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Optical Property of Indocyanine Green in a Tissue Model

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The fluorescence temporal profile has been studied at the symmetrical point of the target in tissue phantom by a time-resolved fluorescence diffuse optical tomography method. Indocyanine green served as the fluorescence target. The results showed that the geometrical symmetry of the fluorescence peak intensity ratio was broken due to target position. By using this parameter, an unknown target location could be identified for fluorescence targeting and further reconstruction of the fluorescence image in a tissue model.

Keywords Fluorescence temporal profile; diffuse optical tomography; fluorescence; absorption; emission; image reconstruction

Introduction

Conventional imaging modalities, including X-ray and ultrasound imaging have been reported with potential applications in biomedical fields. However, these are not sensitive tools for pre-clinical imaging in disease models, such as cancer detection and diagnosis, because they provide small contrast for imaging between normal and diseased tissue. This can be substantially improved by means of the fluorescence diffuse optical tomography (FDOT) method [1–5]. FDOT is an imaging modality that aims at reconstructing the 3-D distributions of fluorescent agents inside live small animals. In this technique, a fluorescent contrast agent is applied to provide further optical contrast in the target with respect to the background phantom. Because the blood vessels in cancers are leaky, the contrast agent tends to accumulate in cancers when the contrast agent is injected intravenously. The emitted fluorescence is then detected and reconstructed into 3-D fluorescence images in order to distinguish between normal and diseased tissue.

Although the FDOT method is expected to be a sensitive one, this has yet to be established. Therefore, such a trial should be carried out. Concerning the FDOT measurement, there are several optical parameters that affect the fluorescence temporal profile, for instance, absorption and scattering coefficients of materials, and target geometry. In this

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paper, the focus is on fluorescence temporal profile changes, relying on target position (centered to the near boundary). A time-correlated single photon counter served as a detection system. Firstly, fluorescence temporal profiles are presented as a function of geometrical configuration at the symmetrical point of indocyanine green target in tissue phantom. Next, an unknown target position was identified using the fluorescence peak intensity ratio. This analysis should be useful to decide the excitation-detection geometry for further aims in optical reconstruction imaging in a tissue model.

Experimental

A fluorescence target of 6 mm in diameter was performed with different target positions (4.5, 7.5, or 15 mm, apart from phantom surface) and concentrations (0.5, 1.0, and 2.0 mM indocyanine green dye in 1% intralipid solution). This target was filled in a tissue phantom in which the top view is shown in Fig. 1. The target was then excited by incident light at position A (90^0). The light source was a Ti:Sapphire laser with a central wavelength of 780 nm. Fluorescence light was detected by a photomultiplier. Detection points were focused at the symmetrical point B (30^0) and D (-30^0), as shown in Fig. 1.

Results and Discussion

Figures 2 (a), (b), and (c) show the fluorescence temporal profiles from a 1.0 mM Indocyanine green (ICG) target 6 mm in diameter with different target locations, namely d = 4.5, 7.5, and 15 mm, apart from the phantom surface. The difference of the fluorescence temporal profile at symmetrical point B (30^0) and D (-30^0) became large when the target was near the phantom boundary or point C (0^0). This was because the total path length

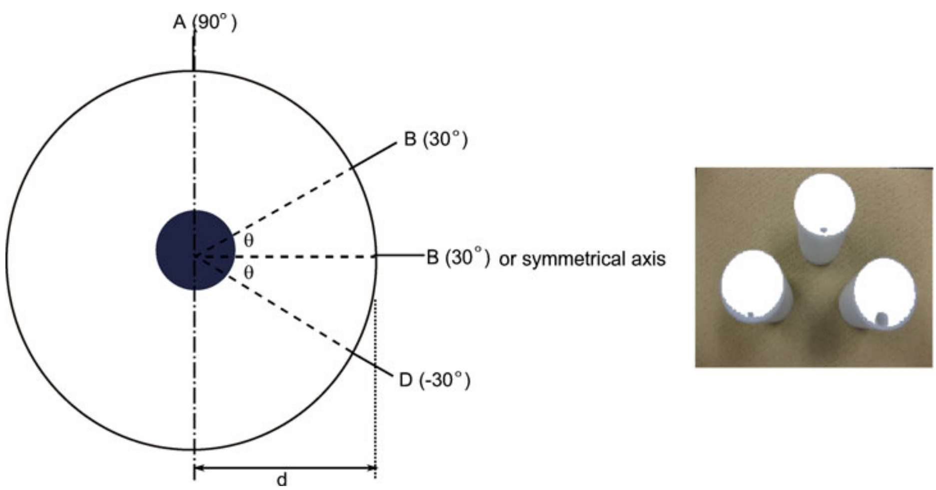

Figure 1. Left: Coordination system of Indocyanine green (ICG) target in tissue phantom of 60 mm in length and 30 mm in diameter. Target position (d) was 4.5, 7.5, or 15 mm, measured from the phantom surface to the target center. The black and white circle represent the ICG target and tissue phantom, respectively. The target size was 6 mm in diameter. The excitation point was defined at position A (90^0). The detection point B and D was 30^0 and -30^0, respectively. Right: Real experimental specimens.

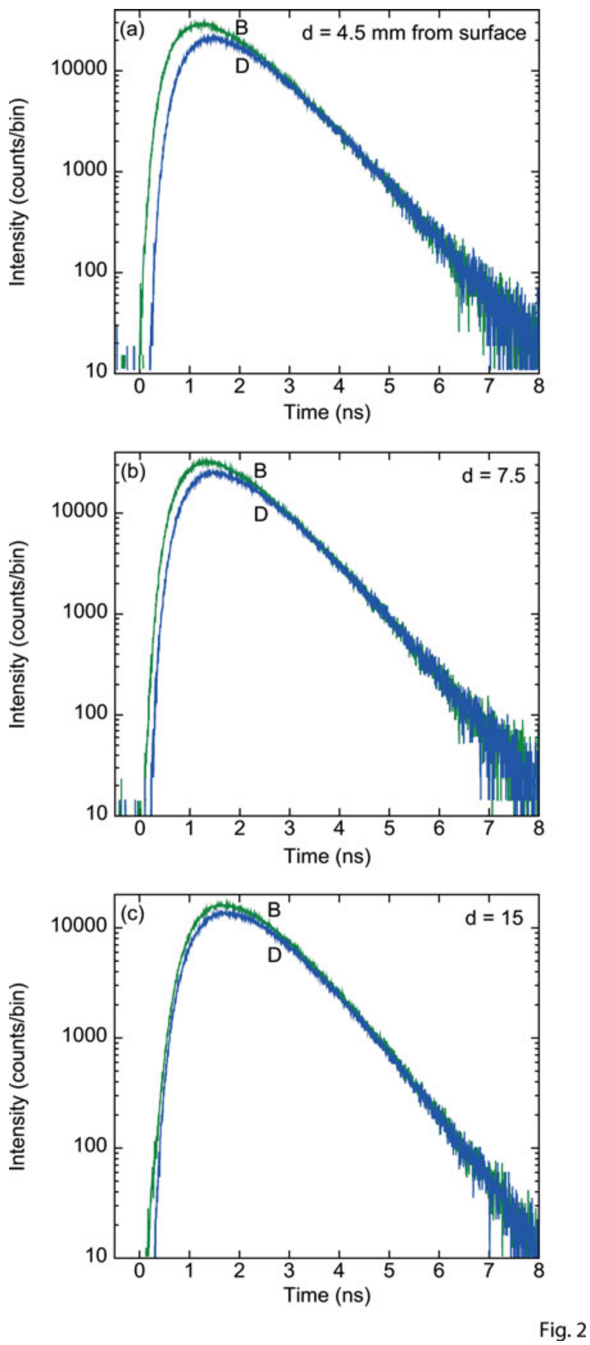

Figure 2. Fluorescence temporal profile as a function of geometrical configuration at different detection points from an Indocyanine green (ICG) target of 6 mm in diameter. The target was located at d = 4.5 mm (a), 7.5 mm (b), or 15 mm (c), measured from the phantom surface to the target center. The target concentration was 1μM ICG solution. The detection point B and D was 30^0 and -30^0, respectively.

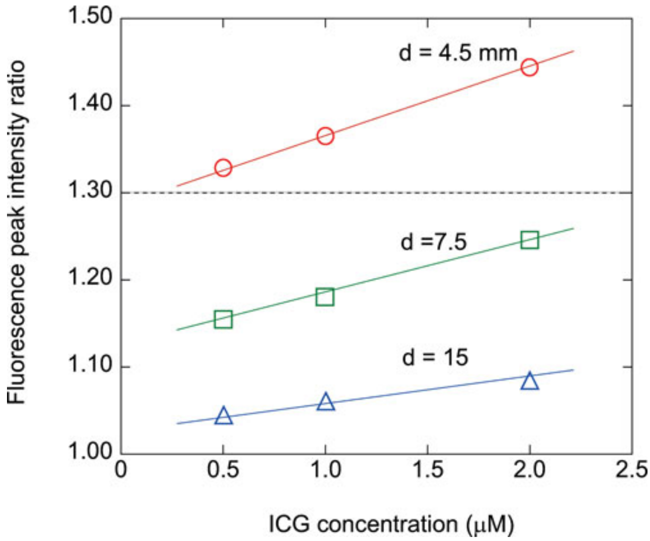

Figure 3. Indocyanine green (ICG) concentration as a function of fluorescence peak intensity ratio at a detection point of $30^0/-30^0$. The target was 6 mm in diameter and was located at d = 4.5 mm, 7.5 mm, or 15 mm, measured from the phantom surface to the target center.

variation between excitation light and emission light in the tissue phantom was increased. Furthermore, the peak intensity and rising edge of fluorescence temporal profile at 30^0 were higher and earlier than those of the profile at -30^0. This result suggested that the front region of the target was more excited than the backside region. Then, the emitted fluorescence travelled a short path length to the detection point. On the other hand, typically the fluorescence intensity would decay as $I(t) = I_0$ exp(-t/t), where t is a fluorescent lifetime. By fitting the observed fluorescence-decay profiles to: $I(t) = I_0$ exp(-t/t), one can obtain t = 0.5 ns.

Next, we characterized the fluorescence temporal profile in terms of fluorescence peak intensity ratio, as shown in Fig. 3. When the target came close to the phantom boundary, the degree of asymmetry in terms of fluorescence peak intensity ratio was further from unity. This indicated that the symmetrical plane of the target with respect to point A (90^0) was broken. Moreover, the degree of this asymmetry was increased when the ICG concentration was increased. Increasing the absorption coefficient of ICG enhanced a gradient of emission intensity at the target region.

These basic results showed a promising approach for fluorescence targeting and further reconstruction of the fluorescence image. The asymmetry of the fluorescence peak intensity ratio was systematically dependent on the target depth and concentration. Therefore, a complete set using this parameter was able to identify an unknown target location. For example, the target size and concentration were known to be 6 mm and 0.5 – 2.0 mM ICG solution, respectively. If the fluorescence peak intensity ratio was beyond 1.3, an unknown target position was expected to be about 4.5 mm or more from the phantom boundary. By contrast, if the fluorescence peak intensity ratio was below 1.3 (dash line), an unknown target point tended to be deeper than 7.5 mm, apart from the phantom surface.

This asymmetrical feature suggests that the fluorescence peak intensity ratio carries geometrical information about the target location. The image quality of the target could then be improved from its fluorescence intensity. On the other hand, our analysis would be useful to decide the excitation-detection geometry and to consider whether this parameter is effective to use in image reconstruction in a tissue model.

Conclusions

Time-dependent measurement of fluorescent light propagation from indocyanine green target in tissue phantom was carried out in order to investigate the fluorescence temporal profile at the symmetrical point of target. The peak intensity ratio of the fluorescence temporal profile was then analyzed. It was shown that the geometrical symmetry of this parameter was broken because of target position. Using this asymmetry feature, an unknown target position was identified. Furthermore, this analysis would suggest better excitation-detection geometry for Fluorescence Diffuse Optical Tomography research.

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