A combined MR- fluorescence tomography system for quantitative small animal imaging: in vivo validation

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Introduction : Multi-modality imaging has become a trend in developing new generation *in vivo* imaging techniques for diagnosis and therapy follow-up[1]. MRI is a high resolution imaging modality, while fluorescence tomography (FT) is becoming an important molecular imaging tool. However, FT's poor spatial resolution and low quantitative accuracy has limited its applications. To overcome this limitation, anatomical *a priori* information provided by MRI has been used to improve the quantitative accuracy of FT [2]. In fact, this approach is similar to the idea of combining nuclear imaging, which is also a low-spatial-resolution functional/molecular imaging modality, with a high-spatial-resolution anatomical imaging modality. Examples of this approach can be found in combined positron emission tomography (PET) and CT systems, combined PET and MRI systems, and combined single photon computed tomography (SPECT) and MRI systems [3-5]. In this study, we show that the concentration of a 4.2-mm diameter Indocyanine Green (ICG) inclusion located 15 mm deep inside a rat can only be recovered within 5% when anatomical *a priori* information from MRI are available.

Method : All animal procedures were approved by the Institutional Animal Care and Use Committee at University of California, Irvine. Transparent thin wall NMR tubes were implanted in a 6-week-old Fischer 344 Rat. The tube had a 4.2 mm inner-diameter and a 0.3 mm wall-thickness. 1% Intralipid and 669 nM ICG were added as the scatterer and fluorophore, respectively. Under general anesthesia, the rat was positioned on a custom-made holder after the surgical placement of the tube. The tube was placed deep inside of the abdominal cavity. For MRI data acquisition, a 4T system was used. High-resolution spin-echo T1-weighted MR images were acquired. The MR acquisition parameters are 300 ms repetition time, 14 ms echo time, 90 degrees flip-angle, 120 mm field of view, 4 mm slice-thickness and 256x256 matrix size. A frequency-domain FT system is used. A picture of the combined MRI-FT interface is shown in Figure 1.b. Optical fibers were used to transmit light to and from the optic interface located in the MRI bore. A 16-leg birdcage coil was built into the interface for transmitting and receiving RF signals. MRI and FT measurements are obtained simultaneously with this hybrid system. The MRI image showed that the tube was 15 mm under the skin, Figure 1.a. This was a very difficult case due to the deep location of the inclusion in heterogeneous tissue. The fluorescence parameters were reconstructed with and without MRI anatomical *a priori* information. The results were compared to demonstrate the benefit of using MRI anatomical *a priori* information for obtaining quantitative FT reconstruction results.

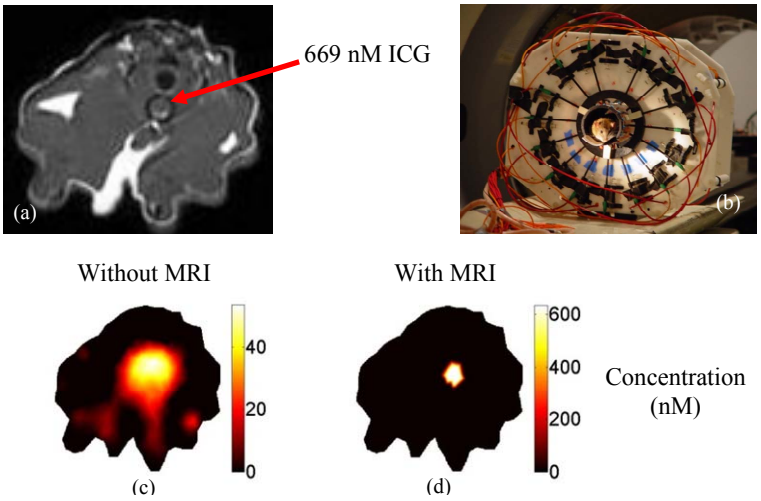

Fig. 1 (a) the MR image of the animal, the tube filled with ICG is indicated by the arrow. (b) The MRI-compatible interface. (c) the reconstructed ICG concentration map without MRI anatomical a priori information. (d) The reconstructed ICG concentration map with MRI anatomical a priori information.

Results : The locations of the fluorophore are indicated by arrows on the MR image, Figure 1.a. As shown in Figure 1.c, the ICG activity can be clearly located on the reconstructed concentration maps. However, the ICG concentration is recovered to 42 nM (94% error). When anatomical *a priori* information from MRI is used, the error is dramatically reduced to 5% with reconstructed ICG concentration at 634 nM. In conclusion, a hybrid frequency domain FT-MRI small animal system was evaluated *in vivo*. A 4.2-mm fluorescence inclusion embedded deep inside a rat was accurately recovered using this system. Without MRI anatomical *a priori* information, recovered ICG concentration maps are only qualitative. The ICG concentration can be accurately recovered *in vivo* when MRI information is used.

Discussion : In this study, we showed that an MRI-compatible FT system for pre-clinical imaging. Currently, only one fluorescence detector unit is used. We are currently upgrading this FT system to increase the temporal resolution.

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