ABSTRACT

ADAPTIVE RADIATION THERAPY OF PROSTATE CANCER

by

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ART is a close-loop feedback algorithm which evaluates the organ deformation and motion right before the treatment and takes into account dose delivery variation daily to compensate for the difference between planned and delivered dose. It also has potential to allow further dose escalation and margin reduction to improve the clinical outcome. This retrospective study evaluated ART for prostate cancer treatment and radiobiological consequences. An IRB approved protocol has been used to evaluate actual dose delivery of patients with prostate cancer undergoing treatment with daily CBCT.

The dose from CBCT was measured in phantom using TLD and ion chamber techniques in the pelvic scan setting. There were two major findings from the measurements of CBCT dose: (1) the lateral dose distribution was not symmetrical, with Lt Lat being ~40% higher than Rt Lat and (2) AP skin dose varies with patient size, ranging 3.2-6.1 cGy for patient's AP separation of 20-33 cm (the larger the separation, the less the skin dose) but lateral skin doses depend little on separations.

Five low risk localized prostate cancer patients were selected for the study. The CTV included prostate and 1cm proximal seminal vesicle. PTV was created by adding 1 cm margin to CTV except 6 mm posteriorly to limit rectal dose. The treatment plans were 7 to 9 fields IMRT. CBCT was acquired before each treatment for online image guidance. The rigid registration was performed online to fuse CBCT to SIM-CT. The patient position was corrected in three translational directions based on registration results.

Dose was recalculated on each CBCT set under the same treatment plan. DIR was performed between SIM-CT and evaluated for each CT sets. Dose was reconstructed and accumulated to reflect the actual dose delivered to the patient. Then the adaptive plans were compared to the original plan to evaluate tumor control and normal tissue complication using radiobiological model. Different PTV margins were also studied to access margin reduction techniques. If the actual dose delivered to the PTV deviated significantly from the prescription dose for the given fractions or the OAR received higher dose than expected, the treatment plan would be re-optimized based on the previously delivered dose. The optimal schedule was compared based on the balance of PTV dose coverage and inhomogeneity, OAR dose constraints and labor involved.

DIR was validated using fiducial marker position, visual comparison and UE. The mean and standard deviation of markers after rigid registration in L-R direction was 0 and 1 mm. But the mean was 2-4 mm in the A-P and S-I direction and standard deviation was about 2 mm. After DIR, the mean in all three directions became 0 and standard deviation was within sub millimeter. UE

images were generated for each CT set and carefully reviewed in the prostate region. DIR provided accurate transformation matrix to be used for dose reconstruction.

The delivered dose was evaluated with radiobiological models. TCP for the CTV was calculated to evaluate tumor control in different margin settings. TCP calculated from the reconstructed dose agreed within 5% of the value in the plan for all patients with three different margins. EUD and NTCP were calculated to evaluate reaction of rectum to radiation. Rectal EUD increased 5-7% in the real delivery of the plan with 10/5 mm margin for all five patients. As the margin was reduced, the percent difference increased to 5-14%. Margin reduction from 10/6 mm to 5/3 mm was a very effective way to reduce predicted GI toxicity. Calculated NTCP was decreased by 6% on average for each patient. As the margin was reduced from 5/3 mm to 3mm, NTCP was decreased by 2% on average. NTCP calculated based on actual dose distribution indicated that possibility was less than 10% to have rectal bleeding with grade level 2 or 3. Similar biological evaluation was performed for bladder. EUD of actual dose was 3% - 9% higher than that of planned dose of patient 1-3, 11%-20% higher of patient 4-5. Smaller margins could not reduce late GU toxicity effectively since bladder complication was directly related to D_{max} which was at the same magnitude in the bladder no matter which margin was applied.

Re-optimization was performed at the 10^{th}, 20^{th}, 30^{th}, and 40^{th} fraction to evaluate the effectiveness to limit OAR dose while maintaining the target coverage. Reconstructed dose was added to dose from remaining fractions after

optimization to show the total dose patient would receive. It showed that if the plan was re-optimized at 10^{th} or 20^{th} fraction, total dose to rectum and bladder were very similar to planned dose with minor deviations. If the plan was re-optimized at the 30^{th} fraction, since there was a large deviation between reconstructed dose and planned dose to OAR, optimization could not limit the OAR dose to the original plan with only 12 fractions left. If the re-optimization was done at the 40^{th} fraction, it was impossible to compensate in the last 2 fractions. Large deviations of total dose to bladder and rectum still existed while dose inhomogeneity to PTV was significantly increased due to hard constraints set in the optimization to reduce OAR dose.

In summary, ART did not show improvements in TCP if the patient was setup with CBCT. However, EUD of rectum and bladder was increased significantly due to tissue deformation, which varied daily. With the power of ART, margins added to the CTV could be further reduced to preserve critical organs surrounding the target.