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International Meeting on Prostate Brachytherapy

Eckert & Ziegler BEBIG

23rd–25th November 2012
Mallorca, Spain

Programme and abstracts

International Meeting on Prostate Brachytherapy

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23rd–25th Nov 2012

Eckert & Ziegler

Foreword

Dear Friends and Colleagues,

These are exciting times in prostate brachytherapy! There are now several new approaches which improve prostate coverage and help to avoid unnecessary radiation – image fusion, partial prostate irradiation, 4D imaging, histoscan, and others. With long-term follow-up, side-effects, complications and quality-of-life can be precisely assessed. Approaches to dosimetry are changing. Lastly, different brachytherapy techniques may be best suited to different clinical settings and prostate cancer risk levels.

In short, it is time to sit and think of the future, time to exchange ideas and to share data. The Eckert & Ziegler BEBIG users' group, meeting during the International Meeting on Prostate Brachytherapy in Majorca from 23rd to 25th November 2012, will be just the forum we need.

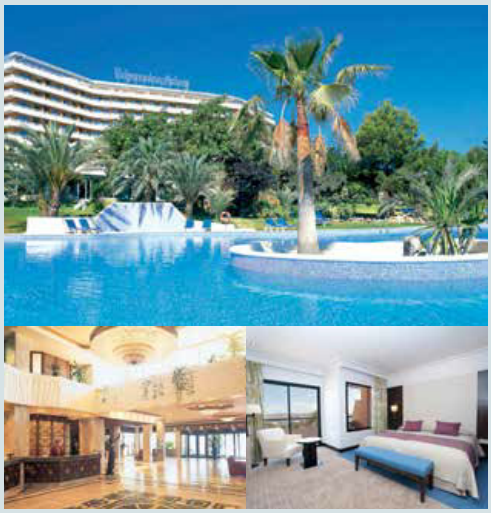
You will see from the programme that we have tried to cover most current questions, leaving only a few aside… But there will be ample time for discussion.

We all hope that Majorca's fine landscapes and food will build the perfect framework for lively conversations and a good time spent with colleagues and friends catching the last sunbeams of the season. We look forward to meeting you in the International Meeting on Prostate Brachytherapy in Majorca.

Best regards,

Prof Pierre Scalliet

Location



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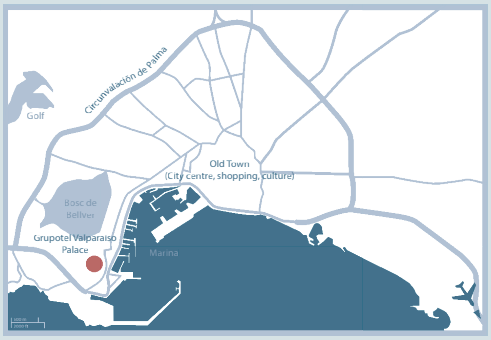

Programme overview

Friday 23th November 2012

6:00 p.m. - 6:15 p.m. Welcome/Introduction
Prof. Pierre Scalliet, Cliniques Universitaires Saint-Luc (president)
Dr. Lurdes Trigo, Instituto Portugues de Oncologia (vice president)

6:15 p.m. - 6:30 p.m. Welcome/Introduction
Abel Luzuriaga, Eckert & Ziegler BEBIG

Saturday 24th November 2012

8:30 a.m. – 09:30 a.m. Opening and kick-off talks
Introduction to the meeting
Prof. Pierre Scalliet, Cliniques Universitaires Saint-Luc (Belgium)
Dr. Lurdes Trigo, Instituto Portugues de Oncologia (Portugal)

Comparative analysis of PSA free survival outcomes.
Results from the Prostate Cancer Results Study Group
Dr. Stefan Machtens, Marien-Krankenhaus Bergisch Gladbach (Germany)

3-D conformal HDR brachytherapy as monotherapy for localised prostate cancer.
Results of > 700 patients treated in one single institution
Prof. Nikolaos Zamboglou, Klinikum Offenbach (Germany)

SESSION I: PCA IN MODERN MEDICINE
CHAIRMAN: PROF. JEAN-MARC COSSET

9:30 a.m. - 10:30 a.m. Quality of life study – Comparison between different treatment options
Prof. Ferrán Guedea, Institut Català d'Oncologia (Spain)

Comparison between existing brachytherapy techniques
Dr. Janusz Skowronek, Greater Poland Cancer Center (Poland)

Consensus paper: ESTRO guidelines in prostate brachytherapy
Dr. Richard Burette, Centre Hospitalier Interrégional Edith Cavell (Belgium)

10:30 a.m. - 11:00 a.m. Coffee Break

SESSION II: CURRENT TRENDS IN PROSTATE BRACHYTHERAPY
CHAIRMAN: DR. THOMAS HENKEL

11:00 a.m. - 1:00 p.m. Focal therapy. Indications, options and role of brachytherapy
Dr. Francisco Gómez Veiga, Hospital Juan Canalejo – Centro Oncológico de Galicia (Spain)

The Paris group experience with focal brachytherapy for prostate cancer
Prof. Jean-Marc Cosset, Institut Curie (France)

Recurrence after low dose prostate brachytherapy: New diagnostic tools and their impact on the management of patients. Perspectives and case discussion
Prof. Thierry Flam, Dr. Dominique Pontvert, Hôpital Cochin/Institut Curie (France)

HDR brachytherapy for prostate cancer: From evidence based medicine to prospective clinical trials
Prof. Jean-Michael Hannoun-Levi, Centre Antoine-Lacassagne (France)

Dosimetric benefits of anatomy-based, inverse planning HDR brachytherapy for prostate cancer
Dr. Luis Felipe Torres, Centro de Control de Cáncer (Colombia)

Fast, intuitive and precise planning of permanent seed implants with PSID 5.0
Dr. Roland Panzer, Imland Klinik Rendsburg (Germany)

1:00 p.m. - 2:30 p.m. Lunch

SESSION III: OUTCOME OF LDR PROSTATE BRACHYTHERAPY
CHAIRMAN: PROF. FERRÁN GUEDEA

2:30 p.m. - 4:30 p.m.

Clinical outcome and dosimetric analysis of 195 low or intermediate risk prostate cancers treated by permanent implant brachytherapy
Dr. Camille Verry (on behalf of Prof Michel Bolla), Centre Hospitalier Universitaire Grenoble (France)

Learning curve experience in LDR prostate brachytherapy
Dr. Thomas Henkel, Ambulantes OP-Zentrum Ullsteinhaus (Germany)

Results of I-125 seed implantation in comparison to radical prostatectomy in men ≤ 60 years
Prof. Alexander Petrovsky, Russian Cancer Research Center (Russia)

Comparison between EBRT and LDR brachytherapy in low and intermediate risk PCa patients
Prof. Gregor Goldner, Allgemeines Krankenhaus der Stadt Wien (Austria)

Sexual function after brachytherapy
Dr. Francisco Díaz, Hospital Regional Universitario Carlos Haya (Spain)

Pregnancy after permanent prostate implants with I-125
Dr. Laurent Chauveinc, Clinique Hartmann (France)

4:30 p.m. - 5:00 p.m. Coffee Break

SESSION IV: PHYSICS IN PROSTATE BRACHYTHERAPY
CHAIRMAN: JACK VENSELAAR

5:00 p.m. - 6:00 p.m.

The impact of interseed effect on treatment planning dose calculation – implant rules and solutions
Dr. Fadi Abboud, Centre Hospitalier Peltzer-La Tourelle (Belgium)

Innovations in brachytherapy: Moving from 2D to 3D and on to IGABT
Dr. Jack Venselaar, Instituut Verbeeten (Netherlands)

Treatment planning and QA in prostate brachytherapy. Clinical practice considerations
Dr. José Pérez Calatayud, Hospital Universitari i Politècnic la Fe (Spain)

Sunday 25th November 2012

SESSION V: IMAGING AND DIAGNOSTICS IN PROSTATE BT
CHAIRMAN: PROF. THIERRY FLAM

9:00 a.m. - 10:20 a.m.

Functional imaging in prostatic brachytherapy
Dr. Alfredo Polo, Hospital Universitario Ramón y Cajal (Spain)

Imaging in brachytherapy delivery
Dr. Stéphane Guerif, Centre Hospitalier Universitaire de Poitiers (France)

Template guided biopsy and focal therapy
Dr. Frank Kahmann, Ambulantes OP-Zentrum Ullsteinhaus (Germany)

Experience with MRI after prostate implant
Dr. Pierre Attignac, Clinique Hartmann (France)

10:20 a.m. - 10:45 a.m.

Closing and farewell
Prof. Pierre Scalliet, Cliniques Universitaires Saint-Luc (Belgium)
Dr. Lurdes Trigo, Instituto Português de Oncologia (Portugal)
Abel Luzuriaga, Eckert & Ziegler BEBIG

Saturday 24th
Oral presentations

Comparative analysis of PSA free survival outcomes. Results from the Prostate Cancer Results Study Group (PCRStG)

S. Machtens[1], L. Grimm, P. Grimm and Prostate Cancer Results Study Group (PCRStG)

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Purpose: The comparison of outcomes from individual studies involving surgery, external beam therapy, brachytherapy, cryotherapy or HIFU remains problematic due to the non-uniformity of reporting results and the use of varied disease outcome endpoints. The Prostate Cancer Results Study Group (PCRStG) was formed to evaluate the comparative effectiveness of prostate cancer treatments.

Material and methods: A comprehensive literature review to identify all studies involving treatment of localised prostate cancer published during 2000-2010 was carried out. Over 18 000 manuscripts were identified on the key criteria: minimum/median follow-up of five years, stratification on risk groups, clinical and pathological staging, accepted standard definition for prostate-specific antigen failure, minimum patient number of 100 in the low-risk and intermediate-risk groups and 50 in the high risk group.

Results: A statistical analysis (standard deviational ellipse) of the study outcomes suggested that, in terms of biochemical-free survival, brachytherapy provides superior outcome in patients with low-risk disease. For intermediate-risk disease, the combination of EBRT and brachytherapy appears equivalent to brachytherapy alone. The combination of EBRT and brachytherapy plus or minus androgen deprivation therapy appears to be more effective in high-risk disease than monotherapeutic approaches.

Conclusion: The metanalysis delivers data to assist physicians and patients in selecting treatment for men with newly-diagnosed prostate cancer.

Key words: prostate cancer, PSA outcome, treatment results, treatment modalities.

Quality of life study – comparison between different treatment options

F. Guedea, F. Ferrer, A. Boladeras, P. Fernández, A. Mariño, G. Sancho, I. Herruzo, A. Hervás, M.J. Ortiz, V. Macías, J.F. Suárez, M. Ferrero and the Multicentric Spanish Group of Clinically Localized Prostate Cancer

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Purpose: To assess five-year biochemical disease-free survival (BDFS) and the impact of treatment-related side effects on quality of life (QOL) after radical prostatectomy (RP), external beam radiotherapy (EBRT) or brachytherapy (BT) in patients with localised prostate cancer.

Material and methods: This was a prospective, observational study of patients recruited from ten Spanish hospitals from 2003 to 2005, with a five-year follow-up. It included consecutive patients with low-risk or intermediate-risk localised prostate cancer (n = 704) as follows: 193 patients treated with radical prostatectomy, 194 with external radiotherapy and 317 with brachytherapy. The Expanded Prostate Cancer Index Composite (EPIC) was administered before treatment and annually thereafter to assess the impact of treatment side effects on QOL. Biochemical relapse was defined as PSA > 0.2 ng/mL after radical prostatectomy or a PSA increase > 2 ng/mL from the nadir after radiotherapy.

Results: Generalized estimating equation models showed that RP patients presented greater deterioration on urinary incontinence and sexual EPIC scales (Beta coefficients: –20.4 and –20.0, at 5 years; $p < 0.001$), but better urinary irritative-obstructive results than BT. EBRT patients showed more deterioration on EPIC bowel and hormonal scales (Beta coefficients: –2.9 and –4.3, $p = 0.01$). Kaplan-Meier estimates of 5-year BDFS 85.4% for BT (95% confidence interval [CI]: 81.4-89.6%), 83.7% for RP (95% CI: 78.5-89.1%) and 77.5% for EBRT (95% CI: 71.3-84.1%).

Conclusion: RP and BT presented similar BDFS, but a distinctive pattern of long-term adverse effects. RP caused greater urinary incontinence and sexual dysfunction than brachytherapy, which produced moderate urinary irritative-obstructive symptoms. EBRT caused long-term moderate bowel symptoms and was associated with more hormonal symptoms than the other treatment options. These results provide valuable information for clinical decisions.

Key words: quality of life, radical prostatectomy, external beam radiotherapy, prostate brachytherapy.

Comparison between existing brachytherapy techniques

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Purpose: Permanent LDR brachytherapy and temporary HDR brachytherapy are competitive techniques for clinically localized prostate radiotherapy. Although, a randomized trial will likely never to be conducted comparing these two forms of brachytherapy, a comparative analysis proves useful in understanding some of their intrinsic differences, several of which could be exploited to improve outcomes.

Material and methods: There are main goals of prostate cancer treatment: cancer control, preservation of urinary control (continence), preservation of sexual function (potency). Indications for monotherapy (based on ABS, ASTRO, GEC-ESTRO recommendations), for brachytherapy as a boost to EBRT and other possible indications are discussed. Contra-indications based on ESTRO/EAU/EORTC recommendations and common side effects (short-term, long-term) are presented. Advantages and disadvantages of both methods are discussed. It is noted that similar clinical results to surgery and EBRT are observed in both brachytherapy techniques. Both techniques are also compared from a technical point of view; costs are also analysed.

Results: Each of these techniques has attributes that advocates for one or the other. First, they represent the extreme ends of the spectrum with respect to dose rate and fractionation and therefore have inherently different radiobiological properties. LDR brachytherapy has the great advantage of being practically a one-time procedure and enjoys a long-term follow-up database supporting its excellent outcomes and low morbidity. On the other hand, HDR is a fairly invasive procedure requiring several sessions associated with a brief hospital stay. Although lacking in significant long-term data, it possesses the technical advantage of control over its postimplant dosimetry (by modulating the source dwell time and position), which is absent in LDR brachytherapy. This important difference in dosimetric control allows HDR doses to be escalated safely, a flexibility that does not exist for LDR brachytherapy.

Conclusions: For the radiation treatment of prostate cancer, a high dose should be delivered for optimal biochemical control. Radiobiological models support the current clinical evidence for equivalent outcomes in localised prostate cancer with either LDR or HDR brachytherapy using current dose regimens. At present, the available clinical data with these two techniques suggest that they are equally effective, stage for stage, in providing high tumour control rates.

Key words: brachytherapy, LDR, HDR, prostate cancer, seeds.

Consensus paper : ESTRO guidelines in prostate brachytherapy

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Purpose: The aim of this paper is to review the GEC/ESTRO-EAU recommendations for transperineal prostate seed implantation (PSI) in case of localised prostate cancer guided by transrectal ultrasound (TRUS) with the same intent to indicate to those embarking in BT 'the factors which may be related to successful outcome'. [Temporary interstitial HDR brachytherapy by Ir192 will not be adressed].

Material and methods: Published by Ash *et al*. (*Radioth Oncol* 2000; 57: 315-21) these recommendations benefit from the evolution of expertise, technologies and data analysis. Twelve years of feedback and clinical studies add to the growing body of literature and to every day clinical practice.

Results: Recommendation evolution for pre-treatment investigations, patient selection, equipment and facilities, clinical team, implant procedure (treatment planning and seed implantation), dose and QA, post-planning, reporting, management of side effects and follow-up are updated demonstrating excellent and durable results of PSI.

Conclusion: Although recommendations are intended to be advisory, the ultimate responsibility remains a medical decision with the patient, his environment and the treating team. This paper represents the evolution of an interdisciplinary group of experts consensus subjected to modifications, as new data and enhancements become available.

Key words: prostate cancer, permanent seeds, recommendations.

Focal therapy: indications, options and role of brachytherapy

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Purpose: The treatment of low-risk prostate cancer is currently a challenge. Many of patients suffer from overtreatment with associated side effects. We reviewed the concept of "Focal Therapy" as an alternative to "Classic" treatment.

Material and methods: The focal treatment and selection should be based on: 1) Biopsy with a minimum of ten cylinders, unilateral tumour, a template biopsy is an alternative. 2) MRI should be another diagnostic tool. 3) Biopsy Gleason ≤ 6, although Gleason 7 could be considered.

4) Clinical stages T1c-T2b. 5) PSA ≤ 10 ng/ml. 6) Prostate volume ≤ 60c.c. Techniques of treatment for focal therapy including: HIFU, cryotherapy, laser, photodynamic or brachytherapy.

Results: Currently, phase II and new phase III studies using various techniques such as "HIFU, cryotherapy, photodynamic, brachytherapy" showed good results related to morbidity, oncological control and the flexibility to repeat "Focal" or "Classic" treatments.

Conclusions: Focal therapy could be an alternative to the radical treatment for prostate cancer, particularly in low-risk patients, just as minimally-invasive brachytherapy is an alternative. Selection of patients must be careful. We must consider that these techniques are experimental in the context of clinical trials.

Key words: prostate cancer, focal therapy, brachytherapy.

References:

1. Eggener SE, Scardino PT, Carroll PR et al. Focal therapy for localized prostate cancer: critical appraisal of rationale and modalities to. International Task Force on Prostate Cancer and the Focal Lesion Paradigm. *J Urol* 2007; 178: 2260 -2267.
2. Langley S, Ahmed HU, Al-Qaisieh B et al. Report of to consensus meeting on focal low dose rate brachytherapy for prostate cancer. *BJU Int* 2012; 109 Suppl 1: 7-16.
3. Wilt TJ, MK Brawer et al. Radical prostatectomy versus observation for localized prostate cancer. *N Engl J Med* 2012; 367: 203-213.

Recurrence after low dose prostate brachytherapy: new diagnostic tools and their impact on the management of patients. Perspectives and case discussion

Thierry Flam, Dominique Pontvert

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With the development of new imaging techniques, notably the PET choline scan and the latest functional endorectal coil MRI of the prostate, we have collected new meaningful data regarding the recurrence patterns in patients treated with brachytherapy for localised prostate cancer. A rise in PSA level within the first two years after an implant is generally considered a bouncing phenomenom and a proven recurrence after brachytherapy is almost always considered an indication for antiandrogen therapy. The new imaging techniques may help to identify a selected group of patients who may be candidates for either salvage radical prostatectomy, second line seed implantation or salvage external beam radiation therapy. The objective of this presentation is to illustrate, with several clinical cases, different situations where the recurrence was proven locally and led to unfamiliar indications. These cases will give an opportunity for everyone to discuss personal experience with such cases and we will encourage the audience to participate in a fruitful debate.

Key words: brachytherapy, recurrence, prostate cancer, MRI, PET choline.

HDR brachytherapy for prostate cancer: from evidence based medicine to prospective clinical trials

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Purpose: To analyse the early toxicity of a high-dose rate brachytherapy (HDRB) boost for prostate cancer using three different fractionation schemes.

Material and methods: From 02/09 to 01/12, after a first course of 3D external beam radiation therapy (EBRT-46 Gy/23f), 118 patients (pts) underwent HDRB boost for low-risk (5 pts – 4%), intermediate-risk (20 pts – 17%) and high-risk (93 pts – 79%) prostate cancers. Pts underwent one insertion (under general anaesthesia) then irradiated according to three different boost fractionation schemes. From 02/09 to 12/09, Group 1 = 18Gy/3f/2d (EQD2α/β3 32Gy/30 pts –25%); from 01/10 to 04/11, Group 2 = 18Gy/2f/2d (EQD2α/β3 43Gy/53pts – 45%); and from 05/11 to 01/12 Group 3 = 14Gy/1f/1d (EQD2α/β3 48Gy/35pts – 30%). Planification CT-scan was performed before each fraction. Organ at risk dose constraints for Group 1 and Group 2 were rV100 = 0 (rectum volume receiving 100% of the prescribed dose-PD) and uV125 = 0 (urethra volume receiving 125% of the PD), while for Group 3, rV90 = 0 and uV115 = 0. Genito-Urinary (GU) and Gastro-intestinal (GI) acute toxicities were assessed at one and six months after boost (CTCv3.0).

Results: Median age was 71 years (50-82). Median follow-up was 19 months (1-35). Ninety-four pts (80%) received an anti-androgen therapy. Median CTV was 34 cc (11-77). Median V100, V150 and V200 were 98% (82-100), 35% (16-81) and 12% (5-33), respectively. Median D10 and D30 were 119% (108-203) and 115% (70-183), respectively. The rate of GU toxicity ≥ G2 was 6% and 0% at one and six months after the boost, respectively. One patient developed G4 sepsis toxicity two days after HDRB and recovered without after-effects. The rate of GI toxicity ≥ G2 was 0% and 1% at one and six months after boost, respectively. GU and GI toxicities at one and six months after boost regarding different fractionation schemes applied are presented in Table 1.

Table 1. Analysis of GU and GI complications observed at one and six months after HDRB boost regarding the complication grade (CTCv3.0) and the different fractionation schemes

Complications	GU		GI	
	GU 1 month (%)	GU 6 months (%)	GI 1 month (%)	GI 6 months (%)
Grades				
0	61	69	74	77
1	33	31	26	22
2	5	0	0	1
3	0	0	0	0
4	1	0	0	0
Fractionation schemes				
G1 (18 Gy/3f/2d)	22*	33	23	45
G2 (18 Gy/2f/2d)	51	63	30	50
G3 (14 Gy/1f/1d)	27	4	47	5
p value	0.41	0.49	0.07	0.34

**Percentages of complication among patients who developed GU and/or GI complications. GU – genito-urinary complications, GI – gastro-intestinal complications*

Conclusions: During the study period, while a significant physical dose-escalation was performed (33% and 10% between Group 1 vs. Group 3 and Group 2 vs. Group 3, respectively), no significant increase in GU and GI acute toxicities was observed.

Key words: prostate cancer, high-dose rate brachytherapy.

Fast, intuitive and precise planning of permanent seed implants with PSID 5.0

Roland Panzer, Imland Klinik Rendsburg, Germany

Prostate cancer is the most common cancer in men. Depending on the stage of prostate cancer, therapy differs from surgery and radiotherapy to wait and see strategies. LDR-brachytherapy or seed implantation is an excepted treatment of low risk prostate cancer (Gleason up to 3+3, PSA < 10 ng/ml, pT1c). Accurate treatment requires an effective treatment planning software such as PSID 5.0 (permanent seed implant dosimetry, Eckert & Ziegler BEBIG GmbH, Berlin). PSID 5.0 supports contouring in live ultrasound images in a preplanning setting as well as in online planning. A digital frame grabber provides the loss-free digital connection to the ultrasound device. In the post-planning setting, seed detection is easily performed and displayed in the 3D image volume. The features of PSID 5.0 are demonstrated using real patient data. Image guidance, image fusion with CT, MRI or histoscanning and adaptive planning are supported. In the near future focal therapy and breast implants could be a possibility. PSID 5.0, as demonstrated, is a fast, powerful, accurate and easy-to-use software for treatment planning in LDR-brachytherapy.

Key words: LDR brachytherapy, prostate cancer, PSID, seeds.

Clinical outcome and dosimetric analysis of 195 low or intermediate risk prostate cancers treated by permanent implant brachytherapy

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Purpose: To report tumour control, dosimetric analysis and toxicity outcomes of a cohort of localised prostate cancer patients treated by permanent Iodine-125 brachytherapy.

Material and methods: Between July 2001 and January 2011, 195 consecutive patients with histologically proven prostate adenocarcinoma were treated with I-125 permanent interstitial implantation using real-time intraoperative treatment planning. The median age was 67 years (51-80). There were 81.5% low risk and 17.5% intermediate risk patients according to the d'Amico classification. The median follow-up time was 53 months (5-119). The biochemical disease free survival (BDFS) was assessed according to the Phoenix criteria and estimated using the Kaplan-Meier method. Morbidity was reported prospectively using "Common Toxicity Criteria AE v2.0" for acute toxicity and "Late Radiation Morbidity Scoring Scheme" (RTOG/ESTRO) for the late toxicity.

Results: The 5-year BDFS was 94.4% (95% CI: 88.2-97.3). The mean D90 was 173 Gy on the real time ultrasound dosimetry versus 158 Gy on the CT scanner based dosimetry performed one month later ($p < 0.01$). D90 emerged as a significant predictor of biochemical outcome. The 5-year BDFS was 99%, 88% and 75%, for patients with D90 > 145 Gy, 130 Gy < D90 < 145 Gy and D90 < 130 Gy, respectively ($p < 0.01$). Acute grade 2 urinary toxicity occurred in 21% and grade 3 in 4%. Late urinary toxicity was rare: 7% of grade 2 and 2% of grade 3. Grade 2 or 3 late rectal toxicity occurred in 3%. No correlation was found between incidence of toxicity and dose at organ at risk.

Conclusion: These 5-year results are consistent with those in the literature with regard to biochemical and overall survival. The occurrence of late toxicity is very low in this prospective study. To optimise the dosimetry and implantation, we are currently working on the following: dose calculation using seed orientation parameters, spatial lo-

calisation of positive biopsies (Urostation, Koelis®) and robot assisted implantation.

Key words: brachytherapy, iodine 125 seeds, prostate cancer.

Learning curve experience in LDR prostate brachytherapy

Thomas Oliver Henkel, Frank Kahmann

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Purpose: Low dose brachytherapy is based on the teamwork of different medical specialities. Dedicated radiooncologists, urologists, physicists, anesthetists and OR-nurses are responsible for the routine performance of a flawless seed implant. In order to achieve this desired quality, many different facets have to be practiced repeatedly by all members of a brachytherapy team. A learning curve represents the changing rate of learning a certain aspect of the implant technique. It can be used as a valuable tool for the sake of comparison, whether for one person or for the entire team.

Material and methods: A learning curve can also reflect the initial difficulty of learning something and how much there is to learn after initial familiarity. These aspects can be demonstrated e.g. in the dosimetry quality (D90, V100) of an implant, in the total OR time of a seed implant, in the required time for creating a dosimetry plan or in the number of seeds required per gram prostate.

Results: We have examined various components of a LDR seed implant which are connected with a learning curve. Our results support the notion that "practice makes perfect" which is reflected in e.g. shorter implant time, shorter dosimetry planning time or reduced number of seeds for adequate dosimetry coverage of the prostate.

Conclusion: Only by means of tedious quality assessment can the learning curve be decreased. All team members should be involved in discussions regarding the learning curve for their respective specialty. This information can be passed on to new individuals within the team as well as to other brachytherapy centres in order to fulfil the requirements of an optimally performed implant as well as to maintain respective standards.

Key words: learning curve, LDR, prostate brachytherapy.

Results of I-125 seed implantation in comparison to radical prostatectomy in men ≤ 60 years

Alexander Petrovsky, Dmitry Roshin, Boris Bukharkin, Vladimir Sholokhov, Mikhail Mechushkin, Vsevolod Matveev

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Purpose: Radical prostatectomy and low-dose permanent brachytherapy are the major treatment options for patients with localised prostate cancer and a life expectancy of more than ten years. The purpose of the study was to compare the results and quality of life in men ≤ 60 years after each of the procedures.

Material and methods: A match-pair analysis of 128 men was performed. Half of them (64) underwent I-125 permanent seed implantation (Group 1) during 2004-2010. The other 64 patients underwent radical prostatectomy (Group 2) and matched the clinical criteria of the consecutive I-125 men. The median age of both groups was 56 years (44-60), the median preoperative PSA was 7.2 ng/ml for Group 1 and 7.8 ng/ml for Group 2. The majority of the patients had Gleason 6 (54 and 57, respectively). The preoperative median IPSS was 7.9 in Group 1 and 8.6 in Group 2. The overall and biochemical disease-free survival rates and quality of life (QOL) using IPSS, QLQ-C30 and IIEF were investigated. The median follow-up was 3.4 years for Group 1 and 4-6 years for Group 2.

Results: The overall and biochemical disease-free survival rates were the same in both groups. QOL was better in Group 1, but not significant ($p = 0.12$). Erectile function was significantly better in Group 1 ($p = 0.02$).

Conclusion: I-125 permanent seed brachytherapy could be safely used in men ≤ 60 years. A longer follow-up period is necessary for a better comparison of survival rates.

Key words: brachytherapy, prostate cancer, radical prostatectomy, seeds.

Comparison between external beam radiotherapy (70 Gy/ 74 Gy) and permanent interstitial brachytherapy in 919 low risk and 890 intermediate risk prostate cancer patients

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Purpose: Aim of this analysis was to compare biochemical no evidence of disease (bNED) rates in low-risk and intermediate-risk prostate cancer patients treated at two centres of excellence using different approaches: permanent interstitial brachytherapy (BT) and external beam radiotherapy (EBRT).

Material and methods: A total of 919 low-risk and 890 intermediate-risk prostate cancer patients, who were treated from 1998 to 2008, were identified in the two local databases. In Utrecht 667 low-risk and 601 intermediate-risk patients received I-125 BT applying a dose of 144 Gy. In Vienna 252 low-risk and 289 intermediate-risk patients were treated by EBRT, applying a local dose of 70 Gy in 82 and 105 patients and 74 Gy in 170 and 184 patients. bNED rates (Phoenix-definition) were assessed.

Results: Median follow-up was 47 months (1-150). Five-year actuarial bNED-rates were for low-risk 94% for BT-patients and 88% for EBRT-patients (p = 0.002) – 84% for 70 Gy-patients and 91% for 74 Gy-patients, respectively. In univariate analysis patients receiving 70 Gy showed a significantly worse outcome compared to BT (p = 0.001) and a difference close to significance compared to 74 Gy (p = 0.06). Five-year actuarial bNED-rates were for intermediate-risk 81% for BT-patients and 75% for EBRT-patients (67% for 70 Gy and 82% for 74 Gy), respectively. In univariate analysis no difference between BT and EBRT could be detected.

Conclusion: Low-risk prostate cancer patients receiving 74 Gy by EBRT showed comparable biochemical control rates to patients receiving seeds brachytherapy, whereas 70 Gy – a significantly worse outcome. In intermediate-risk patients permanent interstitial brachytherapy showed comparable results to EBRT up to 70/74 Gy regarding treatment outcome.

Key words: external beam radiotherapy, permanent interstitial brachytherapy, prostate cancer.

Sexual function after low-dose rate brachytherapy

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Purpose: Sexual function is one of the main determinants the quality of life. The reason why brachytherapy is selected by many prostate cancer patients is to avoid erectile dysfunction. Sexual evolution after low dose rate brachytherapy is evaluated in this paper by the use of a validated questionnaire.

Material and methods: 256 patients with localised prostate cancer treated by low-dose rate brachytherapy with ^{125}I between July 2002 and July 2008 are included; age: 46-79 years, mean 64 years; stage: T1b (1); T1c (178); T2a (66); T2b (11); PSA: 2.1-12.6 ng/ml, mean 6.6 ng/ml; Gleason score: 2 (4 cases); 4 (22 cases); 5 (41 cases); 6 (182 cases); 7 (7 cases); Erectile function is assessed by the erectile function domain of IIEF questionnaire (EF-IIEF) (questions 1-5 and 15) before treatment, at one month, every three months for two years and every six months after the procedure; Follow-up: 2-72 months, mean 40 months.

Results: Number of patients with erectile function before brachytherapy: 172/256 (67.19%); 39/172 patients (22.7%) developed erectile dysfunction after brachytherapy; 27% of the patients had transient erectile dysfunction after brachytherapy; 133/172 patients (77.3%) of the patients remained potent after brachytherapy.

Conclusions: Brachytherapy is a minimally invasive treatment with a low rate of erectile dysfunction. EF-IIEF score shows its lowest level at six months after brachytherapy. There are no statistically significant differences in EF-IIEF scores after nine months regarding pretreatment levels in potent patients.

Key words: prostate cancer, brachytherapy, erectile dysfunction.

Pregnancies after prostate brachytherapy

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Purpose: Brachytherapy is the treatment that best preserves sexual function after prostate cancer. The testicular dose is low and would allow the possibility of conceiving children. In the literature, four cases have been described. Here, we present eight new cases.

Material and methods: Of over 1500 patients treated with low dose rate brachytherapy in the group Institute Curie/Hartmann Clinic, we found eight cases of post treatment pregnancy. The minimum delay is a few months and the longest is eleven years. Two healthy children were born, the other pregnancies were terminated.

Conclusion: Pregnancies after LDR prostate brachytherapy are rare, but possible. Therefore we advise couples to use contraception.

Key words: prostate cancer, prostate brachytherapy, pregnancy.

The impact of interseed effect on treatment planning dose calculation – implant rules and solution

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Purpose: The interseed effect is the attenuation effect of one seed on the dose distribution of all other implanted seeds. Treatment planning systems (TPS) for prostate brachytherapy with seeds use mainly the TG-43 (U1) algorithm for dose calculations. They do not take into account the interseed attenuations due to its complexity. A fast Monte Carlo dose calculation engine, taking into account the interseed effect, has been developed for real-time dosimetry, using the MCNP5 code.

Material and methods: The interseed effect was investigated for the IsoSeed® I25.S06. The MC model of the I25.S06 was carefully validated in comparison with the literature (Hakan *et al.* 2000). A 3D comparison between the Monte Carlo calculation (using MCNP5) and the VARISEED™ programme (using TG-43U1 for clinical cases) was performed for eight real cases. Dose distributions are compared for each ultrasound imaging slide. Moreover, a DVH comparison is also performed for the prostate.

Results: The interseed effect of the I25.S06 on planar dose distribution varied from 4% to 10%, causing a cold spot, especially behind coplanar/aligned seeds. This result is comparable to data published by Chibani and Williamson (2005). Furthermore, this effect becomes more important as the density of implanted seeds by volume unity increases. The interseed effect on DVH is less pronounced than on planar dose distribution.

Conclusions: The interseed effect gives rise to cold spots in planar dose distribution. The influence of cold spots on treatment quality is unknown, but they may lead to prostate cancer recurrence, highlighting the need for the dosimetry to be as precise as possible. Therefore, an accurate and fast system for real-time permanent brachytherapy of the prostate, taking into account the interseed effect was developed. When using VariSeed™ (TG-43), we recommend avoiding as much as possible coplanar-aligned seeds that are separated by less than 10 mm.

Key words: interseed effect, prostate brachytherapy, seeds, TG-43 algorithm.

Innovations in brachytherapy: moving from 2D to 3D and on to IGABT; focusing on the developments of 3D treatment planning algorithms

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Purpose: External beam radiotherapy and brachytherapy are both rapidly evolving technical treatment modalities. When based on modern 3D imaging, brachytherapy is considered to be a state-of-the-art technique and the treatment of choice for several tumour sites and types. The purpose of this presentation is to discuss new developments in treatment planning approaches and their consequences for imaging and accuracy.

Material and methods: In the near future, model based dose calculation algorithms (MBDCAs) will be introduced, complementing or replacing well-known TG-43 methodology. Despite its advantages, there are several drawbacks associated with the use of TG-43 calculations: patient inhomogeneities and tissue composition are not taken into account, neither are patient boundaries and the effects of the presence of other sources, applicators or shields. Errors of a few to several tens of a per cent may occur. The new task group of AAPM and (GEC-) ESTRO, TG-186, will present its recommendations in order to make a giant step forward and to move beyond TG-43.

Results: Instead of assuming the patient to be represented as a large homogenous water phantom, detailed knowledge of geometry, density and tissue composition will be required for accurate dose calculations. In this way, the errors can be avoided and uncertainties in dose delivery reduced. These new processes, however, require optimal use of imaging capabilities. Besides information of active tumour volumes that may be identified by using MRI, fMRI, PET(-CT) and Spect-CT, we will probably need to use dual-energy CT scanning to determine atomic composition. This is a field where much research is still required. Furthermore, as there may be large differences in dose determination depending on whether a $D_{w,w}$, $D_{m,m}$ or $D_{w,m}$ is used for dose scoring, it still must be made clear which of these quantities correlates best with treatment outcomes. Intermediate recommendations from TG-186 will provide routes for a safe introduction of MBDCAs for clinical use.

Conclusion: Due to the consequences for dose recording and reporting, societal co-operations are needed for its safe use.

Key words: accuracy, algorithm, brachytherapy, treatment planning.

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Treatment planning and QA in prostate brachytherapy. Clinical practice considerations

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Treatment Planning and QA in prostate LDR Brachytherapy are well-established techniques widely used in brachytherapy departments. The review of the different steps performed show both well-solved aspects and some remaining weak issues from the clinical practice perspective. Permanent prostate LDR Brachytherapy is based on intraoperative procedures using US for planning and CT-MR for post-planning. A critical point, as general in radiotherapy, is the contouring interobserver variability, which gives significant uncertainty mainly on the base and apex areas. To minimise this uncertainty, well-established acquisition protocols and consensus guidelines are required. Main aspects of the clinical dosimetry procedure are briefly discussed: GEC-ESTRO & ABS recommendations, interactive/dynamic planning, modelling, etc. The air-kerma strength assay and seed deposition of manual vs. robotic systems are addressed. Applications of recommendations when permanent brachytherapy is combined with external RT are not clear. Radiobiology considerations are proposed to obtain the urethra constrain. Independent calculations can be implemented quickly and efficiently in intraoperative LDR brachytherapy procedures using imported data from TPS and specific nomograms. Finally, limitations of current TG-43 based algorithms have to be considered with the main clinical implication when high calcifications volumes are present.

Key words: brachytherapy, prostate, clinical dosimetry, treatment planning.

Sunday 25th
Oral presentations

Functional imaging in prostatic brachytherapy

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Purpose: Modern brachytherapy relies on the paradigm built around the triad dose-volume-fraction. With the advent of CT-based dose planning, more detailed knowledge of this relationship was possible. In the last few years, technological advances in radiology and nuclear medicine gave us more understanding of the topography and metabolism of tumours and a new dimension to optimize radiation therapy, including brachytherapy.

Material and methods: Intraoperative dynamic dose calculation (IDDC) represents a paradigm shift in dose prescription and specification and source delivery for brachytherapy. Initially this concept was devised for permanent seed implantation. It mirrors the IGRT paradigm in EBRT in that an intended prescription dose is adaptively matched to a changing 3D target volume, or selectively "sculpted" to paint the different functional volumes. This process of matching may result in alteration of a previously accepted isodose distribution at any time, until the end of the procedure when a satisfactory dose distribution is achieved. Several workflows have been outlined for intraoperative dynamic dose calculation in the field of permanent seed implantation. The general scheme performing IDDC consists of three steps: first, at some point during the implant, coordinates of implanted vectors are identified; second, vector images are projected onto the reference frame of the intraoperative images for planning; and finally the plan is reoptimized.

Discussion: To accomplish this objective, precise imaging, dose planning and in-vivo dosimetry will be needed. Intraoperative imaging increases the complexity of treatment planning and dose delivery in brachytherapy. It also increases the precision requirement for target volume localisation and for securing geometrical precision before and during irradiation.

Conclusions: Future developments using functional ultrasound (power doppler imaging, elastography) could bring useful imaging into the operating room. Those imaging techniques should have far-reaching therapeutic implications in some tumour localisations, such as prostate cancer. Brachytherapy will gain a clear advantage from these modalities, which could translate into better treatments, more conformity with the target volume, more dose-intensity and less toxicity to the surrounding tissues.

Key words: brachytherapy, IGBT, functional ultrasound.

Template guided transperineal prostate biopsy to enable focal therapy

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Purpose: The concept of focal therapy for the treatment of localised prostate cancer is currently being discussed on a large scale. The current standard is to treat the whole prostate even for very low risk tumours. In order to limit the possible side effects, but to keep the high biochemical free of recurrence rate, a limited treatment of only parts of the prostate, referred to as focal therapy, may be possible. Several studies have shown that the sole treatment of an index lesion of the prostate tumour may be equally effective. In order to get sufficient information about the tumour and to identify tumours with index lesions, prostate biopsy techniques have to be optimised. With the current TRUS guided transrectal biopsies the prostate can not be adequately mapped to obtain sufficient information for focal therapy. Especially lesions in the anterior and apical parts of the prostate are difficult to reach with the current technique. We have implemented a programme to use transperineal template guided biopsies to properly map the prostate. More than 30 biopsies were taken using a specific planning programme, not only to plan, but also to verify the location of the biopsies during the procedure. The transperineal template guided biopsy technique gives detailed information about the spread of the tumour within the prostate, can identify index lesions and reaches all parts of the prostate including anterior and apical parts. This new quality of information about prostate tumours may enable physicians in the future to provide the patients with a more tailored therapy for their prostate disease.

Conclusion: Transperineal template guided prostate biopsies using a planning system will provide systematic information about the spread of the tumour within the prostate. This information is necessary for the implementation of a focal therapy.

Key words: focal therapy, prostate cancer, transperineal template guided biopsy.