Characterization of the Thermal Response of Light Activated Nanoshells in Phantom using MR Temperature Imaging

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Introduction:

Gold-silica nanoshells are a class of nanoparticle that can be tuned to absorb strongly in the near infrared, making them an attractive agent for delivering targeted thermal therapy. This research uses proton resonance frequency based MR temperature imaging as an aid in non-invasively evaluating changes in bulk thermal properties and associated spatiotemporal temperature distribution in gel-based phantoms with varying optical properties and nanoshell construction. Physical parameters, such as thermal diffusivity and absorption coefficient are shown to vary predictably with concentration and demonstrably affect the distribution of temperature and rate of heating region and the intensity of resulting temperatures. Gold-silica nanoshells are constructed from a dielectric core (e.g. SiO_2) surrounded by a gold shell[1]. Controlling the core size to shell thickness allows the plasmon resonances of these particles to be "tuned" to specific optical frequencies. Nanoshells tuned to the near infrared (NIR) region of the spectrum are attractive for the delivery of thermal therapy as light transmission in tissue is optimal in this NIR "window"[2]. These biologically inert nanoparticles can be delivered to a tumor, either by passive extravasation or via targeted delivery methods. Low power NIR laser irradiation is preferentially absorbed by the nanoshells and results in rapid heating of the surrounding tissue to temperatures suitable for hyperthermia or thermal ablation procedures. Aside from properties of the incident photon source, the size, shape and rate of bulk heating is strongly dependent on the optical properties of the manufactured particles. In this work we use proton resonance frequency (PRF) shift based MR temperature imaging (MRTI) to non-invasively evaluate changes in bulk thermal properties and associated spatiotemporal temperature distribution in gel-based phantoms with varying optical properties and nanoshell construction.

Methods:

All experiments were performed in a 1.5T clinical MR scanner (Signa, GEHC, Milwaukee, WI). MRTI was performed using a 2D fast, rf-spoiled gradient-echo sequence with parameters: flip angle 30°, FOV= 12cm, slice thickness 3.0mm, encoding matrix of 256x128, TR/TE = 74.5-ms/15-ms and a 3-inch receive only surface coil. Agar gel phantoms containing nanoshells of various sizes, optical properties and concentrations were prepared (Nanospectra Biosciences Inc, Houston, TX). The cylindrical gels (23mm diameter x 69mm high) were positioned in the MR scanner so that collimated output of a diode laser fiber (808 nm wavelength) could be reproducibly positioned to irradiate gels, thus keeping the beam intensity and beam width constant across the experiments. Each gel was irradiated for 3 minutes at 0.03 W/mm^2 and allowed to cool under MRTI guidance. Nonlinear least squares fitting to the known theoretical behavior for the temperature at the site of maximal heating[3] was performed on the measured data and results plotted to extract estimates of relevant parameters, such as scattering, absorption and thermal diffusivity.

Results:

Figure 1A: shows the difference in heat deposition between two nanoshell concentrations for a fixed size nanoshell. The white line in Figure 1A, 13mm below the surface, indicates separation of the gel layer with no nanoshells above from the gel with nanoshells below. Absorption of NIR energy in the gel without nanoshells was negligible and heating above the line is due to diffusion of heat during irradiation of the gel. Higher concentrations of nanoshells were found to increase the absorption and limit penetration of light, while significantly enhancing the rate of heating. For those shells in which absorption was estimated as a function of concentration, absorption was found to vary linearly with the range of concentrations of nanoshells used to obtain these preliminary results. Figure 1B demonstrates the difference in maximal heating between 150nm (OD=1.55) and the 180nm nanoshells (OD=1.49) engineered to have the same scattering properties. This was confirmed by estimating the scattering coefficients and verifying the temperature difference was due to the different OD's. The time versus temperature curves for these nanoshells can be found in Figure 2 demonstrating the differences in the rate of heating, maximum temperatures reached and diffusive cooling for the differing OD's of these two different sized nanoshells. The data is not linear and was modeled using the method of van Gemert et. al.[3], these simulations are shown as solid lines. Both calculated absorption coefficient and thermal diffusivity were observed to change linearly with nanoshell concentration.

Conclusions:

MRTI can be a useful tool for helping to determining the effects of differing optical and thermal properties of gold silica nanoshells under controlled conditions using gel phantoms. Currently we are expanding this research to characterize a wider range of concentrations, optical properties and nanoshell sizes to observe effects such as the possible tradeoffs between absorption and size. We also plan to investigate the heat deposition patterns using differing light delivery schemes, such as interstitial versus extracorporeal applicators and multiple applicators. New phantoms with tissue-like optical properties are being investigated to observe the changes in bulk thermal properties the nanoshells may present in to a tissue environment. Used in conjunction with more sophisticated modeling techniques (e.g. Monte Carlo photon transport or inverse temperature calculation) MRTI can become a powerful tool for investigating nanoshell properties and the effects of differing light delivery paradigms for use in thermal therapies. Such investigations will play a key role in treatment planning and optimization of treatment delivery. Extensions of these results to in vivo models are the subject of ongoing research.

References:

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3. Martin J.C. van Gemert et.al. Phys. Med. Biol. 41 pages 1381-1399 (1996)

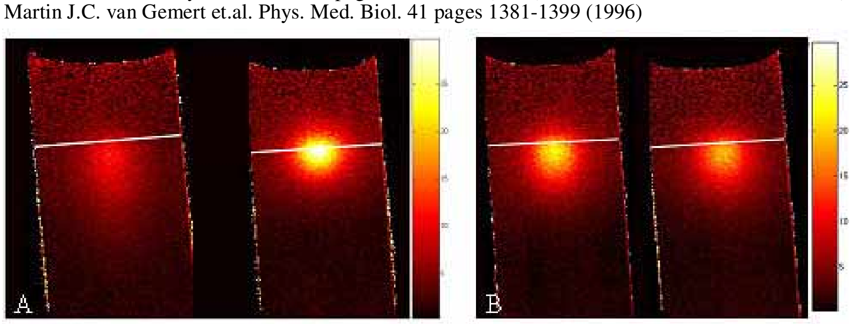

Figure 1A: Temperature images of gels with150nm diameter nanoshells, optical densities are 0.53 and 3.42. White line shows layer below which nanoshells found. 1B: Gels contain 150nm and 180nm diameter shells with OD of 1.55 and 1.49 respectively.

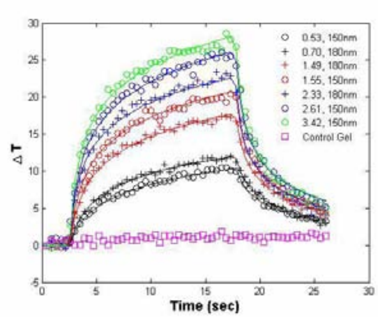

Figure 2: Temperature vs. time of heated region for different optical densities and different diameters.