Experimental Reconstruction in Dynamic Sampling Mode Fluorescence Molecular Tomography with Tikhonov Regularization Method

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Abstract

Fluorescence molecular tomography can obtain a sufficient data set and optimal three-dimensional images when projections are captured over 360° by CCD camera. In order to overcome the obstacle caused by traditional step-mode method in fluorescence molecular tomography, a novel dynamic data acquisition approach, dynamic sampling mode for fluorescence tomography, that allows the synchronization of image capture and mechanical rotation, is proposed. Reconstruction with experimental data obtained in the dynamic-mode process is performed with phantoms. And the Tikhonov regularization based on finite element method is used for the reconstruction. The results demonstrate the feasibility of such an imaging mode.

1. Introduction

Emerging as an important alternative for molecular imaging, fluorescence molecular tomography (FMT) is applied to probing the distribution of fluorescence reporters associated with cellular functions [1,2]. Implementation of the imaging mode of fluorescence tomography in the 360° geometry with CCD-camera-based detection has been proposed to make it possible to achieve high spatial sampling and yield a superior information content data set [2, 3]. In such traditional CCD-camera-based FMT, the step-mode, the rotation of phantom and the exposure of CCD camera were carried out alternately. When the motor stopped, the CCD camera began to capture the photons from the surface of phantom. In order to further improve the optical measurement speed and reduce the unwanted soft tissue movements during living animal experiments when the scan rotation starts and stops, herein an imaging method of dynamic sampling, in which the object rotates continuously during imaging, is proposed. The main purpose of the work presented in this paper is to investigate the feasibility of such an imaging mode through the reconstruction with experimental data. And the reconstruction method adopted is the Tikhonov regularization based on finite element method, taking its advantage of obtaining the stable solution of ill-posedness matrix equation [4].

The paper is presented as follows. In section 2, the mathematical model of photon propagation is initially introduced, along with its finite element solution. Then the Tikhonov regularization applied into its linear scheme is presented. Section 3 shows the reconstruction results with the experimental data in dynamic-mode. Finally, the study results are discussed and concluded in section 4.

2. Methodology

2.1 Forward problem

In a continuous wave (CW) fluorescence imaging experiment, the model of photon propagation can be described by the diffusion theory [4],

$$\nabla \cdot [D_x(r)\nabla\Phi_x(r)] - \mu_{ax}(r)\Phi_x(r) = 0 \tag{1}$$

$$\nabla \cdot [D_m(r)\nabla\Phi_m(r)] - \mu_{am}(r)\Phi_m(r) = -\Phi_x(r)\eta(r)\mu_{af}(r) \tag{2}$$

where r is the position vector, $\Phi_x(r)$ and $\Phi_m(r)$ represent the excitation and emission photon intensity (photons/cm^2/s) at position r respectively, $\mu_{ax,m}$ is the total absorption coefficient at the respective wavelengths, and $D_{x,m}$ is the optical diffusion coefficient equivalent to 1/3($\mu_{ax,m} + \mu'_{sx,m}$), where $\mu'_{sx,m}$ is the reduced scattering coefficient (cm^{-1}). $\eta(r)$ is the fluorophore's quantum efficiency and μ_{af} is the absorption coefficient due to fluorophores (cm^{-1}), which is directly proportional to the fluorophore concentration. The coupled diffusion equations are supplemented by the Robin-type boundary conditions on the boundary [5].

The finite element method (FEM) has been widely used to solve the partial differential equations (1) and (2). Two stiffness matrices are combined for each element, K_x for the excitation equation (1) and K_m for the emission equation (2). Then the solutions of (1) and (2) are obtained by solving the matrix equation $K_{x,m}\Phi_{x,m} = b_{x,m}$, where $b_{x,m}$ is the right-hand side of excitation and emission equations after the finite element transformation [6].

2.2 Reconstruction method

To solve the matrix equation $K\Phi = b$ derived from diffusion equations with FEM [7], Tikhonov regularization [8] is adopted. The regulation method is to make sure that the fluctuation of Φ is not that large when b contains measurement errors. That is,

$$K\Phi = \tilde{b}, \qquad where \ \left\|\tilde{b} - b\right\| \le \delta \tag{3}$$

The solution of equation (3) is $\tilde{\Phi} = (K'K + \alpha I)^{-1}K'\tilde{b}$, and α is chosen to satisfy that,

$$\left\|\tilde{\Phi} - \Phi\right\| \le \sqrt{\alpha}\left\|v_0\right\| + \left\|K^+\right\|\delta \tag{4}$$

Where Φ is the normal solution of $K\Phi = b$, and the vector v_0 satisfies $K'v_0 = -\Phi$. K^+ is the generalized inverse of matrix K. Since $10^{-4} < \alpha < 10^{-2}$, the magnitude order of the right-hand side of equation (4) is equal to δ when α is less than δ in the magnitude order. Thus the fluctuation range of the solution $\tilde{\Phi}$ is the same order of magnitude as the vector $\tilde{b}$, which indicates in theory that the inaccurate measurement due to the rotation might not have a great impact on the reconstruction performance severely with appropriate parameter in the regularization.

3. Results and discussion

The experiment is performed according to our previous setup [9]. Two experiments are designed to acquire the dynamic-mode measurements used for reconstruction. The algorithm is coded in MATLAB 7.1 for flexibility.

In the single-target experiment, the reconstructed target in dynamic mode at the speed of 1° /s (Fig.1 (c)) is not exactly the same as the original one in shape (Fig.1 (a)). However, compared with the actual position of the fluorescent target and the target reconstructed with step-mode data (Fig.1 (b)), the reconstruction results using dynamic sampling data are accurate.

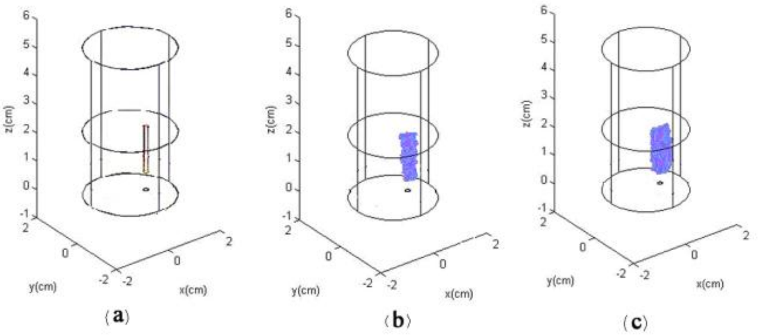

Fig.1 Comparison of the phantom reconstruction results using the data from dynamic sampling mode and step-mode, in which dynamic sampling data is acquired at the speed of 1° /second. (a) Original target position in the phantom. (b) 3D reconstructed result using step-mode data. (c) 3D reconstructed result using dynamic mode data at the speed of 1° /second.

With data set in dynamic sampling mode at different rotation speeds, another comparison between different reconstruction results can be made. Fig.2 shows the reconstruction results on the slide of the phantom. It can be seen that the reconstruction fidelity of the images becomes low as the rotation speed increases. When the rotation speed is set to 0.5° /s, the two targets can be resolved clearly (Fig.2 (a)). When the rotation speed increases to 1° /s, the targets could still be discriminated well, but the reconstructed absorption coefficients of both fluorophores are not so much exact (Fig.2 (b)) since they should have been the same in the experiment. Moreover, the inaccurate calculation leads to the irregular shape of one of the targets (Fig.2 (b)) as compared with Fig.2 (a). The rotation speed of 2° /s may be a critical speed that the targets cannot be distinguished easily during the reconstruction process (Fig.2(c)). And the targets can hardly be resolved when the rotation speed reaches 4° /s (Fig.2(d)). According to the mathematical expressions in section 2.2, we can also get a stable solution by using Tikhonov regularization during the reconstruction process even the measurement data is not that precise. Such reconstruction results in which the targets cannot be resolved clearly at speed of 2° /s and 4° /s demonstrate that the error of CCD readings in dynamic mode is far beyond δ (equation (3)) with these speeds.

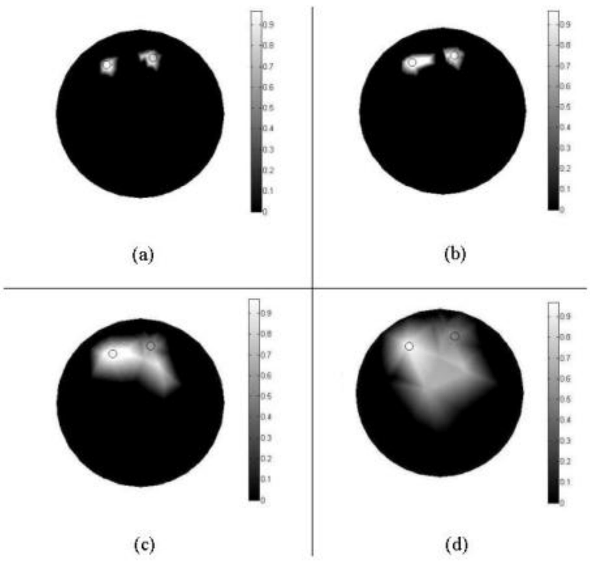

Fig.2 Comparison of the phantom reconstruction results at different rotation speeds, in which dynamic sampling data is acquired with 6s' exposure time of CCD. (a) Reconstructed slice with the rotation speed of 0.5° /s. (b) Reconstructed slice with the rotation speed of 1° /s. (c) Reconstructed slice with the rotation speed of 2° /s. (c) Reconstructed slice with the rotation speed of 4° /s.

4. Conclusion

We have demonstrated from reconstruction that non-contact 360° FMT in a dynamic sampling mode has potential to provide reasonable imaging performance. Although the inaccuracy of dynamic sampling data might compromise the reconstruction performance, especially when the rotation speed is high, the Tikhonov regularization method offers us the stable reconstructed positions of the targets when the rotation speed is appropriately set. Future work will focus on the application of dynamic sampling mode into small animals based on the regularization reconstruction method. Experiments on the comparison between step-mode and dynamic-mode will also be carried out to further demonstrate that our suggested mode has the potential to overcome the obstacles caused by step-mode.

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6. References

1. N. Deliolanis, T. Lasser, D. Hyde, A. Soubret, J. Ripoll. And V. Ntziachristos, "Free-space fluorescence molecular tomography utilizing 360° geometry projections," *Opt. Express*, 0146-9592 (2007).

2. E. E. Graves, R. Weissleder, and V. Ntziachristos, "Fluorescence Molecular Imaging of Small Animal Tumor Models," *Curr. Mol. Med*. 4, 419-430 (2004).

3. R. B. Schulz, J. Ripoll, and V. Ntziachristos, "Experimental fluorescence tomography of tissues with noncontact measurements," *IEEE Transactions on Medical Imaging* 23[4], 492-500 (2004).

4. A. Cong and G. Wang, "A finite-element-based reconstruction method for 3D fluorescence tomography," *Opt. Express* 13, 9847-9857 (2005).

5. R. C. Haskell, L. O. Svaasand, T. T. Tsay, T. C. Feng, M. S. McAdams, and B. J. Tromberg, "Boundary conditions for the diffusion equation in radiative transfer," *J. Opt. Soc. Am. A* 11, 2727-2741 (1994).

6. R. Roy, A. Godavarty, and E. M. Sevick-Muraca, "Fluorescence-Enhanced Optical Tomography Using Referenced Measurements of Heterogeneous Media," *IEEE Transactions on Medical Imaging*, 0278-0062 (2003).

7. X. Song, D. Wang, N.Chen, J.Bai, and H.Wang. "Reconstruction for free-space fluorescence tomography using a novel hybrid adaptive finite element algorithm," *Opt. Express*, 15, 18300-18317 (2007).

8. Kuhnert. *Generalized inverse matrix and regularization method. Chinese version*, Beijing, 1985.

9. G.Hu, J.Yao, Z.Xu, N.Chen, and J.Bai. "Continuous-wave optical tomographic imaging of fluorescent probes in turbid medium with dynamic acquisition dataset," *J. Biomed. Opt.* In review.