Recovery of Nanoparticle Optical Properties Using Magnetic Resonance Temperature Imaging and Bioheat Transfer Simulation: An Inverse Problem Approach

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Introduction: Several types of nanoparticles have been proposed for use in MR-guided laser interstitial thermal therapy (MRgLITT). If the optical resonances of these particles are tuned to the NIR water window and they are taken up by tumor tissue, they can be preferentially heated during a LITT procedure by applying lower laser powers which spare normal tissue. For treatment planning and simulation purposes, the optical properties of the nanoparticles must be characterized to be incorporated into current bioheat transfer models. Gold nanoshells have been studied in great detail because their optical properties can be analytically calculated using Mie theory and tuned by varying the absolute particle size and the ratio of the outer and inner shell radii [1]. Gold nanorods have also been considered for LITT applications because they offer a variety of potential advantages, including size normalized cross sections that are an order of magnitude higher than nanoshells [2]. The most accurate calculations of nanorod optical properties require numerical methods and show a strong dependence on imperfections in particle synthesis [3]. Because of the inconsistencies in reported optical parameters, a method for validating these models in *ex vivo* and *in vivo* environments is desired. In this work we report on our initial investigation of the use of magnetic resonance temperature imaging (MRTI) in conjunction with a parameter search algorithm on bioheat transfer model simulations for both assessing optical properties and validating the resulting simulations in a phantom.

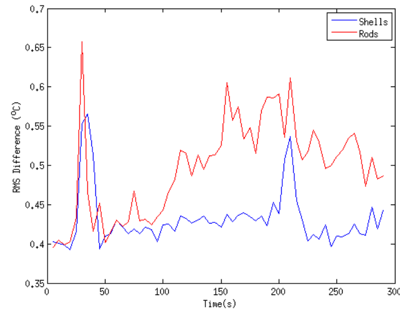

Figure 1- Noise weighted RMS difference between model using optimized parameters and MRTI.

Materials and Methods: Gold nanoshells and nanorods were obtained from Nanospectra Biosciences, Houston Texas. Shells were PEGylated with approximately 120/150 nm core diameters and a resonance peak centered at 812nm. Gold nanorods were measured to be approximately 46nm by 12nm using TEM with a resonance peak centered at 779nm. The nanoparticles were suspended in cylindrical agarose phantoms with an optical density of .695 and irradiated by 808nm laser following the methods of Elliot et. al [4]. Proton resonance frequency MRTI measurements used a spoiled gradient echo with 0.39 mm resolution, slice thickness of 3mm and TR/TE/α of 7.84ms/72.88ms/30° on a 1.5T GE Signa HDxt scanner. A fluoroptic temperature probe was used to independently verify the relative temperature increase and to measure any drift in the main magnetic field. Temperature modeling used a finite element based coupled delta-P1 Pennes bioheat transfer model. The Common Optimization Library Interface (COLINY) pattern search algorithm was used to optimize the absorption and scattering properties of the nanoparticle-agar mixture using the DESIGN Analysis Kit for Optimization and Terascale Applications (DAKOTA) version 5.1. [5]

Results: The COLINY pattern search found the optimal percent absorption to be 63.5% and 89.6% for the shells and rods respectively. These values are within 5% of the expected values of 60.2% for shells [4] and approximately 93% for rods [2,6]. Figure 1 shows the agreement between the optimized model and MRTI using the RMS difference weighted by the voxel by voxel uncertainty in temperature calculated from MRTI. The shells show good agreement with the RMS difference relatively constant at 0.43 °C with the exception of two spikes caused by timing errors when the laser was turned on and off. The nanorod data still shows good agreement with the MRTI but the RMS difference increases by approximately 0.1 °C while the laser is on. Both of these metrics stay within three times the error measured from the MRTI which was 0.20 °C for shells and 0.23°C for rods. Figure 2 shows excellent agreement in the axial heating profiles for each type of particle taken at the maximum valued pixel at t=200s.

Discussion: Modeling nanoparticle heating requires accurate knowledge of optical properties that cannot be easily calculated for nonspherical particles. Furthermore, an experimental method for determining these properties requires that samples be measured with specialized optical equipment. Here we've shown a method that allows the measurement of optical properties directly from MRTI measurements and bioheat transfer modeling. This provides a minimally invasive way of determining the optical properties of a variety of nanoparticle mixtures without the need for complex numerical models beyond a preexisting bioheat transfer model that can be easily extended to studies in *ex vivo* or *in vivo* tissue for validation of treatment planning approaches.

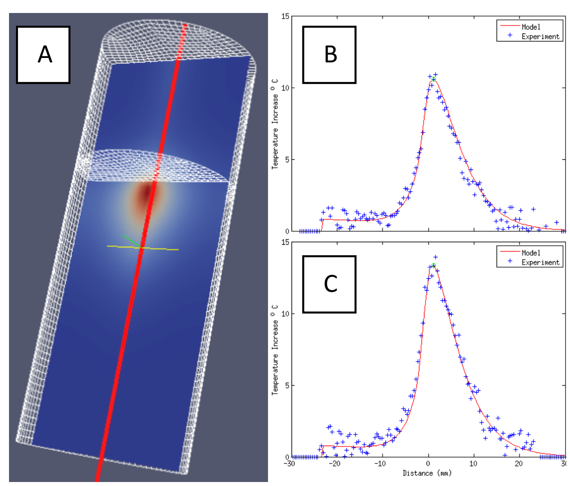

Figure 2- Bioheat transfer solution superimposed on finite element mesh (A). Axial profiles through shell (B) and rod (C) phantoms at t=200s

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