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Abstract. We present the first experimental results of time-resolved diffuser-aided diffuse optical imaging (DADOI) method in this paper. A self-manufactured diffuser plate was inserted between the optode and the surface of a scattering medium. The diffuser was utilized to enhance the multiple scattering that destroys the image information for baseline measurement of turbid medium. Therefore, the abnormality can be detected with the modified optical density calculation. The time-domain DADOI method can provide better imaging contrast and simpler imaging than the conventional diffuse optical tomography measurement. Besides, it also reveals rich depth information with temporal responses. Therefore, the DADOI offers a great potential to detect the breast tumor and chemotherapy monitoring in clinical diagnosis. [DOI: 10.1117/1.JBO.19.4.046008]

Keywords: diffuser-aided diffuse optical imaging; diffuse optical tomography; breast tumor imaging; near-infrared spectroscopy; photon migration.

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1 Introduction

The greatest increase of the incidence of breast cancer has been in Asian countries over the last several decades. The incidence of breast cancer is rising globally and is associated with the increased mortality. The breast cancer had become the first cause of death for the female populations in the developed countries.[1,2] For clinical detection, it mainly relies on the detection of morphological signs and angiogenesis phenomenon with the modern medical imaging technologies such as mammography, sonography, magnetic resonance imaging (MRI), and positron emission tomography (PET).[3,4] However, mammography tends to be difficult to detect malignant lesions in dense breast tissue, which consequently leads to a lower sensitivity for using mammograms to find breast cancers in dense breasts. The detection efficiency of breast sonography strongly depends on the experience and skill of the operators and lack of standardized scanning protocols. Although the active MRI for the "oxygenation dynamics" and the PET for the "gluco-dynamics" have the potential for early detection of breast cancers, they are both very costly and the limitation of a huge size of instruments cannot usually be used for screening or a first line of defense during the regular checkup. Besides, the large size imaging systems cannot provide the diagnosis with completely patient-oriented measurement in clinic.

Over the past decade, diffuse optical tomography (DOT) with near-infrared light illumination has been shown to be an effective tool for measuring the biological properties of breast tissue that can provide both functional and structural information with several benefits such as being noninvasive, less expensive, nonionizing radiation imaging, real-time measurement, long-time monitoring, easy operation, compact design, and completely patient-oriented measurement.[5–11] For human breast imaging, DOT provides pathological tumor contrast directly in vascularity, hemoglobin concentration, and tissue absorption/scattering properties. DOT detects the abnormality of scattering and absorption, i.e., to detect the breast tumor in normal breast background. The process of image reconstruction in DOT depends on the technical algorithms for solving the forward and the inverse problems. In previous studies, the optical properties of normal breast tissue (as baseline) are measured from the contralateral of breast tumor in clinical diagnosis.[12,13] However, human breast tissues are not identical on both sides, which implied the reference signal from the contralateral of detected breast generates concomitant prediction errors of functional image reconstruction. Therefore, we propose a time-domain diffuser-aided diffuse optical imaging (DADOI) method that can reconstruct the images simpler and faster than the traditional DOT approach by monitoring the breast tumor and detects background signal on the same location. Furthermore, the optical properties of the tissue are inferred from the temporal point spread function (TPSF) in the time-domain operation. Thus, time-domain DADOI is a kind of "time-gating" approach to reveal rich depth information.

2 Materials and Methods

Figure 1 shows the scheme of time-domain DADOI system. The system consists of 1 ps laser diode head (LDH-P-780, PicoQuant, Berlin, Germany) as light sources at 780 nm. A computer controlled multichannel laser diode driver (PDL 828 SEPIA II, PicoQuant, Berlin, Germany) was used. The optical power of laser is <5 mW with full width at half maximum (FWHM) <500 ps. The light sources were delivered sequentially to nine locations on the optode by using a 1:9 optical switch (Piezosystem Jena, GmbH, Jena, Germany) for time-division multiplexing. A universal serial bus (USB) interface

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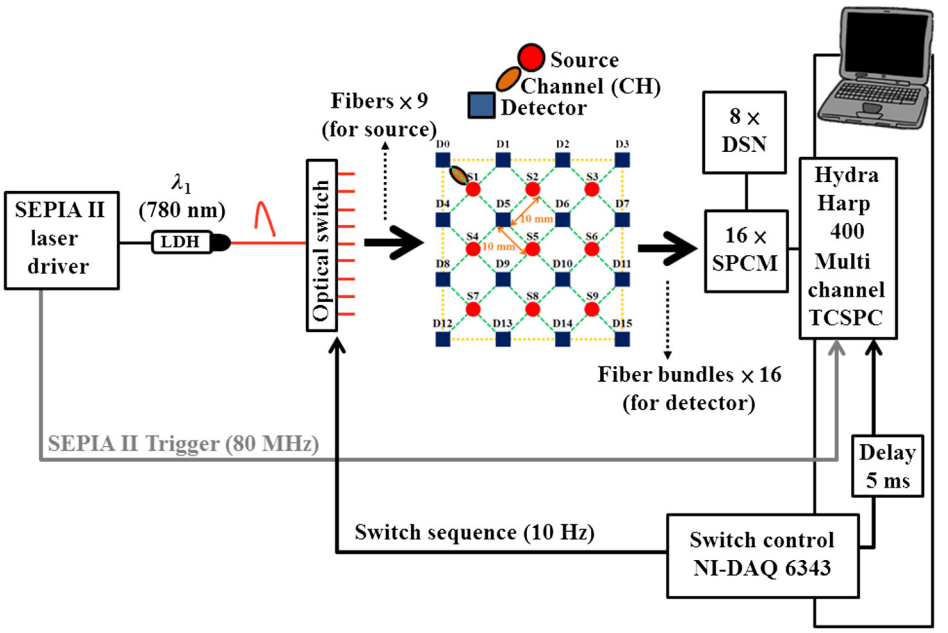

Fig. 1 Schematic of time-domain diffuser-aided diffuse optical imaging (DADOI) system setup. SEPIA II is the computer controlled multichannel diode laser driver, LDH is the picosecond laser diode head, SPCM is the single photon counting module, DSN is the dual SPCM power supply, and HydraHarp is the USB interface board for time-correlated single photon counting.

data acquisition card (NI-DAQ 6343, National Instruments, Austin, Texas) was used for optical switch controlling. The backscattered optical signals from phantom were detected by the use of 16 single photon counting module (SPCM-AQRH-14-FC, Excelitas Technologies, Wiesbaden, Germany) that were controlled and monitored with dual SPCM power supply (DSN 102, PicoQuant, Berlin, Germany). It also provides safety shutdown to prevent SPCM degradation. A multichannel time-correlated single photon counting module (TCSPC) with USB interface was used for acquisition of distribution of times of flight of photons (HydraHarp 400, PicoQuant, Berlin, Germany). The optode array consists of 3×3 array of sources and 4×4 array of detectors in a square geometry with minimum distances of source-detector separation 10 mm. Thus, the whole measurement area was approximately 8×8 cm^2 with 6×6 source-detector pairs corresponding to 36 channels.

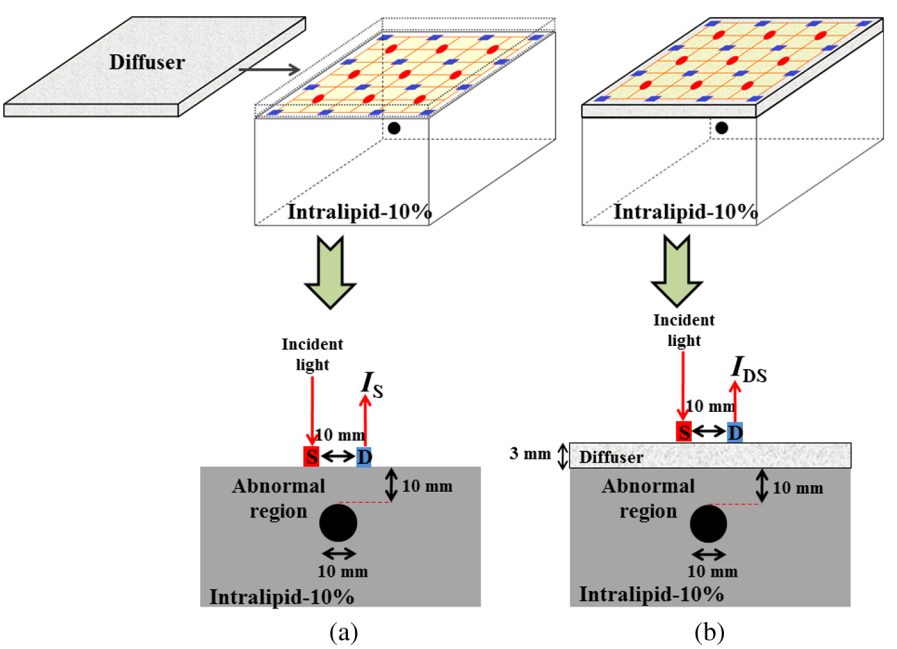

Fig. 2 The experimental setup and principle of time-domain DADOI approach. (a) The measurement without diffuser (or imaging without diffuser). (b) The measurement with diffuser (or imaging with diffuser). The thickness of diffuser plate is 3 mm.

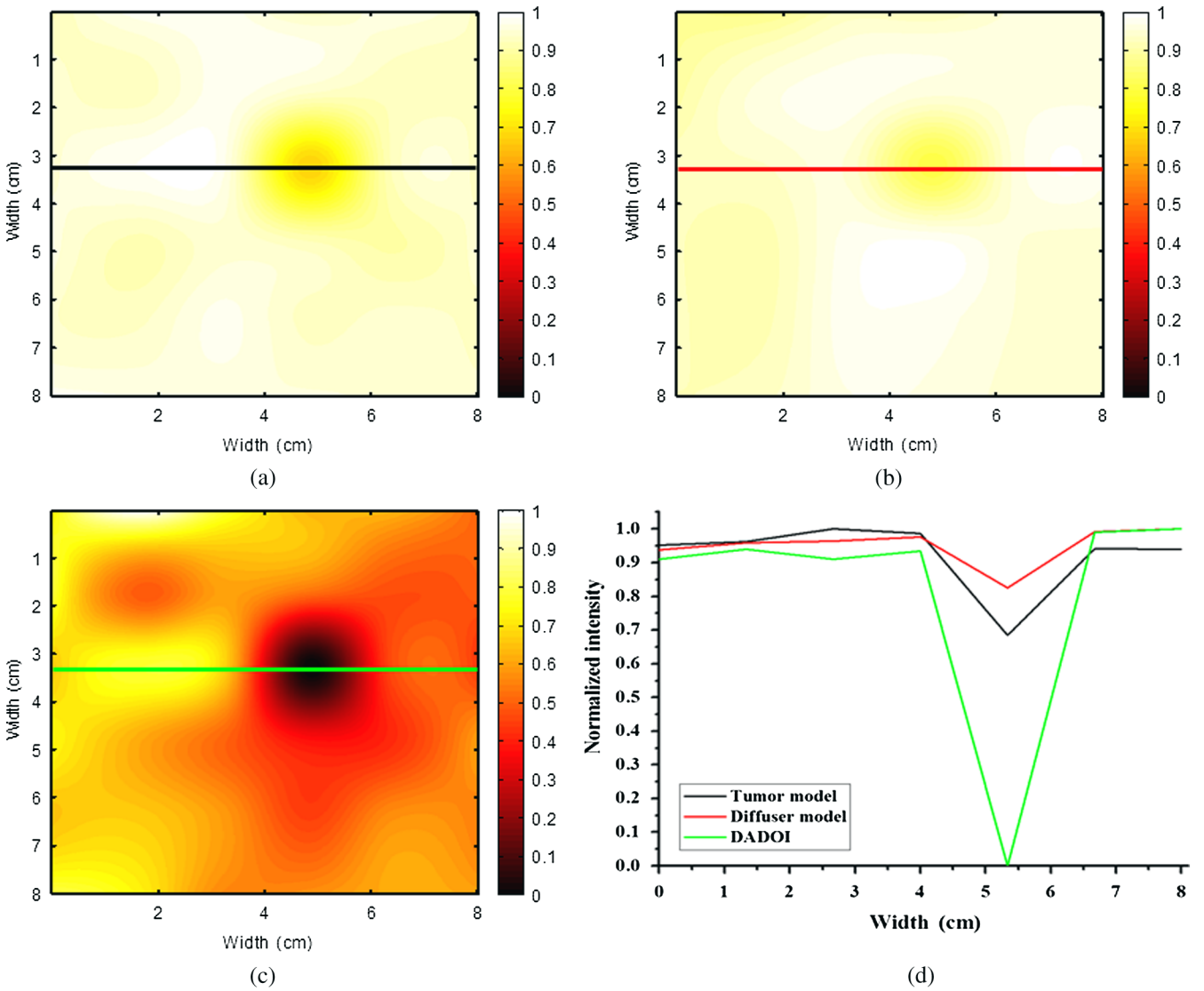

Fig. 3 The DADOI results from the phantom study. (a) Imaging without diffuser [image mapping of $I(t)_S$]; (b) imaging with diffuser [image mapping of $I(t)_{DS}$]; (c) imaging by DADOI method; and (d) contrast comparison among (a), (b), and (c).

The real-time imaging capability of the time-resolved DADOI system was tested on a liquid phantom. The phantom geometry and the principle of time-resolved DADOI method are shown in Fig. 2. The phantom setup consisted of 20 cm× 20 cm × 10 cm tank that filled with the solution of Intralipid and black ink. The scattering coefficient of diluted Intralipid-10% could be similar to breast tissue with given concentration. A 10-mm diameter solid spheroid made of resin was embedded in the tank as an absorbing inhomogeneity. The absorbing inclusion was placed below the middle between the source S5 and the detector D6. The depth from the surface of the absorbing inclusion to the surface of the phantom was 10 mm. The spatial distribution of the detected backscattering light from the surface of phantom without diffuser used was defined as $I(t)_S$ [Fig. 2(a)] and the detected light with a 3-mm thick diffuser plate between the optode and the surface of phantom was defined as $I(t)_{DS}$ [Fig. 2(b)]. The adopted diffuser provides much stronger scattering such that $I(t)_{DS}$ can be a background signal with blurred image information. The signal of time-resolved DADOI can be obtained by calculating the modified optical density with time correlated as Eq. (1). All the backscattering lights $I(t)_S$ and $I(t)_{DS}$ are detected by each source–detector pairs of the optobe (as shown in Fig. 1), then the time-correlated variation of modified optical density was calculated for mapping of spatial distribution

$$\Delta \mathrm{OD}(t) = -\ln \frac{I(t)_{\mathrm{S}}}{I(t)_{\mathrm{DS}}}. \quad (1)$$

3 Results and Discussions

Figure 3 shows the imaging result of time-domain DADOI method. In an experimental result, the temporal responses of received intensity $I(t)_S$ and $I(t)_{DS}$ were summed as an integral intensity to verify the feasibility of DADOI method. Figure 3(a) shows the backscattering image without diffuser plate and Fig. 3(b) shows the backscattering image with inserted diffuser plate between optode and phantom. The calculation of the modified optical density with time correlated is to substitute the complex algorithms of inverse problem of conventional DOT measurement

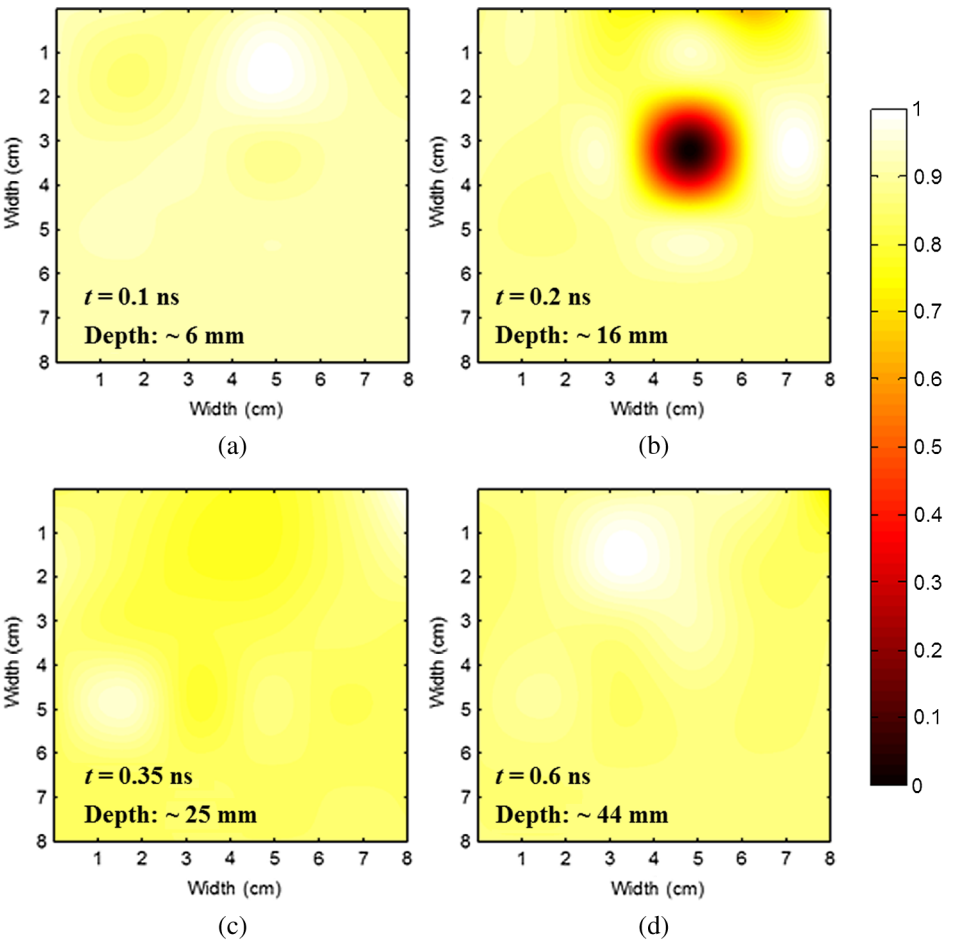

Fig. 4 The tomography of different depths by using temporal responses of time-resolved DADOI method. (a)–(d) The tomography at depth 6, 16, 25, and 44 mm correspond to temporal responses as 0.1, 0.2, 0.35, and 0.6 ns, respectively.

for mapping of spatial distribution. Figure 3(c) demonstrates the contrast image of DADOI method. According to the contrast comparison in Fig. 3(d), the better contrast image can be observed clearly in the DADOI result.

In time-domain DADOI, the depth information can be obtained from the arrival delay of detected photon (time-of-flight signal). In this study, the tomography of depth information was reconstructed simply by using temporal responses of photon migration. Figure 4 shows the tomographic images from four different depths. The depth information was evaluated with source-detector separation, refractive index, velocity of light, and TPSF. With the experimental result of phantom study, the time-domain DADOI method reveals a good feasibility for clinical diagnosis of breast cancer.

4 Conclusions

In conclusion, time-domain DADOI method can provide better imaging contrast and simpler imaging than the conventional DOT measurement. However, the bottleneck of the DOT is still limited by the spatial resolution. In future study, the multi-wavelength sources could be applied to map the images for analyzing and quantifying the vascular and tissue properties such as oxy-hemoglobin, deoxy-hemoglobin, water, and lipids of the breast tissue.

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