

AbstractID: 13425 Title: Optimal Schedule for Localized Radio-sensitization of ^{125}I Prostate Implants

Purpose: Localized radiosensitization may improve the therapeutic ratio of ^{125}I prostate brachytherapy. Spacers used in permanent implants may be manufactured from a drug-releasing polymer. Loading the polymer with radio-sensitizer would allow spacers to deliver protracted release of radio-sensitizer localized to the prostate. Such devices will have a limited drug-loading capacity, and the drug release schedule that optimizes outcome, under such a constraint, is not known. This work seeks optimal drug release schedules for ^{125}I prostate brachytherapy and demonstrates the manufacture of such spacers.

Method and Materials: Mathematical models of cell kill based using quadratic (LQ) models were used to compare biologic effectiveness of a number of drug release schedules where sensitization is present for a limited time (T). A range of radiosensitizations (S) was simulated by incorporating time dependent α and β values in the LQ model and calculating cell survival fractions. To avoid model dependence, a range of baseline α/β values were considered. A limited drug capacity was simulated by comparing schedules with equal products of sensitization and time (ST). To evaluate the ability to create drug-releasing spacers, a gold fiducial marker was coated with a polymer loaded with fluorescent molecules.

Results: Comparing cell kill for schedules with equivalent ST shows that the cell kill is increased more by delivering a substantial sensitization over a shorter time than by sensitizing less for a longer time. Extended duration of radio-sensitization requires a time scale of weeks to achieve increased cell kill given sensitization levels reported for taxol. Polymer coated fiducials show 2-week drug release is technically feasible.

Conclusion: Using brachytherapy spacers to produce localized radio-sensitization over the time scale relevant to prostate brachytherapy is feasible. Both traditional sensitizers and repair inhibitors may be employed to improve the therapeutic ratio of prostate brachytherapy.

Conflict of Interest (only if applicable):