Hierarchical Clustering Method to Improve Transrectal Ultrasound-guided Diffuse Optical Tomography for Prostate Cancer Imaging

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The inclusion of anatomical prior information in reconstruction algorithms can improve the quality of reconstructed images in near-infrared diffuse optical tomography (DOT). Prior literature on possible locations of human prostate cancer from transrectal ultrasound (TRUS), however, is limited and has led to biased reconstructed DOT images. In this work, we propose a hierarchical clustering method (HCM) to improve the accuracy of image reconstruction with limited prior information. HCM reconstructs DOT images in three steps: 1) to reconstruct the human prostate, 2) to divide the prostate region into geometric clusters to search for anomalies in finer clusters, 3) to continue the geometric clustering within anomalies for improved reconstruction. We demonstrated this hierarchical clustering method using computer simulations and laboratory phantom experiments. Computer simulations were performed using combined TRUS/DOT probe geometry with a multilayered model; experimental demonstration was performed with a single-layer tissue simulating phantom. In computer simulations, two hidden absorbers without prior location information were reconstructed with a recovery rate of 100% in their locations and 95% in their optical properties. In experiments, a hidden absorber without prior location information was reconstructed with a recovery rate of 100% in its location and 83% in its optical property.

Key Words: Hierarchical clustering method; DOT reconstruction; detection of prostate cancer.

Prostate cancer is one of the leading causes of cancer deaths in men in the United States (1). Conventional methods for diagnosing prostate cancer include the prostate-specific antigen (PSA) blood test (2) and digital rectal examination (DRE). If the PSA level and/or DRE are suspicious, then in most cases the patient undergoes transrectal ultrasound (TRUS)–guided biopsy. This is because of the fact that the PSA level could be misleading. PSA can be expressed high because of benign prostatic hyperplasia. (BPH) (3). On the other hand, men with a low PSA level (<4.0 ng/ml) can still have prostate cancer (4). Despite recent advances in ultrasound, the grayscale-based ultrasound imaging has an accuracy of 50%–60% only; diagnosis accuracy can be even less in TRUS (5). Thus, TRUS has been used only for guiding a needle biopsy, not for the detection of prostate cancer. In recent years, researchers have made great advances in using magnetic resonance imaging (MRI) and magnetic resonance spectroscopy (MRS) to detect prostate cancer and/or to guide needle biopsy (6,7). Given MRI and MRS cost, bulkiness, requirement for body confinement, and limited accessibility to the general public, it is highly desirable to have a portable office-based imaging tool available to clinicians for an improved detection or screening of prostate cancer and for active surveillance to determine an optimal treatment time.

For the past two decades, diffuse optical tomography (DOT) with near-infrared (NIR) light has been a popular noninvasive imaging modality using nonionizing radiation to provide functional maps about the tissue under study. Because cancer tissues are more vasculature than the surrounding tissue, hemoglobin-based absorption in tumors provides optical contrast in DOT. When imaged at multiple wavelengths, DOT is capable of measuring chromophore concentrations such as oxyhemoglobin, deoxyhemoglobin, and water. Use of DOT for breast cancer detection and diagnosis has been extensively studied for nearly 20 years (8,9). However, investigations on detection of prostate cancer using DOT have been relatively limited compared to those done on breast cancer detection. A previous ex vivo study (10) reported differences in water content between normal

Acad Radiol 2014; 21:250–262

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http://dx.doi.org/10.1016/j.acra.2013.11.003

and cancer human prostate tissues. A recent review article (11) provided a comprehensive summary of optical properties of human prostate cancer tissue at selective wavelengths. Specifically, several reports given in references (12–15) show that light scattering of prostate cancer tissue is higher than that of normal prostate tissue. Transrectal DOT has been reported by several recent studies (16–18) as a possible imaging tool for prostate cancer detection and diagnosis.

DOT instrumentation can be divided into three categories based on the principle of operation: 1) time-resolved systems (19–21), 2) frequency-domain systems (22), and 3) continuous wave (CW) systems (23,24). Measurements are made in transmission geometry, reflection geometry, or both. A time-resolved system relies on photon counting or gated imaging, which provides photons' time of flight through the tissue. However, these systems are costly in comparison with CW systems. A frequency-domain system modulates laser light typically in the radio frequency range (100 MHz) and measures the amplitude and phase shift of the detected signal. A CW system is the simplest, fastest, and most cost-effective system in data collection; it can also be made at a video rate for imaging. However, CW systems measure only the intensity of reflected/transmitted light, so they cannot separate the absorption property from the scattering effect of the tissue (25).

For transrectal DOT to be able to provide excellent reconstructed images for prostate cancer detection, we have to acknowledge our obstacles to find appropriate solutions. One main obstacle is closely associated with the location of measurements: the human rectum, where we have a limited space (allowing a limited number of optodes to be implemented); furthermore, only reflectance geometry of DOT can be used. Given the nature of light scattering in tissues, DOT suffers from poor spatial resolution. Measurements taken using reflectance geometry do not normally achieve the excellent spatial resolution that is more commonly obtained in those taken by transmission geometry. One way to improve the spatial resolution is to couple DOT with other imaging techniques such as MRI and ultrasound. In particular, a combined TRUS and DOT probe for imaging prostate cancer has been studied previously (26), using the anatomical information from ultrasound to reduce the number of unknowns in the DOT image reconstruction. As shown by Xu et al. (26), each anatomical region was considered to be homogeneous; uniform optical properties were reconstructed in each respective region. Although the combined TRUS–DOT method improves accuracy of reconstructed DOT images, it relies highly on the ability of TRUS to locate the prostate cancer lesion. Given that TRUS has a low prostate cancer detection accuracy and that each region is assumed to be homogeneous, the reconstructed DOT images of prostate cancer could be erroneous.

To limit the dependency of DOT image reconstruction on TRUS sensitivity, we have developed a hybrid reconstruction technique by combining a piecewise cluster reconstruction approach with hard prior anatomy of prostate available from TRUS. Our method uses a hierarchical scheme of clustering, where we define a cluster as a group of nodes/voxels within a predefined volume. By using hierarchical clustering, a region of interest (ROI, ie, the prostate) can be transformed into a partially heterogeneous medium, within which we can search and further reconstruct potential cancer lesions. The inverse problem of DOT is solved in multiple steps by changing cluster sizes within the image domain. Multistep reconstruction in DOT has been reported earlier (27) for breast cancer detection based on a frequency-domain study. It is understood according to Srinivasan et al. (27) that the size and location of the absorber were partially or roughly estimated in the first step of reconstruction, after which more steps were used to further improve the quality of reconstructed images. In the TRUS–DOT scenario, however, a rough reconstruction of the first step is futile to effectively detect prostate cancer because of the multilayer tissue compositions, reflectance measurement geometry, limitation in the number of measurements, and particularly the inability of ultrasound to identify prostate cancer lesion or lesions. Thus, to improve the effectiveness and accuracy of prostate cancer imaging, we considered piecewise division of the image domain in DOT, assuming that the domain consists of disjoint subdomains with different optical properties.

Specifically, in our work, we performed the piecewise division of the image domain for a human prostate in the inverse calculation. By doing so, we were able to combine the piecewise division with hard prior anatomic information for DOT image reconstruction. In this article, we present detailed procedures of our proposed method and validate it by showing its performance with the following computer simulations: 1) one anomaly at a depth of 1–3 cm below the measurement surface, 2) two anomalies at 1 cm and at 2 cm, respectively, 3) variable background absorption from 0.005 to 0.015 mm^{-1}), 4) variable noise percentage from 0% to 3%. By the end, we will also validate the performance of the proposed method by laboratory experimental results.

METHODS

Forward and Inverse Methods in DOT

Light transport in biological tissues can be modeled by the diffusion approximation to the radiative transport equation, assuming that light scattering has great effects on light propagation in the tissue. In the frequency domain, the diffusion equation is given by (28,29)

$$-\nabla D(\vec{r})\nabla\Phi(\vec{r},\omega) + (\mu_a(\vec{r}) + i\omega/c)\Phi(\vec{r},\omega) = Q_o(\vec{r},\omega) \quad (1)$$

where $\Phi(\vec{r},\omega)$ is the photon density at the position $\vec{r}$, ω is the modulation frequency of light (in our study we use CW domain, so $\omega = 0$), $Q_o(\vec{r},\omega)$ represents the isotropic source, c is the speed of light in the medium, and μ_a is the absorption