Biologically-guided radiation treatment of the prostate using $^1$H-MRSI

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INTRODUCTION:
The current goal of prostate radiation therapy treatment plans is to achieve a uniform dose over the entire target volume, under the assumption that the cancer is uniformly spread throughout the entire prostate volume. Clearly this assumption does not include biological variations, like regions of acute hypoxia and differences in the spatial distribution of cancer cell density or cancer cell aggressiveness, that are known to exist in the treatment volume. Early work by Ling et al., demonstrated the feasibility of defining biological target volumes (BTV) as identified by functional imaging techniques (i.e. $^1$H-MRSI), and showed the feasibility of performing “dose painting” such regions within the prostate (1-4). To determine what dose needed to obtain adequate tumour control for localized prostate cancer we examine the utility of incorporating spectroscopic imaging data into the radiobiological modeling of prostate cancer. After accounting for the spatial variation of the cancer, we propose to use the spectroscopic data to map regions of the prostate that demonstrate increased metabolic activity and then use the metabolic information (i.e the ratio of Choline=Creatine/Citrate) to directly modify the tumour control probability (TCP) calculation (including its associated radiobiological parameters - α, α/β, number of clonogens) on a voxel-by-voxel basis throughout the prostate. In this study we perform a comparison of two IMRT plans, one with and without the inclusion of spectroscopic imaging data, to demonstrate that spatially varying radiobiological parameters based on spectroscopic imaging data improves the accuracy of treatment through targeted dose escalation.

METHODS:
Seven subjects were scanned on a General Electric 1.5T Signa MR scanner, using an endorectal coil (Medrad Inc.) in combination with a torso phased-array coil. Axial T2 weighted images of the entire prostate gland were acquired as well as $^1$H-MRSI using the optimized CV-MRS and PRESS technique with TE/TR=130/1100 ms with a 16x8x8 phase encode matrix, with a nominal voxel size of 0.42 cm$^3$, and an acquisition time of 19 minutes (5). The combined MRI/MRSI data was corrected for deformations using 3D Slicer, and imported into the radiation treatment plan. A retrospective comparison of two IMRT treatment plans of the prostate were performed with and without the inclusion of $^1$H-MRSI data (IMRT-PROFIT vs IMRT-DIL). We identified the dominant intraprostatic lesion (DIL) based on the (Cho+C)/Cit ratio exceeding 0.74 (see Figure 2A-B). Using a modified TCP formula, which incorporates the $^1$H-MRSI data, we then determined what dose distribution would enable equivalent control of the prostate cancer by escalating the dose to the localized DIL. The TCP and normal tissue complication probability (NTCP) for both plans were calculated, and compared.

RESULTS:
Using standard treatment plan metrics, the TCP was calculated using the parameters from scenario one (i.e. uniform spread of disease through the prostate) and the actual voxel-by-voxel doses to the prostate as estimated in the treatment plan. The mean dose to the prostate clinical target volume (CTV) ranged from 78.6 to 79.7 Gy with a mean TCP of 97.1%±1.1%. The results from the retrospective treatment IMRT plans including the DIL information (IMRT-DIL) demonstrate a mean dose to the prostate CTV was 85.3±1.3 Gy over all subjects with mean TCP values of 98±1.0%. The TCP values calculated using the treatment plans including the DIL and the spectroscopic data are comparable to, but slightly higher than, the predicted TCP values achieved by delivering uniform dose and assuming uniform radiobiological parameters. The radiation treatment plans developed for the IMRT-DIL scenario all met the minimum dose criteria for the PROFIT trial. The target dose volume histograms (DVH) (see Figure 2) demonstrate a tight conformity of the prescribed dose.

DISCUSSION AND CONCLUSION:
In this retrospective radiation treatment study, we have demonstrated a novel way to incorporate the $^1$H-MRSI data into the radiation treatment planning of prostate cancer, using deformable registration to register the MRSI/MRI data to the CT planning data, identifying the DIL using the combined MRSI/MRI, and modifying the TCP calculation to incorporate the MRSI data to determine the appropriate additional dose required by the prostate CTV and DIL that was needed to obtain similar TCP values to those that would be obtained using a standard protocol IMRT plan (without overdosing the DIL and staying within clinical tolerances of normal tissues). This method better characterizes the TCP for the purpose of estimating accurate dose-escalation strategies for the IMRT treatment planning of the prostate. The result of this study indicates that optimizing the dose to the prostate according to $^1$H-MRSI information is possible, and that it can be used to logically derive new prescription doses leading to improved TCP.

References:

Figure 1 (A) MRI with a hypo-intense region along the right peripheral zone. (B) Metabolite ratio map with scaled α/β ratios for each voxel confirming the presence of prostatic cancer. (C) Comparison of dose volume histograms for the CTV and PTV for both treatment plans. In the case of IMRT-DIL treatment plan, the increased dose to the targets, including the DIL, is demonstrated.