Combined MR and Diffuse Optical Tomography for Dynamic Contrast Enhanced Imaging

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Introduction: It has been proven that dynamic contrast enhanced (DCE) MRI detects malignant cancers which are occult on mammography and ultrasound, and as such it is becoming the most popular imaging modality for screening young women with a high risk of developing breast cancer. However, despite its high sensitivity, DCE-MRI also detects many benign lesions presumably due to insufficient selectivity afforded by the low molecular weight clinical MR contrast agents. There have been a number of studies using macromolecular agents to probe the vascular volume and permeability in a more sensitive manner [1]. Nevertheless, there is not any macromolecular MR agent available for clinical use. Indeed, the questionable specificity of DCE-MRI is one of the biggest obstacles for its widespread use. Other imaging modalities can be used as an adjunct to DCE-MRI to improve the specificity by increasing the information content obtained from the breast lesions. For this purpose, we have recently developed a combined MR-Optical imaging system for dynamic contrast enhancement imaging of tumors [2]. This combined system can monitor the enhancement kinetics of both MR and optical contrast agents simultaneously. Hence, two different contrast agents with different sizes can be utilized to increase the specificity in differentiating benign and malignant tumors (i.e. a small molecular MR and a large molecular optical contrast agent). The performance of this novel hybrid imaging system was tested in vivo with animal studies.

Method: The optical imaging system used in this study was a frequency domain diffuse optical tomography (DOT) system. The DOT system was integrated with a 4T MRI system and placed in a separate room, 20 m away from the magnet bore due to the effects associated with the magnetic field. The bore diameter of the MRI was 90 cm, and a homebuilt, small-animal, birdcage-type rf coil was used to transmit and receive signals. Optical fibers are used to conduct light from the light sources to the tissue as well as to transfer the collected light from tissue to detectors. Eight source and eight detector fibers were utilized and coupled to the animal RF coil inside the magnet. The DOT system could acquire a full set of tomographic data that was consisting of 64 measurements in 220 seconds. A finite element based algorithm was developed to reconstruct the absorption and scattering maps from the measurements. The boundary of the animal was extracted from the MR image. Moreover, fiducial markers were used to determine the positions of the source and detector fibers. The performance of the system was tested in vivo. For this purpose, a rat bearing the R3230 breast cancer tumor model was anesthetized and placed in the fiber optic interface. A small molecular MRI contrast agent (Gd-DTPA, 0.1mmol/kg) together with an optical dye (IC-Green, 7.5mg/kg) was injected to the animal intravenously. The enhancement kinetic of both agents was recorded simultaneously with the combined MR-DOT system.

Results: The temporal resolution of the DCE-MRI sequence was 45 seconds and a series of 20 frames were acquired by MRI. The temporal resolution of the DOT system was lower, 220 sec. As a result, only five frames could be acquired with optical imaging system during the experiment. The mixture of Gd-DTPA and IC-Green was injected after the fourth MRI frame. Figs 1.a and 1.b show the MR image of the animal and the finite element mesh prepared based on this image, respectively. The absorption and scattering maps were reconstructed separately for each time point using the data acquired by DOT system. The highest absorption contrast was obtained at the second time point. Fig 1.c shows the highest absorption contrast image superimposed onto the MR anatomical image. The boundary of the tumor was determined by using MR image and indicated with a yellow line in the image. As seen from the image, high enhancement was observed at the tumor as expected. Enhancement maps were obtained using pixel-by-pixel analysis. Later, pixels that belong to the ROI were averaged and mean enhancement kinetic curves were obtained, Fig 1.d.

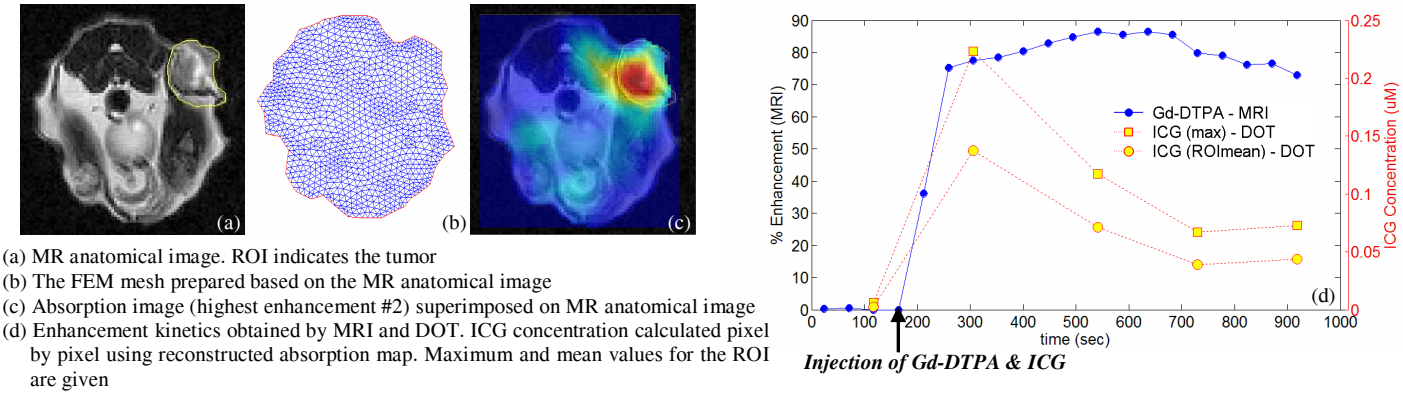

Fig 1. (a) MR anatomical image. ROI indicates the tumor
(b) The FEM mesh prepared based on the MR anatomical image
(c) Absorption image (highest enhancement #2) superimposed on MR anatomical image
(d) Enhancement kinetics obtained by MRI and DOT. ICG concentration calculated pixel by pixel using reconstructed absorption map. Maximum and mean values for the ROI are given

Discussion: In this study, we have shown the feasibility of our combined MR/DOT system for dynamic imaging in vivo. As seen from Fig 1.d, the optical contrast agent, IC-Green, has exhibited very fast kinetics. It is well known that IC-Green rapidly binds to albumin after the injection [3]. Hence, the temporal kinetics of albumin governed the kinetics of IC-Green [4]. Although we could monitor the enhancement kinetics of both agents, the low temporal resolution of our current system did not allow us to catch the fast-rising slope of IC-Green or recover the real peak values of the IC-Green concentration. This was due to non-stationary absorption profile during the time required to take a complete set of DOT data that could also affect the spatial distribution of the recovered absorption map. We are currently constructing a new generation of DOT system that has much higher temporal resolution. Higher temporal resolution will allow us to monitor the uptake of IC-Green more accurately. IC-Green is an FDA approved optical contrast agent and therefore, such a hybrid MR-DOT dynamic imaging system can be immediately applied in a clinical setting. The same system may also be used with novel optical contrast agents with larger molecular weights that will potentially be available in the near future.

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