Diffuser-Aided Diffuse Optical Imaging for Breast Tumor: A Feasibility Study Based on Time-Resolved Three-Dimensional Monte Carlo Modeling

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***Abstract*—This study proposed diffuser-aided diffuse optical imaging (DADOI) as a new approach to improve the performance of the conventional diffuse optical tomography (DOT) approach for breast imaging. The 3-D breast model for Monte Carlo simulation is remodeled from clinical MRI image. The modified Beer–Lambert's law is adopted with the DADOI approach to substitute the complex algorithms of inverse problem for mapping of spatial distribution, and the depth information is obtained based on the time-of-flight estimation. The simulation results demonstrate that the time-resolved Monte Carlo method can be capable of performing source–detector separations analysis. The dynamics of photon migration with various source–detector separations are analyzed for the characterization of breast tissue and estimation of optode arrangement. The source–detector separations should be less than 4 cm for breast imaging in DOT system. Meanwhile, the feasibility of DADOI was manifested in this study. In the results, DADOI approach can provide better imaging contrast and faster imaging than conventional DOT measurement. The DADOI approach possesses great potential to detect the breast tumor in early stage and chemotherapy monitoring that implies a good feasibility for clinical application.**

***Index Terms*—Breast tumor imaging, diffuse optical tomography (DOT), diffuser-aided diffuse optical imaging (DADOI), Monte Carlo simulation, near-IR spectroscopy, photon migration.**

I. Introduction

DIFFUSE optical tomography (DOT) used the harmless near-IR light that is advantageous because it is noninvasive, less expensive, nonradiative imaging, real-time measurements, compact implementation, long time monitoring, easy operation; the diffuse photon of near-IR light has a 1/*e* penetration depth on the order of 0.5 cm; near-IR in the spectral window of 600–1000 nm wavelength can penetrate several centimeters into human breast tissue. Thus far, DOT has generated a lot of scientific interest and has been applied in various deep-tissue applications such as imaging of brain, breast, limb, and joint [1]–[4].

According to the type of operation, DOT can be classified into three modes as time domain (TD), frequency domain (FD), and continuous wave (CW) [2]. In the CW method, the source light is usually time invariant but it sometimes is modulated at LF and constant amplitude to improve the SNR or to encode the source. Though CW method is the fastest and the least expensive, it measures only the change in intensity of the light and is used to detect changes in absorption coefficient. Additionally, CW method contains no direct information about time of flight and hence has the most limited capability for separating absorption from scattering in a heterogeneous medium [5]–[8]. In the FD method, the source light intensity is amplitude modulated sinusoidally at typically hundreds of megahertz, and the reemitted light modulation has reduced modulation depth. The information of absorption and scattering coefficients of the medium is estimated by measuring the amplitude and phase delay of the received light. The FD method, which typically operates at only a single modulation frequency, contains phase information that correlates to mean free path of light [9]–[11]. In the TD operation, the optical properties of the tissue are inferred from the temporal point spread function (TPSF), i.e., the temporal response to an ultrashort pulse of light source. Thus, TD DOT is a kind of time-gating approach to increase the spatial resolution and it reveals rich depth information [12]–[17]. The TD method is mathematically equivalent to the combination of the FD and CW methods. Although measured at many frequencies in a sufficiently broad bandwidth, FD signals can be converted to the TD by using the inverse Fourier transformation. The TD method using the time-gating technique has proved to be more

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sensitive than FD method when applied to a bulky tissue of several centimeters [18]. Among the three methods, TD method is the most information rich despite being the slowest in data acquisition and the most expensive. Therefore, the TD method was adopted for simulation in this study.

The image reconstruction in DOT is an important issue that involves both the forward and the inverse problems. The diffusion equation is usually used to solve the forward problem and provides a good prediction of light distribution on the basis of presumed parameters for both the light source and the object [19]–[21]. However, the early arrived photon without strong scattering is ignored in the diffusion equation that deteriorate reconstructed image in superficial subsurface region of tissue. Monte Carlo simulation is a good tool for the estimation of the optical pathway with various source–detector separations in human breast tissue [22]–[27]. Thus, one of the aims in this study is to observe the photon migration with multiscattering events in a 3-D breast model from MRI based on Monte Carlo simulations. Because the 3-D model from MRI image approaches the realistic human breast, the characteristic of the photon propagation in 3-D realistic breast model and optimal choice of source–detector separation may provide more helpful information for DOT systems design.

As mentioned previously, the image reconstruction in DOT depended on the complex algorithms such as to solve the forward and the inverse problems. Therefore, the main aim of this study is to propose the diffuser-aided diffuse optical imaging (DADOI) approach that can reconstruct the images simpler and faster than traditional DOT based on modified Beer–Lambert's (MBL) law calculation. Besides, DADOI provides rich depth information with time-gating approach.

For human breast imaging, DOT reveals pathological tumor contrast directly in vascularity, hemoglobin concentration, and tissue scattering property. DOT utilizes the abnormal optical properties of scattering and absorption to detect breast tumor with photon migration in breast tissue. Thus, use of diffuse optical technique for breast cancer imaging has been focused in many research groups [29]–[39]. Based on the MBL, the change of vascularity and oxygenation can be observed by utilizing optical measurements at multiple source–detector positions on the tissue surfaces [31]. Usually, the optical properties of normal breast tissue (as baseline) are measured from the contralateral of breast tumor in clinical study [29], [30], [32]. It is expected that the contralateral scan provides the same optical property as monitoring side without tumor. But in fact, human breast tissues are not identical on the both sides, which implied that the reference signal from the contralateral of detected breast generates concomitant prediction errors of functional image reconstruction. To overcome this problem, the DADOI utilize diffuser-aided technique that monitors the breast tumor and detects background signal on the same location. Recently, the diffuser is employed for near-IR light imaging based on the extraction of the near-axis scattered light (NASL) by Takagi *et al*. [40]. Besides, Tseng *et al*. utilize the diffuser for skin monitoring with the measured spectra of absorption and reduced scattering coefficients [41], [42]. The idea of NASL gating is by use of diffuser for intensity modulation of on-axis transillumination in turbid media [42]. In our study, the DADOI is proposed based on the similar concept to NASL gating. A diffuser is utilized to enhance multiple scattering that destroys image information for baseline detection and then the abnormality can be detected by use of subtraction of diffused light background from measured light. The validity of the proposed DADOI is manifested in simulation. The dynamic analysis of photon migration is simulated by time-resolved 3-D Monte Carlo coding with human breast modeling. Although many results have been proposed for the modeling of human breast, as per our knowledge, this is the first paper to show the time-resolved photon migration in the 3-D breast model from clinical MRI with various source–detector separations based on DADOI method. The MBL is adopted with DADOI to substitute the complex algorithms of inverse problem for mapping of spatial distribution and the depth information is obtained based on the time-of-flight estimation. In this paper, the approach of DADOI was implemented by utilizing the time-resolved three-dimensional Monte Carlo simulation and MBL algorithm with the following purposes: 1) to evaluate its feasibility in detecting breast tumor from 3-D Monte Carlo simulation; 2) to demonstrate its capability of diffuse background reduction by use of diffuser; and 3) to illustrate its improved performance over the conventional DOT approach for breast image.

II. Breast Modeling and Optical Simulation

A. Time-Resolved 3-D Monte Carlo Algorithm

In order to test the validity of DADOI approach and achieve breast tumor imaging, the time-resolved 3-D Monte Carlo algorithm is used for simulation. Typically, the behavior of photon migration in breast tissue was determined by 1) the mean free path of a scattering or absorption event, 2) the boundary conditions—refraction and specular reflection, 3) scattering event—deflection and azimuth angles, 4) absorption event—energy loss, and 5) detector location. In addition, Snell's law and Fresnel reflection formulas are applied at each boundary. The absorption and scattering properties of a sphere is described by Mie theory that has been available in previous study [23], [27], [44]. The photons are all traced and recorded in simulation for dynamic analysis. In this study, the Monte Carlo algorithm was coded based on our previous study, which has been described in [28].

B. Three-Dimensional Breast Modeling

In this study, the human breast is modeled based on *in vivo* MRI image as five-layer structure. A 3-D image of breast contains $256 \times 256 \times 130$ voxels. Each voxel is a $0.8 \times 0.8 \times 0.8$ mm^3 from the resolution of *in vivo* MRI image. The layers are assigned as air, skin, fatty tissue, glandular tissue, sternum, and ribcage, respectively. The wavelength of near-IR light source is 800 nm in simulation. The reduced scattering coefficients μ_s' of the five layers are 14 cm^{-1} (skin), 7.67 cm^{-1} (fatty tissue), 8.94 cm^{-1} (glandular tissue), 16 cm^{-1} (sternum), and 39 cm^{-1} (ribcage) that corresponded to 800 nm. Also, the absorption coefficients μ_a of the five layers are 0.23 cm^{-1} (skin), 0.11 cm^{-1} (fatty tissue), 0.06 cm^{-1} (glandular tissue),

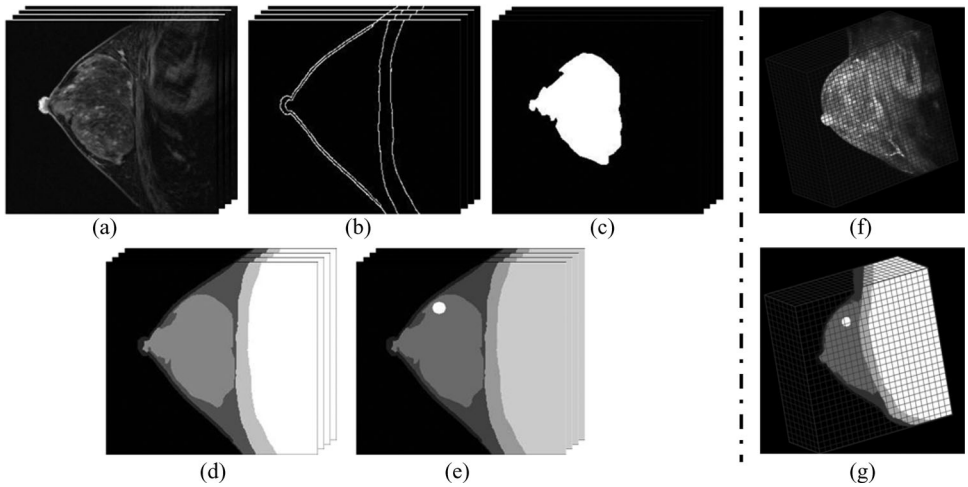

Fig. 1. Modeling process of 3-D human breast from *in vivo* MRI images: (a) original MRI breast slice, (b) boundary image of breast, (c) segmentation of glandular tissue, (d) five-layer breast model, (e) abnormality in breast, (f) 3-D MRI image of breast, and (g) 3-D breast model in Monte Carlo simulation.

TABLE I
OPTICAL COEFFICIENTS OF HUMAN BREAST MODELING

Tissue type	Reduced scattering coefficient μ_s' (cm^{-1})	Absorption coefficient μ_a (cm^{-1})	Anisotropy factor (g)
Skin	14	0.23	0.9
Fatty tissue	7.67	0.11	0.9
Glandular tissue	8.94	0.06	0.9
Sternum	16	0.16	0.9
Ribcage	39	2.8	0.9
Tumor	9.41	6.5	0.9
Diffuser	50	0	0.8

0.16 cm^{-1} (sternum), and 2.8 cm^{-1} (ribcage), respectively. Furthermore, due to the high angiogenesis of tumor, the reduced scattering coefficient and absorption coefficient of tumor are decided as 9.41 and 6.5 cm^{-1}, respectively, as optical properties of hemoglobin around 800 nm. Table I lists the optical coefficients of human breast in each layer [43].

The modeling process of human breast is demonstrated in Fig. 1. The *in vivo* MRI images of human breast were obtained in clinical diagnosis. Fig. 1(a) shows 130 2-D MRI images that were scanned from the right side to left side of human breast and each image contained 256 × 256 pixels. Then, the images were segmented with the layer boundaries and glandular by edge detection and region growing of image processing (see Fig. 1(b) and (c), respectively). The five-layer structure of human breast and tumor is remodeled for Monte Carlo simulation that is illustrated in Fig. 1(d) and (e). Fig. 1(f) and (g) shows the 3-D MRI image and the corresponding breast model we remodeled from MRI in simulation.

C. Optode Design

Generally, while one source illuminates the object, all detectors measure the reemitted light in a DOT scheme. Fig. 2(a) indicates the source–detector arrangement on the surface of human breast model. The distances from light source to six

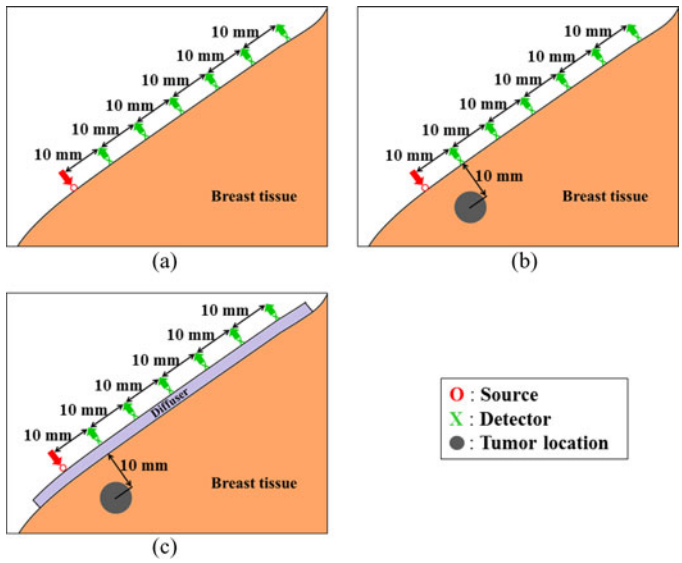

Fig. 2. Scheme of human breast imaging: (a) normal model, (b) tumor model, and (c) diffuser model.

detectors are 1, 2, 3, 4, 5, and 6 cm, respectively. Fig. 2(a) is defined as normal model. For observing the abnormality of a tumor in human breast, a target zones is defined in simulations. Fig. 2(b) shows the tumor location with the same optode configuration as Fig. 2(a). The tumor size is defined as 10 mm^3 and the depth from the center of the tumor to the breast surface is 10 mm. Fig. 2(b) is defined as tumor model. In the Fig. 2(c), the modeling geometry is the same as Fig. 2(b), and then a diffuser slab is placed between optode and the surface of the breast. Thus, Fig. 2(c) is defined as diffuser model. The distributions of received photons from different layers of breast versus source–detector separations are analyzed with time-resolved data of photon migration.

For the DADOI imaging, the geometric configuration of optode for breast imaging is shown in Fig. 3. The optode array consists of 3 × 3 sources and 4 × 4 detectors in a square

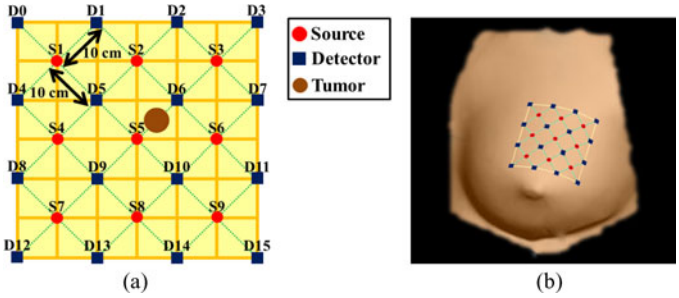

Fig. 3. Geometric configuration of optode for breast imaging: (a) source–detector separations on optode and (b) probing scheme of optode for breast imaging. The optode consists 3 × 3 sources and 4 × 4 detectors with 10 mm shortest source–detector separation. A tumor was located between source S5 and detector D6 with 10 mm depth under the breast skin.

geometry with 10 mm × 10 mm source–detector lattices that is illustrated in Fig. 3(a). A tumor was located between the source S5 and the detector D6, and the depth from the center of the tumor to the surface of the breast was 10 mm. Fig. 3(b) shows the probing scheme with attached optode on the breast surface in Monte Carlo simulation.

D. Principle of DADOI Approach

In the DADOI approach, the spatial distribution of the detected backscattering light from breast surface is defined as I_S and the detected light with a diffuser between optode and breast surface is defined as I_{DS}. In simulation, the backscattering light I_S and I_{DS} are detected on the same location of breast surface. The adopted diffuser provides much stronger scattering such that I_{DS} can be a background signal with blurred image information. The operation of DADOI method is shown in Fig. 4. Fig. 4(a) illustrates the conventional DOT measurement with single channel detection and Fig. 4(b) shows the background measurement by the use of diffuser. Also, the related optical properties of the diffuser are drawn in Table I. The mean free path of I_{DS} is longer than I_S, i.e., the diffuse part of I_{DS} is more than I_S, as can be obviously observed in Fig. 4(c). Then, the signal of DADOI can be obtained by MBL as (1). Based on the method we mentioned previously, all the backscattering light signals I_S and I_{DS} are detected by each source–detector pairs of the optobe (see Fig. 3), then MBL is calculated for mapping of spatial distribution. The optical density (OD) can be mapped as 6×6 image via optode arrangement

$$\Delta OD = -\ln \frac{I_S}{I_{DS}}. \tag{1}$$

III. Result

During the propagation, all the voxels that the photon has passed through are recorded. Therefore, the movie of photon migration in breast can be made with time-resolved 3-D Monte Carlo simulations. This paper has supplementary downloadable material available at http://ieeexplore.ieee.org, provided by the authors. The size of MOV movie file is 1.01 MB.

The light source was located at the 2.5 cm from the direction of 12 o'clock of the nipple. In the video, the movie shows the

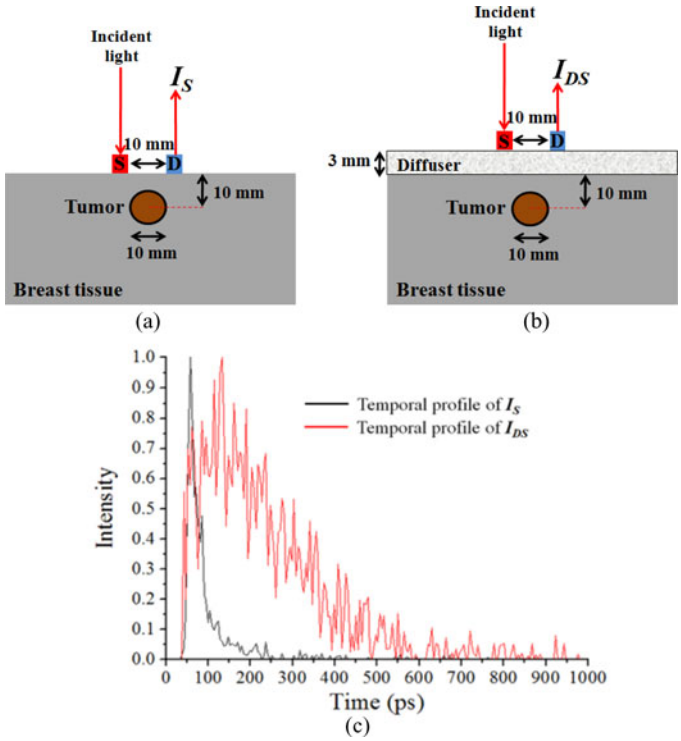

Fig. 4. Illustration of DADOI approach: (a) conventional DOT scheme, (b) diffuser-aided background measurement, and (c) temporal profiles of I_S and I_{DS}.

photon migration of all 10^8 photons in the sagittal section with 800 nm wavelength. The intensity attenuated very strongly at about 4 cm depth in the breast tissue. According to the dynamic distribution of this movie record, we can observe the relevance of attenuation of intensity and the depth of photon migration in breast. Then we demonstrated the photon migration that was detected by detector with various source–detector separations.

Fig. 5 shows that the paths of received photons with various source–detector separations. The red arrow indicates the location of light source and orange one indicates the locations of detectors in each case. The source–detector separations are 1, 2, 3, 4, 5, and 6 cm in Fig. 5(a)–(f), respectively. In the cases of (e) and (f), the detected light is attenuated strongly with deeper penetration (∼4 cm depth). Obviously, the total received intensity was decreasing with the source–detector separation increasing. The 1–4 cm source–detector distances give a banana-shaped pattern revealed by Monte Carlo simulation, which demonstrates a high significant probability of tumor detection at 4 or less cm depth.

Fig. 6(a) demonstrates the distribution of received intensity versus source–detector separations with three cases in simulations. Tumor and diffuser model are the same breast models with a 10 mm depth tumor. The optode in tumor model is attached on the surface of breast as conventional DOT measurement and the diffuser-aided approach is shown in diffuser model that corresponds to Fig. 4(a) and (b).

The normal model describes the normal breast model as conventional baseline and detected light is defined as I_N. In all cases, the decreasing of received intensity accompanies the increasing of source–detector separation. The smaller I_S on 1 cm

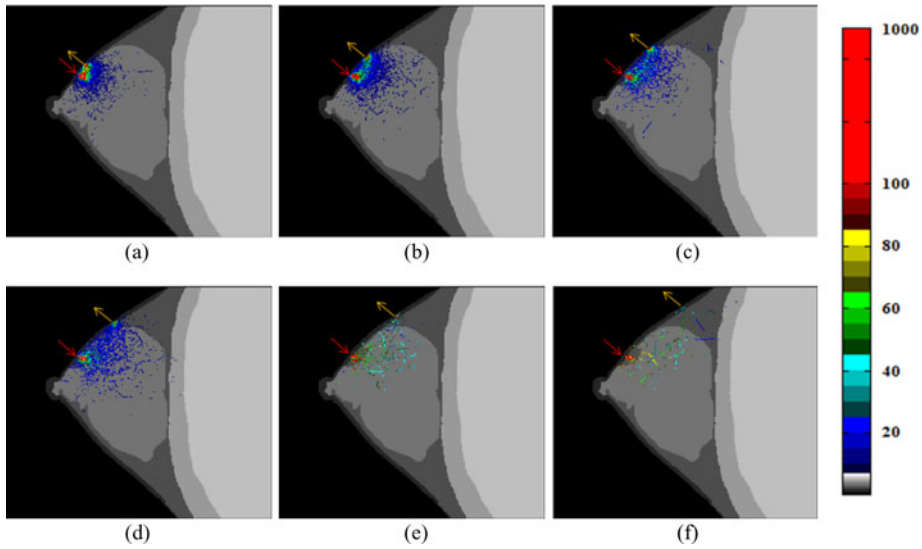

Fig. 5. Propagation pattern of photon migration with respect to various source–detector separations with (a) 1 cm, (b) 2 cm, (c) 3 cm, (d) 4 cm, (e) 5 cm, and (f) 6 cm.

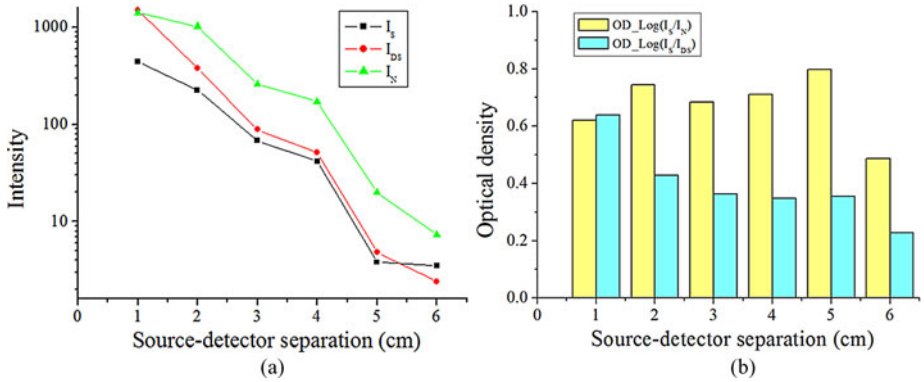

Fig. 6. (a) Distribution of received intensity versus source–detector separations from normal model (I_N), tumor model (I_S), and diffuser model (I_{DS}). (b) Ratios of optical density I_S/I_N and I_S/I_{DS}.

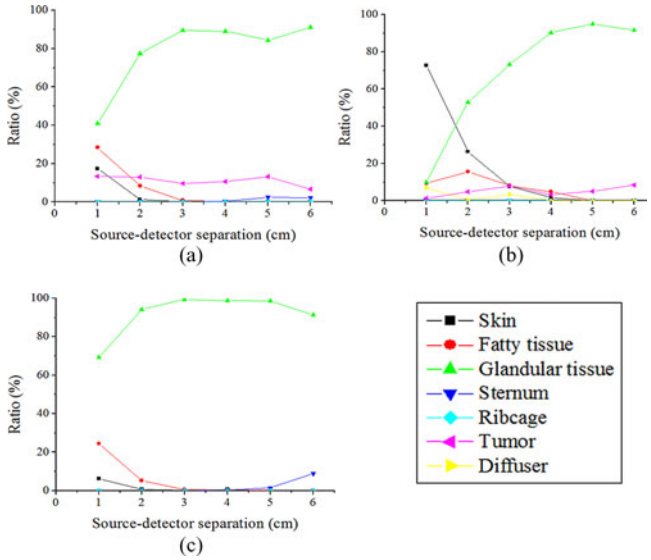

Fig. 7. Distributions of ratio of the received intensity from different layers versus the distance of source–detector separation. (a)–(c) are results that correspond to tumor model, diffuser model, and normal model, respectively.

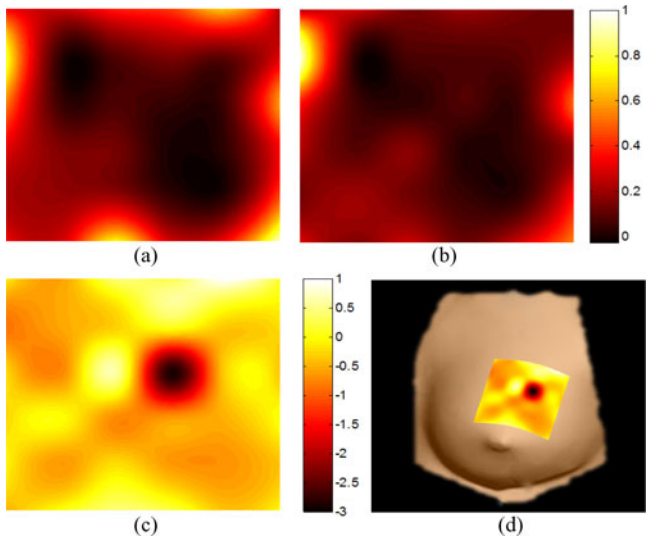

Fig. 8. Imaging result of DADOI approach. (a) Imaging of I_S. (b) Imaging of I_{DS}. (c) DADOI imaging (imaging of ΔOD). (d) Image mapping with respect to optode position on breast surface.

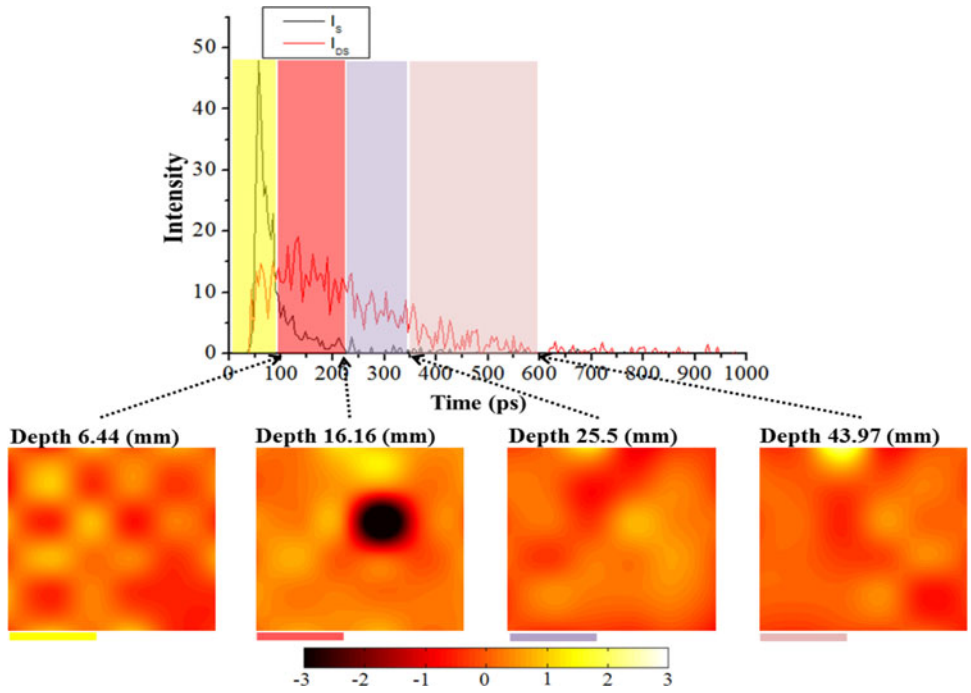

Fig. 9. DADOI via various depths in breast. The pseudocolor represents the summed light intensity of corresponding temporal interval.

separation implies the direct attenuation from tumor. The ratios of optical density I_S/I_N and I_S/I_{DS} are signals of conventional DOT and DADOI that are shown in Fig. 6(b). The better imaging contrast of the tumor location (1-cm source–detector separation) can be observed and it also implies the feasibility of our DADOI approach.

Because all the paths of the received photons were recorded in the simulations, the visited layers of each photon can be marked for postprocess. Fig. 7 shows the ratios of the backscattered intensities from different layer versus the source–detector separation with the three modeling cases. Obviously, the ratio of glandular layer increases rapidly when the distance of source–detector separation increases. In Fig. 7(b), the ratio of glandular layer increases slower than the result of Fig. 7(a) because the path length of the received photons was increased due to the thickness of the diffuser.

Fig. 8 shows the imaging result of DADOI approach (the breast model and optode arrangement were described in Fig. 3). In order to verify the feasibility of DADOI approach, the temporal responses of received intensity of I_S and I_{DS} were summed as an integral intensity in Fig. 8.

The imaging of I_S, I_{DS}, and ΔOD are shown in Fig. 8(a)–(c), respectively. In the conventional DOT measurement, the image reconstruction has to solve the inverse problem with the complex algorithms from backscattering light distribution I_S [see Fig. 8(a)]. In our result, the diffuser-aided approach was utilized to detect the other backscattering light distribution I_{DS} [see Fig. 8(b)], and the better contrast image of breast tumor [see Fig. 8(c)] was reconstructed with MBL as (1) that provide faster and simpler imaging than conventional DOT. Fig. 8(d) shows the DADOI image mapping with respect to optode on breast surface. In the Fig. 8(a) and (b), the pseudocolor indicates the variation of received intensity (I_S and I_{DS}). In the Fig. 8(c), the pseudocolor indicates the variation of ΔOD.

In time-resolved DADOI, depth information can result from the arrival delay of detected photon. Fig. 9 shows the temporal profile of I_S and I_{DS} and the related imaging from different depth. The depth information was estimated with source–detector separation, refractive index, velocity of light, and temporal information. Although the estimation is quite simple, the images from various depths in human breast can be seen obviously in Fig. 9.

IV. Discussion and Conclusion

In this study, the simulation results demonstrate the characteristics of photon migration with different source–detector separations in 3-D human breast model from *in vivo* MRI image. As mentioned before, the time-resolved Monte Carlo method can be capable of performing source–detector separation analysis. The dynamics of photon migration with various source–detector separations are analyzed for characterization of breast tissue and estimation of optode arrangement. As shown in the results in Figs. 5 and 6(a), we observed that the received intensity of the source–detector separation of 5 cm is roughly 10 times smaller than that of 4 cm. Thus, the source–detector separations should be less than 4 cm for breast imaging in DADOI system. Meanwhile, the feasibility of DADOI was manifested in the paper. The result of Fig. 6 shows that the better contrast was obtained with DADOI approach. Finally, the optode array was designed for mapping of spatial distribution, as shown in Fig. 8. In this result, the depth information could not be seen because all the temporal responses of received intensity were summed as CW mode, however, it shows the feasibility of the DADOI approach.

Fig. 9 demonstrates that the depth information can be observed from the time-gated images.

In this study, we can monitor the breast tumor and detect background signal on the same location and simpler to obtain the better contrast image with MBL while the different optical parameters between normal and abnormal areas. In the conventional DOT, the complicated numerical algorithm is needed for image reconstruction. The DADOI approach can provide better imaging contrast and faster imaging than conventional DOT. However, the bottleneck of the DOT is still limited by the spatial resolution for early cancer diagnosis. In the next step, the DADOI will be implemented for breast tumor imaging and chemotherapy postoperative monitoring in experiment.

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