Quantitative molecular imaging with a dual modality MR and fluorescence diffuse optical imaging system: phantom study

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Introduction : Molecular imaging has become an essential tool in characterization and measurement of biological process at the molecular or cellular level. *In vivo* small animal studies have shown the feasibility of using MRI to investigate gene expression and stem cell migration with superparamagnetic iron nanoparticles [1]. However, even though MRI provides excellent anatomical information, the minimum detectable concentration of the nanoparticles is around 10^{-6} M. On the other hand, other sensitive imaging modalities such as nuclear and fluorescence optical imaging can detect smaller amount of molecular contrast agents but suffer from lower spatial resolution. An ideal imaging technique should have both high sensitivity for molecular probes and also provide high-resolution images. Our solution to this demanding requirement is to employ a multimodality imaging strategy. We have previously showed with simulation studies that the fluorophore concentration can only be accurately recovered when the anatomical information from MRI is utilized [2]. In this study, a CCD based non contact fluorescence tomography (FT) system, which could take measurements at multiple views was built, Figure 1. Multi-modality phantoms with both MRI and fluorescence contrast agents were constructed and used in the experiments. Significant improvement has been demonstrated in the phantom results. This combined system has a great potential for quantitative molecular imaging.

Method : FT is based on an external light source that excites the fluorophore and makes it emit light at longer wavelength (emission wavelength). We constructed multi-modality phantoms with multiple compartments to mimic background optical heterogeneity. Indocyanine-Green (ICG), which is the only FDA approved fluorescence contrast agent, was used as the fluorophore. MRI contrast agent Gd-DTPA, a widely used agent in the dynamic contrast-enhanced magnetic resonance imaging (DCE-MRI) was also added to different compartments at different amounts. The phantom composition was determined from the T1-weighted anatomical MR images and used as the structural *a priori* information for the FT reconstruction, see Figure 2, row 1. The inclusion had 0.67 μM ICG and was placed in a transparent tube.

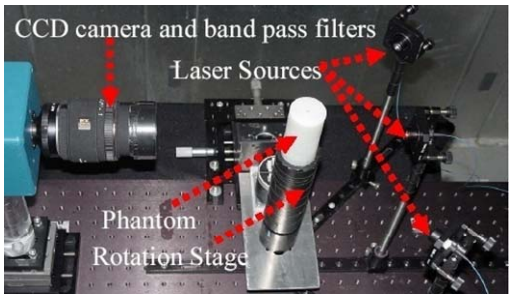

Figure 1. The picture of the FT system.

Table 1. True and recovered mean concnetration.

True (μM)	Without *a priori* (μM)	With *a priori* (μM)
0.67	0.11	0.67

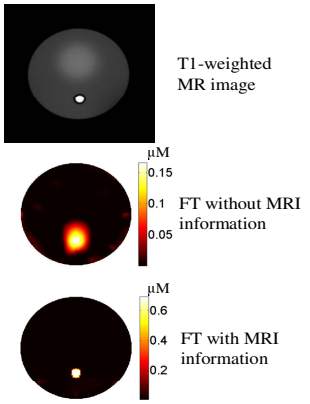

Figure 2. First row shows the MR images of the multi-modality phantoms. The second and third row is the reconstruction fluorophore concentration map without and with the MRI anatomical images.

Results : The structure of the phantom and the location of the fluorophore can be obtained from the T1 weighted image shown in Figure 2. Without the MRI anatomical information, the object could be detected as shown in the second column of Figure 2, row 2. However, the concentration of the fluorophore could not be recovered accurately. The recovered concentration has 80% error. On the other hand, when the MRI structural information is used during the FT reconstruction, the fluorophore concentration is recovered with less than 1 % error.

Discussion: As seen from Figure 2, using structural information in fluorescence optical imaging improves the ability for the system to perform quantitative molecular imaging. Unsurprisingly, the true fluorophore concentration was recovered only if the MRI anatomical information was employed. In fact, we believe that MRI anatomical information would be more essential in the case of in vivo imaging due to the highly heterogeneous background media such as in the case of animal or breast imaging. Currently, we are working on combining such a FT system with MRI to develop a hybrid molecular MR-FT imaging system for human and animal imaging.

References: 1. Weissleder, R. and Mahmood, U. Radiology 219:316–333 (2001). 2. Lin, Y., Gao, H., Nalcioglu, O. and Gulsen, G. Phys. Med. Biol. **52** (2007) 5569–5585.

Acknowledgment: This research is supported in part by the California Institute for Regenerative Medicine through a CIRM training grant T1-00008 awarded to Y Lin and the National Institute of Health Grants # R44 EB007873 and #R01EB008716