDOMISED PHASE III TRIAL

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A randomised phase III trial has compared standard external beam radiotherapy delivering 55Gy in 20 daily fractions over 4 weeks with a combined schedule comprising external beam treatment delivering 35.75Gy in 13 fractions over 2½ weeks followed by HDR brachytherapy delivering 17Gy in 2 fractions. The primary endpoint was biochemical relapse-free survival with secondary endpoints overall survival, toxicity and quality of life. A total of 220 patients were randomised and balanced for important prognostic factors including tumour stage, presenting PSA, Gleason score and use of adjuvant anti-androgens. With a median follow-up of 30 months (range 3-91) a statistically significant improvement in actuarial biochemical relapse-free survival is seen in favour of the combined brachytherapy schedule ($p = 0.02$). This effect was seen across all risk groups and persisted even in those patients receiving adjuvant androgen deprivation. A lower incidence of acute rectal discharge was seen in the brachytherapy group ($p = 0.025$) and other acute and late toxicities were equivalent. Patients randomised to brachytherapy had a significantly better FACT-P score at 12 weeks ($p = 0.02$). The use of HDR brachytherapy in combination with external beam radiotherapy is an effective means of dose escalation in the radical radiotherapy of carcinoma of the prostate with no increase in acute or late toxicity observed so far.

Breast Cancer

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ACCELERATED PARTIAL BREAST IRRADIATION (APBI) USING INTERSTITIAL HIGH DOSE RATE BRACHYTHERAPY (HDR BT) : EARLY TOXICITY AND TECHNICAL ASPECTS

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Purpose/Objectif: APBI using interstitial HDR BT implants, as the sole radiation modality following breast conserving surgery, is currently being used in selected patients (pts) with early breast cancer. The purpose of this analysis is to report early toxicity and technical aspects in a cohort of 42 consecutive pts treated at RHCC.

Materials/Methods: From 11/2004 to 9/2006, 42 pts with a median age of 70 yrs(range: 52-92) and a median tumor size of 1.15 cm (range: 0.4-2.1) received APBI using HDR interstitial BT . Selection criteria: age › 50, Invasive Ductal Carcinoma, Grade I-II, single tumor 2.5 cm. or less in greatest diameter, negative surgical margins, negative axillary LNs. Pts underwent CT scan for target volume definition. The implant geometry was designed according to the rules of the Paris System. Nucletron RABBIT template was used for needle insertion under local anesthesia. Reconstruction was performed using two orthogonal radiographs taken at the simulator. Nucletron PLATO BPS v.14 software was used for treatment planning. Basal dose points were defined midway between catheters in central transversal plane and the average dose for these points was calculated (Mean Central Dose). A dose of 32 Gy in 8 outpatient treatment sessions twice daily during 4 consecutive days was prescribed at an isodose representing 85% of the Mean Central Dose.

Results: Acute toxicity was minimal: 3 pts (7.0%) developed hematoma at the site of the implant, which resolved by itself without any treatment. One patient(2.0%) had local pain, and 3 pts (7.0%) developed minimal erythema. There were no toxicities observed in 17/42 pts with a follow-up of 12-18 months. There were no local recurrences, but the median follow up time (9 months, range: 1 -20 months) is too short to assess long term local control, late toxicity and cosmetic outcome.

Conclusions:

1. Outpatient APBI by interstitial HDR BT is feasible and convenient treatment modality with no serious acute side effects.
2. Technically, the procedure is simple and well tolerated.
3. A longer follow up time is needed in order to assess long term local control rate, late toxicity and cosmetic outcome.

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ACCELERATED PARTIAL BREAST RADIATION: INITIAL EXPERIENCE WITH HDR BALLOON IN IRELAND

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Purpose/Objectif: We present our first experience with accelerated partial breast irradiation (APBI) using MammoSite® balloon implantation. The dosimetry and technical aspects of treatment and treatment monitoring will be presented. All patients were treated on an approved institutional protocol at UCHG

Materials/Methods: Between Oct 2005 and Nov 2006 8 patients were enrolled on protocol, screened and 5 patients treated. The age was from 54 to 78 (mean 64.2) and the tumour size from 10 to 30 mm (mean 29.6mm).The inclusion criteria were: age 45 years or older, have stage 0, I or II breast cancer, low risk, unicentric DCIS, have negative surgical margins (NSABP definition) after final surgery, should have adequate skin spacing between balloon surface (› 7 mm).The balloons were implanted post lumpectomy under ultrasound guidance. The day after balloon insertion, a CT scan (0.2 cm cuts) was performed with contrast inside the balloon. The pre-treatment planning was done using the BrachyVision TPS and all relevant parameters were measured and reported. The dose was prescribed at a distance 10.0 mm from the balloon surface, in a plane transverse to the balloon axis at its centre-single prescription point. Four independent points were added for monitoring dose at the border of PTV volume. Treatment was delivered by HDR GammaMed afterloader with Ir192 source in 10 # of 3.4 Gy-total dose 34 Gy with minimum of 6hrs between the fractions each day. Monitoring the treatment was done by daily CT (daily planning compared with base plan) and afternoon Simulator images. Daily parameters: PTV volume, air and seroma volume, asymmetry source dimension, balloon diameter, DHI, FWHM, balloon surface skin distance were reported.

Results*:* The mean PTV volume for those treated patient was 84.7cm^3(STD± 0.9cm^3)-the balloons had diameter 4-5 cm. The mean dose from all monitoring points were 3.33Gy (STD± 0.06Gy) and was 98% prescribed dose. The coverage index (CI) for those treatments was 88% (STD± 3%). Mean value of DHI was 0.66 with STD± 0.03 and the mean value FWHM was 178cGy with STD ±17cGy. The mean distances between balloon surface and skin for those patients were respectively: 0.93cm, 0.79cm, 0.62cm, 10.2cm and 0.99cm.In one case treatment was stopped after 7 fractions as a result of decreasing distance to the skin surface.

Conclusions: A range of issues was encountered in the first 8 patients. Successful completion rate: 62.5% (8 pts screened and 5 treated).This is in line with international experience for programs in their initial phases. Complications: mild pain tenderness breast, no infection, excellent tolerance, excellence patient satisfaction, excellent early cosmetics. Treatment is short and comfortable for the patient. Daily geometry control requires the use of CT and daily planning is somewhat time consuming. The dose on the skin is not higher than during external beam treatment for patients with a device-to-skin distance of ≥0.7 cm.

85 poster

ACUTE TOXICITY, COSMESIS AND QUALITY OF LIFE AFTER MAMMOSITE (R) BRACHYTHERAPY FOR LOW RISK BREAST CARCINOMA IN PATIENTS OLDER THAN 60 YEARS

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Purpose/Objectif: The MammoSite is a device that was developed with the goad of making breast-conserving surgery (BCT) more widely available. Our objective was to evaluate the MammoSite device performances after an open cavity placement procedure and quality of life in highly selected patients with early-stage breast cancer.

Materials/Methods: From March 2003 to March 2005, 43 patients with T1 breast cancer were enrolled in a phase II prospective study. Twenty-five (58%) were treated with high-dose rate brachytherapy using the MammoSite applicator to deliver 34 Gy prescribed at 1 cm from the balloon surface in 10 fractions over 5 to 8 days. A minimum of 6 hours elapsed between the twice-daily fractions.

Results: The main disqualifying factor was pathologic sentinel node

involvement. Ten out of 43 (23%) patients had the device placed and explanted. There were no device malfunctions, migration or rupture of the balloon. After a median follow-up of 13 months, there were no local recurrences and one contralateral lobular carcinoma. Seventeen (68%), 13 (52%), 7 (28%), 5 (20%) and 4 (16%) patients had erythema, seroma, inflammation, hematoma and infection, respectively. Only 2 patients developed telangiectasia. At 3 months breast erythema grade ⇒ 2 was significantly correlated to cosmetic resultsz (12.5% in the "good to excellent" versus 57% in the "poor to fair" group; p=0.045). The strongest trend of excellent cosmetic outcome was observed in patients with skin spacing ⇒ 19 mm (50%) compared to patients with ‹19 mm (11%; p=0.087). At 1 year the rate of "good to excellent" cosmetic resuts was 84%. Significant changes in QoL were observed for emotional and social well-being between 3 and 12 months. At 24 months only emotional well-being subscore changes were statistivally significant (p=0.015). Parameters such as, the type of hormone therapy administered, adverse events ⇒ grade 2 and cosmetic results did not influence the QoL profiles changes.

Conclusions: To our knowledge, this is the first study since the initial FDA clinical study showing the feasibility of MammoSite brachytherapy procedure following an open cavity technique as a sole therapy in highly selected patients older than 60 years. This is also the first report on QoL during and after APBI using HDR brachytherapy with a MammoSite device. The toxicity and cosmetic results are in the range of previous series with, however, a higher range of skin spacing which allowed a significant reduction of the risk of telangiectasia. QoL evaluation indicates that baseline scores were satisfactory. Changes concerned emotional and social well-being.

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COMPARISON OF TWO TECHNIQUES OF INTERSTITIAL PULSED DOSE RATE BRACHYTERAPY (IBT PDR) AS A BOOST DOSE IN CONSERVATIVE TREATMENT OF BREAST CANCER (BCT).

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Purpose/Objectif: iBT using rigid or plastic tubes is a technique used to deliver an additional dose to the tumour bed following breast sparing surgery. Traditionally BT has been applied following completion of breast EBRT. BT may also precede EBRT, preferably as an intra-operative procedure. We compared selected parameters of implants and natural dose volume histograms in two techniques of iBT PDR applied as a boost in BCT.

Materials/Methods: Data of T1-3N0-1M0 breast cancer pts who underwent iBT as a boost dose in BCT between 05/2002 and 12/2006 were analysed. 74 pts were implanted with rigid tubes after breast EBRT (group A) and 76 had a peri-operative BT with an intra-operative flexible tube placement followed by whole breast EBRT (group B). In both groups PDR BT of 15 Gy (1 Gy/pulse/h) was administered with Paris system rules, and volume optimization was performed using BT planning system PLATO. Statistical comparisons were made with the Student T test.

Results: Two-plane implant was used in 80% of group A pts, and three-plane implant in 80% of group B. 5-13 tubes (mean, 9) and 7-18 (mean, 11) were implanted in group A and B, respectively. The overage volume for the "prescribed dose" (V100) was 35.2±18.9 cm3 (group A) and 39.7±29.9 cm3 (group B); (p=0.4). The respective V50 and V200 were also similar. Quality index (QI) was not impacted by the technique of BT (mean QI was 1.84 and 1.77 for the groups A and B, respectively). Uniformity indexes (UI) in respective groups were 1.59 and 1.50 (p=0.009).

Conclusions: Impant volume encompassed by prescreibed dose is insignificantly lower with intra-operative plastic tubes placement. Based upon the QI these two iBT techniques are comparable. The target volume coverage by the dose distribution as defined by UI is better for the rigid tubes.

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CONTACTS X-RAY (50 KV) IORT AND NIPPLE SPARING TOTAL MASTECTOMY

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Purpose/Objectif: Nipple staring total mastectomy is a standard treatment for extensive ductal in situ breast cancer in many cancer institutes. To prevent the risk of local relapse in relation to residual microscopic cancer cell in the nipple areola plaque adjuvant irradiation can be performed after surgery with electron IORT. As the clinical target volume to be irradiated is very small (2-3 cm diameter, 3-5 millimeter thickness) contact x-ray using 50 kV photons is an attractive approach.

Materials/Methods: In 2006 three patients with the diagnosis of extensive in situ ductal carcinoma of the breast were treated in CAL. Age : 65, 45, 42 years, extensive microcalcifications on mammography, in situ carcinoma proven on macrobiopsy, breast size : 85-90/A-B. Surgery performed was a total mastectomy with skin envelope and nipple areola plaque preservation, and with sentinel node excision. IORT was performed with 50 kV contact x-ray using a localizer of 3 cm and delivered a dose of 12 Gy into the subareolar area which was in direct contact with the localizer. Irradiation lasted less than 2 minutes. In two cases, a small focus of invasive carcinoma was found on the breast pathological examination with margins R0 in all cases. In one patient a pN1 positive sentinel node was found and a postoperative lymph node irradiation was performed with adjuvant chemotherapy. No other adjuvant treatment was given.

Results: No acute or late complication was related to the contact x-ray IORT. The early cosmetic results was good in all three patients with no side effect of the IORT. So far, the three patients are alive with no evidence of disease.

Conclusions: In well selected cases, in patients with small or moderate breast size, contact x-ray IORT appears as an attractive, easy and safe approach to irradiate the subareolar area in case of nipple sparing total mastectomy.

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CORRELATION OF ACUTE SKIN TOXICITY WITH MEASURED SKIN DOSE FROM MULTI-CATHETER HDR ACCELERATED PARTIAL BREAST BRACHYTHERAPY (APBI)

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Purpose/Objectif: To correlate measured skin doses from HDR multi-catheter interstitial breast brachytherapy with actual acute skin toxicity outcomes.

Materials/Methods: Nucletron Plato and Varian Brachyvision treatment planning systems (TPS) were used to determine the location of potential maximum skin doses on 5 interstitial breast brachytherapy patients. Measurements were made using LiF thermoluminescent dosimeter chips (TLDs) which were placed at 5 locations on the breast surface for one fraction per patient. In 4 patients, the readings were repeated with OneDose dosimeters (MOSFET). Patients were followed for acute skin toxicity.

Results: Five patients received APBI to a dose of 34 Gy in ten BID fractions delivered 6 hours apart. The average number of catheters was 19. The range of skin doses measured for all patients for a single fraction with TLDs was 97.7-347 cGy (mean 245 cGy). The range of skin doses as measured by MOSFET was 108-297.7 cGy (mean 237.8 cGy). TLDs were calibrated with 6 MV photons, and the TLD error was estimated to be 5%. No correction factor was used for the MOSFET.

The TLD skin dose measurements strongly correlated with measurements obtained by MOSFET with an r value of 0.92. The correlation between the TPS with either TLDs or MOSFET was poor with r values of 0.16 and -0.07, respectively. Further analysis revealed that when outlier measurements from heavily sloped breast surfaces were removed, the measured skin doses were within 5% of the TPS predicted doses. No patient had worse than a Grade 2 toxicity with a median follow up of 2 months (1-5 months).
Conclusions: Our treatment guidelines produce a maximum measured skin dose of 347 cGy with acceptable acute skin toxicity. In addition TLDs and MOSFET provide reproducible in vivo skin dose measurements which are highly correlated. The lack of correlation between TPS estimates and actual skin dose measurements is likely from small discrepancies in TLD or MOSFET placement which can result in large errors in regions with rapid dose fall off. The TPS continues to provide the simplest method to review potential hot spots. When measuring skin dose, we prefer MOSFETs as they provide instant dose readouts and are less labor intensive than TLDs. We conclude that maintaining the prescription dose within the skin contour yields acceptable acute skin toxicity in patients treated with multi-catheter interstitial breast brachytherapy.

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PARTIAL BREAST IRRADIATION WITH 192-IRIDIUM IMPLANTS AFTER BREAST CONSERVING SURGERY: UPDATED RESULTS OF THE GERMAN-AUSTRIAN PHASE II-TRIAL

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Purpose/Objectif: To evaluate the effectiveness and safety of interstitial multi-catheter partial breast irradiation after breast conserving surgery in patients with early breast cancer.
Materials/Methods: From 11/2000 through 04/2005, 274 women with early stage breast cancer were entered into a protocol of tumor bed irradiation alone using PDR or HDR interstitial implants. Patients were eligible if their tumor was an infiltrating carcinoma ‹= 3 cm, surgical margins were clear by at least 2 mm, the axilla was surgically staged node negative, the tumor was hormone receptor positive and well or moderately differentiated, the tumor did not contain an extensive intraductal component and the patients age was › 35 years. Implants were positioned using a template guide delivering either 49.80 Gy in 83 hours (PDR) or 32.00 Gy in two daily fractions over 5 days (HDR). Local control, toxicity and cosmetic outcome were assessed.
Results: The median follow-up was 37 (9-75) months. The local control was 99% (271/274). Late toxicity: Grade I and II breast pain 6% (17/274) and 2% (4/274). Grade I hyperpigmentation 4% (11/274). Grade I, II, and III breat tissue fibrosis 13% (35/274), 9% (25/274), and 0,4% (1/274). Grade I, II, and III telangiectasia 11% (31/274), 4% (11/274), and 2% (4/274). Good-to-excellent cosmetic results have been observed in 95% (260/274) of the evaluated patients.
Conclusions: This analysis underlined the safety and effectiveness of partial breast irradiation in a carefully selected subgroup with favourable disease characteristics. Of course, longer follow-up and randomised trials are necessary to conclusively assess the potential of partial breast irradiation.

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PARTIAL BREAST IRRADIATION WITH ACCELERATED ENDOCAVITARY BRACHYTHERAPY AND PERSISTENT SEROMA; EXPERIENCE OF A SINGLE INSTITUTE

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Purpose/Objectif: To investigate the incidence of seroma formation after intraoperative placement of the Mammosite catheter for accelerated partial breast irradiation and possible factors associated.
Materials/Methods: This study evaluated from March 2004 to September 2006, 35 patients (pts) who had undergone intraoperative balloon catheter placement at lumpectomy for accelerated partial breast irradiation. Eligibility requirements included the following: age›40 years, mammographyc documentation, tumour≤ 2cm, invasive or in situ ductal histology and all nodal status. Timing procedures of the treatment with Mammosite were: 1st and 3rd day CT-evaluation of the balloon position, status and geometry of the cavity; on 1st day RX standard for 2D/3D treatment planning and on 2nd,4th and 5th for medical choice. After completion of brachytherapy pts were seen every 3 months by their radiation oncologist and baseline mammography/CT scan 6 months after and yearly thereafter. Seroma was verified by clinical examination and CT-evaluation in our Institute. Persistent seroma was defined as seroma that was detectable [3] 6 months after radiotherapy completion. Clinical and treatment related factors were analyzed: patient age, patient weight, history of diabetes, rescission, interval between surgery and radiotherapy, total duration of catheter placement, presence of post radiotherapy infection and concomitant chemotherapy/ormonotherapy.
Results: Local control (median follow-up 16 months): 100%; Seroma appears in all patients but the persistent seroma at 6 months occurred in 23 (65.7%) of 35 pts and after 1 year appears in 15 (42.8%) of 35. Analyzing clinical and treatment related factors: 11 pts‹60y, 12pts›60y with persistent seroma, 0/1pt with diabetes, 0 rescission, 3 days interval between surgery and radiotherapy for all pts and 8 days total duration of balloon placement. One pt with postprocedural infection and concomitant chemotherapy without persistent seroma. A factor correlated positively with the risk of persistent seroma formation is patient weight. Formation of small air zones between tissue and balloon during the positioning procedure is not correlated significantly with seroma formation but is correlated with the time of reduction.
Conclusions: Partial breast irradiation with accelerated endocavitary brachytherapy is associated with the formation of seroma which is positively correlated with patient weight and positioning procedure of balloon.

Gynaecological Tumours

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3-D OPTIMIZED PDR BRACHYTHERAPY FOR CERVICAL MALIGNANCIES: ECONOMIC ASPECTS OF A FRENCH PROSPECTIVE MULTICENTRIC STUDY

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Purpose/Objectif: A prospective multi-centric comparative non randomized study was launched in France in 2005 by the French National Cancer Institute to assess the medico-economic outcomes of an innovative brachytherapy (BT) modality for cervical carcinoma–3D imaging optimized pulsed dose-rate (PDR) brachytherapy (3D PDR)–compared with standard procedures: low dose rate (LDR) Iridium BT (Ir BT); Cesium BT and standard PDR without 3D-optimization, as to obtain objective data for decision making to implement and found this innovation in France. The main economics outcomes are presented.

Materials/Methods*:* The hospital point of view has been adopted, with a micro-costing approach for the direct medical costs. The cost items have been recorded within (1) a "centre questionnaire" (including description of investments for LDR and PDR after-loading unit(s); brachytherapy activity; experience for the innovation...); (2) a "patient questionnaire" (individually measurements of personnel time consuming and consumables and investments requirements for the whole procedure); (3) an industrial questionnaire (investment and radioactive sources costs). The mean costs for the BT procedures have been calculated for the "in routine phase" for each step of the procedure (operation; imaging, treatment planning and irradiation) and according to each cost items (personnel, equipment, consumables…).

Results*:* From January 2005 to December 2006, 18 and 460 centre and patient questionnaires respectively were available for the analysis. A mean number of 24 PDR BT procedures per after-loading unit and per year was observed in 2005. The main costs components for the mean cost per patient for the PDR procedures were the Iridium source (1053€) and the after-loading unit (734€). The mean cost per patient for the imaging and the treatment plan for the 3D PDR were respectively 130€ and 367 € (respectively 47 and 75€ without 3D optimization). The cost differential between the 3D BT and the Ir BT (the least costly procedure) was 2100€ per procedure. This overcost could be reduced to 983€ with a hypothesis of a mean number of 40 PDR BT per after-loading unit and per year. However, a mean 10 years life duration of the projector compared to a 15 years value used for the cost calculations would lead to a 356€ increase of the total cost per procedure. The analysis of the French DRGs for cervical brachytherapy showed that the operative, imagery and treatment planning observed costs were correctly evaluated whereas equipment and Iridium sources were widely underestimated.

Conclusions: The observed costs in this large prospective multi-centric series combined with the medical outcomes data may be used by health authorities as a basis to propose a specific DRG for 3D optimized PDR brachytherapy, in order to assure a medico-economic relevant diffusion of this technique.

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5 YEAR SURVIVAL DATA FOR CANCER OF THE CERVIX USING A HIGH DOSE RATE IRIDIUM 192 AFTERLOADER

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Purpose/Objectif*:* The purpose was to measure 5 year survival for patients diagnosed with cancer of the cervix using hdr afterloader since treatment began in 1995.

Materials/Methods*:* A high dose rate (hdr) afterloader used Iridium 192 (Varisource, Varian UK). Patients had previously received external beam and or chemothereapy. Fletcher Suit Delcos applicators were inserted under general anaesthetic. Two fractions of 7.5 Gy, one week apart,to the mean of the dose to points A,were prescribed. An optimized treatment plan using Cadplan BT (Varian UK) was produced and executed.

Results:
5 year survival data are caluclated. These are:
all patients 54%, radiotherapy alone 42%,
combined chemoradiotherapy 66%,
stage 1 and stage 2 combined 62%,
and,finally, stage 3 and 4 combined 36%.

Conclusions: These data compare well with data published in 2000 of 40% from a UK study and 55% from a European (FIGO) study. The implications of the ESTRO 2006 GYNAE Recommendations are included. The future of the hdr service and its replacement is outlined.

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ADJUVANT HIGH-DOSE-RATE IR-192 VAGINAL BRACHYTHERAPY FOR ENDOMETRIAL CANCER: OUR INITIAL MISGIVING IN DOSE SPECIFICATION AND OPTIMIZATION FOR VAGINAL CYLINDERS APPLICATORS.

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Purpose/Objectif: The most frequent site of first relapse after hysterectomy in high-risk patients diagnosed of endometrial cancer is the vaginal vault. Adjuvant brachytherapy is effective to reduce local relapse. In our institution, we started the high dose rate (HDR) brachyherapy treatments in June 2005. In post-operative vaginal brachytherapy (PVB) three questions appeared: 1) what is the length of clinical target volume (CTV); 2) dose specification: vaginal surface (VS) or at 0,5 cm depth of vaginal surface (0,5-VS)?; 3) dose optimization: lateral vaginal wall (straight portion of the cylinder) or both curved portion of the cylinder dome and the lateral wall?.

Materials/Methods: Data of our first 75 treated postoperative endometrial cancer patients were analysed. In order to determine the length of the CTV, that, in our criteria, it does not have to be greater than the superior third of the vagina, the vaginal length (apex/introitus) was measured in each patient. The dose distribution for varying vaginal cylinders diameters (2–3.5 cm) and varying CTV lengths (3–5 cm) were estimated using a PLATO planning software (Nucletron) for a HDR Ir-192 source (Microselectron) and the dose prescription at VS and at 0,5-VS were analyzed. Two methods of dose optimization were studied: a) only in the lateral portion of the cylinder (lateral optimization, LO) or b) in the apex, curved and lateral wall of the cylinder (total length optimization, TO), taking equidistant points of the cylinder surface, with the aim to give the same weight to the lateral points to those of the cylinder dome.

Results: The measured lengths of the vaginal superior third oscillated between 2,8-4,6 cm. The length of the CTV varies according

to the specification criteria (VS/0,5-VS). Prescribing and optimizing the dose in VS and LO, the mean deviation of the points in SV of the curved part of the cylinder, with respect to the prescribed, go respectively from -23,98% (Ø=2 cm; CTV=5 cm) to +6.42% (Ø=3,5 cm; CTV =3 cm). For TO varies from–1,10% (Ø=3,5 cm; CTV=5 cm) to -0,41% (Ø=2 cm; CTV=3cm). If the prescription and optimization is made to 0.5-SV, the mean deviation of the points of the SV in the curved part of the cylynder, for the TO, respectively goes from a +14,31% (Ø=2 cm; CTV=5 cm) to a +7,40% (Ø=3,5 cm; CTV=5 cm).
Conclusions: In response to our initial questions: 1) vaginal lengths between 3 and 5 cm correspond with the length of the CTV in PVB of endometrial cancer. 2) With TO and prescribing in SV a greater homogeneity of the dose in all the points of the SV is obtained, for all diameters of cylinders and all lengths of treated vagina with respect to the prescription and the optimization to 0.5-SV. 3) With TO a better distribution of dose in all points is obtained (as much in the SV as those of 0.5 cm) for all diameters of cylinders and all lengths of treated vagina with respect to LO.

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ADJUVANT RADIOTHERAPY IN EARLY STAGE ENDOMETRIAL CANCER: THE CASE OF STAGE IB

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Purpose/Objectif: monitor the outcome of patients given adjuvant radiotherapy for stage IB endometrial cancer.
Materials/Methods*:* the database of our Centre was analysed for patients diagnosed for endometrial cancer between January 2002 and December 2006.
Patients eligible for monitoring had to fulfil the following criteria: treated with total abdominal hysterectomy and bilateral salpingo-oophorectomy, pathologic diagnosis of stage IB (FIGO) endometrioid endometrial carcinoma, assessable follow-up.
Results: Sixty-one patients treated for endometrial cancer, stage IB, were present in the database.42 patients fully fulfilled the criteria required to enter this study. Mean age at diagnosis was 60 (range 40-79 years). Mean follow-up was 29 months (range 2-56 months). The tumour was a grade 2 in 29 cases and a grade 3 in 13 cases. Pelvic lymphadenectomy was not carried out routinely in the cases reviewed. G2 tumours were given hypofractionated high-dose rate (HDR) vaginal vault brachytherapy (BRT) only (21 Gy/3 fractions/10 days). Dose was prescribed to the depth of 0.5 cm from the applicator surface. For G3 tumours an external beam radiation therapy (EBRT) course on the pelvis was delivered to the total dose of either 46 Gy/23 fractions or 45 Gy/25 fractions . This encompassed common and internal iliac nodes and tumour bed and was covered with a four-field "box" technique. For G3 tumours, EBRT was followed by a single fraction of HDR BRT to the dose of 5 Gy, with the same dose prescription described above. No patient recurred either locally or at distance. When considering tolerance, one patient suffered from an acute haemorragyc cystitis, leading to treatment interruption. No long-term gastro-intestinal or genito-urinary › G1 was describe, but vaginal stenosis was common.
Conclusions*:* Whilst surgery remains the mainstay for stage IB endometrioid endometrial adenocarcinoma, the best standard of radiotherapy required is still controversial . As cure rate is high, potential acute and long-term side effects must be counterbalanced. We reported a favorable cure rate with an acceptable toxicity. Length of follow-up and lack of a control arm prevent us from advocating a sure benefit with our treatment policy. Briefly, we believe that exclusive HDR BRT for IBG2 and EBRT plus HDR BRT for IB G3, when pelvic lymphadenectomy is not carried out, could be safely proposed as a standard of care.

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BRACHYTHERAPY WITH 192IR- HDR LIKE ADJUVANT TREATMENT FOR PATIENTS WITH EARLY ENDOMETRIAL CANCER

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Purpose/Objectif: Assessment of the results gathered from the192 Ir–HDR Vagynal Brachytherapy performed on patients with I A stage(FIGO) endometrial carcinoma after total abdominal hysterectomy and bilateral salpingo- oophorectomy (TAH-BSO)
Materials/Methods: Between the years of 2001and 2006 398 patients were treated. All of which had I A stage(FIGO) pathomorphologycally well differentiated endometrioid adenocarcinoma with depth of myometrial invasion less than 1/3. The treatment was started between 20-80 days after surgery. The Vagynal Brachytherapy was performed by192 Ir – HDR using Nucleation's Microselectron unit. Between 6-8 sessions by 5 Gy per fraction at 5 mm tissue depth was carried out once a week. The Planning treatment volume was defined individually using Nucleation's (UPS version 10-20) computer planning system based on AP and Lateral localisation X- ray films. Doses of organs at risk were estimated by in vivo dissymmetry performed using LiF capsules placed in the Foley catheter for the bladder and rectal probe for the rectum.
Results*:* Early and late treatment reactions were seen, and the doses delivered at organs at risk were assessed. The patients were monitored for local recurrences. 98% of patients have 5 year surveillance and 2.56 recurrences were seen. The early and late radiobiological reactions were estimated by SOMA-LENT scale. In which 24.8% of the patients had Grade 2, 55.7% had Grade 1 and 19.5 had Grade 0 /according to SOMA/Late toxicity was established in 31 patients- 12 of which had late proctitis 4 years after treatment and 19 had late cystitis three years after treatment
Conclusions*:* Postoperative Vagynal Brachytherapy with 192Ir- HDR has its own important place in the treatment of patients with I A stage(FIGO) endometrial carcinoma after total abdominal hysterectomy and bilateral salpingo- oophorectomy (TAH-BSO). By performing this treatment the late complications were reduced and local control was increased

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CERVICAL RING BRACHYTHERAPY FOR URGENT HAEMOSTATIS. A REVIEW OF THE JOHANNESBURG EXPERIENCE

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Introduction: Johannesburg Hospital Radiation Oncology Department treated about 630 cervical cancer patients in the year 2005 with a similar number estimated in 2006. In addition these patients tend to present at a more advanced stage than in developed countries; with about half at stage three or higher at first presentation and the waiting times to start definitive treatment has been up to six months. As a result acute haemorrhage in untreated patients had required urgent intervention occurred fairly commonly.
Treatment Review: Brachytherapy with a ring only to the tumour with a prescribed dose of 5 Gy at 5 cm on two consecutive days is a recognised treatment option (1) for patients who have not responded to more conservative measures and may obviate the need for more aggressive surgical intervention. Its efficacy is, however still subject to review (1).
Study: We present a retrospective review of thirty-two patients treated with a ring applicator only for acute haemorrhage from a

cervical carcinoma from 1st January 2006 to 31st January 2007. The patients were analysed for efficacy only, as defined by a cessation of bleeding within three weeks of the intervention, but are broken down according to age, histology, stage and compliance. Only four failed treatment and six others failed to comply giving a success rate of 86%. This strongly supports using this method, in particular to avoid more invasive and costly interventions that may be rendered unnecessary. Further sub analysis as to its efficacy in relation to other parameters may well be justified.

Reference:

1. Grigsby P.W. et al. High dose rate cervical ring applicator to control bleeding from cervical carcinoma. Int. J. Gynaecol. Cancer 2002, 12, 18-21.

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COMBINED IMRT AND HDR BRACHYTHERAPY FOR CERVICAL CANCER: A DVH ANALYSIS

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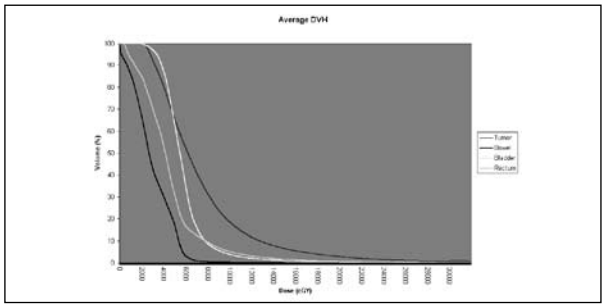
Purpose/Objectif*:* We combined intensity modulated (IMRT) and brachytherapy (BT) treatment plans to determine dose delivered to pelvic structures in patients treated for cervical cancer.

Materials/Methods*:* We evaluated the IMRT and BT treatment plans for eight patients with stage I-III cervical squamous cell carcinoma treated with radiochemotherapy. The IMRT plan was generated after PET/CT simulation. IMRT planning delivered 50.4 Gy to the pelvic lymph nodes (PLN) and 20 Gy to the cervical tumor. Patients were treated with six weekly high-dose-rate (HDR) BT insertions with tandem and ovoids (T&O), each delivering 650 cGy to point A . After each T&O insertion and prior to BT administration a BT treatment planning CT (BCT) was obtained with the patient in their IMRT treatment position. The brachytherapy treatment plan was generated with BrachyVision for each HDR treatment. Each BCT was fused to the IMRT plan using pelvic bones for alignment and a summation plan was generated. We reviewed cervical tumor, rectal, bowel and bladder dose distributions of the summation plan. A dose volume histogram was generated for each patient and the data were summed to attain a mean DVH for all patients. Spearman rank test was used.

Results*:* Each of the eight patients had six HDR BT implants and completed IMRT as prescribed. A DVH for the mean cervical tumor, rectal and bladder doses for the summed IMRT and BT treatments was generated (see figure). Seven patients experienced acute grade one diarrhea. There were no acute bladder complications. There was no significant difference in acute side effects based on dose delivered to bowel, bladder or rectum on combined plans. Two patients had residual uptake on PET at six-week follow-up.

Conclusions: Combined IMRT and HDR treatment planning is feasible for patients treated definitively for cervical cancer with radiochemotherapy. Summed IMRT and HDR DVH analysis can be performed.



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CONFORMAL VAGINAL BRACHYTHERAPY USING THE HDR MULTICHANNEL VAGINAL APPLICATOR.

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Purpose/Objectif*:* Vaginal lesions in stage 3b and recurrent endometrial carcinomas and cervical carcinomas, and primary vaginal carcinomas are amenable to local treatment with intravaginal brachytherapy. The multi-channel vaginal applicator (Miami Applicator™, Nucletron) allows dose optimisation to the area of interest. The additional outer sleeves assist in reducing the surface dose. The results of treatment in ten patients are presented.

Materials/Methods: Ten patients have been treated since March 2006; three with primary cancers of the vagina; one with stage 3b cancer of the endometrium and six with recurrent cancers of the endometrium. Patients are examined under conscious sedation (intravenous Midazolam and Fentanyl) and when possible stainless steel markers are inserted to delineate the area of disease. The dimensions of the disease and the vaginal length and diameter are recorded. The patients then undergo a CT scan (2.5mm slices) with the applicator in place. The target volume is defined together with the OAR (rectum and sigmoid). The target volume is defined at 5mm from the surface of the applicator in those patients with surface disease, and at 10mm in those with palpable disease. In those patients treated with radical vaginal brachytherapy the dose prescription is 42Gy @ 5mm from surface in 6#, 2# per week to the high dose volume (disease with 3cm margin) and 28Gy @ 5mm from surface to the low dose volume (rest of vagina with sparing of the lower vagina and introitus if possible). In those who have received pelvic radiotherapy to a dose of 45Gy in 25#, the prescription for the vaginal brachytherapy boost is 20Gy @ 5mm from surface in 4#, 2# per week to the high dose volume, and 12Gy @ 5mm from surface to the low dose volume. Dose optimization was performed to achieve a V100 to the high dose volume of 90% and to the low dose volume of 95%, while observing the cumulative dose volume constraints (EBRT+BT) of the D2cc rectum and sigmoid to Diso (2Gy equivalent) ‹ 75Gy (a/b = 3Gy).

Results*:* Median follow-up is seven months (3-11 months).Three patients had palpable disease between 5mm and 10mm and achieved complete resolution of disease within three months of completing treatment. All patients are disease free at the time of last follow-up (three monthly). Treatment is well tolerated with no serious acute or long term side effects.

Conclusions: The multi-channel vaginal applicator allows conformal vaginal brachytherapy with dose optimization to the target volume and dose limitation to OAR.

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CONVENTIONAL INTRACAVITARY BRACHYTHERAPY WITH SIMULTANEOUS APPLICATOR-GUIDED IMRT BOOST FOR 3-D IMAGE-BASED BRACHYTHERAPY : NOVEL APPROACH FOR IMPROVING CERVICAL TUMOR DOSE COVERAGE

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Purpose/Objectif*:* Our image-based treatment planning study confirmed that the pear-shaped dose distribution of conventional high-dose-rate (C-HDR) brachytherapy often fails to cover the entire gross tumor volume (GTV), especially in large volume tumor. Dosimetric study of cervical cancer demonstrates that intensity-moduated radiotherapy (IMRT) can improve GTV coverage. However, there is a concern that IMRT is unable to deliver significantly high doses in the

center of GTV which is a typical dose distribution for intracavitary brachytherapy (ICBT). This presentation is to evaluate our novel approach which maintains C-HDR but adding simultaneous applicator-guided IMRT (AG-IMRT) boost to the area of under dose by C-HDR.

Materials/Methods*:* Six patients with cancer of the uterine cervix (3 IB2, 3 IIB) received whole pelvic irradiation of 45 Gy and underwent C-HDR brachytherapy. CT and MRI images of the pelvis were done with plastic HDR applicators in place. For dosimetric study, we replicated the C-HDR plans in 3-D treatment planning system. GTV and organs at risk (OARs) were outlined on the CT images with the assistance of MR images. CTV was defined as GTV with 3 mm margin (GTV+) plus the uterus. The four plans (C-HDR, Optimized (O)-HDR, IMRT alone, C-HDR/IMRT boost) were compared by dose-volume histograms. For the C-HDR/IMRT boost technique, the C-HDR plan was modified to reduce the bladder and rectum dose below 80% of the prescription dose and IMRT boost plan was subsequently optimized based on the HDR dose to compliment the dose coverage of CTV. To preserve anatomy from deformation, the IMRT boost plans would be delivered immediately following HDR treatment with applicator in place. The percent volume receiving 95% of prescription dose was used to evaluate CTV coverage, and the minimum doses in 2.0 cm3 volumes receiving the highest dose (D2) were calculated to compare doses to OARs.

Results*:* C-HDR failed to provide adequate tumor coverage (53% average tumor coverage). The O-HDR, IMRT, and C-HDR/IMRT techniques yielded substantially improved tumor coverage: 98%, 95% and 100%, respectively. However, the O-HDR technique resulted in unacceptably high average D2 dose to bladder, rectum and bowel. The IMRT and C-HDR/IMRT boost plans both provided sufficient sparing to the bladder, rectum and bowel. However, the C-HDR/IMRT boost technique provided significantly higher integral tumor dose than IMRT alone.

Conclusions*:* Our novel approach, integrating C-HDR with simultaneous applicator-guided IMRT boost, provides excellent tumor coverage while maintaining conventional ICBT dosimetry with reasonably low doses to OARs.

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HDR CERVIX BRACHYTHERAPY: DOES INTRA-OPERATIVE ULTRASOUND (US) HELP?

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Purpose/Objectif: The availability of CT/MRI compatible applicators for cervix brachytherapy has allowed for many advances in treatment planning. Unfortunately, computer-assisted treatment planning based on 3D imaging cannot correct geometrically unfavourable intracavitary implants. To take full advantage of sophisticated imaging and planning tools, the assessment of applicator positioning prior to leaving the operating room is needed. An imaging modality such as US is readily available in most departments and allows real-time visualization of applicators relative to adjacent structures. We prospectively implemented the use of trans-abdominal US guidance to assess the following: 1) Does intra-operative US guide the accurate placement of the tandem (minimizing risk of perforation) within the uterine cavity? 2) Does direct visualization at the time of insertion influence the specifics (length, angle) of the tandem used? 3) Is routine use of US feasible without radiology consultation?

Materials/Methods: Twenty-six insertions were performed in 15 women between July 2006 and January 2007. The bladder was instilled with 200cc of normal saline for better visualization of anatomy. Cervical dilation, tandem selection and subsequent insertion were guided by trans-abdominal ultrasound (Restitu, Resonant Medical). Final placement of the applicator system was also confirmed by US. We used CT imaging for treatment planning, to measure perforation rates and assess applicator suitability for given anatomy. The benefits of US were also measured in terms of overall insertion time and requirement of assistance from gynecologic surgical oncology.

Results: Dilation of the cervix and intrauterine tandem insertion was successfully guided by US in all procedures (26/26). CT imaging confirmed accurate placement within the uterine cavity compared with a historic institutional perforation rate of up to 10%. Visualization of patient anatomy during the procedure aided in the selection of suitable tandem length and angle in 46% of cases and resulted in more optimal applicator selection and placement. The average insertion time has not significantly changed (decreased from 34 to 26 minutes (p=0.17)). Request for assistance by gynecologic surgical oncology has declined from 38% to 7.7% of procedures. The use of US has been successfully implemented with staff and equipment from radiation oncology.

Conclusions: The use of trans-abdominal US is feasible in the application of cervix brachytherapy. It provides real-time feedback for accurate intrauterine tandem placement and aids in the selection and positioning of applicators. By essentially eliminating the risk of uterine perforation, there is less risk of prolonging overall treatment time and OR time is used more efficiently. Geometric improvements in applicator positioning may lead to enhancements in the therapeutic ratio. The efficient use of trans-abdominal ultrasound is applicable to a radiation oncology department, without assistance from diagnostic radiology.

101 poster

INTERSTITIAL BRACHYTHERAPY: MUPIT TRANSPERINEAL IMPLANT. RESULTS AND TOXICITY ANALYSIS

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Purpose/Objectif: Pelvic tumors are not an exceptional situation of the Radiotherapy Departments. When the surgery has been rejected, the radiotherapy remains as the unique option of treatment in these patients. Over the time, the brachytherapy has been essential in these cases; mainly with endocavitary treatments, due to its capacity of irradiate with high doses avoiding dose limiting structures. But in several situations, the transperineal approach with CT imaging for the dosimetry are preferable, because of its better dose distribution and more capacity of volume to be reached. The purpose of this study is the toxicity.

Materials/Methods: From Sep 2004 to Feb 2007, 9 patients have been treated for pelvic tumors using the template "Martinez Universal perineal interstitial template" (MUPIT) guide for high dose rate brachytherapy (HDRB). 2 males & 7 females. Median age was 63 years (range 37–77 years). Two patients of gastrointestinal origin (rectal cancer and anal canal), six ginecologic malignances (cervix) and one vagina metastases from a clear cell kidney tumour. In all patients the MUPIT implant was part of the primary treatment. The indications for the Mupit in the gynecological cases have been: bulky cervical with or without vaginal affectation, parametrial involvement, geometrically unfavorable anatomy or macroscopic disease on the cervical stump.The implant was made with epidural anesthesia. We have done in all cases a CT imaging following needle implantation to identify tumor volume and critical normal structures, dose optimization was performed keeping care on hot volumes in relation with prescribed dose. All the gynecological patients have been treated with 6 fractions of 400 cGy, twice a day. The median of previous external beam radiotherapy dose have been 5000 cGy (4500 – 5040 cGy). The patient with an vaginal recurrence of a clear cell adenocarcinoma of kidney was treated exclusively with HDR brachytherapy with 6 fractions 450 cGy. The patient of the rectum adenocarcinoma received 8 fractions of 300 cGy after 25 Gy (5x500 cGy) and 30.6 (180 cGy) administrated in another hospital. The pa-

tient with the canal anal tumor received 3 fractions for 300 cGy after 66 Gy (180 cGy) with external beam radiotherapy.
Results: The acute toxicity side effects were scored according to RTOG/EORTC scoring system. The 6 patients treated with gynecological tumors have had asymptomatic vaginitis grade 2 one month after the implant. The patient with a vaginal recurrence had vaginitis grade 3 controlled with analgesia. The two patients with gastrointestinal tumors had proctitis grade 2 needing narcotic analgesia and topic treatment. All these side effects were recover 1.5 months after the implant.
Conclusions: Interstitial transperineal approach with CT based dosimetry, represents an elective technique with better dose distribution in bigger volumes, achieving more adaptative treatments.

102 poster

INTERSTITIAL HDR BRACHYTHERAPY AND 500KHZ HYPERTHERMIA COMBINATION FOR CERVICAL CANCER PATIENTS. A PHASE I/II STUDY.

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Purpose/Objectif: Intracavitary brachytherapy (ICBT) is a treatment of choice in advanced cervical cancer (CC). However, in many cases it is not possible to take advantage of this modality due to unsufficient tumor regression after initial external beam iradiation and chemotherapy (RT/CT). Interstitial approach (ISBT) makes brachytherapy possible in such a patients. Hyperthermia has a proved effectiveness in CC radiotherapy. Thus a combination of ISBT and hyperthermia seems to be a promising treatment option.
Materials/Methods: From 2004 to 2006 44 advanced CC patients (FIGO stage IIb-IIIb) unfit for ICBT due to a lack of sufficient regression after standard RT/CT or expected poor ICBT dose distribution. ISBT was performed using intrauterine probe and 2-6 interstitial metal needles (depending on the tumor size)inserted into the cervix and, if necessary into the parametria. The same applicators were used both for brachytherapy and hyperthermia. Radiofrequency hyperthermia treatment was performed for 45 minutes during every ISBT. Total dose of ISBT was 20Gy/4 fr (after 64Gy/32fr RT/CT) or 30Gy/4fr (after 46Gy/23fr RT/CT). Temperature was measured by a set of 3 thermocouples inserted into the applicators (intracavitary and interstitially).
Results: No case of treatment intollerance was detected. Temperature of over 42,5 oC (up to 49 oC or up to patient's temperature tollerance limit) was mantained during the whole hyperthermia session in every case. Excellent local control in 40/44 (90%) cases was observed. Follow up time was 7- 26 months (median 18 months)
Conclusions*:* Concurrent ISBT and radiofrequency hyperthermia is a well tollerated, simple and effective treatment of advanced CC patients. A randomized trial based on results of this study was started in November 2006.

103 poster

INTERSTITIAL PULSED-DOSE-RATE BRACHYTHERAPY IN TREATMENT OF VAGINAL ENDOMETRIAL CANCER RECURRENCE

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Purpose/Objectif*:* Interstitial PDR brachytherapy has been the preferred method of treatment for patients with vaginal recurrences of endometrial cancer at our institution since 2001.
Materials/Methods: Between 2001 and 2006, 22 patients with endometrial cancer were treated with interstitial PDR brachytherapy. Median age at recurrence was 71 years (range 47-83). According to the FIGO stage classification the diagnoses were: IB-2, IC-7, II-7, III-5, IV-1. There were adenocarcinoma endometriale histological grades: G1-6, G2-10 and G3-6. 10 patients had received prior external irradiation and the vaginal recurrences were diagnosed 2-53 months after the primary treatment. Remaining 12 of 22 patients with locally advanced endometrial carcinoma were treated with PDR brachytherapy in combination with external beam radiotherapy. In this group of patients vaginal recurrences were diagnosed before the start of irradiation. All patients received whole pelvis external beam radiation therapy in a box technique at a linear accelerator to a total dose of 40-50Gy, followed by interstitial implantation. Eight patients had suburethral recurrences and fourteen in the lower two-thirds of the vagina. The size of mean tumor was 3.2cm (range 0.5-7cm). Median total prescribe dose was 35Gy (range 30-40Gy) to the implant volume with interstitial in 2-3 applications, at a dose rate of 1Gy per pulse for an hour. This study analysed toxicity and preliminary result of PDR interstitial brachytherapy treatment.
Results: The follow-up period for patients group is 2-60 months, with a median 20 months. Complete response was achieved in 19 (86.4%) patients with 3 patients having persistent disease. Ten (45%) patients came into complete remission. Seven (31.8%) of these 19 patients developed recurrences at a time of 4-36 months–4 developed distant metastasis (2 in paraaortic area, 1 in lung, 1 in spine) and 3 local recurrences. Two patients failed to follow-up 4-6 months after the treatment. No patient had acute Grade 3 or 4 morbidity. In 12 patients acute vaginitis and in 9 patients urinary toxicities Grade 1 (5 pt.) and Grade 2 (4 pt.) were noted. Using the RTOG late radiation morbidity scoring criteria, there were no Grade 3 and 4 complications.
Conclusions: PDR interstitial brachytherapy is a safe and effective method of the treatment of local endometrial recurrences in vagina.

104 poster

ON BEHALF OF THE « STIC PDR » GROUP. PRELIMINARY RESULTS OF A PROSPECTIVE MULTICENTRIC FRENCH STUDY OF PDR 3D BRACHYTHERAPY FOR CERVIX CARCINOMA : PATIENTS TREATED BY EXTERNAL BEAM THERAPY AND BRACHYTHERAPY FOLLOWED BY SURGERY.

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Purpose/Objectif: In 2005 a French multicentric non randomized prospective study ("STIC PDR*") was initiated to compare 2 groups of patients treated for cervix carcinoma according to brachytherapy method. For the first group of patients (2D group), dosimetry was performed on orthogonal X Rays; for the second group (3D group) dosimetry was planned on 3D imaging and performed with Pulsed Dose Rate Brachytherapy. The study will end after 2,5 years accrual and the enrollment of 850 patients, half in each group. 850 patients, half in each group. This study describes the first 262 patients treated by external beam therapy (EBT) and brachytherapy (bT) followed by surgery.
Materials/Methods*:* Clinical data are available for 262 patients: 122 in the 2D group, 140 in the 3D group. The 2 groups were comparable in terms of clinical presentation: respectively 83 and 76% were squamous cell carcinomas, 17 and 22% adenocarcinomas; 30% of patients presented with stage I disease, 60 and 53% with stage II disease, and 10 and 13% with stage III disease; 36 and 43% had pelvic adenopa-

thies on CT scan. Respectively 28 and 34% of the patients had a pelvic lymphadenectomy performed at time of diagnosis; 26 and 19% positive nodes were found among them. EBT was performed as first treatment, followed by brachytherapy, and then by surgery. In both groups, ICRU bladder and rectal points were drawned; "isodose 60 Gy" corresponded to 60–EBT dose; the volume of isodose 60 Gy was measured ; in the 3D group, CTV volumes were delineated according to GEC ESTRO recommendations (High Risk CTV (HR CTV) and Intermediate Risk CTV (IR CTV)), as were the external wall of the organs at risk (bladder, rectum and sigmoid); cumulative DVH were performed on CTV and organs at risk. The dose to 100% (D100) and 90% (D90) of CTV and the Volume of CTV receiving 60 Gy (V60) were analysed.

Results: More than 90% of patients in the 2 groups received irradiation limited to the pelvis; the median dose delivered was 45 Gy in 25 fractions. More than 92% of the patients received concomitant chemotherapy consisting in weekly cisplatyl most of the time. Brachytherapy Data are available for 157 patients (51 in the 2D and 106 in the 3D group). Results are comparable between the 2 groups in terms of isodose 60 Gy volume (123 and 130 cc respectively), dose to ICRU bladder point (13 and 12,5 Gy respectively) and rectal point (15 and 16,5 Gy); TRAK was a little higher in the 3D group (85 vs 122 Gy.cm2). In the 3D group, for a median prescription of 15 Gy, median D100 and D90 for HR CTV were 12 and 18 Gy respectively; V60 was 97%. For IR CTV median D100 and D90 were 8 and 14 Gy respectively; V60 was 85%. Median dose delivered by bT to 2cc of bladder was 16 Gy, and to 2cc of rectum was 12 Gy. Surgical data are available for 130 patients; 80% had a colpohysterectomy, associated with pelvic lymphadenectomy in 72 and 57% of the cases respectively in 2D and 3D groups; 15% in the 2D group and 6% in the 3D group had pelvic positive nodes. The same proportion of patients had a complete cervical pathologic remission in the 2 groups (51 and 54%). After surgery pathologic data were available for 39 patients in the 3D group; 24 were in partial remission, 15 in complete response. There was no significant difference in terms of coverage of CTV between complete and partial remission in the 3D group.

Conclusions*:* In this series of patients there appears to be no difference in treated volume or pathological remission between 2D and 3D groups. This preliminary experience may correspond to a learning curve during which physicians didn't modify to a large extent their mode of prescription while evolving towards 3D brachytherapy, especially as surgery was scheduled after brachytherapy. *Grant from the French Ministry of Health

105 poster

ON BEHALF OF THE « STIC PDR » GROUPPRELIMINARY RESULTS OF A PROSPECTIVE MULTICENTRIC FRENCH STUDY OF PDR 3D BRACHYTHERAPY FOR CERVIX CARCINOMA : PATIENTS TREATED BY BRACHYTHERAPY FOLLOWED BY SURGERY

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Purpose/Objectif*:* In 2005 a French multicentric non randomized prospective study ("STIC PDR*") was initiated to compare 2 groups of patients treated for cervix carcinoma according to brachytherapy method. For the first group of patients (2D group), dosimetry was performed on orthogonal X Rays; for the second group (3D group) dosimetry was planned on 3D imaging and performed with Pulsed Dose Rate Brachytherapy. The study will end after 2,5 years accrual and the enrollment of 850 patients, half in each group. This study describes the 120 first patients treated by brachytherapy followed by surgery

Materials/Methods*:* Clinical data are available for 120 patients: 63 in the 2D group, 57 in the 3D group. The 2 groups were comparable in terms of clinical presentation: respectively 65 and 60% were squamous cell carcinoma, 30 and 37% adenocarcinomas; 84 and 89% of patients presented with stage IB1 disease; 2 and 3% had pelvic adenopathies on CT scan.

Respectively 37 and 18% of the patients had a pelvic lymphadenectomy performed at time of diagnosis; 17 and 10% positive nodes were found among them. Brachytherapy was performed as first treatment, followed by surgery 4-6 weeks later. In both groups, ICRU bladder and rectal points were drawned; the volume of isodose 60 Gy was measured; in the 3D group, CTV volumes were delineated according to GEC ESTRO recommendations (High Risk CTV (HR CTV) and Intermediate Risk CTV (IR CTV)), as well as the external wall of organs at risk (bladder, rectum and sigmoid); cumulative DVH were performed on CTV and organs at risk. The dose to 100% (D100) and 90% (D90) of CTV and the Volume of CTV receiving 60 Gy (V60) were analysed.

Results:

Dosimetric comparisons

Data are available for 106 patients (51 in the 2D and 55 in the 3D group).

Results are comparable between the 2 groups in terms of isodose 60 Gy volume (102 and 122 cc respectively), dose to ICRU bladder point (28 and 32 Gy respectively) and rectal point (42 and 40 Gy), or TRAK (435 vs 453 Gy.cm2).

In the 3D group, median D100 and D90 for High Risk CTV were 46 and 69 Gy respectively; V60 was 90%. Median D100 and D90 for Intermediate Risk CTV were 34 and 53 Gy respectively; V60 was 78%. Median dose to 2cc of bladder was 61 Gy (30-133 Gy), and to 2cc of rectum 35 Gy (6-67 Gy).

Surgical data are available for 69 patients; 90% had a colpohysterectomy associated with pelvic lymphadenectomy in 69 and 89% of the cases respectively in 2D and 3D groups. 14% in the 2D group and 8% in the 3D group had pelvic positive nodes.

The same proportion of patients had a complete cervical pathologic remission in the 2 groups (57 and 56%).

After surgery pathologic data were available for 39 patients in the 3D group; 24 were in partial remission, 15 in complete response. There is no significant difference in terms of coverage of CTV between complete and partial remission.

Conclusions*:* In this series of small tumors, there appears to be no difference in terms of treated volume or pathological remission between 2D and 3D groups. This preliminary experience may correspond to a learning curve during which physicians didn't modify to a large extent their mode of prescription while evolving towards 3D brachytherapy.

*Grant from the French Ministry of Health

106 poster

PATTERNS OF CARE AND OUTCOME IN ELDERLY CERVICAL CANCER PATIENTS : A SPECIAL FOCUS ON BRACHYTHERAPY

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Purpose/Objectif: The mean age of the general population has been prolonged and the incidence of cancer in elderly patients has increased. The purpose of the present study was to evaluate the efficacy in terms of patterns of failure and outcome, complication rates and survival rates of brachytherapy (BT) as part of treatment in uterine cervix cancer patients.

Materials/Methods: From January 1997 to March 2006, 1073 patients diagnosed with uterine cervical cancer with stage I to IV (FIGO) have completed BT at the Institut Gustave Roussy. Among them, 121 patients were over 70 years old. A retrospective analysis was carried

out with 113 patients treated by conventional low dose-rate (LDR) BT as a part of their treatment. This population was divided into 2 groups: Group 1 with patients 70 to 79 year- old, and Group 2 with patients 80 years and older.

Results*:* The mean age was 74.5 years (ranging from 70.7 to 79.7) in Group 1, and 84.9 years (ranging from 80 to 94.4) in Group 2. More than 80% of the patients presented a squamous cell carcinoma. Fifty-two percent of the patients were treated by a sequence excluding surgery. The BT treated volume was significantly different between both age groups (172 versus 119 cm3). The ICRU bladder and rectal points were strictly equivalent between both age groups and their mean dose values were 30 and 33 Gy, respectively. In Group 1, rectal, small bowel and urinary tract complications assessed at least 6 weeks after completion of BT were observed in 19 (24.1%), in 4 (5.1%), and in 13 patients (16.5%), respectively. In Group 2, rectal, small bowel and urinary tract complications assessed at least 6 weeks after completion of BT were observed in 6 (20%), in 1 (3.3%), and in 3 patients (10%), respectively. With a median follow-up of 3.1 years, 10 patients have developed distant metastases and 10 others local relapses. The 3-year specific overall survival rate is 88.6% and the corresponding disease-free survival rate was 81%.

Conclusions: Elderly women with cervical cancer tolerated BT well and had excellent local disease-free and specific survival rates. Age did not influence the effectiveness of BT in elderly patients and BT should be considered whenever possible, even in elderly patients presenting with a cervix cancer.

107 poster

PREVENTION BY INTRAVESICAL HYALURONIC ACID (CYSTISTAT®) OF ACUTE RADIATION-INDUCED CYSTITIS IN RADIOTHERAPEUTIC MANAGEMENT OF CERVICAL CANCER

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Purpose/Objectif*:* One of the main objectives in the radiotherapeutic management of cervical cancer cancer is to the treatment in a period nonsuperior to 8 weeks, since there is evidence that by every day that surpasses this period of time, there is a 1% of loss in the probability of both tumor response and tumoral control. In this therapeutic strategy is fundamental to avoid and control the appearance of secondary toxicity to the treatment that causes these interruptions. The incidence of acute radiation-induced cystitis (RIC) during treatment varies, in the literature, between 3-6.7%. Concomitant use of chemotherapeutic agents may work synergistically to increase the risk of developing bladder injury from radiation. The treatment with intravesical hyaluronic acid (IV-HA) (Cystistat®) has demonstrated its effectiveness in different forms from interstitial cystitis. We present our initial experience in the use if IV-HA instillations in the prevention of RIC in patients diagnosed of cervical neoplasia and treated with a curative chemo-radiotherapy protocol.

Materials/Methods*:* We presented the preliminary data from the first 14 diagnosed patients of cervical carcinoma treated with curative intention (external beam radiotherapy (EBRT): 46-50 Gy + concomitant (weekly) cisplatinum (40 mgr/m2) chemotherapy; high-dose rate (HDR) brachytherapy: 5,5, Gy x 5 fr) and treated with IV-HA instillations. If posible, we start HDR-brachytherapy in the fourth week of treatment. The day of HDR-brachytherapy, no EBRT or chemotherapy are administred. The IV-HA (40 mg/50 ml, during at least 30 min) schedule treatment consists of: 1) one instillation in the week -1; 2) weekly instillations during EBRT; 3) one instillation on each HDR-brachytherapy applications; 4) a weekly instillation in the following four weeks to the conclusion of the treatment. Overall time of IV-HA treatment: 13 weeks. The scale of vesical toxicity (RTOG/EORTC) was evaluated previosuly to each instillation.

Results*:* No patients developed grade III toxicity. No treatment was disrupted due to bladder toxicity. Four patients developed grade 2 toxicity and 2 patients grade 1 toxicity, all of them when the HDR-brachytherapy treatment was started. All the patients were free of vesical toxicity after the second week of conclusion of treatment.

Conclusions*:* Although these are preliminary results, and prospective studies are necessary to confirm this efecct, in this short serie of patients the use of IV-AH instillations had a protective effect on the vesical mucosa in the prevention of RIC, allowing finalizing the treatment in the scheduled time. In our opinion the treatment must be started from the beginning of chemo-radiotherapy schedule treatment, since the radiation injury takes place already from initial days of the treatment. The study in ongoing in order to have more complete data in the next future.

108 poster

PULSE-DOSE-RATE (PDR) BRACHYTHERAPY COMBINED WITH PET/CT GUIDED INTENSITY-MODULATED RADIOTHERAPY (IMRT) IN PATIENTS WITH LOCALLY ADVANCED CERVICAL CANCER (CCU) AND LYMPHNODE METASTASES.

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Purpose/Objectif: PET/CT in CCU can detect pelvic and paraaortic lymphnode metastases and IMRT allows dose-distributions, which sharply conform to the planning tumor volume with a reduction of dose delivering to critical structures. The goal of this study was to evaluate the feasibility of PET/CT guided pelvic IMRT in combination with concomitant chemotherapy and low-dose PDR brachytherapy in the treatment of locally advanced CCU and to determine the potential impact on acute and long-term toxicity.

Materials/Methods*:* Data of 20 consecutive pts treated between October 2004 and November 2006 for locally advanced CCU and PET positive lymphnodes were analyzed retrospectively. All pts underwent a whole-body scan, using customized immobilization, in a GE Discovery PET/CT scanner and the dose planning was done in Eclipse dose-planning equipment (Varian). GTV, CTV and critical structures were defined on the 3-D reconstruction based on the fused PET/CT images. The IMRT treatment was given as a 5 or 7-fields technique using 6/18 MV photons. 50 Gy/32 F were delivered to CTV and the cervical tumor and 64 Gy/32 F to PET positive pelvic or paraaortal lymph nodes, respectively. Brachytherapy was performed by insertion of a ring- and intrauterine applicator (Nucletron) and delivery of a standard dose plan as 17.5 Gy/10h x 2 / 1 pulse/h, given to point A (BrachyVision,Varian). Pts were treated twice with one week apart on a PDR microSelectron (Nucletron). Prior to the first treatment, the applicator position was controlled on a CT scan. The treatment was combined with concomitant chemotherapy (cisplatin 40 mg/m2/week).

Results: One pt never received concomitant chemotherapy due to unacceptable renal function. Due to hematological toxicity grade 2/3, diagnosed in 15 pts, 76 % of the planned cycles of concomitant chemotherapy were given (87/116). One case of long-term thrombocytopenia has been reported. Overall, 4 pts and 3 pts experienced acute grade 2/3 diarrhea and nausea, respectively. 2 pts had grade 2 abdominal pain and one pt was diagnosed with a recto-vaginal fistula after treatment. By December 2006, 3 pts died of their cancer and 2 pts relapsed 3-9 months after first line treatment.

Conclusions*:* PET/CT guided pelvic IMRT given in combination with concomitant chemotherapy and PDR brachytherapy is generally is feasibly and treatment-related toxicity has been manageable. Sparing bone marrow could be an option to deliver the planned chemotherapy in the curative settings.

109 poster

TWO YEARS EXPERIENCE IN 3D IMAGE-BASED GYNAECOLOGICAL BRACHYTHERAPY: PRELIMINARY RESULTS

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Purpose/Objectif*:* Brachytherapy techniques are nowadays supported by distinct imaging modalities. Images from CT, US or MRI allow the implant reconstruction and the delineation of the target volume and of the organs at risk. The treatment plan evaluation can then be based on calculated dose distributions, dose-volume histograms and dose volume indexes.

The purpose of this work is to present the results of two years experience (2004-2006) concerning the assessment of dose-volume indexes correlated with the organs at risk (bladder and rectum) in gynaecologic HDR brachytherapy implants. It is also our aim to report the preliminary results from patients follow up.

Materials/Methods*:* The gynaecologic HDR brachytherapy implants have been performed using the Standard applicator from Nucletron. The Plato BPS, version 14.2.4., and the microSelectron TCS treatment unit, both from Nucletron, have been used. Since 2004 the treatment plan for each implant is based on a 3D-CT image set, acquired with the patient lying in supine position. The bladder and rectum have been delineated by the physician as OARs. Given the limitations of CT images, the target volume has not been delineated, so the dose was prescribed to points AA, following the rules of Manchester System. The total dose delivered to each of the prescription points is the main criteria for the clinical acceptance of the treatment plan.

Results: Regarding the OARs, the dose-volume indexes reported are: $D_{0.1cc}$, D_{1cc}, D_{2cc}, EQD2 (α/β=3), V_{100} and V_{50}. The dose delivered to points AA, V_{ref} and TRAK were also reported.

33 patients, with uterine cervix epidermoid carcinoma IIB-IIIB (Figo's classification), were treated from 2003 to 2005 with concomitant quimiotherapy (cisplatine) and radiotherapy. The RT schedule was: pelvic RT to 50.4 Gy/28 fr/ 51/2 weeks + BT HDR intrauterine and vaginal 8.5 Gy/2 fr/1 week or pelvic RT to 59.4 Gy/33 fr/ 61/2 week (with field reduction at 50.4 Gy) + BT 7 Gy/2 fr/1 week. The follow-up was 12 months–36 months with clinical evaluation of bladder and rectum (OR) symptoms

Conclusions: The locally adopted methodology has followed the international recommendations for modern brachytherapy techniques. The calculation and report of dose-volume indexes for the OARs has allowed a partial assessment of the treatment plan quality and a more consistent follow up of treatment outcome. It contributes to the establishment of clinical acceptance criteria for treatment plans. Following the GEC-ESTRO recommendations, it is our goal to delineate the target volume. To accomplish this, the acquisition of a MRI unit by our hospital will definitely bring a crucial contribute.

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UTERINE PERFORATION FROM 837 CERVICAL BRACHYTHERAPY IN FRANCE

C. Kerr

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Purpose/Objectif*:* From a "STIC PDR" multi-centric study with 19 French Centers between January 2005 and May 2006 we listed the perforation during the brachytherapy.

Materials/Methods*:* A questionnaire of three pages has been sent to each leader of this stud. First part is to determine practices in gynaecologic brachytherapy of every center:- How long have you been using gynaecologic and PDR brachytherapy?- Do you have an ultrasonograph? Which one? Since when?- Is there a radiologist?Second part of the questionnaire is focused on patients taking part of the "STIC PDR" study which needed imagery 3D (group A-412 women)- How many perforations? When do you note it? What is the TNM state and previous treatment?- What have you done about perforations (brachytherapy, antibiotic, increase of the numer of hospitalisation days?The last part is focused on patients not taking part of the "STIC PDR" study (group B-425 women). In this group dosimetry can be done by using orthogonal pictures in 2D. The same questions than in the second part have been asked.

Results*:* 5/19 Centres have a scan at the brachytherapy department. There were 837 brachytherapy done and 15 perforations have been observed (1.8%).1. T1a2/2T1b1 and 2T1b2/2T2a and 4T2b/3T3b and 1Tx Group A: 8 perforations Group B: 7 perforationsDistribution: 5 notices during the brachytherapy / 8 just a scanner or MRI/ 2 no precise details.Decision:- 5 cancel / 5 modified / realized- 0 surgery but 1 nodes control no realized / 1 hematoma- 5 days ‹ antibiotica ‹ 10 days / 1 treatment less / 4 no precise details.

Conclusions: This study shows no difference in perforatioin number between the 2 groups and no delay for the brachytherapy neither for the way out. For 3 Centres, the use of Misoprostol® 2 days before the brachytherapy allows cervix dilatation and reduce risks of perforation. The scan is a good assistance.3D imaging for the PDR after-loading technique analyse type of perforation (intra uterine muscle or transcervical), position of intestine and make easier the treatment management.

Head and Neck Cancer

111 poster

DOSIMETRIC ANALYSIS OF TREATMENT PLANS FOR THE BRACHYTHERAPY OF THE BASE OF TONGUE

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Purpose/Objectif*:* To make quantitative comparisons between traditional X-ray film and CT based planning in the brachytherapy (BT) of cancer of the base of tongue, and to analyze treatments plans for external boost irradiation (EBI) and brachytherapy of base of tongue cancer regarding dose to normal tissues.

Materials/Methods: Between January 1992 and June 2000 thirty-seven patients with base of tongue cancer were treated with brachytherapy boost. Before interstitial treatment traditional planning with the use of X-ray films (n = 27) or CT based planning (n = 10) was applied. Quantitative analysis was performed to evaluate and compare the plans made by these two methods. For the analysis the V100, V150, DNR (dose non-uniformity ratio) and CI (coverage index) parameters were used.

In 10 patients conformal plans made for EBI and interstitial brachytherapy using the same CT images were compared with regard to dose exposure of critical organs (mandible, parotid gland, spinal cord). Dose exposure was calculated by means of dose-volume histogram. The dose homogeneity was characterized with the ratio of the maximal dose (Dmax) and the prescribed dose for EBI and with the DNR for BT. In the critical organs the maximal dose was calculated for both treatment modalities.

Results*:* The coverage of the target volume by the reference dose (CI) was better in the conformal plans compared to the traditional ones, the CI was 87 % vs. 78 %, on average. In the comparison of EBI and BT boost plans the dose exposure to the critical organs was higher in external radiotherapy. Maximal dose of the mandible always exceeded the prescribed dose with an average of 6 % in the EBI, while with 33 % less than the prescribed dose in BT plans.

Conclusions*:* CT based planning is recommended for accurate localization of the target volume and for improvement of the target coverage by the reference dose. For quantitative comparison of treat-

ment plans the use of V100, V150, DNR and CI is recommended. Boost BT is more unfavourable from the point of view of dose homogeneity, but more advantageous in terms of radiation exposure to surrounding normal tissues than percutaneous irradiation.

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ENDOSCOPY GUIDED PERI-OPERATIVE HDR BRACHYTHERAPY (PHDRB) FOR RECURRENT SPHENOID SINUS CARCINOMA: A CASE REPORT

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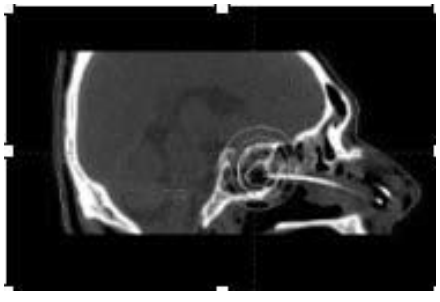
Purpose/Objectif*:* To examine the role of endoscopic resection and placement of after-loading catheters and PHDRB in recurrent malignancy of sphenoid sinus.
Materials/Methods*:* A biopsy proven carcinoma of the sphenoid sinus was treated with radical concurrent chemotherapy and radiotherapy. The patient developed a recurrence twelve months post treatment. Pre-operative 3-D treatment planning with virtual placement of after-loading catheters on MRI was done. The tumor was endoscopically resected. Post resection 3 after loading Teflon catheters were positioned in the tumor bed. The positions of catheters were confirmed fluoroscopically on table and retained in situ with the help of Merocel®. CT simulation was performed. CT and MRI fusion was done. GTV, CTV and OARs were delineated. 3D treatment planning was done. A total dose of 30 Gy in 12 fractions at 2.5 Gy/fraction over 6 days was delivered [Biologically equivalent dose (BED) „l 37.5 Gy]. Two fractions per day with an interfraction interval of six hours from third post-operative day were delivered. After loading catheters were removed on the 8th post-operative day.
Results: Resection was R1 (microscopic positive margins) category. 85% (2.9cc of 3.2cc) of CTV received 85% of the dose. The mean dose received by right optic nerve, left optic nerve and optic chiasm 7.2 Gy, 3.6 Gy and 1.8 Gy respectively. Patient developed radiation therapy oncology group (RTOG) grade 0-1 complications.
Conclusions*:* With complete endoscopic surgical resection followed by HDR brachytherapy, the treatment time, morbidity and cosmetic deformity have been minimized. Endoscopic guided placement of endocavitary after loading catheters is accurate and a feasible option for irradiation by PHDRB. The doses to normal tissues were Tolerable.



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ESTIMATION OF ACUTE AND LATE TOXICITY USING CTC AE AND MODIFIED DISCHE SCORING SYSTEM IN PATIENTS WITH ORAL CAVITY CANCER TREATED WITH HDR INTERSTITIAL BRACHYTHERAPY AND IMRT TELERADIOTHERAPY.

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Purpose/Objectif*:* To evaluate acute and late toxicity and function preserving in patients with oral cavity cancers treated with interstitial HDR brachytherapy and IMRT.
Materials/Methods: Data charts of 20–18 (90%) male and 2 (10%) female patients treated between January 2002 and November 2004 in Institue of Oncology In Gliwice were evaluated. Median age was 55 years. There were 15 (75%) patients with lip cancer and 5 (15 %) with oral cavity cancer. There were 12 (60%) patients with T2 and 8(40%) with T1 tumour. Total dose to the primary tumour and local lymph nodes (level I and II) ranged from 50Gy to 60Gy in 2Gy per fraction. All patients were treated using IMRT technique to spare the critical stuctures like parotid gland, mandible and mucosal membrane of phanynx and larynx. All patients were treated with interstitial brachytherapy with. median total dose ranging from 15 to 21Gy in 3Gy per fraction/BID/ and median treatment time was 4 days. All patients were examined at least 2 times per week during whole treatment, and monthly after its finishing. Acute toxicity was evaluated with CTC scale and modified Dische scoring system. Late complications–with CTC ver.3-scale. Median follow up was 24 months.
Results: After median follow all patients are alive. 2 (10%) patients, developed local recurrences and both were salvaged with surgery. During teletherapy all patients developed grade 2 mucositis estimated with CTC scale. Medial, maximal acute mucosal reaction during IMRT according to Dische scale reached 10 points. During and after brachytherapy acute mucosal reactions, with confluent mucositis (grade 3 with CTC scale) in 15 (75%) patients, were noticed, but did not exceed 15 points in Dische scale. No implant-related toxicity was noticed. Medially 6 months after treatment 15 (75%) patients developed grade 1 CTC, and 5 (25%) grade 2 CTC of xerostomia. 10 (50%) patients presented localized oedema of head and neck tissues without function impairment (grade 1 CTC). In 5 (25%) patients, after 12 months periodontal disease in grade 1 was noticed. All patients with tongue cancer, medially 15 months after radiotherapy developed moderate (grade 2 CTC) fibrosis of irradiated tongue muscles. 4 (20%) patients, all with tongue cancer presented cranial nerves (XII) neuropathy estimated by neurologists as grade 1 CTC (3 patients) and grade 2 (1 patient). One patient (5%), after 7 moths developed osteoradionecrosis of mandible bone (grade 4 of CTC scale). Precise evaluation of treatment plans and case history indicated that inadequate teeth extraction was the most probable reason of the complication. Neither cosmetic nor functional deficits were reported by the patients.
Conclusions*:* Our results suggests that combination of IMRT and interstitial HDR-brachytherapy is safe treatment of T1-2 tumours of oral cavity. The function of the tongue and other treated important structures is preserved. Toxicity of proposed modality is acceptable and well tolerated by the patients. In our opinion combined IMRT and interstitial HDR brachytherapy should be considered as valuable option in T1-2 oral cancer patients.

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HIGH DOSE RATE BRACHYTHERAPY IN PATIENTS WITH TONGUE CARCINOMA.

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Purpose/Objectif: The aim of this study is to present our clinical experience in the treatment with high dose rate 192-Ir brachytherapy (HDR) in patients with tongue tumours and to get a survival analysis and their complications.

Materials/Methods*:* A retrospective audit identified 53 patients (p.) treated of tongue carcinoma with HDR, between September 1999 and November 2006, 47 of oral tongue, 4 of floor of mouth and 2 of base of tongue. The incidence was double in males (36:17). The mean age was 59 years old. Histology showed 52 squamous carcinoma and 1 verrucous carcinoma. The distribution by stages was I:17, II:13, III:13, IVa:7 and 3 cases treated for recurrence. Nodal involvement was present in 29%. Five p. had been previously treated with radiotherapy for other primary head and neck tumours. Chemotherapy was administered to 13 p. (24%). Exclusive brachytherapy was given to 18 stage I-II p. (34%) and complementary to external beam radiotherapy (EBRT) to 35 p. (66%). A perioperative technique was used in 12 p. to get a conservative management at the time of surgery. The median total dose was 44 Gy (40 – 49) when HDR was used alone and 18 Gy (15 – 24'5) when HDR was administered in conjunction with EBRT, total dose 50 Gy (44 – 70). The median dose per fraction was 4 Gy (3 – 4) with exclusive HDR and 3 Gy (2'5 – 4) with EBRT, twice a day with a minimum interval of six hours. Survival was calculated using the Kaplan-Meier method.

Results: Thirteen patients have died, 6 p. by local recurrence, 2 by skin metastasis, 4 by a second neoplasm and 1 by intercurrent disease. Two p. are alive with lymph node metastasis but local control. The median follow-up was 31 months. Actuarial overall survival at 5 years is 57%. Actuarial free of disease survival at 5 years is 76%, in early stages (I-II) is 90% and in advanced stages (III-IV and recurrences) is 56% (p‹0'01). Local failure has developed in 8 p., two of them salvaged with surgery. Actuarial local control at 5 years with HDR is 65%, in early stages is 90% and in advanced stages is 53% (p‹0'1). The group of p. treated with exclusive HDR gets 100% local control and the combined group (EBRT+HDR) 58% at 5 years (p‹0'05). With salvage surgery, actuarial local control at 5 years is 84%. All patients treated with perioperative technique have got local control. Late effects related to radiation therapy have been observed in 10 p. (19%), 8 soft tissue necrosis (15%), solved with a conservative procedure, and 2 bone necrosis (G2, G4) (3'8%).

Conclusions*:* HDR brachytherapy is an effective method for the treatment of tongue carcinoma, with very good results in early stages. The results are equivalent to low dose rate brachytherapy studies but late effects are less than expected, probably due to the optimization and a reduced dose to the mandible. The perioperative technique promises effective results.

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PALLIATIVE HDR AND PDR BRACHYTHERAPY IN RECURRENT TONGUE AND FLOOR OF THE MOUTH CANCER

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Purpose/Objectif*:* A large majority of patients with recurrent tongue and floor of the mouth cancer are disqualified from radical treatment and constitute a group of bad prognosis. Some of them can be qualified for salvage surgery and treated mostly with a palliative intent. In some cases brachytherapy can be a treatment of choice. The paper is to present results of HDR and PDR brachytherapy (HDR, PDR – BT) in a described group of patients

Materials/Methods*:* Thirty six patients with recurrent tongue and floor of the mouth cancer were treated with HDR–BT and PDR–BT since October 2000 till September 2005 in Greatpoland Cancer Center. The age of patients ranged from 45 to 83 years, average 59 years. The group consisted of 7 women (19.4%) and 29 men (80.6%). Clinical locations of recurrence were: tongue (n=3, 8.3%), floor of the mouth (n=5, 13.9%), both locations (n=14, 38.9%), massive recurrence in floor of the mouth and circumjacent tissues (n=7, 19.4%) and neck infiltration (n=7, 19.4%). In all cases squamous cell cancer was diagnosed. 28 (77.8%) patients were previously both operated and irradiated, 7 were irradiated (19.4%) and 1 was operated (2.8%) as a single modalities. Primary lesions were irradiated most often with total dose of 70 Gy. Median time between primary tumor and its recurrent appearance was 20.4 months (min. 2 and max. 168 months) and it was longer than 12 months in 10 cases. 23 patients were treated with HDR – BT and 13 – with PDR–BT. PDR–BT was given most often with a single fraction of 20 Gy in 25 pulses by 0.8 Gy hourly. In 1 case PDR fraction was repeated in view of small size of a tumor and relative good response after first fraction. In HDR – BT most often 5 fractions of 4 Gy were used. The assessment of the results was performed in 1st months after completion of the treatment and then after 3, 6 and 12 months.

Results: Median survival time carried out 7.7 months (1 – 18 months). In 1st month after the end of the treatment complete remission (CR) was found in 5 (13.9%), partial remission (PR) in 16 (44.4%), lack of remission (NR) in 14 (38.9%) cases, and progression in 1 (2.8%) case, respectively. In 3rd and 6th months remission (CR + PR) was observed in 20 (55.6%) and 13 (36.1%) patients, respectively. In 24 cases (66.7%) superficial necrosis was observed in first and third months of observation, in 2 cases we found fistulas.

Conclusions: 1. HDR and PDR brachytherapy can be an efficient palliative treatment of recurrences in patients previously irradiated with external beam radiotherapy and/or surgery. 2. It appears to be, that in some cases brachytherapy improve local control of tumor. 3. To confirm the above a comparative investigation of a larger group of patients is needed.

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RESULTS OF HIGH DOSE BRACHYTHERAPY F AND CERVICAL NECK DISSECTION FOR HEAD AND NECK CANCER

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Purpose/Objectif*:* Reports highlighting the use of interstitial high dose rate brachytherapy (I-HDR) as adjuvant treatment for cervical cancer is scarse the literature. We evaluate the results and morbidity asdsociated to an institutional treatment policy, using I-HDR as sole adjuvant treatment or in combination with external beam radiotherapy (EBRT).

Materials/Methods*:* Charts of 42 patients with a median follow up of 36 months (range 8-111) and treated from 1994 to 2003 were revised. Age of patients ranged from 31 to 76 yo and the ratio male to female was 4.25:1. Thirty five patients had previous irradiation with EBRT, with doses ranging from 30 Gy to 65 Gy (median 52). The total dose of I-HDR ranged from 12 Gy to 48 Gy (median 24), given in 3 to 14 fractions (median 6 fractions), in 2 to 8 days (median 4).

Results: The total treatment time ranged from 19 to 83 days (median 35 days).The 5- and 8-year overall (OS) and relapse-free survival (LRFS) rates were 52.5%, 48.1%, 48.5% and 38.1%, respectively. The only statistical significant prognostic factor for LRFS and OS at 5- and 8-year was margin status, p= 0.0050. On multivariate analysis no predictive factor was found to be statistical significant. Four patients

(9.5%) presented late adverse effects as local dehiscence (2), local ulcer (1) and extensive neck fibrosis (1), not related to a higher dose to the skin or graft.
Conclusions: In view of these results we suggest that I-HDR can be recommended in selected patients with first presentation lesions, local recurrences or second primary carcinomas, even with a previous course of EBRT, but further studies are eagerly awaited to delineate the optimum schedule for this treatment combination modality.

Miscellaneous

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A PHASE I/II STUDY OF PER-OPERATIVE PERMANENT IMPLANT (POPI) USING 103PD SEEDS FOR ADJUVANT LOCALISED CANCER

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Purpose/Objectif: Per operative irradiation (POI) has regularly been evaluated by different ways. External Beam Radiotherapy (EBRT) with photons and/or electrons and by Brachytherapy (BT). In terms of dose delivery, BT kernel is probably the most effective and less expensive way compared with modern IMRT IGRT and ART techniques. Phase I-II studies showed interest in using POI but no phase III or straightforward conclusions were drawn from literature due to technical, human resources or cost problems. With Permanent Prostate Implant (PPI) and Permanent Breast Implant (PBI), data from clinical studies has confirmed effectiveness and potential of PI in cancers control and the purposes of this study is to evaluate feasibility and local control results of a new method using Pd103 strands for POPI (Per Operative Permanent Implant). In combination with new interactive treatment planning system guided by images is now feasible using modern Image Guided BT technology and experience acquired in POI PBI PPI.
Materials/Methods*:* Per operative Permanent Implant (POPI) based on a new type of stranded Pd103 sources A phase I-II study is then promoted using Visicoil° clips and plastic tubes insertion in OR with the surgeons. After staging and anatomo-pathological mapping, images acquisitions from CT is transferred for virtual 3D treatment planning dosimetry and optimisation in dose volume. Optimised spacing of Optiseed° strands and Pd103 activity enable remote after loading and final withdrawal of plastic tubes to cover incomplete resections after surgery.
Results: Thoracic and abdominal indications have been selected in the first flow for feasibility study and appropriate local control enhancement. These early data give first patients results with short term follow in regard with the phase I preliminary study.
Conclusions: The early feasibility and early local control results are really encouraging and opening a new field of application for permanent implants. The figures and data will be presented in order to promote collaboration with other teams.

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ADJUVANT HDR BRACHYTHERAPY FOR HIGH GRADE COMPLETELY RESECTED SOFT TISSUE SARCOMAS OF THE SUPERFICIAL TRUNK OR EXTREMITIES- A PROSPECTIVE PHASE I–II DOSE ESCALATION STUDY.

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Rational: adjuvant brachytherapy (BT) has been proven to decrease local recurrences after conservative complete resection (R0) of high grade sarcomas of extremities or superficial trunk (SEST) to 10- 15 %, comparable to external beam radiotherapy (EBRT), although there is no randomized study BT vs EBRT. The ABS recommended dose is 42- 45 Gy in LDR BT or 3 Gy/ fr x 12 fractions (fr), bid, for HDR BT, the latest being equivalent (Eq) to only 39 Gy assuming an $\alpha/\beta = 10$, but "compensated" by a different prescription point for LDR vs HDR. There is scarce evidence about exclusive HDR BT after R0 high grade SEST, and the results with such schedule seem to be less good than with LDR. Purpose: dose escalade prospective analysis of toxicity and efficacy of HDR BT for Ro primary SEST.
Materials/Methods*:* From November 2004 to July 2006, 15 patients with T1-2NoMo high grade primary SEST received interstitial perioperative Ir192 HDR BT after a Ro conservative resection. Patients referred by other institutions with R1 or unknown margins were re- operated in our center to ensure the R0 status. There were three groups: first receiving 12fr x 3.5 Gy/bid (47.2Gy Eq), second 12 fr x 3 Gy/ bid (39 Gy Eq) and third 13-14 fr x 3Gy/bid (42.2- 45.5 Gy Eq).BT started no sooner than five days after surgery. Dose was prescribed at 1 cm from the catheters axis (parallel, equidistant needles or plastic tubes, 12 to 15 mm apart). Dose optimization was done for reducing the 200% isodose maximum diameter under 10 mm and skin dose under 70% of prescribed dose, on CT based dosimetry verified by in vivo measurements during first fraction. Most patients received chemotherapy after BT. Majors nerves or vessels were embedded in gelfoam to avoid direct contact with BT catheters.
Results*:* With a median follow- up of 16 months (6 to 26 months), the local control was 100 % and there were no G3-4 acute or late complications. However, we noticed 40 % late G2 skin fibrosis and 20 % G2 neurotoxicity in the 3.5 Gy arm compared to 20 % and 0 % for the 3 Gy/fr groups.
Conclusions*:* Dose escalation from 3Gy/fr to 3.5 Gy/fr HDR BT, 12 fr bid (ie 39 Gy Eq to 47.2 Gy Eq) seem not to increase acute or late severe toxicity. Longer follow up and larger effectives are warranted, but our results suggest that keeping the dose/fr at 3 Gy induce less G2 toxicity and that probably 42Gy/ 14fr, bid could be more appropriate, as equivalent to ABS recommendations.

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ADJUVANT LOW AND HIGH-DOSE-RATE BRACHYTHERAPY IN THE MANAGEMENT OF KELOIDS

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[3]European Institute of Oncology, *Plastic and Reconstructive Surgery, Milano, Italy*

Purpose/Objectif: Surgical resection of the keloids alone has been shown to result in a recurrence in 50–80% of the cases, and the resulting keloid is even larger than the original one. Therefore, adjunctive procedures have been proposed in the literature to improve therapeutic and cosmetic outcomes. We describe our experience with adjuvant low dose rate (LDR) and high dose rate (HDR) brachytherapy with 192Ir.
Materials/Methods*:* Between April 1999 and June 2006, 62 patients (pts) with a total of 95 keloids had been irradiated by LDR (37 pts) or HDR (25 pts) brachytherapy after complete surgical excision. The applicator-guide for brachytherapy (BRT) was a flexible 5 or 6-french dedicated plastic tube. During the surgical procedure the catheter was inserted about 4-5 mm deep in the derm through the centre of the wound.
Each treatment was simulated using standard X-ray or CT with dummy-sources. BRT dosimetry was done using the PLATO TPS and the irradiation was administered within 4–6 hours after surgery.
The active length was calculated according to the length of the surgical wound, considered as the target volume.
Thirty-seven pts with 61 keloids were treated with LDR BRT. The reference isodose is located 5 mm (range 4–7) from the long axis of the source. A median total dose of 16 Gy was given with a median dose rate of 0.4 Gy/h .

Twenty-five pts with 34 keloids were treated with HDR BRT. The reference isodose is located 4 mm from the long axis of the source and optimized on dose points to avoid skin toxicity. All patients but 2 received a total dose of 12 Gy in 4 fraction of 3 Gy b.i.d.

Results*:* We evaluate the cosmetic outcome of therapy with a scale from 1 (poor) to 3 (excellent). In the LDR group, 4 pts with 8 keloids were lost to follow-up. After a median follow-up of 36 months (range 18–72) 66% of the keloids are without any evidence of recurrence. Cosmetic results were considered to be good or excellent in 25 pts (36 keloids).

In the HDR group, 3 pts with 5 keloids were lost to follow-up. After a median follow-up of 8.5 months (range 1–18) 86.2% of the keloids are without any evidence of recurrence. Cosmetic results were considered to be good or excellent in 21 pts.

Conclusions*:* Adjuvant irradiation with brachytherapy of keloids is an effective and very well tolerated therapy modality with few side effects, because it involves less normal tissue in the treated volume than external radiotherapy, particularly in the treatment fields with irregular surface.

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BRACHYTHERAPY COMBINED WITH STENT PLACEMENT IN PALLIATIVE TREATMENT PATIENTS WITH ADVANCED OESOPHAGEAL CANCER–OWN EXPERIENCES

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Purpose/Objectif: Brachytherapy and stent intubation, each of them are very effective as a single method in palliative treatment in patients with advanced oesophageal cancer. Time to tumour overgrowth after stent placement is relatively short but this method offers a rapid relief of the dysphagia. The purpose of presenting work was estimation if brachytherapy added to stent placement influence its effect and improve it.

Materials/Methods*:* 20 patients with comfirmed advanced oesphageal cancer were treated in Brachytherapy Department between July 2003 and February 2006. All of them underwent the stent intubation before brachytherapy. Two weeks after we started the intraluminal irradiation. The total, prescribed dose was 18 Gy in three fractions of 6 Gy each, specified 0.5 cm from the surface of the aplicator, 1 fraction per week . 4 weeks after treatment first examination with X-rays of the oesophagus and/or oesophagoscopy was performed.

Results: In all but one cases recurrence of dysphagia was not observed during follow-up. In one case malignant stricture was found at oesophagoscopy above upper tip of stent. In two cases fistula formation was observed (one oesophageo-mediastinal and one oesophageo-bronchial), one patient died because of fatal haemorrhagia from GI. Median survival was 5 months. Despite lack of dysphagia improvement of quality of life was not observed. All patients complained severe, prolonged somatic pain in chest which required stronger analgesis, ie morphin-like drugs.

Conclusions: Addition brachytherapy to stent intubation into the oesophagus slows down the overgrowth of the tumour and prolongs time to dysphagia. But severe, somatic pain after combined treatment gets QoL of the patiens worsened. There was no improvement in overall survival. Because of these reasons simultaneous using described above methods was ceased.

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BRACHYTHERAPY FOR CARCINOMA IN SITU OF THE GLANS PENIS

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Purpose/Objectif*:* Carcinoma in situ of the glans penis (CISGP) is rare and the treatment is a penis-preserving strategy consisting of one of the following options: topical applications of 5-fluorouracil cream, laser therapy, cryotherapy, local excision combined with reconstructive surgery and brachytherapy (BT). The goal of this study is to analyze the results of BT for CISGP.

Materials/Methods: Between 1970 and 2004, 12 patients (pts) with CISGP were treated by BT, 5 of them being treated previously by conservative surgery for a primary CISGP 25 to 39 months before BT. The median age at the time of BT was 65 years (40-76). The median diameter of the lesion was 10 mm (3-30). Biopsy and circumcision were performed before BT which was realized using the hypodermic needles technique loaded with Iridium 192 wires. The median radioactive line number was 4 (2-11) in a median number of 2 planes (1-3). The median radioactive length per needle was 4 cm (2-6) and the median radioactive length per pt was 11 cm (3-55). The median delivered dose according to the Paris system rules was 63 Gy (56-71). The median treated volume was 7.7 cm3 (1.5-68) and the median dose rate was 4.7 μGy/cm/m^2/h (3.8-7.6).

Results*:* The median follow-up was 88 months (31-181). Three pts had a local relapse (all CISGP), 6, 13 and 57 months after BT. Salvage treatment consisted in: local excision (1 pt), partial amputation (1 pt) and second BT (1 pt), all pts being controlled without disease at the date of the last news, 13, 27 and 47 months after the local relapse. Relapses were not statistically related with previous history of CISGP. Complications were correlated with: the number of needles (p=0.04), the number of planes (p= 0.03), the total radioactive length (p=0.05) and the treated volume (p=0.06) (Mann-Whitney Test).

Conclusions*:* Our limited series shows that BT provides a tumor control in 75% of CISGP, almost half of the pts having a previous history of CISGP and all recurrences are CISGP. Total radioactive length should be limited to avoid complications.

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CT ASSISTED 3D HDR BRACHYTHERAPY IN THE TREATMENT OF SKIN CANCER

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Purpose/Objectif*:* Our purpose was to present the feasibility of 3D CT assisted HDR brachytherapy (HDR-BT) in the complex treatment of skin cancers using individual molds. In this study we have also focused on the usefulness of volumetric indices in the plan evaluation process.

Materials/Methods: Between December 2003 and December 2006 20 patients (9 male, 11 female) with 21 basal cell or squamous cell carcinomas on the face were treated with 3D CT assisted HDR-BT. Mean age was 70 years (range 59-85). 18 patients received brachytherapy as a boost treatment after external beam radiotherapy (EBRT), while in the remaining 2 cases brachytherapy was used alone. A total of 8 patients were irradiated as first-line therapy, while the remaining 12 patients had local recurrences or incomplete R1 resection. In all cases individual molds were constructed to get a well reproducible, fix geometric arrangement for the catheters. After clinical placement of the moulage planning CT was performed. After delineation of the PTV and organs at risk 3D conformal planning was carried out using dose point optimization. For plan evaluation the following volumetric indices were used: coverage index (CI), homogeneity index (HI), spill ratio (SR). The average dose of EBRT was 41 Gy (39.6-50.4 Gy). The mean of HDR-BT dose administered was 23 Gy (8-50.4 Gy) with a mean of 13 (4-28) fractions. The average fraction size was 1.9 Gy (1.6-2.5 Gy).

Results*:* All patients with macroscopic tumors (10 pts) had complete remission. During the median of 14.2 months (range 2.5-26) follow up period there were no local recurrences as well as regional or distant failure. According to the RTOG scoring system no grade

3-4 acute and late side effects were noted. The reproducibility of the catheters and the treatment tolerance were excellent in all cases. The mean volumetric indices were as follows: CI: 98%, HI: 80% and SR: 20%. The average time needed for treatment planning and was 20 min., while the total time of daily procedures was only 15 min.
Conclusions: Individual molds combined with CT based 3D treatment planning seem to be feasible, safe and accurate method in HDR-BT of skin tumors facilitating its application as a sole modality. Besides DVH analysis volumetric indices seem to be promising and useful parameters for quantitative evaluation of surface 3D HDR-BT. A systematic use of these parameters is planned in our institution. Higher number of patients and longer follow up are needed to properly establish local tumor control, functional and cosmetic results.

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DOSE NEAR THE RIM AND BEHIND A RU-106 PLAQUE

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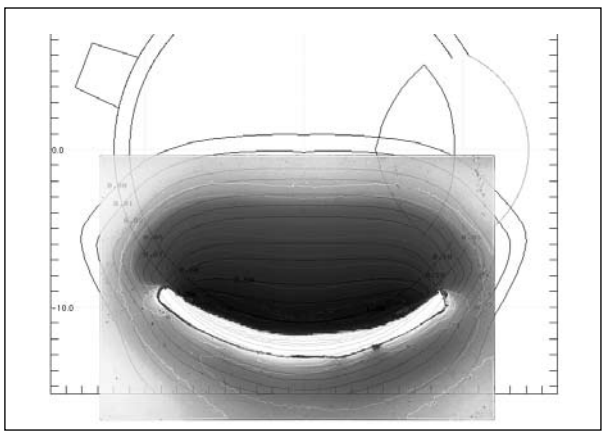
The BEBIG Ru-106 plaques used in the treatment of ocular tumors have the shape of a spherically concave silver bowl with an inner radius of curvature of about 13 mm, and a total thickness of 1 mm. The radioactive nuclide is deposited on the concave surface a 0.2 mm thick silver target foil which is sandwiched between the concave surface of a 0.7 mm thick layer of silver (back) and the convex surface of a 0.1 mm thick layer of silver (window). The Ru-106 (halflife 368 days) disintegrates via low energy ß- decay to radioactive daugher Rh-106 which is actually the primary contributor to therapeutic dose. Rh-106 decays with a halflife of 30 s to the stable element Pd-106. It primarily emits a spectrum of beta particles with a mean beta energy of about 1.4 MeV. About 20% of Rh-106 decays also emit photons of 0.5 MeV, and about 2% of decays emit photons with energies in excess of 1 MeV. The 0.7 mm thick silver backing of the plaque should effectively shield the patient and orbit of the eye from the beta particles, but the relatively hard photons can not be significantly attenuated by any material in the space available to on eye plaque.
The dose delivered to objects near the rim and immediately behind a Ru plaque was studied by cutting a slot into GAFChromic film to match the contour of a model CCD plaque. The plaque was inserted into the slot for several days. The film was then digitized and isodensity lines plotted and compared to isodose calculations using the BEBIG Plaque Simulator software. The accompanying figure illustrates that the measured film optical density from 1 to 2 mm behind the plaque corresponds to about 5% of the dose that would be delivered to the base of a tumor 1 mm in front of the plaque. The film density 3 mm away from the plaque corresponds to about 2 to 3% of the basal tumor dose. A dose buildup region is evident in the 1st mm adjacent to the plaque rim and back surface. This observation is consistent with the premise that the dose behind the plaue is being delivered by the hard photon component of the Rh-106 decay.



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FROM CONTINUOUS LDR TO OFFICE-HOURS PDR IN BLADDER BRACHYTHERAPY

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Purpose/Objectif: To evaluate the efficacy and safety of a pulse dose rate (PDR) office hours schedule in interstitial brachytherapy of bladder cancer.
A trimodality approach, transurethral resection (TUR), external beam irradiation (EBI) and interstitial brachytherapy, is an effective treatment for a solitary bladder cancer ‹ 5 cm. The 5-year DFS reaches 70% and approximately 70-80 % patients can preserve their bladder. These numbers are based on both Dutch and French low dose rate (LDR) experience. The Arnhem Radiotherapy Institute has a long history of LDR interstitial brachytherapy. In 1998 we replaced the LDR mSelectron by a PDR mSelectron and kinking catheters troubles forced us to abandon the standard continuous irradiation schedule and to introduce an office hours schedule for this particular indication.
Materials/Methods: The LDR-based protocol: T1G3 tumors: external beam irradiation (EBI)–3 fractions of 3,5 Gy followed immediately by 60 Gy(range 55-65 Gy) delivered by brachytherapy. T2 tumors: EBI–20 fractions of 2 Gy followed within 1 week by 30 Gy delivered by brachytherapy. In the PDR-based protocol the EBI schedules remained unchanged. To deliver a biological dose equivalent to 30 Gy LDR, a slight reduction to 28 Gy physical dose was required for the PDR schedule of T2 tumors and from 64 Gy to 60 Gy for T1 tumors. Radiobiological calculations were performed with a linear quadratic model including incomplete mono-exponential repair with the following parameter values: for late responding normal tissues α/β ratio=5 Gy and repair half time =1-3 h; for tumor α/β = 10 Gy and repair half time = 1 h. Applying these parameters, two PDR schedules were designed with the following characteristics: For T2 tumors: 28 Gy delivered in 3 days with 10 daily fractions on two consecutive days and 8 fractions the third day, with a fraction dose of 1 Gy and a period time of 1 h. For T1 tumors: 60 Gy in 6 days, 10 fractions of 1 Gy each day with a period time of 1 h.
Conclusions: The local control and (mild) late toxicity are comparable for both schedules. The acute toxicity (wound infections, pneumonia, temporary ileus) is higher in the PDR population, however not significant (p=0, 30). Log-rank tests indicate no significant differences between LDR and PDR in local control and in disease specific survival. The office-hours PDR schedule has been shown to be a very workable and effective alternative for LDR in the treatment of bladder cancer.

Results

	LDR	PDR
Time period	1983-1997	1998-2007
Number of patients	61	28
F/M	5/56	8/20
Age Mean/Median	67.2/67.2	71.1/73.2
T1G3/T2	10/51	5/23
Days of hospitalization (mean ± SD)	16 ± 6	13 ± 6
Acute toxicity G1,G2 G5 (cardiac mortality)	13	9 1
Late toxicity (G1,G2_only)	6	4
5 yr. Local control	67 %	78 %
5 yr. DFS	76 %	62 %

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FUSION OF 3-D ULTRASOUND (US) AND (PET)CT IMAGES FOR REAL 3-D INVERSE DOSE PLANNING OF INTERSTITIAL BRACHYTHERAPY OF ANAL CANCER. A FEASIBILITY STUDY.

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Purpose/Objectif*:* Palpation in general anesthesia and concomitant 2-D ultrasound is a common procedure for the clinical staging of anal cancer and dose-planning of interstitial brachytherapy. The Paris system was an international accepted system to define doses of interstitial brachytherapy of anal cancer.
3-D US is the imaging technique with the highest resolution in the anal canal, even better than MRI. Furthermore, PET/CT gives biological information of tumor metabolism.
To calculate more conformal interstitial brachytherapy and to introduce PDR technique new imaging methods are needed to detect the GTV more precisely. We introduced 3-D US stepwise in staging- and dose planning procedures of interstitial brachytherapy of anal cancer as previously described. Until now we could not use all ultrasound information for thru 3-D dose planning because of lack of a DICOM format. We have developed a new method to import 3-D US in the dose planning system and to fuse it with CT- or PET/CT scan.
Materials/Methods: The anal implants are performed by using an anal template and stainless straight needles (Nucletron). A pre-operation 3-D US rectal scan is performed followed by the implantation and completed by a post-operation 3-D US rectal scan. The pre-operation scan defines the coordinates for the implant. We are now able to import the post-operation US scan into the dose planning system (BrachyVision, Varian), and fuse it with a CT- or PET/CT scan. This method makes it possible to reconstruct the needles in situ, the GTV and the organs at risk in 3-D. The inverse dose plan is also based on the fused images. Brachytherapy is performed on the PDR micro-Selectron (Nucletron).
Results: The lack of a DICOM format has been a limiting factor for importing 3-D US in dose-planning systems and calculating a thru 3-D conformal dose plan. We have developed a new method to import 3-D US in the dose planning system and fuse it with CT- or PET/CT scan. The fusion of these imaging techniques gives the possibility to define the tumor and risk organs more precisely and calculate a better inverse dose plan.
Conclusions*:* This is the first study, which demonstrates the feasibility of fusion of 3-D US rectal scan with PET/CT scans as a new method for optimizing the dose planning of interstitial brachytherapy of anal cancer.

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HDR BRACHYTHERAPY OF SKIN CANCER - GREATPOLAND CANCER CENTRE EXPERIENCE

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Purpose/Objectif*:* To analyze treatment results of HDR brachytherapy (BT) in patients with skin tumors.
Materials/Methods*:* 179 patients with skin tumor were treated with HDR BT in Greatpoland Cancer Center between May 1999 and May 2004. There were 93 man (52 %) and 86 woman (48%), age ranged from 27 to 96 years (median – 70.8 years). Most frequently diagnosed tumor was squamous cell carcinoma (n=102, 57%) and basal cell carcinoma (n=52, 29%). In most of cases tumor was diagnosed in early clinical stage (T1 – n=79, 44.1%, T2 – n=60, 33.5%). HDR BT of 50–60 Gy in five or six fractions counted in distances 0.5 to 2 cm from tube axis was used. Most frequently 6 fractions of 10 Gy were used (n=110, 61.5%). Patients were observed during a period of 12 months in terms of local remission rates depended on chosen prognostic factors (age, sex, clinical stage, location, histopathology and method of treatment.
Results: Complete remission (CR) assessed in 4 weeks after treatment was observed in 152/179 (84.9%) of patients, partial remission (PR) – in.16 (8.9%), no remission (NR)–in 9 (5%), progression in 1 case, respectively, 1 patient died. Significant correlation was observed between remission rate and clinical stage, location and method of treatment (Principal Component Analysis). After 12 months CR in 146/179 cases (81.6%), progression–in 16 cases (8.9%), were observed, respectively. Five of patients (2.8%) died, 12 patients (6.7%) were lost (lack of information). Early complications were assessed in 4 weeks after treatment: they occured in all cases: Ist grade in 126 cases (70.4%), 2nd – in 31 cases (17.3%) and 3rd grade–in 22 cases (12.3%), respectively. Late complications (assessed in 6 month after treatment) were observed: Ist grade (n = 66/179, 36.9%), 2nd grade (n = 21, 11.7%) and 3rd grade (n = 6, 3.4%).
Conclusions*:* 1. HDR BT is high effective treatment metod of skin tumors. Complications rate is acceptable and treatment costs are low. 2. In some tumors (great skin lesions in sculp, near eyes or on the nose) BT allows great dose reduction in surrounded heath tissues. 3. Higher remission rate is observed in tumors in lower clinical stage, treated radically and localised in face.

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INTRALUMINAL HDR IR-192 BRACHYTHERAPY IN THE PALLIATION OF MALIGNANT BILE DUCT OBSTRUCTIONS: A DOSE-ESCALATION STUDY

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Purpose/Objectif: Previously, we have shown that a single dose 10 Gy of intraluminal brachytherapy (BT) combined with metal stents is effective in the palliation of malignant bile duct obstruction. The treatment yielded a high stent patency without increased acute or late morbidity. In the present investigation, we evaluated the efficacy and side effects of an escalated dose of 15 Gy using an equivalent patient material.
Materials/Methods*:* A total of 23 consecutive patients during 2002-2006 received 15 Gy at 10 mm from the center of the non-centering 6F afterloading catheter. At the time of drainage procedure 18/23 patients had a biopsy-proven malignant extrahepatic disease. A self-expanding metal stent (diameter 10 mm) was inserted during a drainage procedure using percutaneous transhepatic catheterisation (PTC) as a palliation to biliary obstruction and/or pain. Insertion of an afterloading catheter was performed through the 8F percutaneous introducer sheath. Survival, stent patency and acute and late side effects were registered from patient records.
Results*:* Median and mean survival was 4.2 and 6.6 months (range 0.3-23.7 mo). 4 patients needed a repeated operation due to stent occlusion at 6, 16, 17 and 18 months. Acute side or late effects that could be associated with BT were not encountered.
Conclusions: Median and mean survival for 22 patients in our previous 10 Gy group (1998-2001) was 2.8 and 7.0 months (range 0.3 – 38.9 mo). Although the median survival in that series was short, the mean survival was long due to three patients surviving until 2.0, 2.2 and 3.2 years. One patient required a repeated drainage procedure at 18.0 months due to a stent occlusion. In the present investigation with 15 Gy and same stent length (88 mm), the mean survival was nearly equal but the median survival suggests for survival benefit (4.2 vs. 2.8 mo). Although the stent patency was lost with long-term survivors, it is evident that a single escalated dose of 20 Gy with BT

could not prevent a late stent occlusion. To avoid a repeated PTC procedure an alternative could be a stent-targeted external beam single dose at one year to long-term survivors.

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LOCAL CONTROL AND SURVIVAL IN PATIENTS WITH SOFT TISSUE SARCOMA TREATED BY LIMB SPARING SURGERY IN COMBINATION WITH INTERSTITIAL BRACHYTHERAPY AND EXTERNAL RADIATION

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Purpose/Objectif*:* The purpose of this study was to evaluate local control, survival and complication rate associated with pulsed-dose rate (PDR) interstitial brachytherapy and external beam radiotherapy (EBRT). This study reports the long-term outcome and experience from our centre with this combined treatment modality.

Materials/Methods*:* A retrospective review of soft tissue sarcoma patients who underwent primary limb-sparing surgical intervention, combined with PDR interstitial brachytherapy 20 Gy and additional postoperative EBRT 50 Gy. From 1995 to 2004, 39 adult patients (femal/male= 25/14, mean age 51(range 21-78) years were treated with curative intent for soft tissue sarcomas. Liposarcoma (n=18), myxofibrosarcoma (n=5) and leiomyosarcoma (n=4) were the most common histological types. Six patients had grade 1, 17 grade 2, and 16 grade 3 tumours. The median tumour size was 8,6 (range 3-19) cm. Resection margin were classified as wide (n=13), marginal (n=15) and intralesional resection (n=9).

Results*:* Five patients developed local recurrence. The probability of local recurrence free 5 years survival was 83.4%. Ten patients had died and 29 patients were still a live; mean follow-up 4.7 (0.8-10.9) years. The overall survival was 70% at 7,1 years of follow-up. Four (10,2%) patients required surgical intervention because of skin necrosis. Twelve (30.7%) patients had persistent pain. Distal limb oedema was observed in 16 (41%) patients and 19 (48,7%) patients suffered from some degree of decreased force or function of the affected limb. No treatment related bone fracture or nerve damage was seen.

Conclusions*:* The results of this study demonstrated that limb sparing surgery, combined with interstitial BRT and EBRT can result in excellent local control in patients with soft tissue sarcomas. Brachytherapy is an effective modality with good cosmetic results and acceptable toxicity.

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LONG TERM RESULTS OF BRACHYTHERAPY FOR CARCINOMA OF THE PENIS CONFINED TO THE GLANS OR THE PREPUCE (N- OR NX)

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Purpose/Objectif: To analyze the results of the classical indication of brachytherapy (BT) for squamous cell carcinoma (SCC) of the penis (Jackson stage I classification), in a large series with a long follow-up. Patients with carcinoma in situ or pathological inguinal lymph node involvement were excluded of the study.

Materials/Methods: Between 1970 and 2006, 145 patients (pts) of median age 62 years (26-94) were treated by exclusive BT for a carcinoma of the penis confined to the glans or the prepuce. Inguinal nodes dissection was performed in 20% of pts (all N -). After a wide circumcision, BT was performed using the hypodermic needles technique in the GAG applicator. The median radioactive Iridium line number was 6 (2-18). The median number of planes was 2 (1-5). The median radioactive length per needle was 4 cm (2-6) and the median radioactive length per patient was 24 cm (4-108). The median delivered dose according to the rules of the Paris system was 65 Gy (37-76). The median treated volume was 22 cm3 (2-110) and the median dose rate was 4.7 μGy/cm/m^2/h (1.6-10).

Results*:* The median follow-up was 67 months (0.5-353). The 5 and 10 year risk of local relapse were 12% (CI 95%: 6-18) and 21% (CI 95%: 12-30) and more than 95% of local recurrence were locally controlled by salvage partial (57%) or total (29%) amputation, excision (5%) or a second BT (9%). The 10 year risk of inguinal lymph node relapse and metastases were 11% (CI 95%: 5-17) and 7% (CI 95%: 3-11). The 10 year specific survival was 91% (CI 95%: 86-96). Previous history of SCC, differentiation of SCC, macroscopic aspect and size of the tumor had no significant impact on relapse. Urethral stricture was observed in 24% of pts and pain (requiring medicine) in 23% of pts, 8% of the pts requiring surgery for these complications. Complications were correlated with: the number of needles (p=0.02), the number of planes (p= 0.06), the total radioactive length (p=0.06) and the treated volume (p=0.02) (Mann-Whitney Test).

Conclusions: Brachytherapy is an effective conservative treatment for SCC confined to the glans or the prepuce. In case of local relapse, salvage local treatments are efficient. Specific deaths are mainly due to the rare lymph node or metastasis recurrences as first events or combined with local recurrence. Late complications are clearly related to BT parameters.

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POSTOPERATIVE RADIOTHERAPY WITH HIGH DOSE RATE IRIDIUM 192 MOULD FOR PREVENTION OF EARLOBE KELOID

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Background: Simple excision of earlobe keloids can result in 50-80% recurrence rates. Many modalities including radiotherapy have been suggested to reduce the risk of the recurrence postoperatively. Objective: The aim of this study was to determine the efficacy of postoperative radiotherapy by a high dose rate Iridium 192 mould in the prevention of earlobe keloids.

Materials/Methods: Between March 1999 and March 2003, 22 patients with 24 earlobe keloids were treated by radiotherapy immediately following surgical excision. A dose of 15 Gray in 3 fractions was delivered at a point placed 5 mm from the axis of the Iridium sources.

Results: Twenty two patients with 24 keloids were treated; 15 cases with 16 lesions were followed for a minimum of 6 months. A recurrence occurred in two lesions (12.5%). There were no severe adverse effects.

Conclusions*:* Postoperative radiotherapy by high dose rate Iridium 192 mould was an effective prevention of earlobe keloids. It was well tolerated and did not present any significant side effects.

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STATUS OF BRACHYTHERAPY FACILITIES AND APPLICATIONS IN POLAND IN 2006

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Purpose/Objectif*:* One of the current ESTRO projects by is named The Pattern of Care for Brachytherapy in Europe (PCBE). The first stage of this project was a survey of brachytherapy facilities in the entire European area for 2002. This data has been assembled from almost all European countries and will ultimately help to shape future European brachytherapy policy. This paper presents the current state of brachytherapy facilities and applications in Poland, updated for 2004 and further for 2006, according to PCB recommendations.
Materials/Methods*:* In 2003, an ESTRO Questionnaire on Brachytherapy Practice in Europe was distributed to 25 Polish centers with brachytherapy facilities. They provided data on brachytherapy infrastructure in Poland for 2002. The same questionnaire has been sent out to collect the data for 2004 in order to observe the actual trends and to compare with the estimates given in the previous questionnaires. A new, redesigned questionnaire was sent to the radiotherapy centers in January 2007.
Results*:* In Poland, there are 25 brachytherapy facilities. The numbers of afterloaders installed in these facilities, as of 2004 were: LDRu201322, HDRu201313, PDRu20134. The brachytherapy afterloading equipment is modern and in good technical conditions. The population of Poland is 38.5 million and the total number of patients undergoing brachytherapy irradiations is about 8000 per year. This is a very large number as compared to other European countries. The brachytherapy is applied for virtually all tumour localizations (HDR), however about 78% brachytherapy is used for treating gynecological tumours (still mostly LDR technique, slowly being replaced by HDR/PDR).
Conclusions: Current number of brachytherapy facilities seems to be adequate taking into consideration the population and estimated cancer incidence in Poland.There is a need for further training of radiation oncologists in more complex HDR techniques in order to take full advantage of the existing equipment. The PCBE study should be continued in order to monitor the changes and progress in brachytherapy development.

Physics

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ANALYSE OF OUR PERMANENT PROSTATE BRACHYTHERAPY IMPLANTS LEARNING CURVE

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Purpose/Objectif: The objective of this work is to analyse the 125I permanent prostate brachytherapy implant learning curve in our instituition after one hundred aplications.The implant method used follow the recommendations of several organizations, such as ABS, AAPM and ESTRO, and use the AAPM TG 43 formalism for dosimetry. The prescription dose was 145 Gy. We make TRUS real-time intra-operative dosimetry, using BK biplanar transducer, and Varian Variseed 7.1 software. The sources are IsoSeed I25.S06 125I from Bebig and we mix loose and strand seeds. A CT was performed one month after the implant for post-implant dosimetric analysis.
Materials/Methods*:* We begin this technique in June 2004, and one hundred patients were treated. To investigate any changes with time, we divided them in three groups of 33 (34 for the last one). The learning curve analyse was made by two ways: first we analyse the total activity implanted versus prostate volume, for all patients, and for the three study groups; and then we analyse of the post implant quality indices, using Dose Volume Histograms, such as V100 (the percentage of prostate volume receiving 100% of the prescibed dose) and D90 (dose to 90% of the prostate volume).
Results: Table 1 summarise the results for the total activity implanted / prostate volume ratio, V100 and D90, with the standard deviation, for all patients and groups.No statistical differences were found in the relation between total activity implanted and prostate volume in all study groups, but standard deviation (SD) becames smaller along time.The results for V100 and D90 become better with time, and the bigest increased was for the second group of patients.
Conclusions*:* With this work we show the learning curve for 125I permanent prostate brachytherapy implants. Time evolution analysis for total activity implanted per unit prostate volume and for dosimetrisc quality indices show that we are in the right way.

		Group 1 (SD)	Group 2 (SD)	Group 3 (SD)	All patients (SD)
Act./Vol. (mCi/cc)		0.77 (0.18)	0.82 (0.16)	0.79 (0.14)	0.79 (0.16)
V100 (cc)	Min	70.1	70.1	71.9	-
	Med	84.1 (6.9)	86.5 (6.2)	86.9 (6.6)	85.8 (6.6)
	Max	97.2	96.8	96.6	-
D90 (Gy)	Min	91.6	104.0	111.4	-
	Med	131.8 (16.0)	139.0 (14.2)	140.3 (13.9)	137.0 (15.1)
	Max	169.2	171.5	168.1	-

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BROAD BEAM TRANSMISSION CURVES FOR NEW RADIONUCLIDES IN BRACHYTHERAPY

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Purpose/Objectif*:* The characteristics of the radionuclides used in High-Dose-Rate (HDR) and Pulsed-Dose-Rate (PDR) brachytherapy combine a high specific activity with the emission of relatively low-energy photons, i.e. mostly below 100 keV, and a half-life suitable with regular source exchanges in the afterloader. These radionuclides must maintain similar dose distribution in the clinical range around the sources. Among these radionuclides are the classic Cs-137, Co-60, Au-198, Ir-192 and the new Yb-169, and other promising radionuclides such as Tm-170, W-181, Ga-153, Ce-144 and Sa-154 that may be considered for use in new types of afterloading equipment. However, the complexity of the spectrum of these isotopes and the scarcity of radioprotection data for the low-energy range in the literature makes it difficult to determine the required thicknesses of protection material for the design of the protecting walls. The purpose of the present study is to calculate broad beam transmission curves for the radionuclides mentioned above.
Materials/Methods*:* With the help of the GEANT4 Monte Carlo code, basic data required for the design of HDR-PDR brachytherapy treatment room facilities have been derived. The results are presented in the form of broad beam transmission curves through concrete and lead walls. Half Value Layer (HVL) and Tenth Value Layer (TVL) have been derived. Also an analytical expression for the calculation of lead and concrete barrier thicknesses necessitated by any combination of distance, dose limit, and occupancy and facility workload is presented. The potential effect of attenuation within the patient to

radiation shielding calculations is also evaluated.
Results*:* From the transmission curves HVL and TVL for both lead and concrete were obtained for each radionuclide. HVL for concrete are: 20 mm (Ce-144), 20 mm (Tm-170), 20 mm (W-181), 14 mm (Ga-153) and 8 mm (Sm-154). HVL for lead are: 0.13 mm (Ce-144), 0.17 mm (Tm-170), 0.14 mm (W-181), 0.08 mm (Ga-153) and 0.06 mm (Sm-154). Furthermore, the attenuation by the patient in a typical gynaecologycal application vary between 0.5 (Ir-92) and 0.2 (Sm-154) depending upon the radionuclide.
Conclusions: The radionuclides studied are of potential use in brachytherapy. The broad beam transmission curves have been obtained using Monte Carlo methods and HVL and TVL values have been deducedfrom these curves. The reduction of HVL values for these new radionuclides compared to those for Ir-192 are significant.

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DEPENDENCY OF IN VIVO DOSIMETERS RESPONSE, USED IN MDR/LDR BRACHYTHERAPY, ON TEMPERATURE AND THE ANGLE OF THE INCIDENT BEAM

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Purpose/Objectif*:* Dependency of diode detectors, designed as in vivo dosimetr, on temperature and incident beam angle for MDR/LDR intracavitary Brachytherapy, using Cs-137 sources, was investigated.
Materials/Methods*:* Semiconductor detectors (PTW, type 9112 and type 9113) were irradiated using Cs-137 sources, with apparent activity of 34.9 mCi, incorporated in a Selectron machine as well as using Manchester applicators. Firstly, detector dependency on the temperature was investigated with the immersion of probes into a water tank for a range of possible temperatures. Varying the temperature from 25°C to 35°C in 2°C steps, the experiment was then repeated three times under a dose rate of 187.5 cGy/h (MDR) at 3 cm distance. Secondly, to investigate the variation of the radiation beam angle on diodes response, the sources were placed at 5 cm distance from diodes at 0°, 30°, 44° and 53° angles, under the dose rate of 21.48 cGy/h with constant temperature of 26°C.
Results*:* A slight increase of diodes responses was observed with the increase of the temperature. The linear regression of three series of results was found to be on average 0.08% per degree Celsius. A linear decrease on the diodes responses was also observed with the increase of the radiation angle (-0.09% per degree).
Conclusions*:* The current study showed that the there is no significant variation in the response of diodes with the temperature for MDR Brachytherapy. However, radiation beam angle variation led to a decrease of diode response significantly. In conclusion, the observed temperature effects can be neglected and the impact of the radiation beam angle variations should be taken into consideration using possible corrections in diode readings. The achieved results were found to be different from diode response reported for HDR sources.

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DISPOSITION ESTIMATION OF RADIATION DOSES IN GYNAECOLOGICAL PATIENTS USING CYLINDRICAL APPLICATOR

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Purpose/Objectif: The aim of the work is the analysis of the position displacement of the cylindrical applicator and dosimetric sonds used in the group of patients treated by HDR brachytherapy in the Department Brachytherapy. The next step is to evaluate the dependence of total dose of the four fraction from the measured displacement of the applied cylindrical applicator and dosimetric sonds.
Materials/Methods: Analysis of the position displacement of cylindrical applicator in the successive applicators in the Department. Planning of the dose disposition was carried out using Plato-BPS system.A correlation has been notified, in dosimetry in vivo, between planned and measured doses. The change of position of he beginning or the end of the applicator in the examined group of patients has a statistical influence on the percentual differences of the registered doses in vivo in six points, which don't change their position between the fractions, in the same patient.
Results: It can be stated that the position of the dosimetric points in the bladder and rectum in the individual fractions is not identical. Therefore it is essential to check the localization of those points and the position of the applicator in order to apply proper fractional and total dose as well as to assume the probability of complications in the critical organ.
Conclusions*:* Reasonable seems to be, to plan the disposition of the doses in case when the position change of the applicator in patient is bigger than 1 mm between fractions. In those cases disposition of the doses differ statistically between invidual fractions in a patient.

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HARMONISATION OF THE PRATICES OF BRACHYTHERAPY IN GYNECOLOGY WITH OPTIMIZATION OF DOSE

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Purpose/Objectif*:* The beginning of a new technique like pulse dose rate Brachytherapy in gynecology with 3D dosimetry, needs a specific quality assurance program.
Materials/Methods*:* The regrouping of several departments in the program of support for the diagnostic and therapeutic innovations expensive (supported by the french gouvernement) allowed to establish a common program of quality assurance: · A mandatary participation in the external quality control proposed by Equal Estro in brachytherapy a. geometrical quality control of the planning systems of treatment, b. quality control of the calculated and delivered dose. · A control of the projectors of source. · A control of the systems guaranteeing the safety of the treatment for the patient. · A harmonization of the definitions of organ risk and target volumes, in collaboration with the physicians. · A comparison of the methods of optimization.
Results*:* The results of the external quality controls will be presented as well as various points of internal quality control. The differences in delineation will be presented in order to illustrate the importance of the harmonization of the definitions of the organs at risk and target volumes. Various methods of optimization will be described with their advantages and disadvantages.

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IN VIVO DOSIMETRY IN BREAST CANCER BRACHYTHERAPY (APBI TECHNIQUE)- PRIMARY RESULTS

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Purpose/Objectif: The topic of the study was examination of the relationship between measured and calculated skin dose in a pilot study of lumpectomy and high-dose-rate interstitial brachytherapy for breast cancer.
Materials/Methods*:* For some of the patients with the breast cancer the HDR technique using APBI (accelerated partial breast irradiation)

method with a Nucletron microSelectron afterloader have been applied. 8 patients treated by interstitial brachytherapy using plastic catheters (system Comfort from Nucletron), were irradiated during 4-days period. The total dose was 32Gy in 8 fractions of 4Gy . The minimal interval between the daily fraction was 6h. For each patient, the planning target volume has been defined as the tumor excision cavity plus margin, which was defined individually (2cm from the tumor). The dose distribution has been calculated and optimized by the Plato treatment planning system (TPS) based on CT. The doses to the skin, calculated by the TPS in selected points defined on the basis of the CT examination, were measured during subsequent fractions with TLD polycrystalline detectors (Li:Mg, Ti) in a form of round sinter (4.5 mm diameter and 0.9 thickness). Detectors have been placed and taped to the skin at the four points, easily defined by position of the scar: nipple, middle part of the scar, middle plane of the entry and the end of the applicators from breast of the patient. For each of patients, 3 to 7 measurments were pursued and than that dose was compared with dose calculated with TPS. After each irradiation the detectors were read out with a Fimel PCL3 TLD reader.

Results: In patients qualified to the study the planning and irradiation dose strictly followed the adopted protocol. In the most of the cases measured dose of the skin was less then the dose calculated from treatment planning system (TPS). The mean percent difference of the dose was 17.42% (range 6.32%–27.31%).

Conclusions: The measurment doses may differ from the calculated doses due to the edema of the breast during treatment and the small discrepancies in positions of the detectors because of their size. One of the advantages of the APBI technique is expected good cosmetics effect, depending on the total skin dose. Thermoluminescence dosimetry has provided useful quality assurance information on the doses received by patients.

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INVESTIGATION ON THE PRACTICES IN PULSED DOSE RATE BRACHYTHERAPY IN GYNECOLOGY WITH OPTIMIZATION

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Purpose/Objectif*:* Within the french group entitled " Utilisation de la curiethÉrapie pulsÉe gynÉcologique (PDR) avec optimisation de la rÉpartition de la dose et dosimÉtrie tridimensionnelle ". An investigation was carried out with the 20 centers taking part in the STIC. It related to the practices, the methods of imagery available, the methods of optimization, as well as the associated quality control.

Materials/Methods*:* Each center described the material used as well as the methods of imagery available. The determination of the lengths of the active sources and the initial prescription had to be described. The methods and criteria of optimization were specified, as well as the associated quality control.

Results: The physicists described with precision their method of reconstruction of the catheters, on orthogonal X Rays and/or directly on the 3D imaging. Many centers let cohabit the 2 methods during th learning curve. Uncertainty on the position of the sources depends on the slice thickness (about 3 mm). this uncertainty is to be compared with the precision of the determination of the volumes by the physician. 3D dosimetry is performed on CT-scan in a majority of cases, the use of MRI tends to increase, the 2D remains as a control. The diagnosis imagery is often made with another method than the dosimetric imagery. By visualizing volumes on the 3D imagery the physician tends to modify (even modestly) thedose distribution compared to that obtained without optimization. Optimization is done while varying the dwell times of the source, manually or graphically. The inverse planning is not used at present

Conclusions: The STIC made it possible for the teams to concentrate their efforts on one method in brachytherapy. The exchange of experience between the centers made it possible to accelerate the evolution towards 3D brachytherapy with optimization. The superiority of MRI for the delineation of volumes leads the teams to use it more often. With MRI, the difficulty of the reconstruction of the sources delays its generalization. It is necessary to note the absence of use of dosimetric indices and common rules of quality control of the distribution of dose

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THE ANALYSIS OF GEOMETRIC IMPLANT PARAMETERS IN MULTICATHETER HDR BRACHYTHERAPY IN ACCELERATED PARTIAL BREAST IRRADIATION

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Purpose/Objectif*:* Treatment plans in multicatheter HDR brachytherapy in Accelerated Partial Breast Irradiation (APBI) can be calculated on the base of fluoroscopic images (IBU) and/or CT scans. Evaluation of dose distribution depends on imagining method. For IBU plans, dosimetric indexes deriving from natural dose volume histogram, inform about dose homogeneity and quality of the implant. The aim of this study was to analyze what are the values of geometric implant parameters that result in satisfactory dosimetric indexes in order to employ them to a new treatment plan in future.

Materials/Methods*:* We treat APBI patients with HDR monotherapy with 4 Gy per fraction BID to total dose of 32 Gy in 5 days. Treatment plans for all patients are calculated on the base of IBU and CT images. For the purpose of this study, six consecutive IBU based treatment plans were selected, then transferred to respective CT scans to get lung and skin dose. Next the following dosimetric parameters: DHI (dose homogeneity index), QI (quality index), and NDR (natural dose ratio), all calculated on the base of DVHs, were analyzed as a function of needle density index DI (combination of the needle number and distance between them within target volume, own definition).

Results: In our IBU plans, maximum skin dose didn't exceed 51%, 1% of lung volume received 39,6% of the reference dose, while mean value of dose delivered to 50% of lung was 6,6% of the reference dose. Satisfactory DHI above 0,7 was received only for DI in range of 0,12–0,14. The formula DHI(DI) was found to describe DHI as a function of DI. In our data, while DI decreased QI index value increased ($r = -0,79$, $p = 0,062$). No statistically significant correlation between NDR and DI has been found.

Conclusions: In our IBU plans, the relation between dose homogeneity and proposed density index has been found. We hope that in future such relation may be helpful in optimization of pre – planning procedure (before needle implantation) giving us suggestion as for number of needles, distance between them and target volume.

Prostate Cancer

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A SEVEN-YEAR EXPERIENCE OF HDR BRACHYTHERAPY BOOST FOR LOCALIZED PROSTATE CANCER: BIOPSY AND PSA OUTCOME

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Purpose/Objectif: To evaluate PSA failure free survival and 24-month prostate biopsy outcome in patients with localized prostate cancer treated with inverse-planned HDR brachytherapy boost.
Materials/Methods: We analyzed the information collected prospectively from 120 patients treated between 1999 and 2005 for localized prostate adenocarcinoma. They received external beam pelvic radiation (44 Gy) followed by HDR Ir-192 prostate boost. Patients were given 18-20 Gy in 2-3 fractions to the prostate gland using inverse-planning with simulated annealing (IPSA). Post-treatment quarterly PSA and two-year control biopsy have been reviewed and analyzed.
Results*:* The median follow-up is 38.28 (18-82) months. Median age is 64 years. In this study, clinical stage distribution is 42.5% T1, 53.3% T2 and 4.2% T3. Population is distributed in three categories of Gleason score: ≤ 6 (38.3%), 7 (55%) and ≥8 (6.7%). Initial PSA is ≤10ng/ml for 60.8%, 32.5% between 10-20 ng/ml and 6.7% is ≥20 ng/ml. Also, 55.8% of patients received hormonotherapy. Categorized by risk of progression, 11.7% of patients are low risk, 72.5% intermediate and 15.8% are high risk. The 24 months prostate biopsies are negative in 62/68 patients (91.2%) and additional 3 show undetermined result. All three positive patients have not demonstrated biochemical failure. Furthermore, biochemical control at 36 months is 98% (135/137) with ASTRO failure definition and 2005 Houston definition. The two patients who present biochemical failure have a follow-up of two years and just experiment PSA raise. On the other hand, PSA bouncing („d2 ng/ml elevation with spontaneous resolution) is found for 19/120 patients and is limited in the first two years. 1 patient died during the follow-up from a cardiac cause.
Conclusions: The use of inverse-planning with simulated annealing (IPSA) HDR brachytherapy prostate boost produces an excellent tumor control rate with biochemical response (98% at 36 months) and negative two-year biopsy rate (91.2%). Moreover, raise of PSA with spontaneous resolution (PSA bouncing) is seen in 16% of patients and seems to be restricted in the first two years. Conservative approach is recommanded in face of a raise of PSA in this window of time.

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ASSESSMENT OF TOLERANCE FOR RE-IRRADIATION WITH USE OF HDR BRACHYTHERAPY TECHNIQUE APPLIED PATIENTS WITH LOCAL RECURRENCE OF PROSTATE CANCER

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Purpose/Objectif*:* Prostate cancer is apart fron lung, the most cammon male cancer. Not long ago just one treatment in cases of failure after radical procedures was pharmacotherapy. For patients with local recurrence of prostate cancer paliative interstitial HDR brachytherapy was started in July 2000 at Brachytherapy Department in Cancer Center in Warsaw.
Materials/Methods*:* Aim of the analysis is assessment of early tolerance for re-irradiation applied to patients with local recurrence after radical radiotherapy. Results for group of 20 patients were evaluated. Patients were irradiated since July 2000 still December 2003. Age of patients was between 51 and 78 years with median of 65,12. Starting PSA level in range of 1,1 to 51,7 and clinical advances from T1NxM0 to T3NxM0. In all cases HDR brachytherapy were used and 30 Gy in 3 fractions (with 3 weeks intervales) was given.
Results*:* Early tolerance of re-irradiation was good. In all cases complete treatment was finished. The most commonly observed toxicity were problems with nycturia. In 5 cases catheters in bladder for 2-3 mounts were necessary.
Conclusions*:* In our analysis re-irradiation of prostate seems good method of paliative treatment local recurrence.

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BRACHYTHERAPY WITH TRANSPERINEAL 125IODINE SEEDS FOR LOCALIZED PROSTATE CANCER

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Purpose/Objectif*:* To evaluate treatment results after permanent prostate brachytherapy in localized prostate cancer.
Materials/Methods*:* Between June 2004 and December 2006, 33 patients with T1-T2b N0 M0 prostate cancer were treated with transperineal 125Iodine seed implants in the Department of Radiotherapy at the S. Orsola-Malpighi Hospital (Bologna, Italy).
Tumors were classified as T1c in 9 patients, T2a in 7 patients and T2b in 6 patients. The mean pre-treatment PSA was 6.06 ng/ml. The mean prostate volume was 35.5 cc (range 16-60 cc) and the mean preimplant urinary flow rate was 19 ml/sec (range 15-29 ml/sec).
The 125Iodine seeds were implanted transperineally under transrectal ultrasound guidance. An average of 86 seeds (range 60-117) were implanted. The dose to the periphery of the prostate was 145 Gy.
In order to evaluate urinary symptoms patients underwent the International Prostate Symptom Score (IPSS) questionnaire before implant and during the follow-up.
Results*:* The mean follow-up was 10.36 months (range 2-24). At this moment all patients are alive without biochemical relapse. Genitourinary acute toxicity such as nicturia, dysuria, increased frequency, were temporary symptoms and they never exceeded the grade 1 score. Acute urinary retention occurred in one patient. One patient developed urgency. Proctitis grade 2 was observed only in one patient. No gastrointestinal toxicity were detected. Three patients reported erectile dysfunction but only one of them had impotence after 4 months from brachytherapy treatment.
Conclusions*:* Transperineal 125Iodine seeds brachytherapy in localized prostate cancer is a very low toxicity treatment; however preimplant urinary flow rate was the most important factor predictive of postimplant acute urinary retention. An increased number of seeds implanted also, near urethra especially, is involved in urethral irritation and in development of acute urinary morbidity. In our investigation all patients had a complete remission with shotdown of PSA after 8 months.

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COMPARISON OF IMRT TO EXTERNAL BEAM AND BRACHYTHERAPY BOOST DOSE-VOLUME PARAMETERS EXPRESSED AS BIOLOGICALLY EQUIVALENT DOSES FOR PROSTATE CANCER.

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Purpose/Objectif: To investigate differences in dose-volume parameters between external beam (IMRT) and external beam combined with brachytherapy expressed as biologically equivalent doses for the treatment of prostate cancer.

Materials/Methods: The CT data sets of 20 consecutively treated patients were selected for this study. Patients were treated with external beam radiotherapy (EBRT) combined with pulsed dose-rate (PDR) brachytherapy. For all these patients a five beam IMRT plan was made up to a dose of 46 Gy prescribed on the PTV (prostate plus 8 mm margin). Additionally a 70 Gy IMRT plan (8 mm margin) was generated with a concomitant boost to 76 Gy on a sub volume (8 mm margin, 0 mm rectum). Also two other plans were made for which the patients received first the 46 Gy IMRT plan, followed by either a brachytherapy plan of 24 fractions PDR or 3 fractions high dose-rate (HDR). The prescribed dose for the brachytherapy plan was on the periphery of the prostate without margin. To facilitate comparison the total biological equivalent dose (BED) given by the combined IMRT and brachytherapy plan was made equivalent to 70 Gy in 2 Gy fractions IMRT, assuming an a/b-ratio for the prostate of 1.5 Gy and 10 Gy respectively. The a/b-ratio for the organs at risk was assumed to be 3 Gy. For both IMRT plans daily positioning variations were taken into account when calculating BED's. One of the evaluated parameters was the BED95 for prostate (BED95p), which represents the minimal BED to 95% of the prostate volume. In the same manner the BED90p and BED50p as well as the minimal BED for 2 ml of the rectum, bladder and 10% of the urethra volume were calculated. An association between treatment modality and BED values was analyzed by two-way-analysis of variance. Pairwise comparisons between groups were performed by the Bonferroni method.
Results: A statistically non-significant association was found for BED90p and treatment modality; P=0.510 (a/b=1.5 Gy) and 0.175 (a/b=10 Gy). For a/b-ratio=1.5 Gy the mean BED95p for IMRT minus PDR and IMRT minus HDR were 5.01 Gy and 4.81 Gy, respectively (all P-values ‹0.001). On the contrary the mean BED50p differences were –24.06 Gy and –29.96 Gy, respectively (all P-values ‹0.001). The mean BED2ml-rectum, BED2ml-bladder, and BED10-urethra for IMRT minus PDR and IMRT minus HDR were 15.33 Gy and 22.14 Gy (both P-values ‹0.001), 14.91 Gy and 22.39 Gy (both P-values ‹0.001), and –11.52 Gy (P‹0.001) and 2.80 Gy (P=0.111), respectively. Similar results were found for a/b-ratio=10 Gy for prostate.
Conclusions: If a biologically equivalent dose is prescribed to the prostate PTV, the minimal BED to 90% of the prostate is similar for the different modalities. The coverage with IMRT is slightly better resulting in a higher BED95p compared to the brachytherapy modalities. However because of high doses in an implant the resulting BED50p for brachytherapy is much higher than for IMRT. Better sparing of rectum and bladder is achieved with combined EBRT and brachytherapy.

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CORRELATION BETWEEN TOXICITY AND DOSIMETRY IN HIGH-DOSE-RATE (HDR) BOOST FOR LOCALIZED PROSTATE CANCER

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Purpose/Objectif: To evaluate urinary and digestive toxicity along with erectile dysfunction in relation with dosimetry for patients with localized prostate cancer treated with inverse-planned HDR brachytherapy boost.
Materials/Methods: The information has been collected prospectively between 1999 and 2005 from 125 patients (median age of 64) treated for localized prostate adenocarcinoma with external beam pelvic radiation (mostly 44 Gy) followed by HDR Ir-192 prostate boost. Patients were given 18-20 Gy in 2-3 fractions to the prostate gland using inverse-planning with simulated annealing (IPSA). At each follow-up visit (median of 38 months, range 19-86), patients filled questionnaires detailing urinary (IPSS), gastrointestinal and sexual symptoms. IPSS score was categorized as mild (0-8), moderate (9-19) or severe (20-35); digestive toxicity rated according to the frequency of the symptoms (none, occasional or regular) and erectile dysfunction without hormonotherapy as severe or not. The worst episode in the acute (≤ 6 months) and late (› 6 months) periods are reported while late erectile dysfunction represents the evaluation at the last visit.
Results: Categorized by risk of progression, 10.4% of patients had low (T1 and GS ≤ 6 and PSA ≤10ng/ml), 72.8% intermediate and 16.8% high (T3 or GS ≥8 or PSA ≥20 ng/ml) risk disease and 76 of them (60.8%) received hormonotherapy. In the acute period, 41.1% and 3.6% of the patients reported moderate and severe urinary symptoms respectively; 17.9% and 2.7% of the patients reported occasional and regular gastrointestinal symptoms respectively; 23.1% had severe erectile dysfunction. Urethral V100 was the only dosimetric factor associated with acute urinary toxicity: mean of 1.65±0.6cc for patients with moderate to severe acute urinary symptoms compared to 1.34±0.5cc for patients with mild acute symptoms (p=0.018). In the late period, 43.2% and 11.9% of the patients reported moderate and severe urinary symptoms respectively. 35.9% and 2.6% of the patients reported occasional and regular gastrointestinal symptoms. 28.9% of patients became impotent at long term. Urethral V100 was also the only dosimetric factor associated with late urinary toxicity: mean of 1.65±0.6cc compared to 1.35±0.5cc for patients with mild late symptoms (p=0.014). No dosimetric factor was significantly related to gastrointestinal symptoms. However, higher urethral doses (V100, V150 and V200) were significantly related to severe erectile dysfunction.
Conclusions: Our clinical study provides evidences that HDR brachytherapy prostate boost using inverse-planning with simulated annealing (IPSA) produces low urinary (based on IPSS-score) and digestive toxicity, even in acute or late phase. Only urethral doses have been found to be prognostic of urinary and sexual function toxicity. Moreover, majority of patients keeps long term potency.

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COSTS OF LOW DOSE RATE 192IR OR 125I BRACHYTHERAPY AND SURGERY AS PRIMARY TREATMENTS OF EARLY PROSTATE CANCER

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Purpose/Objectif: To investigate the costs of low dose rate 192Ir or 125I brachytherapy (BT) and surgery (S) in order to identify possible ways to reduce healthcare costs while still improving quality of care.
Materials/Methods: We reviewed hospital 5 year expenses linked to treatments of the first 35 patients treated with the 3 different approaches since 01/1999 in our institution. We separated expenses of the first 6 months in relation with the primary treatment and the management of acute side effects from the rest of the period, reflecting more the expenses linked to treatment of late side effects.
Results: Considering the first 6 months, median (min-max) expenses were 6617 (2066–47 885) € for S, 7506 (2722–56 944) € for 125I BT and 5759 (2384 -11 629) € for 192Ir BT. 2/3 of the costs resulted from hospitalisation expenses (2955 €) and surgeons fee (1344 €) for S, from radioactive products (4598 €) and radiation treatment (843 €) for 125I BT and from hospitalisation expenses (3282 €) and radiation treatment (902 €) for 192Ir BT. Considering the second period from 6 months to 5 years after treatment, median (min-max) expenses were 1474 (1–20 096) € for S, 275 (31–11 286) € for 125I BT and 455 (15–21 527) € for 192Ir BT. 4/5 of the costs after S came from hospitalisation expenses (763 €) and surgeons fee (381 €).
Conclusions: Costs of S and 125I BT are equal, and higher than 192Ir BT. The highest costs come largely from hospitalisation expenses for S or 192Ir low dose rate BT and from radioactive products for 125I BT. Reducing hospitalisation time to around 4 days with laparoscopic

techniques for S, and with pulsed dose rate irradiation for 192Ir BT while reducing costs of new radioactive products for permanent implants could improve global expenses. However, the costs of late follow up in the surgery arm resulted from more hospitalisation periods, reflecting probably a higher rate of minor technical problems linked to this treatment method.

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EARLY BIOCHEMICAL OUTCOMES OF PERMANENT SEED INTERSTITIAL IMPLANTATION AS MONOTHERAPY FOR PATIENTS WITH PROSTATE CANCER AT THE EUROPEAN INSTITUTE OF ONCOLOGY

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Purpose/Objectif*:* To report the incidence of acute and late toxicity and the biochemical outcome after transperineal ultrasound-guided permanent prostate brachytherapy (PPB) in a single institutional group setting.

Materials/Methods*:* From October 1999 to May 2006, 246 patients (pts) underwent PPB using either 103Pd (16 pts) or 125I (230 pts) for primary clinical T1a/T3a N0M0 (1997 AJCC) adenocarcinoma of the prostate gland (237 pts) or local recurrence after surgery and/or external beam radiotherapy (9 pts). Risk group distribution was as follows: low risk 172 pts (73.8 %), intermediate risk 48 pts (20.6 %) and high risk 13 pts (5.6 %); 4 pts with Gleason Score not valuable. A total of 146 pts (59%) were treated with neoadjuvant hormones mainly to downsize the prostate volume. The first 60 pts were treated using a pre-operative preplanning, the following 186 pts were treated using a perioperative treatment planning with dedicated hardware and software available at our Institute from April 2001. Urinary symptoms (International Prostatic Symptom Score, IPSS) and uroflowmetry were evaluated before treatment. Biochemical disease-free survival (bNED) was defined by the ASTRO 1997 consensus definition. Bounces were defined as any rise in PSA level that was followed by a fall of any magnitude.

Results: The median follow-up was 35 months (range 1–72) with a median of 8 PSA-dosages per patient. Ten patients were lost to follow-up. Specific overall survival was 98.5%. The bNED and bounce rate using risk stratification was 79.7% and 10.5%, 39.7% and 25%, 30.7 % and 7.7% in patients at low, intermediate and high risk group, respectively. Fourteen patients (5.7%) developed acute urinary retention, requiring either a Foley catheter or temporary suprapubic cystostomy. All patients removed the catheter in a few weeks. No patient developed urinary incontinence.

Conclusions*:* PPB offers acceptable bNED in pts affected by clinically localized prostate cancer. After PPB, serious adverse symptom are rare, with low incidence of urethral stricture requiring TURP. Postoperative urinary retention is a relatively common event not translating in late toxicity. These early results are comparable with literature, but longer follow-up is needed to confirm the efficacy and safety of this treatment.

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HDR BRACHYTHERAPY AS A EXCLUSIVE TREATMENT FOR LOCALIZED PROSTATE CANCER. 3-YEARS RESULTS . PILOT STUDY

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Purpose/Objectif: HDR brachytherapy seems be very effective and elegant methode for localized prostate cancer. In most of the trials brachytherapy is combined with diffirece schemes of exteranal irradiation. New technologies in visualization and planning with protection of "high risks" organs giving a chance for use the HDR brachytherapy as a exclusive treatment for the patients with locaized ane well defined prostate cancer

Materials/Methods: Between 10.2001-02.2003 15 pts with localized prostate cancer were treated in Warsaw Cancer Center Brachytherapy Department. In all cases PSA level was below 10, Gleason score less than 7, T stage 2 (a or b), and age › 70. Combined treatment was performed with 6 mths of MAB and in the middle of hormonal therapy HDR brachytherapy was performed. Routinly 3 fractions 15 Gy each were given every 21 days to the total physical dose 45 Gy. Specification was done on the gland capsule with 90% of covering. Dose for urethra was calculated no more than 80% and for rectum wall on the level of 30%

Results: In all ceses no any site effects were observed inc. bladder, urethra or rectum wall. During at least of 3 years of obsevation no any late effects were observed. All pts are alive with PSA level below 0,5 and no any TRUS symptoms of reccurence of disease. Late effects are detected by colonoscopy and cystoscopy once a year. Mean follow up for the whole group is 42 mths

Conclusions*:* For the exctracted of low risk grup of patients with prostate carcinoma HDR brachztherapz as a exclusive treatment seems be safe and quite

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HEXAGONAL COORDINATE SYSTEM AS NEW TEMPLATE GEOMETRY FOR INTERSTITIAL BRACHYTHERAPY OF PROSTATE–A COMPARISON OF CARTESIAN AND HEXAGONAL IMPLANT GEOMETRY

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Purpose/Objectif: To analyse quality of dose distribution in the prostate using different arrangement of needle coordinates "traditional" Cartesian and "new" hexagonal implant geometry respecting the necessity of protection of the urethra and to have the best values of dose parameters regarding target tissue (prostate) as D90, V90, V100.

Materials/Methods: Different arrangements of Cartesian or hexagonal coordinates of needles were recontstructed and dose distribution calculated in original ultrasound prostate pictures of 20 patients with prostate cancer. We compared our "traditional" template with Cartesian coordinates and a "new" developed template with hexagonal raster. Using hexagonal raster minimum rounding errors were accepted, so that four coordinates of right-angled overlays were in cover with cooresponding of the hexagonal raster (yardstick). As planning system for calculation of dose distribution including geometric optimisation and also for analysis we used Plato BPS (V14.2.6, Nucletron B.V. The Netherlands). The differences of the implant quality were determined on the basis different quality indices.

Results*:* The communication between physician and medicine physicist during implantation of needles is easier using Cartesian coordinate system than using a hexagonal one. It is particularly because of the early identification of shifted positions of the needle tips. The calculated quality indices are better using a hexagonal coordinate

system for needle insertion. Nevertheless the differences–advantages of hexagonal coordinate system–are not convinsingly. A detailed analysis of all differences will be presented.
Conclusions: The use of hexagonal coordinate system as new template geometry for interstitial brachytherapy of prostate is possible. An improvement of the quality of the implant is however not very large, but this implant geometry is more flexible, versatile and make possible to build templates in future with coordinates for needle insertion more closely. Here further analyses are necessary.

149 poster

HIGH DOSE RATE INTENSITY MODULATED BRACHYTHERAPY WITH EXTERNAL BEAM RADIOTHERAPY FOR PROSTATE CANCER: OUR EXPERIENCE

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Purpose/Objectif: We evaluated our experience with high dose rate brachytherapy (HDR) boost in localized carcinoma of prostate.
Materials/Methods: From August 2004 to November 2006, 80 patients were treated with a combination of HDR brachytherapy and external beam (EBRT). Patients ranged in age from 55–79 years, median 69 years. All patients underwent conformal external radiotherapy to the pelvic region or the area of prostate and seminal vesicles in the dose of 45–50.4 Gy. Brachytherapy was applied in two fractions during the 3rd and the 5th week of external radiotherapy at a dose of 8 Gy per fraction using the interstitial transperineal application technique with HDR–Ir192 source. Based on the initial PSA levels, Gleason score, and T classification, patients were divided into three groups according to the relapse risk: low risk group (25 % pts.), medium risk group (37.5 %), high risk group (37.5 %). We used intraoperative planning with Tuned inverse optimization followed by graphical optimization (GOTIO). The dose volume histogram (DVH), dose to the anterior rectal wall and dose to the urethra were evaluated in each patient. The maximum determined dose was 125 % of the dose prescribed at the reference isodose for the urethra, and 85 % of the reference isodose for the anterior rectal wall, respectively. Calculated parameters were verified on in vivo dosimetry. We evaluated acute toxicities of treatment according RTOG.
Results: Treatment volumes ranged from 18.4 cm3 to 93.5 cm3, median 34.70 cm3. Median number of needles was 12 (range: 5–18). Median V100 was 85.51% (range: 50.67–95.8 %). Median D90 was 7.40 Gy (range: 1.42–8.95 Gy). We analyzed volume of PTV with 100% dose. The number of implantation with V100 › 85% was 86 (55.9%), with V100 ‹ 75 % was 18 (11.7 %). The acute toxicities are recorded in table. We compared calculated doses with measured doses in uretra. The measured dose was smaller in 70.3 % cases, mean deviation was 0.48 Gy. In vivo dosimetry in rectum is very orientational. The measured doses are ranged 0.68–4.79 Gy, median 1.96 Gy.
Conclusions*:* Pelvic EBRT interdigitated with transrectal ultrasound guided real–time conformal HDR prostate brachytherapy boost is both a precise dose delivery system and a very effective treatment for prostate cancer. These results, coupled with the low risk of complications, the advantage of not being radioactive after implantation, and the real–time interactive planning, define a new standard for treatment prostate.

		1 m. after RT	4 months	7 months
GU toxicity	G 0	48,0 %	70,9 %	74,0 %
	G 1	40,0 %	25,4 %	24,0 %
	G 2	10,7 %	3,6 %	2,0 %
	G 3-4	1,3 %		
GIT toxicity	G 0	81,4 %	92,8 %	96,0 %
	G 1	17,1 %	7,2 %	4,0 %
	G 2	1,5 %		
	G 3-4			

150 poster

INTEGRAL DOSE TO PROSTATE AND URINARY SYSTEM CONSIDERING GEOMETRICAL CHANGES IN IMPLANT AND PROSTATE GEOMETRY AFTER I-125 SEED IMPLANTATION

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Purpose/Objectif*:* After prostate implantation, dose calculation is usually based on a single imaging session, assuming no geometrical changes occur during the months of dose accumulation. In this study the effect of changes in anatomy and implant geometry on the integral dose in prostate and urinary system was investigated.
Materials/Methods: At three different moments (1 day, 1 month and 3½ months) after seed implantation, a combined TRUS-CT scan was made of thirteen patients. The consecutive scans were used to determine the changes in dose rate distribution in prostate, urethra and bladder. The "geometry corrected" dose distribution in each organ was estimated by integrating interpolated dose rates. Some physical characteristics of the implants, such as shrinkage and shift were evaluated.
Results: Parameters representing high dose volumes in prostate and urethra were largely underestimated when based on the day-1 scan: V150 of the prostate 18±10 % (p=0.0001) and V120 of the urethra 47±32 % (p=0.0001). The dose to a 2 cm3 hotspot in the bladder wall (D2cc), determined at day-1, was 31±35 % higher than the geometry corrected value (p=0.003). The shrinkage of the implant in time appeared to be largest in cranio-caudal direction (1.8±0.8 mm).
Conclusions: Values indicating the adequacy of dose coverage of the prostate, V100 and D90, were not influenced by geometrical changes and independent of the post-implant scan date. Other parameters representing high dose volumes changed strongly within the first month after implantation. Remarkably, the shrinkage of seed implants over time was non-isotropical and largely exceeded the volume reduction of the prostate.

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INTERSTITIAL HIGH DOSE RATE (HDR) BRACHYTHERAPY UNDER LOCAL ANESTHESIA FOR EARLY STAGE PROSTATE CANCER

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Purpose/Objectif: Transrectal Ultrasound (TRUS) guided interstitial implant for prostate cancer using Low Dose Rate (LDR) and High Dose Rate (HDR) techniques has been reported with results comparing very favorably to external beam radiation therapy. TRUS interstitial implant of the prostate has been traditionally performed under general or spinal anesthetic in an operating room. We report our results with a technique performed under local anesthesia in a Department procedure room.
Materials/Methods*:* Patients with T1 and T2 localized prostate cancer were judged to be candidates for TRUS guided interstitial implant.
Results: Between 2002 and 2007, 312 TRUS guided prostate implants were performed under conscious sedation + local anesthesia. Conscious sedation consisted of intravenous Morphine (12-22 mg) and Versed (6-14 mg), or intravenous Demerol (50-175 mg) and Versed (3-12 mg). Local anesthetic was given with a mixture of of 1% Lidocaine, 0.25% Marcaine, 1:100,000 Epinephrine, and 4% Sodium Bicarbonate neutralizing solution (20-120 cc). Local anesthesia was given to a 5 x 5 cm perineal area to a depth of 10 cm under TRUS guidance. The implants were placed under mobile multi-plane prostate template (Radiation Therapy Products Prostate Template) guidance using from 3 to 4 planes, and 12-22 needles. Needle spacing was 1.0 cm. The implant procedure

included sigmoidoscopy and cystoscopy. Median implant time was 45 minutes (range : 30 to 150 minutes). HDR treatment was given using the Nucletron afterloading system. The implant volume received 2,250 cGy in 3 fractions prescribed to the 100% Isodose line, given over 24 hours. Urethral dose points were followed, and limited to ‹ 105% of the prescription dose. The procedure was well tolerated, with all patients having completed the procedure. One patient developed respiratory suppression, and required reversal with Narcan. He recovered uneventfully. Otherwise, there have been no complications to date.

Conclusions: TRUS interstitial implant of the prostate under conscious + local anesthesia is feasible, and well tolerated. Implant time and complications compare favorably to general or spinal anesthetic technique.

153 poster

NOVEL PROSTATE BRACHYTHERAPY TECHNIQUE–EFFECT ON DOSIMETRY AND POTENCY

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Purpose/Objectif*:* Erectile dysfunction (ED) following prostate brachytherapy (BXT) has been reported to be related to dose received by the penile bulb. To minimise penile bulb dose, whilst preserving prostate dosimetry, we have developed a novel technique for I125 seed BXT using both stranded seeds and loose seeds delivered with a Mick applicator, and implanted via the sagittal plane on trans-rectal ultrasound.

Materials/Methods*:* Post-implant dosimetry and potency rates were compared in 94 potent patients (IIEF score ›11) treated with prostate BXT. In Group 1, 64 patients were treated using a conventional (Seattle) technique of stranded seeds implanted in a modified-uniform distribution. From January 2005 a novel second-generation technique was developed using stranded seeds peripherally and centrally distributed loose seeds implanted via a Mick applicator (Group 2). The latter technique allows greater flexibility when implanting the seeds at the prostatic apex which contribute to penile bulb dose. Each patient was prescribed a minimum peripheral dose (mPD) of 145 Gy. The penile bulb was outlined at 5mm intervals on the day 1 post-implant CT scan. No patients received external beam radiotherapy or hormone treatment. There was no significant difference in mean age between the two groups.

Results*:* The new technique delivers lower penile bulb doses (D25 as %mPD–Group1: 60.7 +/- 35.1, Group 2: 27.4 +/- 12.2, p‹0.0001; D50 as %mPD–Group1: 45.5 +/- 26.4, Group 2: 20.1 +/- 8.4, p‹0.0001) whilst improving prostate dosimetry (D90–Group1: 147 Gy +/- 20.7, Group 2: 160.3 Gy +/- 16.5, p‹0.05; V100–Group 1: 90.7% +/- 5.9, Group 2: 93.4% +/- 3.9, p‹0.05). At 12 months, the potency rate (IIEF ›11) was also improved: Group 1–60.9%, Group 2–83.3% (p=0.017).

Conclusions: The second-generation BXT technique using both peripheral stranded seeds and central loose seeds delivered via a Mick applicator results in lower penile bulb doses, improved prostate dosimetry and appears to result in higher potency rates as well.

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OPTIMIZED PULSED DOSE RATE BOOST BRACHYTHERAPY FOLLOWED BY EXTERNEL BEAM RADIOTHERAPY IN LOCALIZED PROSTATIC CANCER

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Purpose/Objectif*:* To assess the feasibility and interest of 3D optimized pulsed dose rate (PDR) boost brachytherapy and 3D external beam radiotherapy (EBRT) planning for localized prostatic cancer.

Materials/Methods: Since February 1995, 214 patients have been treated in the « Centre FranÇois Baclesse» by an association of 192 Ir LDR brachytherapy delivering 25-Gy on the most posterior prostatic point (2D planning) and an EBRT delivering 34-Gy on prostatic volume (2D planning). Brachytherapy procedure consists in an implantation of 4 to 6 non parallel needles by perineal poncture under anesthesia. We have treated in 2006 another 10 patients (aged from 52 to 75) using the same technique but with 192 Ir PDR brachytherapy 3D system delivering 25-Gy plus a 3D EBRT planning delivering 34-Gy in 17 courses on CTV (prostate). The pre-plan scanner is performed and the patients are positioned in decubitus; positioning needles is controlled under fluoroscopy. A post-operative scanner is performed 6 hours later. DVH are obtained after contouring of CTV, bladders and rectum. The minimal target dose on CTV is 25-Gy, delivered in 50 pulses (one pulse by hour). 3D LDR and optimized PDR treatments plans are realized and compared with each patient. The dose constraints (brachytherapy + EBRT) are :–for the rectum 65 Gy, both on 25% and 2 cm3 of rectal wall,–and 95 Gy for urethra (maximal dose).

Results*:* The average volume of prostate is 59 cm3. The dose distribution of PDR brachytherapy is V25Gy = 100%, V30Gy = 98.2%, V40Gy = 84.2% and V50Gy = 65% against V25Gy = 98%, V30Gy = 93%, V40Gy = 75% and V50Gy = 56% for LDR brachytherapy. The LDR brachytherapy didn't allow to cover 100% of the target volume by the minimal target dose (25Gy) but only 22.2 Gy (meandose) whereas the PDR increased the dose by 3.6 Gy, 4.7 Gy, 4.3 Gy and 5 Gy respectively on D100%, D95%, D90% and D85%. On average the total added dose (brachytherapy and EBRT) are 74 Gy (D85%) and 84 Gy (D65%) with optimized brachytherapy Vs 69 Gy (D85%) and 79 Gy (D65 %) with LDR brachytherapy. The acute toxicity is reported with RTOG criterias. There was no urinary retention; 1 patient shown a rectal bleeding under platelet suppression agent and another one shown once a hematuria stage which was probably linked to the puncture in itself.

Conclusions*:* A PDR interstitial brachytherapy, as a boost of EBRT, is feasible and allows to improve the dose distribution into the CTV in comparison to LDR brachytherapy; respecting the rectal and urethral constraints. A later trial is necessary to validate this technique based on the late effects and biochemical relapse-free survival.

155 poster

PERMANENT IMPLANT BRACHYTHERAPY FOR PROSTATE CANCER WITH AN AUTOMATIC LOADER AND LOOSE SEEDS. DOES POSITIONING OF AN APEX ADDITIONAL SPACER AFFECT THE DOSIMETRIC PARAMETERS?

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Purpose/Objectif: To assess prospectively the impact of adding an additional (extra) spacer, placed at the end of each seed row, on the dose distribution calculated the day of implant (d0) on TRUS and thirty days post-implant (d30) on CT scan images.

Materials/Methods*:* From march 2005 to december 2006, 172 patients with prostate low-risk carcinoma were treated with permanent I125 loose seed implant alone. The implantation was realized with real time dosimetry and loading with an automatic loader. The prescribed dose was 160 Gy. The study was realized prospectively, on two groups of patients, 99 implanted with an extra spacer added after the last seed, at the end of each row, to avoid seed aspiration beyond the apex (group 1), and 73 patients without (group 2). The dosimetric results obtained the day of implantation and thirty days later were compared between the 2 groups.

Results: The 2 groups of patients were not statistically different according to prostate volume (mean volume group 1: 35 cc, group 2: 37 cc), number of needles (22 in each group), or number of implanted seeds (respectively 74, 70). The following dosimetric pa-

rameters were studied on the dosimetry performed at d0 and d30 : D90, V100, V90, V150, U30, RV160. None of them were statistically different. In particular, mean value of D90 was 181 Gy in each group at d0 (p=0.83), and 155 versus 159 Gy at d30 (p=0.21). Moreover the number of seeds found positioned beyond the apex was not correlated to the addition of extra-spacers. (0.9 versus 0.8) (p=0.59).
Conclusions*:* The addition of an apex spacer at the end of each seed row does not influence the dose distribution on the final dosimetry.

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PROSTATE BRACHYTHERAPY–UPDATED UK 5-YEAR BIOCHEMICAL RELAPSE-FREE SURVIVAL DATA

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Purpose/Objectif: 926 patients have undergone low dose rate (LDR) prostate brachytherapy in our unit to date. In response to NICE's call for UK brachytherapy data, we present prospective outcome results for the first 400 treated patients.
Materials/Methods*:* Data was analysed from a prospective database of 400 consecutive patients treated with LDR interstitial I-125 prostate brachytherapy between March 1999 and December 2003. Patients were stratified into low (49%), intermediate (36%) and high (15%) risk as defined by the Memorial Sloane Kettering Prognostic Index. Patients received 145Gy brachytherapy (BXT) alone (42%), BXT with 3 months neoadjuvant androgen deprivation (NAAD) (38%), 45Gy external beam radiotherapy (EBRT) with 110Gy BXT (3%), or a combination of NAAD, 45Gy EBRT and 110Gy BXT (17%). Biochemical freedom from disease and PSA nadirs were analysed for risk groups and for treatment received in each risk group.
Results: Median follow-up was 54 months (range 36-93 months) with a mean patient age of 63 years. Prostate cancer-specific survival was 99.5%. 26 patients (6.5%) experienced biochemical failure according to the "Houston" definition (PSA ≥nadir plus 2 ng/ml)): 7 (1.75%) low risk, 14 (3.5%) intermediate risk, and (1.25%) 5 of the high risk patients. When stratified by treatment group for low, intermediate and high risk patients, the 5-year actuarial BRFS was 92%, 84%, 100% for BXT alone; 80%, 64%, 94% for NAAD and BXT; 100%, 75%, 80% for EBRT and BXT; and 100%, 86%, 92% for NAAD, EBRT and BXT respectively. Overall 4- and 5-year PSA ≤ 0.5 ng/ml was achieved by 87% and 84%, and a 5-year PSA ≤ 0.2 ng/ml was achieved by 77%.
Conclusions:
This prospective study updates our previously published biochemical relapse free survival, and demonstrates that the excellent USA reported outcomes for BXT are reproducible in the UK.

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PROSTATE VOLUME VARIATION DURING REAL-TIME DYNAMIC PERMANENT BRACHYTHERAPY

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Purpose/Objectif*:* The use of real-time dynamic brachytherapy (RTDB) has been extended because it is the current most recommended treatment option. During the implant process, the prostate volume can be increase because the edema. The intensity of this edema has a high variability and apparently is patient specific. The purpose of this study is to compare the prostate volume at the operating room prior to needle insertion and after seed implantation. The correlation between this variation and some clinical-physical parameters is studied in a preliminary set of patients.
Materials/Methods*:* A group of 15 consecutive patients underwent RTDB with I-125 seeds, has been included in this study. Automatic afterloading SeedSelectron (Nucletron, The Netherlans) was used in combination with the TPS SPOT-PRO (Nucletron, The Netherlans) to perform prostate implants. For 6 patients RTDB was the exclusive treatment with 145 Gy prescription dose (PD) and for the others 9 patients (intermediate risk) it was combined with external radiotherapy with 100 Gy PD. 13 patients were previously treated with androgenic blockade. Prostate anatomy is scanned and contouring prior to implant in order to get the plan updated after the needle insertion. For this study, once seed implant is finished, a new scan was acquired where prostate was newly contoured and its new volume was compared with the previous one. This variation has been correlated with the initial prostate volume, needle number, androgenic blockade (if applicable) and RTDB (if applied exclusively or as complement of External RT).Data were analyzed with SSDS statistic package.
Results*:* The initial volumes ranges from 11.5 cm3 to 39.5 cm3 with mean of 24.6 cm3 and standard deviation 9.2 cm3 (k=1). The number of needles ranges from 12 to 22 with mean of 17.7 and standard deviation 2.6 (k=1).The relative volumes increased range from 2.2% to 47.8% with mean of 20.0% and standard deviation 13.7% (k=1). When the edema volume values were compared with inserted needle number, with or without External RT and with or without androgenic blockade, no correlations were found. Despite the low patient number in this preliminary study, the impression of the data graphical tendency supports the former results.
Conclusions: Although the edema volume varies from patient to patient, none of the analyzed parameters in this study shown significant correlation with this fact. Nevertheless, a major sample size should be desirable in order to confirm these data.

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PULMONARY MIGRATION OF PERMANENT INTERSTITIAL LOOSE SEEDS IN PATIENTS UNDERGOING PROSTATE BRACHYTHERAPY : THE ROLE OF EXPERIENCE

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Purpose/Objectif*:* Our group previously reported on the percentage of pulmonary migrating seeds in a series of 170 patients treated by the real-time technique with loose seeds (Isoseed Bebig), between September 2001 and August 2002 (Chauveinc et al, Cancer/ RadiothÉrapie, 8 (2004) 211-216). In this first series, one (or occasionally several) seed(s) were found on the systematic post-operative chest X-ray in 27 patients (15.9 %). Moreover, a total of 32 seeds were found to have migrated to the lungs, out of the 12,179 which were implanted (0.26 %). Those numbers grossly corresponded to what was reported in the literature at that time .
Materials/Methods*:* Four years later, after more than 1300 implantations performed by our group, we re-evaluated the pulmonary seed migrations for the 203 patients treated between September 2005 and August 2006, again with a systematic post-operative chest X-ray for all patients.
Results*:* The percentage of patients with pulmonary migrating seed(s) was found to be very significantly reduced in our last cohort (6.4%in the 2005-2006 cohort versus 15.9% in the 2001-2002 cohort ; p=0.003), as well as the percentage of seeds having migrated to the lungs(0.11% versus 0.26%; p=0.006).The table below shows the detailed comparison of the two series .

Conclusions: Out of 1,000 implanted seeds, only one migrated to the lungs in our 2005-2006 series, a very significant gain when compared with what was observed in our 2001-2002 cohort.Based on our experience, specific attention devoted to the strict intraprostatic implantation of the loose seeds under real time ultrasound guidance is probably responsible for such an improvement.

	Sept.2001-Aug.2002	Sept.2005-Aug.2006	
% of pts with pulmonary migrating seed(s)	15.9 % (27/170)	6.4 % (13/203)	$p = 0.003$
% of pulmonary migrating seeds	0.26 % (32/12,179)	0.11 % (14/12,458)	$p = 0.006$

159 poster

QUALITY OF LIFE AND SYMPTOMATOLOGY SELF-REPORTED BY PROSTATE CANCER PATIENTS TREATED WITH RADIOTHERAPY; RADICAL EXTERNAL BEAM RADIOTHERAPY (EBRT) AND OR PROSTATE BRACHYTHERAPY (PERMANENT I125 BRACHYTHERAPY OR HIGH-DOSE-RATE (HDR) BRACHYTHERAPY)

C. Springer

Windsor Regional Cancer Ctre, *Department of Radiation Oncology, Windsor, Ontario, Canada*

Purpose/Objectif*:* A prospective, descriptive, correlative study with a convenience sample 220 patients with localized, pathologically confirmed adenocarcinoma of the prostate treated and followed at the WRCC Treatment options included permanent I125 implant alone (78 patients), or combined with external beam radiotherapy (26 patients), and EBRT alone (81 patients), or combined with high-dose-rate brachytherapy (35 patients).

Materials/Methods*:* A baseline demographic assessment, and questionnaires regarding decision-making, and information access were administered at entry into the study. Assessments instruments used included the European Group Quality of life questionnaire (EUROQOL), Symptom Distress Scale and the American Urological Association (AUA) questionnaires administered at base line, 1 month, 3 months, 6 months and 12 months post-treatment. Data was collected prospectively during the period 1999 to 2005.

Results: There were some significant differences in mean age between the groups with the patients in the EBRT group tended to be older and patients receiving HDR brachytherapy younger. Information preference was based on the treatment available and the likelihood of cure. Decision was primarily based on physician-family interaction. The physician-nurse team was identified as the most helpful during the decision-making process, treatment and follow-up. There was a general decline in erectile function at 12 months compared to pretreatment function: I125 implant (47/48%), HDR+EBRT (43/60%), I125implant+EBRT (54/48%), and EBRT alone (59/78%). The predictors of quality of life at 12 months varied with the choice of treatment. Bladder and sexual dysfunction were the main predictor for patients receiving I125implant alone or combined with EBRT, whereas bowel dysfunction was the main predictor for patients receiving EBRT. The analysis failed to identify a main predictor for patients choosing combined HDR brachytherapy and EBRT.

Conclusions*:* The cohort of prostate cancer patients generally based their treatment choice on the likelihood of cure of available treatment and the physician-family interaction. The radiotherapy treatment options offered were generally well tolerated but the sample size was too small to discriminate between them in terms of associated symptomatology and effect on quality of life. One-half of the group, whose average age was 67 years, reported an inability to have an erection at base line. The largest decline occurred the EBRT group.

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REAL-TIME DYNAMIC PERMANENT PROSTATE BRACHYTHERAPY: DAY 1 AND DAY- 30 CT-MR ANALYSIS

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Purpose/Objectif: The use of real-time computer assisted dosimetry on operating room for prostate brachytherapy has become on an important improvement over the implant quality (real-time dynamic brachytherapy–RTDB). It is well know the subjectivity defined prostate volume in the CT if it is used alone. The other hand, MR represents the current gold standard in definition of prostate anatomy. The purpose of this study is to compare the dose assessment assumed on the operating room with those of the day-1 and day-30 plans, in order to know the benefices of this technique and the edema influence, using MR for pos-implant anatomy delineation.

Materials/Methods*:* A set of 10 patients underwent RTDB with I-125 seeds. Automatic afterloading SeedSelectron (Nucletron) was used in combination with the TPS SPOT-PRO. On day-1 and day-30, CT and MR were performed for each patient fussing both into the TPS software. These two post-plans were compared with the resulting ultrasound based plan on the operating room (ORP) once needles and seeds were updated and optimized. For each plan, the parameters stored have been: Prostate (Volume, D90, D100, V100, V150, V200), Urethra (V150, Dmax, D90), this last one was not obtained on day-30. For Rectum D0.1 cc was obtained too on day-1 and 30 plans. These parameters were compared for the three plans to evaluate: 1) The similarity of ORP, with day-1 plan to evaluate effects of eventual intra-implant movements and anatomy variation. 2) The evolution of dosimetric parameters because edema comparing day-1 and day-30 plans. 3) The improvement of RTDB comparing the operating room plan with the day-30 one, where the edema factor is minimized.

Results: In this study, which is planned to be completed with large patient number, the most representative preliminary results are:The prostate volume increases due to edema but finally day-30 volumes are close to the ultrasound based delineating volume. The main therapeutic parameter D90 decreases significantly from ORP to day-1 but is recover on day-30, keeping 110-130% of Prescription Dose (PD). V150 in Urethra are maintained from ORP to day-1 and after, very close to 0 cc volume. D0.1 on Rectum are maintained from day-1 to day-30, with maximum values around 70-90% of PD.

Conclusions: The effort involved on adapting the plan with needles-seeds on ORP contributes to the improvement of day-30 plan (currently reference plan for this technique). Urethra dose is maintained from ORP to day-1 plan and after.

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REAL-TIME PROSTATE BRACHYTHERAPY USING MAINLY PERIPHERAL STRANDED SEEDS

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Introduction: a new technique for prostate seed brachytherapy (BXT) was introduced recently at this centre which consists of peripherally distributed stranded seeds and centrally implanted loose seeds using the Mick applicator. Positioning of the pre-loaded peripheral needles was based on a pre-treatment plan using ultra-

sound images acquired approximately 3 weeks before implantation to localise organs of interest. A study of the new technique is presented.

Materials/Methods*:* A tracked stepper and a laptop with a VariSeed 7.1 incorporating a twister software are connected to the U/S unit prior to starting the live procedure. In the real time procedure, adjustments to needle positioning and live planning of the central loose seeds is done using U/S images acquired intra-operatively. A seed activity of 15.5 MBq was used. The dosimetric parameters V100, V150 and D90 for the prostate were determined using post treatment CT images.

Results: Initial analysis to date of the dose volume (DV) data for the real time technique:

V100: Mean = 93.8% Range = 90.7-97.9
V150: Mean = 53.5% Range = 37.6-76.6
D90: Mean = 159 Gy Range = 148-184

Conclusions: Initial analysis shows favourable post treatment DV results. This real-time technique using mainly peripheral stranded seeds has clear advantages. As peripheral needles are currently preplanned and pre-loaded, cost time and irradiation of staff is kept to a minimum. This real time procedure takes less than 1 hour and there is no wastage of seeds. Performing an implant with a live update of dosimetric quality alerts ensures DV parameters for prostate and critical sites are kept within desired limits.

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SUB-ACUTE AND LATE MORBIDITY FOLLOWING IODINE 125 PROSTATE BRACHYTHERAPY

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Purpose/Objectif*:* Current evidence on the safety and short to medium term efficacy of low dose rate brachytherapy for localised prostate cancer appears adequate to support the use of this procedure. The aim of this retrospective study is to report the sub acute and late side effects caused by permanent radioiodine seed implant.

Materials/Methods*:* Forty-two consecutive patients with localized prostate cancer underwent permanent interstitial brachytherapy between January 03 and October 06.Mean patient age was 70 years old (range 54 to 83) .Median follow- up was 33.3 months (1.9- 47). The sub acute and late side effect were analysed retrospectively. The RTOG scoring system was used for assessment of urinary function at 6 months for sub- acute toxicity and for late toxicity occurring more than 12 months after the procedure. Erectile dysfunction was also monitored. We analysed the effect of patient and tumour factors, and implants characteristics on the severity of post implant morbidity. The implant was done using a 3 D- ultrasound guided intraoperative technique.

Results: Disease stage was T1c and T2a for 71 and 28 % of patients respectively. All the Gleason score were below or equal to 6.Median PSA level at implantation was 7.45 ng/ml (4.5- 10.9). Dosimetric data were as follows: the mean value of D90 (dose received by 90 % of the target volume) was 163.36 Gy(140- 183).Median urethral D 30 was 173 Gy (143- 202). Median Prostate V 100, V 150 and V200 values(volume of prostate receiving 100, 150 and 200 % of the prescribed dose) were 95.2,53, 17.53 % respectively. No rectal dose limits were specified. Grade 1, 2 and 3 sub- acute urological morbidity was seen in 21.2, 12.2 and 3 % of patients respectively(78 % evaluated). Grade 1, 2 and 3 late urological morbidity at 2 years was seen in 7.1, 2.4 and 2.4 % respectively(60 % evaluated). No grade 4 toxicity was reported. Erectile dysfunction was seen in 47.7 % of patients(67 % evaluated).We noted a correlation between vesical toxicity and initial prostate volume which showed a trend towards significance (p= 0.07) Urethral dose didn't predict any vesical toxicity. A significant correlation(p=0.02) between V 100, V 150 and V 200 and vesical toxicity was found at 6 months . Rectal side effects were minimal, with 96 % of patients having normal bowel function at 2 years.

Conclusions*:* Prostate brachytherapy is a well tolerated treatment modality in patients with localized disease. Urinary morbidity of our patients was well managed with oral medication. Approximatively half of the patients with no major erectile dysfunction pre- implant retained useful function after treatment. No major rectal complications were noted.

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TECHNICAL FEASIBILITY OF TRANSPERINEAL MR-GUIDED PROSTATE INTERVENTIONS IN A LOW-FIELD OPEN MR SYSTEM: CANINE STUDY

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Purpose/Objectif: MRI provides excellent visualization of the prostate, its substructure and surrounding tissues, making it the modality of choice for guiding and monitoring interventions like brachytherapy and biopsy. Our objective was to demonstrate the feasibility of transperineal MR-guided prostate interventions in an open MR unit and to present our clinical experiences on canines.

Materials/Methods: The procedures were performed on 4 canines in an open-configuration 0.35 T MR scanner. For interventions an MR compatible custom-made device was used consisting of 3 major parts: template-obturator rod, immobilization arm and patient tray. The canines were placed feet first in the right lateral decubitus position. Template reconstruction, trajectory planning, target and OAR delineation were based on T2 FSE images. For image guidance and target confirmation, fast gradient spoiled echo (FSPGR) sequence was used; images were obtained in 10 seconds. MR compatible coaxial needles were inserted through the perineum to the base of the prostate. After satisfactory position was confirmed, brachytherapy catheters were placed through the coaxial needles, which were then removed. Verification of transport induced possible needle displacements were done by X-ray and MR images.

Results*:* MRI allowed clear definition of the prostate, periprostatic tissues, needles and catheters. Mean and standard deviation of the needle displacements at 10.5-11.5 cm target depth was 2.2 mm±1.2 mm, with a median of 1.9 mm. 90% of the errors were less than 4.0 mm; maximum error measured was 4.5 mm. Implantation induced prostate motion was measured with a mean of 10.3 and 2.3 mm in cranio-caudal and transverse directions. Significant movement was only observed during the first 4 needle insertions. Based on MRI and X-ray findings, no appreciable motion of needles was noted after transport. The average time needed for each step was: setup and positioning – 20 min., initial imaging – 15 min., template registration and trajectory planning – 10 min., insertion of 7 needles – 45 min.

Conclusions: A system for transperineal MR guided prostate intervention has been developed and applied successfully on canines. This method seems to be a promising approach for performing feasible, accurate, reliable and high-quality image guidance within a reasonable time span. Our results facilitate us to introduce MR guided high-dose-rate (HDR) brachytherapy as well as biopsy into the daily clinical practice in the near future.

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THE USE OF A SEED-PROJECTOR FOR EXCLUSIVE IODIN-125 PROSTATE BRACHYTHERAPY: THE FRENCH PRELIMINARY EXPERIENCE.

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Purpose/Objectif*:* To analyse a new technique for prostate brachytherapy with permanent Iodine implants characterized by the use of a seed projector after a 3D dosimetric per-operative treatment planning (FIRST technique)
Materials/Methods*:* Between November 2002 and December 2005, 395 patients have been treated in France with this technique in six radiotherapy centres for a localized prostate cancer.
Results*:* Thirteen patients (3.3%) developped a urinary retention, and respectively 7.8% and 26.5%% an acute RTOG grade 3 and 2 toxicity. The 6-weeks IPSS score was equal or lower to 15 in 73% with a 11 median IPSS value. A failure of the loading with the seed-projector, leading to a manual loading of the seeds, occurred in 9 patients (2.3%) in two centres, directly related to the loading procedure with the seed-projector in 5 cases.
Conclusions*:* This multicenter study establishes the feasibility of the routine use of a seed projector for permanent I125 prostate implants with an initial tolerance similar to the best results published for other implants techniques.

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TRANSPERINEAL PROSTATE SEED IMPLANT (TPI) WITH I 125: C.R.O.B"S EXPERIENCE

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Purpose/Objectif: Transperineal prostate seed implant (TPI) with permanent low dose rate seed sources is a popular modality for definitive treatment of early-stage prostate cancer. Dose escalation has became an essential component of radiotherapeutic advances for the treatment of prostate cancer. Increased dose of radiation yields improved biochemical control, particulary for locally prostate carcinoma.
During TPI, radioactive sources are placed in the patient's prostate under ultrasound guidance with to help of a template often with fluoroscopic assistance and based on a pre-implant treatment plan.
Materials/Methods: The experience of perineal implantation for the treatment of prostate cancer at the Oncologycal Hospital C.R.O.B. begins in June 2003. Criteria for permanent implantation were: good general health, localized tumour (T1 and T2a, T2b),moderate or well differentiated, ultrasound measured prostate volume ® 20 cm3 and ‹ 60 cm3 and no or only small TURP defect. Pre-treatment evaluation included palpation and TRUS to establish tumour stage, needle biopsy or small TURP to establish histological diagnosis and grading, PSA level, routine blood examination, bone scan and CT scan of the pelvis to exclude distant metastases. Regional lymph node dissection (either laparoscopic or open) was optional, but was not indicate in patient with well-differentiated tumours and PSA values of ‹ 20 ng/ml [1]. At the Oncologycal Hospital C.R.O.B., Rionero in Vulture, 50 patients were treated by perineal implantation between June 2003 and October 2005. Average age was 71,74 (range 56-85). Stage was: T1, 29%; T2, 71%. Average initial PSA level was 7,108 (range 0,64–14,36). Average Gleason was 5,16 (range 2–8). Average prostate volume was 31,95 cm3 (range 15cc – 65cc). Prostate LDR Brachytherapy consists of I-125 seed implantation and was performed with Rapid Strand, with a high number of seed. Permanent iodine-seed implantation was made with modern techniques including ultrasound guided perineal placement of the needles. The complete treatment was developed in various phases: study of preplanning and post-planning. Treatment was performed under spinal anesthesia in the lithotomy position. A Foley catheter was placed before the introduction of the needles and prophylactic antibiotics were given for 5-7 days. The number of seeds was calculate according to estimated volume of the prostate during ultrasound imaging, according to the pre-plan. Avarage seeds implanted were 78 (range 46 – 135); average seed activity was 0,38 mCi. After implantation of seeds and retraction of needles the positioning of the seeds and the total number was established by fluoroscopy. The patient was hospitalized for 3 days, the day after implantation the catheter was removed and the patient received instructions for radiation safety. One month after, patients were invited for TC-images to verify the positioning of the seeds. We always aimed at a dose of 145 Gy according to TG 43 [2] of the American Association of Physicists in Medicine. All patients were followed alternately by the radiation oncologist and the referring urologist, for the first year at 3 months interval and thereafter at 6 months.
Results: Iodine-seed implantation is patient friendly, with few side-effects, tanks to modern techniques and is well accepted from all the patients. Generally mild effects resolve spontaneously and are well tolerated from patients. CT and MRI images give all information for the elaboration of post-planning. The evidence of a good final result is correlate to a better volume coverage. The dose that covers 90% of the prostate gland (D90) must be ensured, the volume of prostate gland that is treated with 100% of dose (V100) is › 98%.
The short duration of the treatment and the good tolerance of it justifies this procedure particularly in the older man. We conclude that permanent seed implantation is a good alternative for radical surgery and external beam irradiation for patients with localized prostate cancer. Although results are related to treatment period in our experience, we believe that a long experience is important to evaluate better the results.

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WHAT ARE THE PROGNOSTIC FACTORS FOR PATIENTS WITH INTERMEDIATE AND HIGH RISK PROSTATE CANCER RECEIVING HIGH-DOSE RATE BRACHYTHERAPY AND EXTERNAL BEAM RADIOTHERAPY?

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Purpose/Objectif*:* Patients with intermediate and high risk features probably benefit from dose escalation and High-dose-rate (HDR) brachytherapy is a logical treatment modality to deliver the boost dose to an external beam radiation therapy (EBRT) treatment. We studied the influence of different risk factors and neoadjuvant androgen deprivation (NAAD) on treatment outcomes.
Materials/Methods*:* We evaluated 131 patients considered of intermediate or high risk for biochemical failure, who were treated with combination of EBRT (44-50 Gy) and HDR (20-24 Gy, 4 fx, BID) from 1997 to 2004 at Hospital ACCamargo, Sao Paulo, Brazil. HDR was performed after the course of EBRT and the total treatment time should not exceed 7 weeks.

Results*:* Median follow-up was 65.9 months. Median age of patients was 68.7 years (range 47-83). Fifty-nine patients (45%) had no NAAD, 22 (16.8%) had central and peripheral blockage, and 50 (38.2%) had only peripheral blockage. Estimated disease specific survival (DSS) according to ASTRO-Phoenix definition was 84.8% in 5 years. On univariate analysis patients with iPSA ‹ 10 ng/ml and Gleason score (GS) ‹ 6 had a better DSS (p=0.038 and p=0.0230). Table 1. On multivariate analysis the only predictive factor for DSS was GS (p=0.042), 95% CI (1.02-2.7). Patients with GS ›6 had a HR of 1.7 times of dieing of cancer.

Conclusions: Our results suggest that Intermediate and high-risk patients who receive primary EBRT and HDR did not benefited from NAAD, but other factors, as GS, initial PSDA value and clinical stage shall be used in the decision of the need of adjuvant AD.

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WHICH INDEX IS MOST USEFUL AND SENSITIVE WHEN COMPARING DIFFERENT DOSE PLANS?

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Purpose/Objectif*:* At Radiumhemmet, patients diagnosed with prostate carcinoma, have been treated with brachytherapy since 1998. Pre-treatment dose plans, which are based on transrectal ultrasound images of the prostate, are used. Over the years the technique for making dose plans has changed, i.e. the number of needles used has increased. The aim of this study was to evaluate different variables and indices which could be used to compare different dose plans regarding homogeneity.

Materials/Methods*:* 80 patients were randomly selected from two time periods: 40 patients treated during 1999, and 40 patients treated during 2005. For the early treated patients the dose planning system NPS (Nucletron, the Netherlands) was used and for the newly treated patients the dose planning system BrachyVision 7.10 (Varian Medical System, USA) was used. All dose plans were made using manually adjusted dwell-times. The dose plans made with BrachyVision were also graphically optimized. The patients from the different time periods were divided into two groups each according to the volume of the prostate, ‹30 cc and ≥30 cc.For all patient groups the number of needles was recorded. The variables V100(%) and V150(%) were evaluated and the overdose- (OI), the homogeneity- (HI) and the conformal- (COIN) indices were calculated.

Results*:* When comparing data from 1999 with that from 2005 and also between the two volume groups all results show an increase in the number of needles (p‹0.0001). They also show a statistically significant decrease in V150(%) and OI and an increase in V100(%) and HI. However, the COIN index did not show any apparent change.

Conclusions*:* Our dose planning technique has changed during the years especially when changing the dose planning system. The statistically significant changes in V150(%), HI and OI indicate that our present dose plans are more homogeneous compared to the old ones. A major contributory to this improvement is the increased number of needles which result in shorter dwell-times than in the early days. However, the present dose plans show as good coverage of the target as the old ones. As the COIN-index did not show any obvious change on comparison between dose plans the OI and HI indices and the V150(%) seem more useful and sensitive to detect differences in homogeneities in different dose plans.

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