PSMA-directed biologically-guided radiation therapy of castration-sensitive oligometastatic prostate cancer patients

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Purpose/Objectives:
Local ablative treatment to oligometastatic (OM) patients can result in long term disease-free survival in colorectal, sarcoma and lung cancer patients. The importance of consolidating all macroscopic tumor deposits in prostate cancer in the modern era is an area of active investigation. Stereotactic ablative radiation (SABR) is highly focused, high-dose radiation, but further dose escalation is still limited by target motion, localization uncertainties and difficultly irradiating multiple metastases simultaneously. Biology-guided radiotherapy (BgRT) is currently being developed to utilize PET emission data to guide radiotherapy delivery in real-time and to multiple targets simultaneously. With this modality, the PET signals act as a biological fiducial that inherently tracks target motion and treatment setup uncertainties. Prostate membrane specific antigen (PSMA) is a cell surface protein that is overexpressed preferentially in prostate cancer and radiolabeled-ligands have been used for unprecedented molecular imaging in prostate cancer. Here we report on a pilot study examining PSMA-directed BgRT using a cohort from our Phase II randomized trial of SABR to men with recurrent low volume (1-3 metastases) metastatic hormone sensitive prostate cancer (HSPC) who have been imaged with PSMA PET-CT.

Materials/Methods:
Patients are randomized 2:1 to SABR:observation with minimization to balance assignment by primary intervention, prior hormonal therapy, and PSA doubling time. All men treated with SABR were imaged with PSMA PET-CT at day 1 prior to SABR and day 180 from randomization. Four patients from this trial were used for a proof-of-concept study to compare conventionally planned SABR treatments versus BgRT treatments generated from a prototype treatment planning system (TPS). BgRT treatment plan prescriptions were duplicated from the conventional SABR treatment plans and the dose constraints for organs-at-risk (OARs) followed AAPM TG101 guidelines. No additional dose shaping structures were used for the BgRT plans.

Results:
All patients had one metastatic site and the breakdown was n= 2 node & n= 2 bone with an average PTV of 5.1 cc (range = 1.8-9.5 cc). All four BgRT plans met pre-specified planning objectives and were qualitatively acceptable even without the use of optimization structures, and with minimum planning efforts. The BgRT plans displayed better PTV coverage, V95=96.9±2% versus V95=95.6%±1 for conventional SABR planning, were more heterogeneous [average Dmax of the prescription dose was 149% (range = 137-164%) for BgRT versus 123% (112-131%) for the conventional SABR] and gave more dose on average [Dmean 123% (range = 117-127%) for BgRT versus 112% (range = 109-116%) for conventional SABR] but had similar and in many cases better avoidance of OARs.

Conclusions:
This is a pilot BgRT planning study from the first randomized Phase II study evaluating the safety and efficacy of SABR in OM HSPC who have been imaged with PSMA PET-CT. Our study suggests comparable treatment plans between conventional and BgRT planned SABR and demonstrates the feasibility of PSMA-directed BgRT-guided SABR for OM HSPC.