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A hybrid imaging method based on diffuse optical tomography and optomechanical method to detect a tumor in the biological phantom

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ABSTRACT

In this study, a new combined method to detect abnormality inside the biological phantom is presented. We describe a new approach to breast imaging based on diffuse optical tomography and optomechanical imaging. In this method, the diffusion of photons inside compressed breast phantom is used to detect the location of abnormalities. The variation of optical properties of phantom induced by compression can affect on diffusion of photons. Therefore, these variations of optical properties of phantom must be considered in this imaging method. In current study, the ability of this method to detect the location of tumor inside biological phantom is evaluated. The results show that the accuracy of this method is better than diffuse optical tomography.

1. Introduction

Breast cancer is the second leading cause of cancer deaths among women [1–3]. So, the breast cancer screening has an important role in oncology. Currently, the optical imaging methods such as diffuse optical tomography (DOT) and photoacoustic spectroscopy method as a complementary method to mammography are tested for breast cancer screening [4]. These optical imaging methods have disadvantages. The low optical depth due to diffusion of photons inside biological phantom is a complicated problem of bio-optical imaging. The low spatial resolution of diffuse optics is due to scattering as is well known [4]. For improving the diagnostic potential of DOT for breast cancer detection, some hybrid techniques like “DOT-MRI” and “DOT-X ray have been presented [5–14]. Theses research groups employ spatial *a priori* information from MRI and X-ray within the image reconstruction frame to improve the accuracy of reconstructed images. These come with the additional benefit that it makes the interpretation of the multimodal data simpler without the need for complex algorithms to remap the images of different modalities onto a common space [11–13].

In 2000, the first key paper using both DOT and MRI was published by Ntziachristos et al. [5]. In this paper, they presented the clinical application of this combined method to perform magnetic resonance imaging (MRI)-guided DOT and noninvasively retrieve functional tumor characteristics in deep tissue. The combination of the optical and MR measurements into the same tomographic scheme yields additional benefits that cannot be achieved simply by acquiring MR and optical images as stand-alone techniques. This is because the use of a priori information, such as the anatomical or functional information from MRI, can significantly improve the quantification accuracy of the optical method by constraining the DOT image reconstruction procedure [6]. In 2005, Brooksby and his colleagues presented an imaging system that simultaneously performs DOT and MRI. Their results illustrated that this hybrid method can be used to improve the spatial resolution and quantitative accuracy of reconstructed optical parameter [7]. In spite of these benefits, the DOT-MRI system needs huge accessories and so, it is very expensive [12,13].

In 2005, Zhang et al. presented first hybrid optical and X-ray mammography imaging system, together with an image reconstruction technique suitable for imaging the breast [8]. Then in 2011 Fang and his colleagues presented results of a clinical trial by DOT-X ray between April 2006 and June 2009. In this trial, 155 subjects were enrolled (normal: 52 subjects, malignant: 50 subject and benign: 53 subjects) [9]. The results presented in this project illustrated that normalized value of total hemoglobin concentration (Hb_T) which is estimated by this method can be used to differentiate cancerous tumors from solid benign lesions and fibroglandular tissue of the same breast. While X-ray mammography (with some limitations) may be utilized several times without major health risks, it does not readily provide metabolic information which may be the key-parameter that changes rapidly and often [11].

As was discussed earlier, MRI based modalities are prohibitively

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expensive and unavailable for such use. On the other hand, X-ray does not readily provide metabolic information, and X-ray modalities also provide superior lateral resolution, but its depth discrimination is relatively poor because of the restricted angular views, which also can cause artifacts such as ghosting [10,17]. Therefore, a noninvasive, inexpensive, nonionizing-radiation-based detection modality sensitive to metabolic and physiological changes is expected to be of critical importance [11,16–18].

Another new method to breast cancer imaging is optomecanical imaging [1,13]. In 2007, Xu et al. developed and tested a handheld optical probe for dynamic imaging and characterization of biological tissue systems *in vivo* [13]. This schema measures the relative changes of tissue physical and physiologic properties in response to an external compression stimulus. They hypothesize that the tumor oxygen dynamics in response to the external stimulus may provide important information regarding tissue viscoelasticity, metabolic demand, and vascular perfusion that may ultimately help to identify malignancy [13]. In 2011, Al abdi et al. presented an optomechanical imaging system to breast imaging based on the interaction between controlled applied mechanical force and tissue hemodynamic [1]. They applied the method of optomechanical imaging as a basis for obtaining new contrast features in the hope of improving the diagnostic potential of NIR imaging methods for breast cancer detection. Central idea to this technique is the ability to simultaneously measure the viscoelastic properties of the breast while observing time-dependent changes in hemodynamics induced through precisely controlled articulation [1,16]. Carp et al. in 2013 applied this method to breast imaging. They illustrated that compression-induced hemodynamics can differentiate malignant breast tumors from the surrounding tissue. The main feature observed is a persistent blood volume reduction in the tumor area in contrast with a slow reperfusion in the normal tissue. This characteristic is statistically significant, and can be detected using a single compression cycle with 60 s of follow-up during compression [15].

As mentioned, elastic properties and optical properties can be applied to differentiate between normal tissues and tumors, that is because these properties of tissue are changed by variation of physiological properties of tissues [16,19]. Localized physiological properties such as total hemoglobin concentration (Hb_T), tissue oxygen saturation (StO_2), and water percentage (H_2O) can be quantified diagnostically in tissue with optical and optomechanical methods [16,20]. It seems that the combination of DOT and optomechanical can simply yield additional benefits compared with DOT and optomechanical imaging as stand-alone techniques. For example, as mentioned in Ref. [4,21] the penetration depth of NIR photon is restricted by multiple scattering occurred in the biological tissues which results in a decrease in the spatial resolution of DOT. In addition, the accuracy of DOT highly depends on the knowledge of the tissue optical heterogeneities [22]. Hence, this combination can improve the accuracy of DOT.

In this study and due to abilities of DOT and optomechanical imaging method, a combination of these two methods has been evaluated. In optomechanical, the variation of elastic properties is measured and these changes are applied for imaging. But, in the current study, the changes of optical properties under compression are applied for imaging. The mechanical pressure can deform the geometry of breast and change the optical property of breast. In the current hybrid method, the small value of pressure is applied on phantom and therefore the deformation of shape is insignificant [23]. The key result of this study is the evaluation of a new hybrid method based on DOT and optomechanical method. To evaluate this presented method, first the propagation of diffused photons inside breast tissue phantom are studied by this hybrid method and then the location of an abnormality defect is detected.

The optical and mechanical properties of constructed phantom must be consistent with breast tissue. Most volume of breast is made of adipose (fatty) and fibroglandular tissue overlying the anterior chest wall. So, construction of real breast phantom could be complicated. It seems that an inhomogeneous breast phantom with multiple inclusion must be conducted (at least three levels of optical properties, one for adipose, one for firoglandular and one for tumor are needed). Some research groups have measured the optical properties of adipose, fiberglandular and breast tumor [24,25]. Troy et al. in Ref. [24] have measured *in vitro* the absorption and reduced scattering coefficient of breast in near infrared spectrum. Measurements were conducted on 115 tissue samples collected from 88 patients. In the study of Troy et al. although no statistically significant difference was observed in reduced scattering coefficient of ductal carcinoma and fatty or fibrous normal tissue on 115 pooled samples from 88 patients, measurements of normal and diseased breast-tissue samples from the same patient showed significant difference in optical parameters [24,25]. The measured data in Ref. [24] show that the values of reduced scattering coefficients are two orders of magnitude greater than value of absorption coefficient. Therefore in near infrared spectrum, the diffusion of photons in breast phantom actually depends on the value of reduced scattering coefficient. By this point, Ghosh et al. measured *in vitro* the optical properties of the breast tissue included adipose and fibroglandular [25]. So, based on results presented in Ref. [23–26] and in NIR region, an approximated simple inhomogeneous phantom with one inclusion as tumor can be used. It should be emphasized that in this study, the constructed phantom is used purely to evaluate the accuracy of presented method and it is not used to design or calibrate a commercial optomechanical mammography system for real breast.

If the inclusion similar to real compressed breast is assumed to be non-isolated, the procedure of image reconstruction is very complicated. That is because in real tomography situations the absolute true values as well as the distribution of the inclusion in the breast tissue are not known and cannot be fed into the reconstruction algorithm as a priori information [27]. As mentioned in Ref. [28], a practical way for initializing the iterative reconstruction process is to start off with a uniform distribution of optical properties at the approximate value of the average background medium [28]. In this study, three different simulation cases are distinguished: Case a: Homogeneous breast phantom with known optical properties; Case b: Inhomogeneous phantom (with one inclusion) with known optical properties; Case c: Inhomogeneous phantom with unknown size and location of inclusion.

Case a can be used to evaluate the accuracy of simulation. Moreover, the changes of optical signals measured by DOT under different pressure can be used to determine the variation of optical properties of homogeneous phantom. For example, in case a, the proportionality factor between optical properties and value of pressure can be estimated.

In the second case, the simulation is done using an inhomogeneous breast phantom. It is assumed that all optical properties, size and location of inclusion are known and provided as *a priori*-information to the reconstruction process. In this case, the proportionality factor between optical properties and value of pressure can also be estimated. The sensitivity of this hybrid method can be evaluated by this ideal case. In case c, we can try to determine the optical properties, size and location of inclusion (the shape and angle of inclusion is known).

Briefly, in this study, the phantom is compressed by mechanical pressure and so, this compression changes the value of measured diffused reflectance. As we presented in Ref. [23], these changes in diffused reflectance can be explained by variation of optical properties induced by pressure. Then, the pressure dependence of optical properties of phantom is estimated. After that, we add this