# Quantitative molecular imaging with a combined fluorescence diffuse optical tomography and MRI system

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**Introduction :** Molecular imaging has become an essential tool in characterization and measurement of biological process in molecular or cellular level. Several molecular imaging studies have shown the feasibility of the MRI to investigate gene expression and stem cell migration by using superparamagnetic iron nanoparticles [1]. However, due to the low sensitivity of the MRI, the minimum detectable concentration of the nanoparticles is around $10^{-6}$ M. Other more sensitive molecular imaging modalities such as nuclear and optical imaging suffer from low 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. In this study, we show the feasibility of using a combined MRI and optical fluorescence imaging approach to quantitatively resolve the fluorescence contrast agent concentration. Furthermore, we investigated the improvement in the recovered fluorophore concentration using MRI anatomical information during the fluorescence tomography reconstruction. Significant improvement has been demonstrated in the simulation results. We are also working on the development of a combined MR-FT imaging system. This combined system would be the first of its kind and have a great translational potential for human studies in the near future.

**Method :** Fluorescence imaging is based on an external light source that excites the fluorophore and makes it emit light at longer wavelength (emission wavelength). Traditional planar imaging approach which simply measures emission photon density at surface is only qualitative. On the other hand, tomographic approach, namely fluorescence diffuse optical tomography (FT) is able to provide more quantitative images in the presence of heterogeneous turbid media [2]. For the simulations, the animal mesh was generated from the MR image (Figure 1a), and three different fluorescent object sizes were simulated (2, 4, and 6 mm) with an inclusion with 100nM concentration. The object and background contrast was 50:1 for concentration which is the typical contrast ratio in small animal fluorescence imaging. The optical properties, absorption and scattering coefficients, were assigned to different organs according to the MR image. The FT reconstruction was achieved without and with anatomical MRI information. In the latter case, the size and the location of the object was assumed to be obtained from the MR image and used to constrain the reconstruction algorithm. Simulations were performed with 1% amplitude noise added to the synthetic data.

**Results :** First column in Figure 1b shows the true concentration and position of the fluorescence inclusion within the background. In all cases, without the MRI anatomical information, the object could be detected as shown in the second column of Figure 1b, however; the concentration of the fluorophore could not be recovered accurately. Moreover, the error in the recovered fluorophore concentration increases as the object gets smaller. For example, the error increases from 29% to 63% as the object size reduces from 6mm down to 2mm. Table 1 gives the recovered mean concentration values for the fluorophore for all cases.
On the other hand, the true concentration is recovered regardless of the size of the object with the utilization of MRI "anatomical" information. Figure 1 column three clearly reveals the importance of using the MRI anatomical information. The error of the recovered fluorophore concentration is less than 1% as shown in Table 1.

Table 1: True and recovered mean concentration for ROI

| Object diameter (mm) | True (nM) | Without *a priori* (nM) | With *a priori* (nM) |
|---|---|---|---|
| 2 | 200 | 74 | 200 |
| 4 | 200 | 95 | 200 |
| 6 | 200 | 142 | 201 |

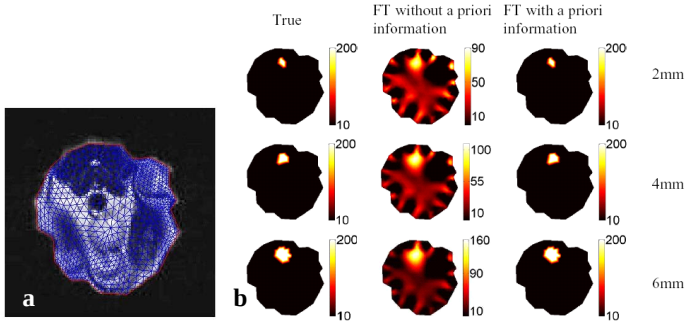


Figure 1: (a) The FEM mesh superimposed on the MR image of the small animal. (b) First column shows the true position and optical properties of the inclusion. The second and third columns show the reconstruction results without and with MRI anatomical information, respectively.

**Discussion:** As seen from Figure 1b, combining MR and fluorescence optical imaging improves the ability for a system to perform quantitative molecular imaging. The true fluorophore concentration was recovered only if the MRI anatomical information was employed. MRI anatomical information was vital especially if the inclusion was relatively small. 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 undertaking phantom experiments with a combined MRI-FT system to show the feasibility of this approach.

**References:** 1. Weissleder, R. and Mahmood, U. Radiology 219:316–333 (2001). 2. Ntziachristos, V. Ann. Rev. Biomed. Eng. 8:1–33 (2006)

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