A Combined Diffuse Optical Tomography (DOT) - MRI System for Small Animal Imaging

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Purpose:

Recently, there has been a great deal of interest in further improving the in-vivo characterization of tumors by interrogating tissues with multiple simultaneous image based measurement techniques that provide complementary information about the functional state of the tissue under investigation. Besides offering the possibility of complementary information, multi-modality techniques could also be used to improve the measurements done by either modality as well as providing cross validation measurements. Magnetic resonance imaging (MRI) and near-infrared diffuse optical tomography (DOT) are two techniques that, when combined, can provide complementary structural and functional information. MRI can be used to obtain detailed structural and metabolic information regarding tumors. On the other hand, DOT can be used to determine local quantitative information regarding tumor composition and metabolism [1]. Thus, a combined system consisting of MRI and DOT has the potential to enhance understanding of the complex biological processes in tumors. In this work, we describe the design of the hybrid DOT-MRI system.

Methods:

The MRI system being used with the DOT is a homebuilt 4T scanner with a Marconi Medical, Inc. console. The bore diameter is 90cm and a birdcage type, and a small animal, transmit-receive RF coil is utilized for the animal studies. Due to the effects associated with the 4T magnetic field, the optical instruments were placed in a separate room, 20m away from the magnet bore. Optical fibers were used to conduct light from the sources to the tissue as well as to transfer the collected light from tissue to detectors. Gradient index, 62.5mm core diameter fibers were used as the source fibers, while 1.1mm core diameter step-index fibers were used as the detector fibers. The source and detector fibers were coupled to the animal RF coil inside the magnet. For this purpose, an adaptive interface was constructed. It consists of 8-source and 8-detector fiber probes with radially adjustable holders. The RF coil was fixed in the center of the fiber interface and 16 holes were prepared for fiber probe entrances as seen in Figure 1. The frequency-domain DOT system employs four different wavelengths, namely 665nm, 785nm, 800nm and 830nm. The laser diodes are driven by a DC current source and a network analyzer. The network analyzer provides the RF modulation signal at 110MHz. A fiber optic switch is used to multiplex the laser diode outputs through the source fibers. Eight photomultiplier detectors are used at the multiple detection sites. Because of the detection geometry, the detectors nearest to the source can receive orders of magnitude more incident light than those that are the farthest. To be able to adjust the light level, a filter wheel is inserted between PMT-fiber coupling systems, Figure 2. The network analyzer was used to measure the amplitude and the phase information from each detector. For each of the 8 source locations, measurements were done for 8 detector locations, thus 64 measurements were performed for each wavelength. The measurement time for one wavelength was less than 1 minute. Figure 3 shows the measurements and the calculated data from the finite element forward problem solver for a cylindrical phantom, which was 95mm in diameter with optical properties: μa=0.0045 mm^{-1}, μ's=0.3 mm^{-1}. Each probe contains H2O-CuSO4 solution, which is clearly distinguishable in the MR image. These markers make it possible to find the exact fiber positions in the MR image and use this information in the FEM reconstruction program. A rat was anesthetized and placed into the rf coil and the hair around the area corresponding to the fiber plane was shaved. The fiber probes were radially adjusted until they were in contact with the skin. The selection of the oblique MRI slice that covered the rat body and that coincided with the optical imaging plane was achieved by using these markers. Figure 4 shows the T2-weighted images using a fast spin-echo (FSE) sequence with TR/TE= 5500/105 ms, echo train= 8, field of view (FOV)= 10.5 cm, Image-Matrix= 128 x 256 and 5mm in slice-thickness. The fiber probes filled with H2O-CuSO4 solution can be easily seen in the MR image.

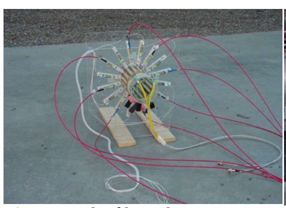

Figure 1. The fiber adaptive interface and the small animal rf-coil

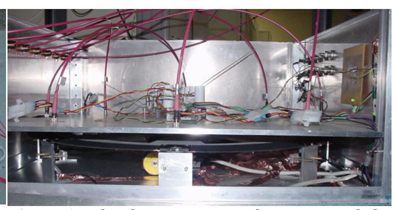

Figure 2: The detection unit: The PMTs and the detector fibers were arranged in a circular geometry and fixed. A rotation stage was used to change the positions of the filters.

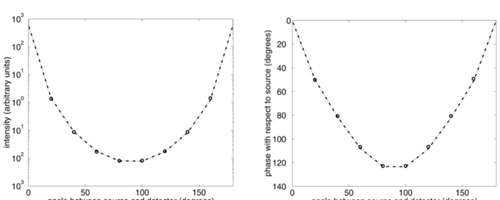

Figure 3: Comparison between experimental data and the FEM calculation for the homogeneous cylindrical phantom (μa=0.0045 mm^{-1}, μ's=3.0 mm^{-1}).

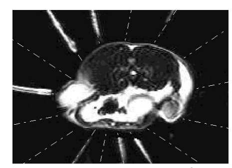

Figure 4: Axial MRI of a rat with DOT fibers in place. Some of the markers contained H2O-CuSO4 solution and are clearly visible in the image. The locations of the remaining fibers are marked on the image.

Discussion:

We have designed and constructed a DOT system and integrated it with a 4 T MR system. Once the system development is completed, the hybrid system will be evaluated in-vivo using animal models. DOT techniques can generate volumetric reconstruction of the optical properties such as μa and μ's. With the acquisition of μa images at a sufficient number of wavelengths, fat, water, the oxygenated and the deoxygenated hemoglobin maps can be produced. A priori information obtained from the MRI can be incorporated at two different stages of the optical reconstruction scheme. First, the structural information obtained from MRI images can be used to find the exact boundary and source/detector locations. In addition to this, by utilizing an automatic segmentation program, the imaging volume can be divided into regions. Photomultiplier tubes (PMT) are generally used as detectors for DOT measurements due to their high gain and low noise properties. However, due to the limited operational wavelength range of PMTs, it is very difficult to obtain an accurate fat and water concentration for the imaging volume. This, in turn also affects the accuracy of the reconstructed oxy- and deoxy-hemoglobin concentration maps. In general, an average bulk water and lipid content can be used for the concentration of these two chromophores [1]. The fat and water concentrations obtained from MRI can be incorporated into the final stage, where the concentrations of chromophores are found. At that stage, instead of using an average bulk water and lipid content, fat and water distribution acquired from the MRI images can be utilized. In addition to these, the fat/water concentration and blood vascular volume parameter obtained from MRI could be compared with the parameters obtained from the DOT measurements. The fat and water concentrations can be obtained from MRI by utilizing Dixon technique [2] and vascular volume parameter could be derived from the pharmacokinetic modeling analysis of the intra-tumor kinetics of MR contrast agents [3].

References:

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