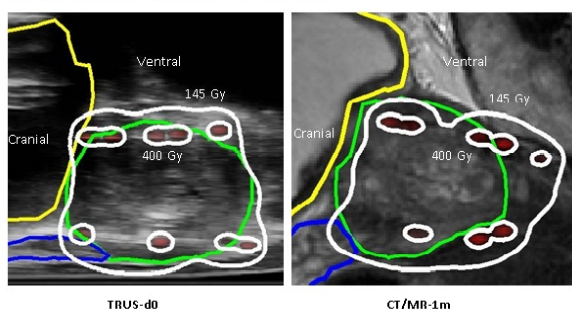


However, this displacement was larger for ventral seeds compared to dorsal seeds (see Fig. 1): 4.4 ± 3.1 mm versus 1.7 ± 2.6 mm ($p < 0.001$). Of the ventral seeds, cranial seeds showed larger displacements than caudal seeds: 5.3 ± 3.1 mm versus 3.5 ± 3.1 mm ($p < 0.001$).

Fig. 1 Displacement of ventral seeds in caudal direction



Conclusions: Due to prostate volume changes and seed displacements after the seed implantation, a reliable quantitative assessment of dose-volume parameters for the prostate cannot be made at the end of the implantation procedure at the OR. A qualitative determination of possible cold spots, however, can be made if a potential displacement of ventral seed strands in caudal direction is considered.

OC-0134

Choline/PET CT and MRI detection of recurrences after I-125 seed implant brachytherapy of prostate cancer

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Purpose/Objective: For low (LR)- and intermediate-risk (IR) prostate cancer, I-125 seed implant is a highly successful treatment modality. However, a small proportion of patients show tumor recurrence at some point. Salvage options depend on the location of tumor progression. With multi-parametric MRI and Choline PET, patterns of failure can be established. The purpose of this study was therefore to identify the location and timing of tumor progression after brachytherapy.

Materials and Methods: Between January 2003 and January 2011, 328 patients with Gleason ≤ 7 , PSA < 20 , clinical stage T1-T2 and a maximum prostate volume of 60 cc, were implanted with I-125 seeds (145 Gy). Date of progression was scored at either increase of PSA > 2 $\mu\text{g/L}$ above nadir, or established recurrence by biopsy and/or imaging, whichever was first. A PSA bounce (> 2 $\mu\text{g/L}$ increase) with spontaneous recovery was not scored as progression. Diagnostic procedures (including bone scan, multi-parametric MRI, Choline/PET CT, biopsies) were performed in most cases as a part of routine follow-up after rising PSA levels, determining the location(s) of first relapse. Cumulative incidences were estimated using Kaplan-Meier analysis.

Results:

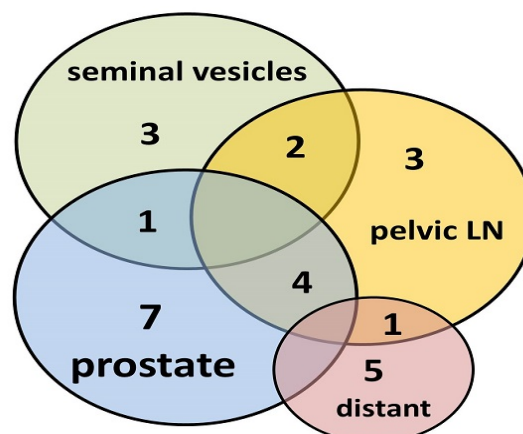


Figure 1. Location of first recurrence.

At a median follow-up of 4.9 years (range 0.3 - 10.4), 5-year freedom from failure was 92 % for LR ($n=214$) and 88 % for IR ($n=114$). Six patients showed a PSA bounce > 2 $\mu\text{g/L}$ increase. Tumor Relapse was scored in 30 patients; in 4 cases follow-up imaging was lacking due to severe comorbidity or a wait and see policy. The first relapse location(s) are summarized in Fig 1 ($n=26$). Local failure within the gland as (part of) a first event occurred in 46 % of the identified failures (12/26) with an estimated cumulative 5y incidence of 3.9 % in LR and 3.5 % in IR patients (Log Rank $p=0.8$). Local failure in the prostate only (all pathology confirmed) occurred in 7 cases after a median follow-up of 4.3y (range 1.5 - 7.0) and a median PSA nadir of 0.6 $\mu\text{g/L}$; in 5 cases salvage prostatectomy was performed afterwards. Increased uptake in the seminal vesicles on follow-up Choline/PET CT ($n=6$) was observed 2 to 6y post-implantation ($n=1$ pathology confirmed). Patients who were diagnosed with distant failure as first site ($n=5$) had early relapses within 2 years and a high nadir (1.9 - 13.9 $\mu\text{g/L}$). Cumulative 5y incidence of failures occurring completely outside the gland ($n=14$) was 3.5 % for LR and 6.2 % for IR patients, which was a non-significant difference ($p=0.15$).

Conclusions: Using multi-parametric MRI and Choline/PET CT, patterns of failure after brachytherapy were identified. Options for salvage treatment could be adapted accordingly, improving patient care. For solitary recurrences a local salvage treatment, such as prostatectomy, may be effective. The cases of early tumor progression completely outside the prostate gland, suggest that pre-treatment screening with MRI may improve patient selection and outcome for brachytherapy.

OC-0135

A biological approach to optimisation of permanent I-125 prostate implants for focal brachytherapy

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Purpose/Objective: To demonstrate the application of a biologically based inverse optimization algorithm for low dose rate (LDR) prostate focal brachytherapy treatment planning.

Materials and Methods: The treatment plans for ten patients treated with a conventional approach to prostate LDR brachytherapy (145 Gy to entire prostate) were compared with plans for the same patients created with a biologically based inverse optimization planning process. To demonstrate functionality of the model, the biological optimizer applied a non-uniform distribution of tumor cell density through the prostate based on known and expected locations of tumor. Using an iterative local search approach, the algorithm determined the optimal needle and seed placement to achieve the target TCP value whilst constraining urethral doses. A range of optimization objectives were considered based on maximizing the TCP and minimizing dose to the urethra and the volume of tissue posterior to the prostate. For each clinical plan, 3 focal plans were generated based on 3 different planning approaches. The robustness of the plans was tested in the presence of random displacement of seeds.

Results: Depending on the planning approach, the volume of the urethra receiving 125% of the conventional dose prescription (145 Gy) was reduced on average from 64% (SD 17%) for the clinical plans to below 13% for the focal plans whilst maintaining high values of TCP through use of a biological optimization approach. The average number of planned seeds was reduced from 85 to less than 74 in all 3 focal planning approaches. The robustness of the plans was not inferior to the conventional plans when considering clinically realistic seed displacements. Clinically, this planning approach will use a combination of in-vivo multi-parametric MRI imaging (mp-MRI) data and biopsy data to populate the radiobiological model with patient specific tumor characteristics. Early work demonstrates that T2w, DCE, DWI and BOLD imaging are capable of providing a voxel map incorporating tumor location, tumor cell density, cell proliferation and hypoxia information. Future work is focused on modeling uncertainties in mp-MRI data and incorporating a statistical model to generate clinically robust focal brachytherapy plans using LDR or high dose rate brachytherapy.

Conclusions: We have demonstrated, using a combination of clinical and synthesized data, that a biologically based inverse planning approach to LDR treatments has the potential to maintain high rates of tumor control whilst minimizing dose to healthy tissue. The software is designed to use mp-MRI and biopsy data to inform the biological model.

OC-0136

Rectal dose constraints for total and focal salvage Iodine-125 prostate brachytherapy

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Purpose/Objective: Organ-confined prostate cancer recurrences after primary radiotherapy can be curatively treated with salvage Iodine-125 brachytherapy (I-125 BT). Options include a complete re-implantation or focal salvage directed only at the recurrent tumor area. This study assesses the differences in rectal dosimetry between these two approaches and provides dose constraints to reduce late severe gastro-intestinal (GI) toxicity (>90 days after implantation).

Materials and Methods: Intraoperative dosimetry for 20 focal salvage (FS) and 28 total salvage (TS) BT patients was evaluated. Patients were treated from December 2001 until October 2012. The dosimetry recommendations for primary BT according to the American brachytherapy society (ABS) and the European Society for Radiotherapy and Oncology (ESTRO) were used. GI toxicity was evaluated using the CTCAE version 4. Differences between dosimetry variables were analyzed with a Mann-Whitney U test. Receiver operating characteristic (ROC)-analysis was used for dosimetry cutoff values to prevent late severe (\geq grade 2) GI toxicity.

Results: FS I-125 BT leads to a significant dose reduction in all analyzed parameters for the rectum compared to TS I-125 BT. Median reductions in D0.1cc, D1cc, D2cc and V100 were 38Gy ($p=0.002$), 46Gy ($p<0.0001$), 46Gy ($p<0.0001$) and 0.41cc ($p=0.0001$) for FS patients compared to TS patients (table 1). No late severe (\geq grade 2) GI toxicity was observed in the FS group. TS patients with severe GI toxicity (41%, $n=11$) showed significantly higher doses to the rectum than TS patients without GI toxicity (59%, $n=16$). The median difference in the D0.1cc, D1cc, D2cc and V100 were 29 Gy ($p=0.0009$), 17 Gy ($p=0.001$), 28 Gy ($p=0.0007$) and 0.45cc ($p=0.001$) between TS patients with and without late severe GI toxicity (figure 1). With ROC-analysis, restrictions for the D0.1cc, D1cc, D2cc and V100 are <160Gy (AUC 0.881, 95%CI: 0.755-1.000), <119Gy (AUC 0.869, 95%CI: 0.735-1.000), <102Gy (AUC 0.892, 95%CI: 0.772-1.000) and < 0.38cc (AUC 0.875, 95%CI: 0.747-1.000), respectively.

Conclusions: FS I-125 BT reduces the dose to the rectum significantly compared to TS. Centers performing TS I-125 BT have to be aware of the risk of cumulative rectal dose and subsequent severe GI toxicity. Based on these findings, the rectal D0.1cc, D1cc, D2cc and V100 should remain below 160Gy, 119Gy, 102Gy and 0.38cc.

Table 1: dosimetry differences between the focal and total salvage treatment plans

Organ	Variable	TS group (n=28)	FS group (n=20)	Median reduction	Recommendations*	p-value for difference
Rectum	D0.1cc, Gy	166 (90 - 289)	128 (90 - 181)	-38 Gy	< 200 Gy	0.002
	D1cc, Gy	130 (59 - 185)	84 (61 - 111)	-46 Gy	NA	<0.0001
	D2cc, Gy	111 (46 - 145)	65 (38 - 88)	-46 Gy	\leq 100% (=145 Gy)	<0.0001
	V100, cc	0.43 (0 - 2.02)	0.02 (0 - 0.39)	-0.41cc	<1 cc	0.0001
	V150, cc	0.01 (0 - 0.59)	0 (0 - 0.04)	-0.01cc	NA	0.037

Abbreviations: FS, focal salvage; TS, total salvage; Gy, Gray. Medians and their corresponding ranges are depicted.

*The recommendations are from the American Brachytherapy Society (ABS) and European Society for Radiotherapy and Oncology (ESTRO).

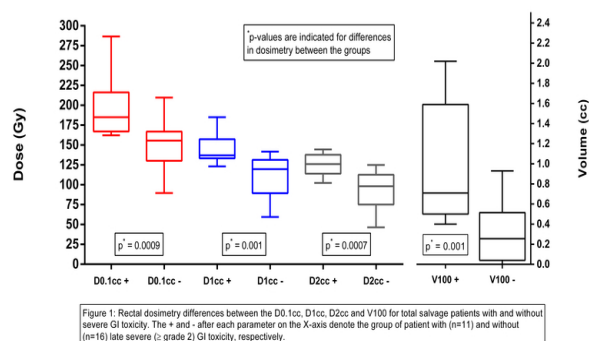


Figure 1: Rectal dosimetry differences between the D0.1cc, D1cc, D2cc and V100 for total salvage patients with and without severe GI toxicity. The + and - after each parameter on the X-axis denote the group of patient with (n=11) and without (n=16) late severe (\geq grade 2) GI toxicity, respectively.