AbstractID: 8814 Title: Biologically-based optimization of Volumetric Modulated Arc Therapy (VMAT) for prostate cancer including boost for hypoxia and urethra sparing

Purpose: To establish a formalism for biologically-based optimization of intensity-modulated radiation therapy (IMRT) for overcoming prostate tumor hypoxia while sparing the urethra. **Method and Materials:** A formalism based on the concept of equivalent uniform dose (EUD) was used to construct the objective function for biological optimization of IMRT. IMRT planning using VMAT (Volumetric Modulated Arc Therapy) was performed based on hypothetical hypoxic regions manually drawn on CT scans. The developed formalism accounts for impact of chronic and acute hypoxia on cell surviving fraction and re-oxygenation in chronic hypoxia regions. EUDs for urethra, rectum, bladder and femoral heads were calculated based on power-law dose-volume histogram reduction. CT data sets from 25 prostate cancer patients who recently received external beam radiation therapy were selected. VMAT plans optimized with dose-volume constraints were used for comparison. **Results:** Significant dose boost in the target volumes designated as chronic or acute hypoxia regions was achieved. EUD in the PTV exceeded 80 Gy, despite accounting for the effects of hypoxia. This increase was achieved with only minor changes in the dose to normal tissue compared to the dose-based VMAT plans. Notably, urethra sparing was excellent with a EUD of approximately 64 Gy. The robustness of the proposed approach was validated using various settings of acute and chronic hypoxia consisting of a range of hypoxic volumes, regions and re-oxygenation patterns. **Conclusion:** The comparison of IMRT plans obtained with biological and dose-volume constraint based optimization showed that the biologically-guided IMRT planning approach is more suitable for critical structure sparing dose painting. In particular, a sterilizing dose may be delivered to hypoxic regions in a variety of scenarios while ensuring rectum, bladder and urethra sparing.