Localized Chemo-Radiation for Prostate Cancer

**ABSTRACT**

Prostate cancer is the second leading cause of cancer related deaths in men. While 5-year survival rates are high, prostate cancer is slow-growing and recurring tumors that are often unresponsive to treatment. Salvage brachytherapy offers a second chance for cure but leads to high rates of rectal toxicity. We aim to locally radiosensitize the prostate throughout the duration of brachytherapy treatment to enable the use of lower radiation doses with lower toxicities for a greater chance of cure. Currently, brachytherapy uses inert spacers for spatial guidance during the one-time injection of radioactive seeds. We leverage the use of these spacers to create a new modality of chemo-radiation therapy, replacing the spacers routinely used in brachytherapy with biodegradable spacers doped with radiosensitizing drug (docetaxel). This approach provides localized in-situ delivery of the chemotherapeutic sensitizer directly to the tumor and avoids the toxicity associated with current systemic delivery. This work presents a biodegradable spacer loaded with docetaxel and inserted intratumorally in mice as a monotherapy as well as combined with radiation for local chemo-radiotherapy. As a monotherapy, in vivo efficacy of the localized spacer versus the standard systemic dosing was tested. The therapeutic benefit of spacer proved to be significantly greater with fewer toxicities than standard clinical treatment. The localized chemo-radiosensitizer was then combined with radiotherapy to demonstrate a synergistic effect at lower doses. The combined treatment showed the highest degree of tumor suppression with significant growth inhibition by day 90. This work demonstrated clinical promise for high therapeutic benefit and lower toxicities.

**IMPORTANCE & INNOVATION**

- **Prostate cancer** (PCA) is 2nd leading cause of cancer related deaths in men
- 220,800 new cases (53k localized PCA) and 27,540 deaths estimated in the US in 2015.
- 20-30% chance of relapse with recurrence: high toxicities from added treatments with high chance of tumor resistance.

- Localized Chemo-Radiation Therapy (LCRT) aims to radiosensitize the tumor site to decrease systemic toxicities and increase chance of cure.

**REFERENCES**