

in detecting local relapse after radical prostatectomy for prostate cancer by analysis of post-prostatectomy fossa appearance in pre- and post salvage radiotherapy DCE-MRI.

Methods and Materials: 33 patients undergoing DCE-MRI without endorectal coil before salvage radiotherapy (RT) without evidence for metastases were selected retrospectively and evaluated using information of post treatment DCE-MRI with an interval ≥ 12 months and response of Prostate-specific antigen (PSA) after RT, median <0.01 ng/mL (mean 0.02 ng/mL, range, <0.01 –0.08 ng/mL). The median PSA at diagnosis of biochemical recurrence before salvage RT was 0.34 ng/mL (mean 0.57 ng/mL, range 0.08–2.38 ng/mL). Pre-RT DCE-MRI scans were compared with post-RT-DCE-MRI-scans to assess behaviour of any suspicious lesions.

Results: 22/33 patients had 24 enhancing nodules in the post-prostatectomy fossa in pre-RT-DCE-MRI at a median PSA of 0.51 ng/ml (mean 0.74 ng/mL, range 0.11 to 2.38 ng/mL). These pre RT enhancing nodules disappeared in post treatment DCE-MRI while PSA showed biochemical remission after RT. Therefore these nodules were considered as highly specific for macroscopic local prostate cancer recurrence. 11/33 patients had normal post-prostatectomy MRI findings at median PSA of 0.22 ng/mL (mean 0.24 ng/mL, range 0.08 and 0.53 ng/mL) without changes after salvage RT. Calculated sensitivity for the MRI identification of the location of the source of the PSA recurrence within the prostatic bed was 72% per lesion for all cases and reached 100% at PSA-levels >0.53 ng/mL. Specificity was 100%.

Conclusions: Enhancing nodules in the DCE-MRI of the post-prostatectomy fossa can be detected depending on the PSA-level with high sensitivity and specificity. Thus DCE-MRI without endorectal coil, which can simultaneously be used for RT planning, may be a valuable tool to detect local recurrence even at low PSA-levels (>0.11 ng/mL), and may be used for dose escalation on macroscopic sites of local recurrence.

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POSTER DISCUSSION

The Impact of Rectal Distension Present on Planning Scans on Localized Prostate Cancer Outcomes in the Era of Image-guided Radiotherapy

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Background: Rectal distension (RD) at time of radiation planning has been associated with lower rates of biochemical progression free survival (bPFS). Use of daily image-guided radiotherapy (IGRT) on prostate may overcome prostatic displacement from RD. We review the impact of RD on prostate cancer outcomes in patients treated with daily IGRT.

Methods and Materials: 189 localized prostate cancer patients were treated with daily IGRT on implanted fiducials from 2001–2003. Patients treated with neoadjuvant/adjuvant hormone therapy were excluded. All patients received 79.8 Gy in 42 fractions delivered via 3D conformal radiotherapy (88.9%) or intensity modulated radiotherapy (11.1%). Clinical target volume (CTV) was prostate +/- seminal vesicles. The planning target volume was a 10 mm expansion on the CTV in all directions except for posteriorly where a 7 mm margin was used. Six RD parameters were measured on CT simulation scans: rectal length (RL); rectal volume (RV); average cross sectional area (CSA); superior rectal diameter (SRD); inferior rectal diameter (IRD); and average rectal diameter (ARD). The primary end-point was the impact of the RD on bPFS using the PSA nadir + 2 definition. After adjusting for T-stage (T1 vs T2+) and risk-category (low vs intermediate vs high), associations between bPFS and RD were determined through multivariate analysis using a Cox-proportional hazard model. Secondary end-points were physician scored RTOG acute/late gastrointestinal (GI) and genitourinary (GU) toxicity scores.

Rectal distension parameter	Median distension (range)	Hazard Ratio	95% Confidence Interval
Rectal length	7.9 cm (5.6–12.4)	0.98	0.74–1.31
Rectal volume	49.8 cm ³ (20.9–123.6)	1.00	0.99–1.02
Average cross-sectional area	6.4 cm ² (3.1–13.4)	1.03	0.89–1.18
Superior rectal diameter	3.0 cm (1.3–6.4)	0.87	0.62–1.21
Inferior rectal diameter	2.6 cm (1.5–4.3)	1.14	0.61–2.10
Average rectal diameter	2.9 cm (2.0–4.3)	0.95	0.47–1.94

Results: Median follow-up was 7.7 years for patients alive at last visit. 84.1% of patients had a T-category of T1a-T2a (T2b/T2c 14.3%; $>$ T2c or Tx 1.6%). Low or intermediate risk disease was 92.6% of patients, while 7.4% had high-risk disease. The 7-year bPFS rate was 78.7%. There were

no significant associations between any of the RD parameters and bPFS (see table). Acute GI toxicity grade ≥ 2 was 0%. Acute GU toxicity grade ≥ 2 was 5.3%. There were 2 events of acute grade 4 urinary obstruction requiring catheterization. Late GI toxicity grade ≥ 2 was 1.1%. Late GU toxicity ≥ 2 was 1.1%. No late GU or GI grade 4 toxicities were reported.

Conclusion: RD does not appear to impact bPFS when patients are treated with daily IGRT on prostate. Severe acute or late toxicity was uncommon and bPFS is consistent with other reports.

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POSTER DISCUSSION

Cellular and Humoral Immune System Activation by Sipuleucel-T – Preliminary Data From the OpenACT Phase 2 Trial

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Background: Sipuleucel-T is an autologous cellular immunotherapy designed to stimulate an immune response against prostate cancer. It is made from peripheral blood mononuclear cells (PBMCs) cultured ex vivo with a recombinant fusion antigen, PA2024 comprising prostatic acid phosphatase [PAP] linked to granulocyte-macrophage colony-stimulating factor (GM-CSF). Sipuleucel-T has demonstrated improved overall survival (OS) in men with asymptomatic or minimally symptomatic metastatic castrate resistant prostate cancer (mCRPC). OpenACT is a Dendreon-sponsored Phase 2 trial, designed to further evaluate the safety and immune responses in mCRPC patients (pts). Survival follow-up is ongoing.

Materials and Methods: Sipuleucel-T was administered every 2 weeks (wks) $\times 3$ and antigen presenting cell (APC) activation (CD54 upregulation) was assessed by flow cytometry. In vivo responses to PA2024 and PAP antigens were assessed at baseline and 2 wks after the 3rd infusion by IFN γ ELISPOT, ³H-thymidine T cell proliferation assays; humoral responses were measured by ELISA. Cytokines were profiled during manufacture of sipuleucel-T and in pt serum before and after treatment (multiplex MSD assay).

Results: 104 pts were enrolled. Following the manufacture of sipuleucel-T, CD54 upregulation was greater at the 2nd and 3rd infusions, suggesting a prime-boost phenomenon. Analysis of the culture supernatants showed an increase in T cell activation-associated cytokines (IL-2, IL-4, IL-5, IL-6, IL-10, IL-13, IFN γ , and TNF α) after the 1st infusion. Cytokines associated with APCs (IL-8, IL-12p70, IL-1 β , MCP-1, MIP-1 β , TARC, and Eotaxin) were elevated. Compared to baseline, humoral responses against PAP and PA2024 after therapy were robust ($P < 0.001$ for both). Post-treatment IFN γ ELISPOT responses to PA2024 and PAP were increased from baseline ($P < 0.001$ and 0.073, respectively) as well as proliferative responses ($P < 0.001$ and 0.003, respectively). Serum cytokines associated with immune activation were increased from baseline (IL-6, TNF α , and IL-10 [$P < 0.05$]). Prior docetaxel exposure (28% of treated pts) did not adversely affect immune responses. Adverse events reported here were comparable to those reported in the pivotal Phase 3 IMPACT trial.

Conclusions: Sipuleucel-T generates a prime-boost immune response in pts with mCRPC by activating the immune system. The humoral response to PAP and newly reported serum cytokine profiles provide support for sipuleucel-T's mechanism of action.

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POSTER DISCUSSION

Patients Treated With Sipuleucel-T Who Had Prior Docetaxel Had Positive Immune Responses and Survival Benefit

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Background: Sipuleucel-T, an FDA-approved therapy for men with asymptomatic or minimally symptomatic metastatic castrate resistant (hormone refractory) prostate cancer, has been demonstrated to prolong