809 POSTER

## Use of MOSFET detectors for in-vivo dosimetry during permanent low-dose-rate prostate implants

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**Purpose:** Prostate volume and shape can change during trans-perineal interstitial permanent prostate brachytherapy due to edema caused by the trauma of needle insertion, making it difficult to achieve the planned implant geometry and hence the desired dose distribution. An instant in-vivo dose measurement device would be useful to facilitate adjustment of the seed distribution in response to changing geometry during the implant procedure.

The purpose of this work was to evaluate specially designed MOSFET detectors for in vivo dosimetry inside the bladder and along the urethra immediately post-implant.

**Materials and Methods:** The detectors used for the in vivo measurements were dual Metal Oxide Semiconductor Field Effect Transistors (MOSFETs. Angular response of the MOSFETS was measured in the 100 kVp orthovoltage beam, which has an effective energy similar to that of the 125I seed. Calibration in terms of dose per unit response of the detector was done in a solid water phantom using a special high activity 125I seed. Prior to use for in-vivo measurements all MOSFETs were sterilized. MOSFET detector was inserted into the lumen of the Foley catheter. Measurements were taken at 1 cm intervals from base to apex of the prostate. For each measurement point, the distance between the MOSFET and the lower edge of the Foley balloon was recorded to provide the reference to the internal bladder wall.

**Results:** We have performed the measurements of the initial dose rate along the urethras of several patients. The dose rate increased with the distance from the bladder, reaching a maximum inside the prostatic part of urethra. The value of this maximum for different patients ranged from 10 to 16 cGy/hr, corresponding to the total absorbed dose of 205 to 328 Gy. The shape of this dose rate curve can help to evaluate an overall implant quality. The in-vivo measurements agreed well with the post-implant treatment plan calculations.

**Conclusions:** Specially designed MOSFET detectors are very useful for in vivo dosimetry of permanent prostate implants. When inserted into the urethra, they can measure in real time the initial dose rate received by this organ. This can serve not only as an indicator of possible treatment complications due to excessive dose to the urethra, but also as a measure of the overall quality of the implant.

810 POSTER

## Pulmonary migration of permanent interstitial sources in patients undergoing prostate brachytherapy

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**Purpose:** Permanent prostate brachytherapy can be performed by a number of techniques, of which the most popular are the pre-plan method using linked sources and the real-time method using loose seeds deposited by an applicator. An inherent advantage to the strand method has been the potential to reduce seed migration to the lung. When CXR were taken the day after the procedure Tapen found an incidence of 0.7%(Int J Rad Oncol Biol Phys 42:1063, 1998). A study with longer follow-up in patients treated with linked sources, found 25% with at least one seed in the lung(Merrick et al, Int J Rad Oncol Biol Phys 46:215, 2000). To date, the incidence of pulmonary migration of seeds has not been reported with the real time technique.

**Methods:** 238 patients were implanted with either I-125 (146) or Pd-103 (92). Patients were implanted with the real time method using the Mick applicator to place the sources. The implant was peripherally based (75%) and care was taken to place the sources just underneath the prostate capsule rather than outside of the gland. Post-implant dosimetry was performed at 1 month. Following implantation, routine chest x-ray (CXR) was obtained at a minimum of 3 months post implant. 24 patients had a second CXR.

**Results:** Of the 238 patients 141 (59%) had stage < T2b and 175 (73.5%) had Gleason score < 7. The median PSA was 7.5 ng/ml (range 1.3-124), 118 (50%) were treated with 6-9 months of hormonal therapy and 39 (16.4%) had a combination of implantation and external beam irradiation. A total of 21,654 seeds were implanted (median 89, range 27-220). Post-implant CXR were obtained at a median of 912 days (range 147-3023). Of the 238 patients, 4 (1.7%) experienced at least one seed embolus to the lung. 10/21654 (0.005%) seeds were found in the lungs. All 4 patients had received an I-125 implant, giving the pulmonary embolus rate for I-125 at 4/146 (2.7%) and for Pd-103 0/92. No patients experienced a subsequent seed migration if it was not seen on the initial film. The median D90 for all I-125 was 172 Gy and for the 4 with migration was 174 Gy.

**Conclusion:** Seed embolism to the lungs is a rare event when patients are implanted using the real time method. The most likely explanation for the low migration rate is that the sources are placed just inside of the capsule rather than outside of the prostate. While migration appears to be slightly higher with I-125 compared to Pd-103, there is no negative effect on post-implant dosimetry results.

811 POSTER

## Intravenous vinorelbine (i.v.VRL) and estramustine (EMP) in patients (pts) with androgen-independent prostate cancer (AIPC): final results

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**Purpose:** The single-agent activity of both i.v.VRL and EMP is well established in AIPC. The two-drug combination formed then the basis for a phase II trial. The main objective was to assess clinical efficacy and tolerance of i.v.VRL in combination with oral EMP in pts with AIPC previously untreated by chemotherapy.

**Methods:** From 1996 to 1999, 51 pts with Karnofsky PS * 60% and median age= 69 years, were included. They were given i.v VRL (25 mg/m* i.v. (D1-D8) every 3 weeks) and EMP (600 mg/m* continous oral daily). PSA response represented the main evaluation criterion. Tumour response in pts with measurable disease and clinical benefit were evaluated.

**Results:** A median of 5 administrations was given. The median relative dose intensity was 98.1% for VRL and 98.2% for EMP. Decrease in PSA by >50% and >80% were seen in 41% and 33.3% of the pts, respectively. Out of the 7 pts with measurable disease, two (28.5%) had a partial response, and out of the 36 evaluable pts for clinical benefit, disease control (responder + stabilisation) was observed in 66%.The median progression free survival was 4.7 months, and the median survival was 14.3 months. The toxicity was acceptable. Neutropenia grade (3-4) was seen in only three pts (6.1%). Thrombocytopenia (grade 4) occurred in 1 patient (2%).Thirteen pts (25.5%) experienced vomiting (< grade 3), nausea (< grade 3) was observed in 28 pts (24%). Thrombotic complications (grade 3-4) occurred in 2 pts (4%). Cardiac dysrythmia(grade 4) and cardiac ischemia (grade 4) were reported in 3 pts (1.1%). Three pts (1.1%) experienced (grade 3) cardiac dysfunction.

**Conclusions:** The present study showed that i.v.VRL in combination with EMP is an effective regimen in pts with AIPC previously untreated by chemotherapy. VRL can be administered safely in combination with EMP. Further clinical studies especially with various schedules and doses of estramustine are warranted.

812 POSTER

## Association of a G915C (ARG25PRO) polymorphism of the TGF-beta1 gene with prostate cancer

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**Purpose:** Links between disease susceptibility and genetically determined variation in human cytokine expression have recently been described. Transforming Growth Factor-b1 (TGF-beta1) plays an important role in the regulation of growth and differentiation of prostatic cells. A Gà C transition at nucleotide 74 of the TGF-beta1 gene results in a Argà Pro substitution at amino acid 25 of the signal peptide. We have examined a possible association of TGF-beta1 genotype with prostate cancer.

**Methods:** Blood samples were obtained from 51 healthy male blood donors (HD), and 50 prostate carcinoma patients (PC). DNA was extracted from the blood samples through salting-out. The polymerase-chain reaction (PCR) allowed the genotyping of the samples in G915C using two sets of primers describe previously by other authors: each set amplified the gene containing the G or the C nucleotide.

**Results:** We found that 45% (23/51) of the HD were heterozigotes, presenting a CG genotype; all the other HD presented a GG genotype. Only 14% (7/50) of the PC were heterozigotes, with all the other patients presenting the GG genotype.