AbstractID: 13246 Title: Release kinetics of radio-sensitizers from nanoporous coatings on gold fiducials : Biological in-situ dose-painting for IGRT

Purpose: Image-guided radiation treatments routinely utilize radio-opaque implantable devices, such as fiducials or brachytherapy spacers, for improved spatial accuracy. We study the hypothesis that the therapeutic efficiency of IGRT can be enhanced through simultaneous in-situ delivery of radiosensitizers, contained within nanoparticles and nanoporous polymer matrices coating gold fiducial markers or spacers implanted in the tumor (BIS-IGRT, Biological In-Situ Image-Guided Radiation Therapy).
Methods and Materials: Biocompatible polymers loaded with model molecules were coated as a thin film on gold fiducials. The nanoporous morphology of the polymer coatings allowed controlled release of molecules and nanoparticles. Two experimental approaches were studied: (i) a free drug release system, (Doxorubicin, a hydrophilic drug in Poly(methyl methacrylate (PMMA) coating) and (ii) Poly(D,L-lactic-co-glycolic acid) (PLGA) nanoparticles loaded with Coumarin-6, a fluorescent model for a hydrophobic drug, in a chitosan matrix applied as gold fiducial coating. Measurements of temporal release kinetics in buffer and spatial release profiles in agarose were carried out using fluorescence spectroscopy.
Results: For gold fiducials coated with Doxorubicin in PMMA matrix an initial release of Dox within the first few hours was followed by a sustained release over the course of next 3 months. Release of Dox from within PMMA matrix is dependent on the concentration of Dox, ratio of PMMA/Dox, thickness of PMMA/Dox coating on gold surface. The release profile of coumarin-6 loaded nanoparticles from chitosan film on gold fiducials showed that (63±10)% of NPs were released in twenty days, and after that, the release became slower and additional 37% of release was observed after additional twenty-days. Spatial release profiles in an agarose phantom were also measured and compared with release kinetics models.
Conclusions: The results show that dosage and rate of release of these radiosenstizers can be precisely tailored to achieve the desired release profile for BIS-IGRT.