MRTI Evaluation of SPIO Core Gold Coated Nanoshells for Thermal Therapy and as T2* Contrast Agent

A. M. Elliott[1], A. M. Shetty[1], M. P. Melancon[2], X. Ji[2], B. Taylor[1], J. D. Hazle[1], C. Li[2], and R. J. Stafford[1]

[1]Dept. of Imaging Physics, University of Texas M.D. Anderson Cancer Center, Houston, Texas, United States, [2]Dept. of Experimental Diagnostic Imaging, University of Texas M.D. Anderson Cancer Center, Houston, Texas, United States

Introduction:

Laser Induced Thermal Therapy (LITT), when used in conjunction with gold-silica nanoshells has proven to be an effective method for effecting thermal therapy of tumors[1]. These nanoshells are a class of nanoparticle tuned to absorb strongly in the near infrared. The presence of such particles in a tumor act to amplify the effectiveness of LITT treatments within the volume of the tumor. These gold-silica nanoparticles can also be constructed by using superparamagnetic iron oxide particles as their core[2]. This gives these nanoshell the added ability of changing the magnetic susceptibility and hence the T2* contrast in any region where they collect in high enough concentrations. The potential dual use of these nanoshells makes them attractive for study in magnetic resonance temperature imaging (MRTI). We present phantom and *in vivo* results showing the effectiveness of these nanoshells in temperature imaging and there ability to change T2* contrast.

Methods:

All experiments were performed in a 1.5T MR scanner (Signa, General Electric, Milwaukee, WI). Phantom experiments were performed with MRTI 2D fast GRE sequence with parameters: flip angle 30°, FOV= 9x5cm, slice thickness 3.0mm, encoding matrix of 256x192, TR = 20.7ms, an echo spacing of 9.6ms, 16 echoes collected and a 3-inch receive only surface coil. These experiments were prepared using a 1.5% /wt agar gel phantoms; the phantoms were mage in two levels, the lower level of each contained different concentrations of nanoshells while the upper level contained no shells. Each gel could then be subjected output powers of 7.6W/cm^2 from an 810nm laser (Diomed 15 Plus EVLT, Sigmacon Medical Products, Ontario, Canada). *In vivo* experiments were performed using MRTI, 2D , multiecho, FGRE sequence with parameters: flip angle 40°, FOV= 6x3cm, slice thickness 3.0mm, encoding matrix of 128x128, TR = 70ms, an echo spacing of 3.1ms, 16 echoes collected and a 3-inch receive only surface coil. To demonstrate how the presence of the SPIO nanoshells would affect the T2* contrast, two tumor-bearing mouse (A431 human epidermoid carcinoma) were injected intratumorally with nanoshell, one with a concentration of 10^{12} nanoshells/ml while the other was with 10^{11} nanoshells/ml.

Results:

Figure 1: shows the results of phantom experiments for a nanoshell concentration of 6.7x10^{11} nanoshells/ml; these nanoshells are contained in the lower (dark) part of the phantom while the upper (light) part contains no nanoshells. The phantom is shown with the thermal distribution form the laser seen at the point of maximum heating. Temperature change as a function of time is also shown at the point of maximum heating for the three different concentrations of nanoshells used. Temperature response was found to vary linearly with nanoshell concentration. Figure 2: shows the maximum temperature reached by the mouse tumor during treatment. Time vs. temperature data was taken from the region of the black square and shows the temperature rise and fall off characteristics during treatment.

A number of mice had the nanoshells injected directly into the tumor at the time of imaging, T2* measurements were performed on the mice both pre and post injection. Mouse1 injected with 10^{12} nanoshells/ml showed a 68% change in T2* at the injection site, while mouse2 injected with 10^{11} nanoshells/ml showed a 55% change in T2* value.

Conclusions:

We have demonstrated the effectiveness of gold-coated SPIO-core nanoshells for use with LITT both in phantom and *in vivo*. The potential dual -imaging capability of these SPIO-based nanoshells as T2* contrast agents is also demonstrated.

References:

1. L.R. Hirsch *et. al.* PNAS 100 (23) pages 13549-13554 (2003)
2. Xiaojun Ji *et. al.* J. Phys. Chem. C. 111 (17) pages 6245-6251 (2007)

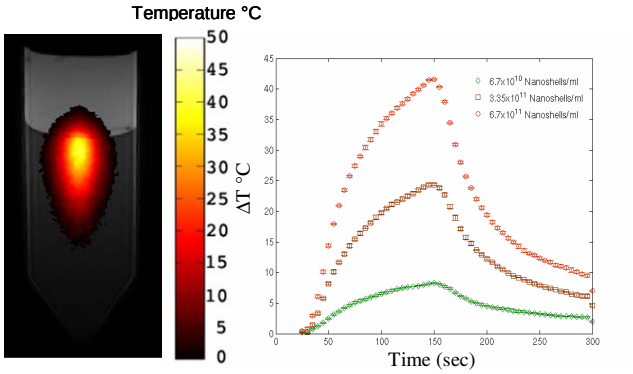

Figure 1: Phantom results show thermal distribution in gel containing 6.7x10^{11} nanoshells/ml. The nanoshells are contained in the lower part of the gel, this is the reason it is darker. The graph shows temperature vs. time plots for three concentrations of nanoshells. Thermal response

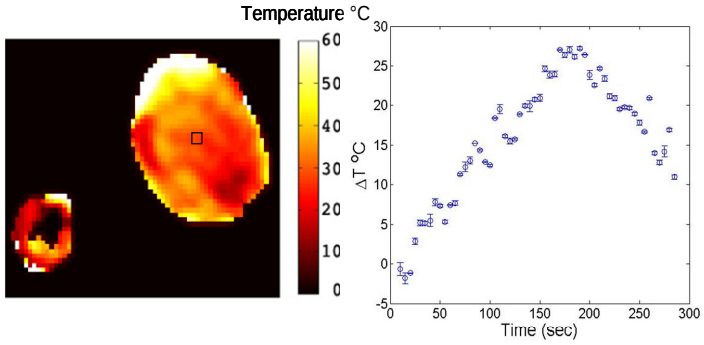

Figure 2: Shows temperature distribution throughout mouse xenograph (A431 human epidermoid carcinoma) tumor. The tumors were grown subcutaneously on the hind leg of the mice. The time vs. temperature plot represents data taken form the region indicated by the black square.