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Rapid Diagnosis of Inhomogeneity in Turbid Media

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ABSTRACT

In this work, a novel approach is proposed that would be able to rapidly diagnose the presence and location of inhomogeneity in turbid media. In this approach, ultrafast pulse laser is used as a detecting source and the time-resolved backscattered light signals are collected around the boundary of the target. The log slopes in the decaying log tail of the detected signals will be analyzed and used for the detection and image of embedded inhomogeneity. The relatively high absorption in the foreign object will result in a steeper log slope when the detector is located close to the object. A slim graphite of 1.6 mm in diameter embedded in a tissue phantom has been successfully detected in a preliminary experiment and the location of the graphite is determined from the v-groove profile of log slopes. A Monte Carlo program has been developed to further simulate and investigate the feasibility and quality of this method to diagnose the presence of a tumor-like material embedded inside a highly scattering media. A 2D reconstructed image confirms the potential of this novel method to detect and image accurately and rapidly the presence of tumors in biological tissues.

Keywords: detection, transient radiation transfer, turbid medium, backscattering, ultrafast laser, optical tomography.

1. INTRODUCTION

Cancer is the second leading cause of death among Americans. The American Cancer Society estimates that, in 2002, about 1.3 million Americans will receive a new diagnosis of cancer and about 550 thousands more will die from this disease. It is also estimated that the direct medical expenses cost up to $60 billion annually and a significant portion of it goes to diagnosing stage. There are several methods available for diagnosing cancers. MRI and X-ray computed tomography are commonly adopted in detecting tumors. But these methods are very costly and require large facilities. A great desire exists for new noninvasive methods that are low cost, less safety concern, and widely available to large segments of humanity. Optical imaging method is an excellent candidate as an alternative non-invasive or minimally-invasive imaging modality. Particularly, near-infrared (NIR) optical imaging is attracting increasingly attention in recent years because NIR radiation is non-ionizing and the device is very compact and low cost. NIR light is being applied to image thick tissues such as breast and brain [1-3].

In order to get optical images of foreign objects embedded in a certain depth of human tissues and/or organs, one has to consider an inverse model as well as a forward model. The forward model is to solve radiation transport in highly scattering turbid media either with radiation transfer theory or diffusion approximation. The inverse model is used to reconstruct tomographic or 3D images based on an optimization procedure using measured data around the boundary and iteratively forward modeling. The inverse problem not only is inherently ill-posed, but also requires huge amount of computation time. These have impeded real time clinical applications of the optical imaging method.

In this paper, a rapid approach used to detect and image the presence of inhomogeneity in a highly scattering medium is proposed. This method is particularly designed to accommodate the need of an initially inexpensive and swift screening of the presence of tumor in human body before performing a comprehensive tomographic scan or biopsy examination. Our new method directly resolves the presence of inhomogeneity through a straightly forward analysis of the decaying tail of the detected signal. It is ideal for real time application because it does not require the inverse model. The apparatus consists of an ultrafast laser diode, fiber optics, reflectance probe, PMT detector and a computer. These equipments are fairly low-cost, safe to operate and require no radiation shielding.

The detection principle is simple in theory and is based on the study of the log slope characteristic of the detected time-resolved signals in turbid media. Brewster and Yamada [4] have shown that the asymptotic log slope of a homogeneous semi-infinite slab is steeper as the scattering albedo decreases. A study conducted by Zaccanti et. al. [5] also shows that there is a significant dependence between scattering coefficient of a homogeneous medium and the broadening of laser pulse, thus affecting the steepness of asymptotic log slope. More recently, Guo and Kim [6] further showed that the log slopes of reflected signals in a finite 3D geometry are proportional to the absorption coefficient of the embedded inhomogeneity.

This paper will be dedicated to demonstrating the feasibility of the novel detection method. An experimental result in detecting the presence of a graphite inclusion embedded inside a tissue phantom will be presented. A corresponding Monte Carlo simulation will be deployed to investigate the extension of this method under different circumstances. We will also demonstrate the applicability of this method as a preliminary tumor diagnostic tool.

2. THEORY

The simulation is performed using a Monte Carlo multidimensional transient radiative transfer program adapted from Guo et. al. [7]. The Monte Carlo simulation mimics photons propagation in homogeneous turbid medium by calculating the movements of a large number of photon bundles. Each emitted photon bundle begins from its initial position and time and makes its way into the participating medium by a certain path length determined from statistical distribution and time of flight. It will experience scattering, absorption as well as reflection. Scaled isotropic scattering is used to reduce CPU time in calculations although the scattering of tissue phantom is anisotropic. Such an approximation does not introduce obvious errors in the diffusion part of the signal as shown by Guo et. al [8]. Fresnel reflection [9] at the tissue-air boundaries consideration is incorporated because there is a significant refractive index mismatch between them ($n_{air}=1$, $n_{tissue}=1.40$). Total internal reflection occurs when the incoming angle is greater or equal to the critical angle while partial specular reflection occurs otherwise. The energy attenuation of each photon bundle is determined using the scattering albedo method.

2.1 GRAPHITE INCLUSION

Additional subroutines are developed in this study to simulate light propagation inside a turbid medium with the presence of a graphite cylinder inclusion. The graphite inclusion is treated as a highly absorbing and low reflecting material. As such, large amount of radiative energy will be absorbed when the scattered photon bundles come into contact with the graphite's surface. The exact values of absorption and reflection for graphite are unavailable, but we assumed 95% absorption and 5% reflection. Actually, the log slope changes less than 1% for results with absorption ranging from 90% to 100% because only a small fraction of emitted photon bundles interact with the tiny graphite inclusion. Interacting photon bundles will be specularly reflected with a substantial loss of energy content and no photon bundles are allowed to penetrate the graphite inclusion.

2.2 TUMOR INCLUSION

A Monte Carlo simulation to investigate the effectiveness of this method on tumor inclusion is performed. Unlike graphite, tumor is not totally opaque to near infrared laser. Tumor's property is similar to most tissue except that the gene expression is abnormal, having higher density and blood concentration. The accumulation of deoxygenated blood, which is an absorptive material for light in the near infrared spectrum results in a higher absorption coefficient in the tumor region. In this paper, we consider a spherical tumor with scattering coefficient of $1mm^{-1}$ and absorption coefficient of $0.2mm^{-1}$. The effective absorption may be enhanced with use of ICG dye to highlight the presence of tumor more clearly.

3. SIMULATION/EXPERIMENTAL MODEL

3.1 TISSUE PHANTOM

Overall simulation model consists of a rectangular tissue phantom implanted with a tiny graphite cylinder that serves as a source of inhomogeneity. The tissue phantom is made from a mixture of polystyrene matrix and silica microspheres of 1μm (±10%) in diameter with 1.46 refractive index value. Silica microspheres are used as scattering agent and have a concentration by volume of 0.86% of the entire tissue phantom that measures 16.1mm x 96.6mm x 39.1mm in height, length and depth. The above preparation of tissue phantom yields a quasi-homogeneous turbid medium with scattering coefficient of $0.37mm^{-1}$ and negligible absorption for visible wavelengths as no artificial absorbing agent is added during the process. The refractive index of this phantom matrix at 532nm wavelength is found to be 1.59. The tissue block is held on a translation stage and is free to move from left to right during scanning process. A tiny piece of graphite cylinder measuring 1.6mm in diameter and 39.1mm in length is inserted horizontally at the center of the tissue block.

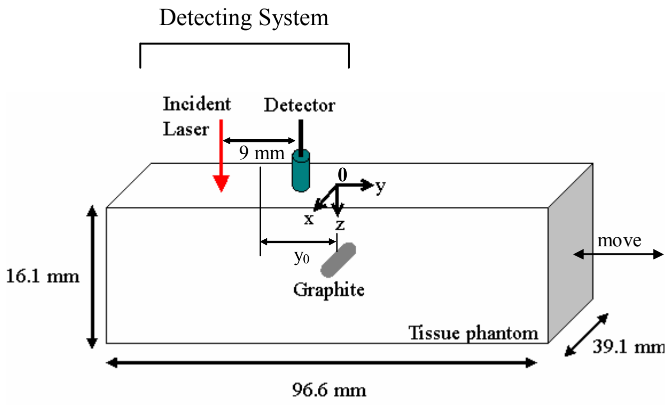

Figure 1. -Sketch of the experimental model: The laser and detector head is scanning over a tissue phantom with a graphite inclusion, through horizontally moving the sample.

Graphite is a highly absorbing material and therefore, most photons that interact with it will be absorbed before they pass through. However, a small percentage of the photons will be reflected back into the tissue phantom for further internal scattering.

3.2 INCIDENT LASER AND DETECTOR CONDITIONS

The pulse laser source is generated via a Nd^{3+}:YAG mode-locked laser which has a pulse width of 60ps at a repetition rate of 76 MHz. The setup of laser system has been given in Guo et. al. [8]. Laser beam is delivered to the surface of the tissue block via window output. The beam is incident at the top face of the tissue. The beam's diameter is 1.3mm and the temporal Gaussian pulse is describe by the equation below

$$I = I_0 \exp\left[-4\ln 2 \times (\frac{t}{t_p} - 2.0)^2\right] \qquad (1)$$

where I_0 is the maximum pulse intensity, and t_p, the pulse width. In the present Monte Carlo simulation, a total of $1x10^8$ photon bundles are used for an impulsive input where Duhamel's theorem of superposition is applied to incorporate the input pulse profile in a method as described by Guo and Kumar [10].

In the experiment, the detector which is positioned at a fixed distance of 9mm away from the laser incident location in the positive y-axis direction. The laser beam and optical fiber are collectively known as the detecting system and y_0 is the detection position refers to the distance. y_0 is measured from the origin of Cartesian coordinate to the mid-point between laser and detector. The detector which is an optical fiber approximately 100μm in diameter connected to an ultrafast optical oscilloscope. The optical oscilloscope model is OOS-01 made by Hamamatsu and has a photon counting capability with time resolution of 10ps. The Monte Carlo's detection routine is set to match the experimental model.

3.3 TUMOR DIAGNOSIS SIMULATION MODEL

Previous simulation and experimental model of a graphite inclusion tissue phantom is a first step to verifying the feasibility of this novel detection method because the absorption of graphite is extremely high. However, this section deals with a leaner absorptive inclusion (tumor) to investigate its potential as a biomedical imaging tool. *Figure 2* shows a sketch of a homogeneous tissue phantom embedded with a spherical tumor. The scattering and absorption coefficients of the tissue phantom are $1.0mm^{-1}$ and $0.01mm^{-1}$ respectively - similar to human's soft tissue. The tissue phantom size is 20 x 20 x 20 mm^3. A spherical tumor is placed at the center of the tissue phantom. It has a scattering and absorption coefficients of $1.0mm^{-1}$ and $0.2mm^{-1}$ respectively. The diameter of the tumor is 6 mm.

The diagnosis tool consists of an ultrafast near infrared pulse laser source, reflectance probe and an ultrafast photon detector. The laser source is conditioned to emit laser impulse, δ-function. The reflectance probe will collect signals throughout a scanning grid predefined on surface of the tissue phantom. The scanning grid is a 19 by 19 equally spaced mesh with a spacing of 1 mm. Two steps of scan will be performed. The first is to obtain a 2D scan with the presence of spherical tumor. Secondly, the same 2D scan is performed, but without the presence of the spherical tumor. The result without the presence of tumor will serve as a background to be subtracted from the result with the presence of tumor to eliminate noise from the edge effect. It also serves as a datum for calculating relative absorption magnitudes.

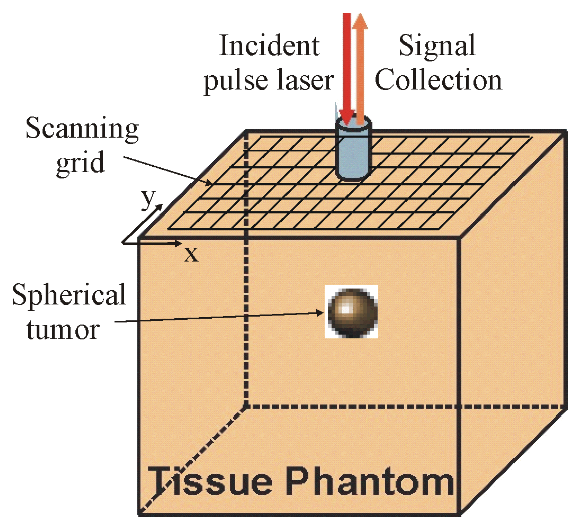

Figure 2. – Sketch of spherical tumor embedded in homogeneous tissue phantom with detector scanning over the surface.

4. RESULTS ANS DISCUSSIONS

4.1 CHOICE OF LOG SLOPE

Figure 3 shows typical detected laser signals in both linear and log scales, where the results of MC simulation are also plotted. There exists a nearly straight decaying tail in the log scale and its log slope can be calculated for each detecting positions. The representative results in *Fig. 3* are from the case that the detecting system is positioned at -3mm from the center with a graphite implanted at the rectangular tissue center. The log slope varies with localized absorption coefficient. Regions with higher absorption portray steeper log slope than those region with lower absorption coefficient. Therefore, it is possible to detect a localized area with high absorption property inside a turbid medium by performing scans across the surface of the medium.

Figure 4 shows the representative log slopes, in the interval 400-500ps used in our analysis for signals collected at y_0 = -25mm and y_0 = -3mm, respectively. The log slope is calculated by fitting an exponential function over this interval. At -25mm, the absorption effect from the graphite inclusion is very slight. Therefore, the log slope profile is a result of purely laser diffusion in the homogeneous region. For detection position near the presence of graphite inclusion, such as at y_0 = -3mm, the influence of absorption is great and tends to create steeper log slopes. When the analysis is applied to all signals detected from various positions, the location of the graphite inclusion can be determined.

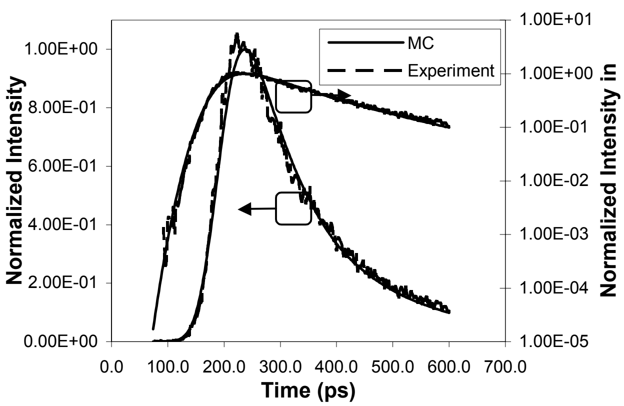

Figure 3. –Experimental and MC simulated laser signals detected at y_0=-3mm.

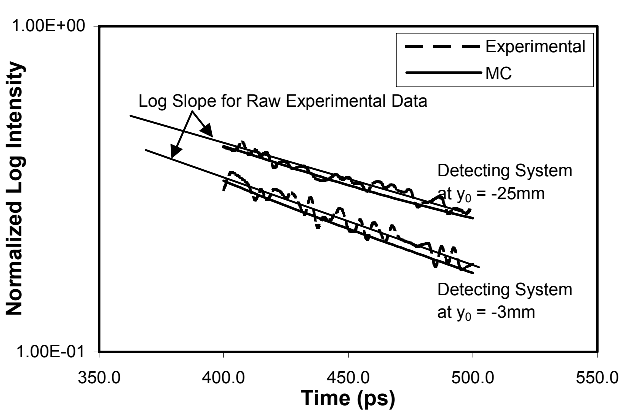

Figure 4. –Log intensity between 400-500ps for signals detected at y_0 = -25mm and -3mm.

4.2 DETECTION OF INHOMOGENEITY

Laser signals collected at various detection positions in experiment and Monte Carlo simulation are investigated. The Monte Carlo simulation is performed on a PC with a 1.7GHz Pentium 4 processor equipped with 256 MB RAM. The result from each detector position with $1x10^8$ incident photon bundles requires approximately 1.4hrs computation time. This value of photons is chosen to reduce computation time without compromising the accuracy. The simulation for each detector position is repeated for a total of 10 times to obtain a statistical error. Experimental procedures have been performed for 3 times for each detector position.

Figure 5 shows the average log slope values plotted with respect to detecting positions from the center of coordinate system. The raw signals from both experiment and Monte Carlo simulation are normalized before their respective log slopes are calculated. The v-shape log slope profile in *Fig 5* has demonstrated the feasibility of detecting highly absorbing inhomogeneity in turbid media by utilizing decaying log slope characteristic. The tip of the profile indicates the position of the graphite inclusion, but the profile is not symmetric because of the 9mm gap between laser and detector in the experimental design. However, the exact size of the inhomogeneity (ϕ=1.6mm) is not clearly available in the v-shaped log slope profile. The affecting region in *Fig. 5* is about 10mm. This may be caused by the fact that there is a 9mm gap between the laser and detector is present. Since we used a window output type laser system, we could not put the detector to a closer distance to the laser incident spot to avoid the intervention of reflection from the detector and the collection of directly reflected light from the surface of the incident spot. It is also noted that there is a slight mismatch between the experimental and Monte Carlo results. This mismatch is probably due to the fact that the prepared tissue phantom's optical properties are quasi-homogeneous and not homogeneous as assumed in Monte Carlo simulation, and that the relatively strong noise in experiment associated with the photon counting technique.

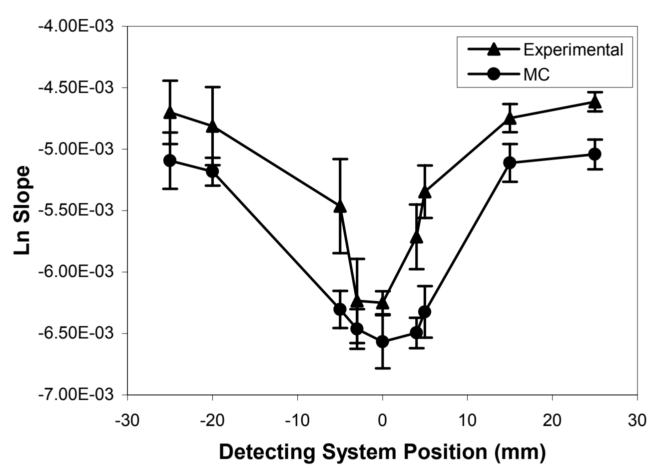

Figure 5. – Experimental and Monte Carlo comparison: average log slope with error bar versus detector position.

4.3 EFFECT OF GRAPHITE INCLUSION DIAMETER

The effect of graphite inclusion diameter in inhomogeneity detection is being investigated numerically. The optical properties of tissue phantom, the position of graphite inclusion and the detecting system remain unchanged. *Figure 6* shows the average log slope plotted with respect to the position of detecting system for the case where laser and detector are separated by 9mm. The depth of v-shape groove begins to diminish with reduction in graphite diameter as expected because less radiative energy is absorbed. The minimum detectable graphite diameter presuming 3% standard deviation in log slope uncertainty measurement is found to be about 0.1mm. The depth of v-shape groove is strongly related to the diameter of the inclusion. The larger the diameter is, the deeper is the v-shape groove.

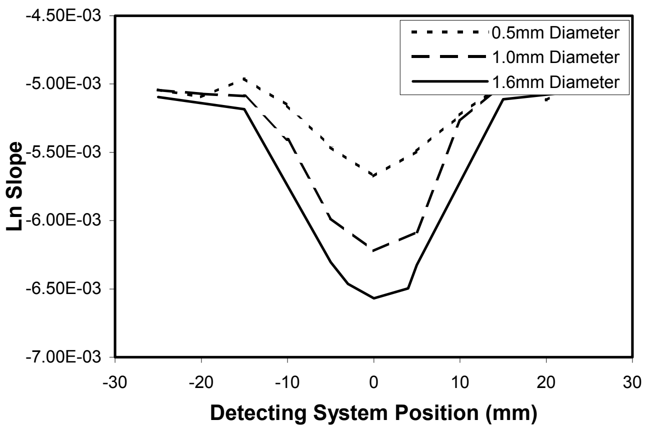

Figure 6. –Effect of graphite's diameter on log slope: laser and detector distance is 9mm.

4.4 EFFECT OF DEPTH OF GRAPHITE INCLUSION

The effect of depth of graphite inclusion in inhomogeneity detection is being investigated. Unlike the original experimental setup, the Monte Carlo program is modified to simulate the case when the position of laser and detector coincide with each other. Such a modification is try to eliminate the influence of the gap between the laser beam and detector and can easily be achieved experimentally by the use of a fiber optic reflectance probe. *Figure 7* shows the v-shape grooves for graphite embedded at 5.05mm, 8.05mm and 12.05mm below the surface respectively using this new simulation design. The profile is now symmetry along the centerline, i.e. where the graphite inclusion is located. The width of the groove in *Fig. 7* is smaller as compared to previous plots. Apart from that, the overall magnitude of log slope has increased because the detected signal is less diffused and relatively narrower than the 9mm gap laser-detector counterpart. The percentage of graphite inclusion's volume over the entire volume of radiation propagation decreases drastically as the depth of which it is embedded increases. The v-shape deepens when the inclusion is closer to the surface because of increase in absorption. It may be possible to reckon the depth by characterizing the strength of the v-shape

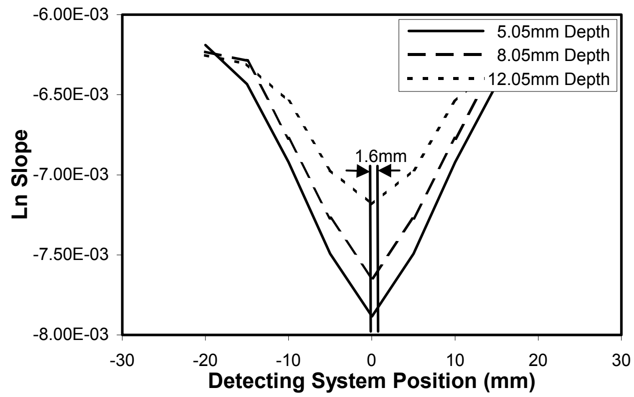

Figure 7. –Effect of graphite inclusion's depth on log slope: laser and detector coincide with graphite diameter 1.6mm.

4.5 TWO DIMENSIONAL TUMOR IMAGING

Figure 8 shows the reconstructed two dimensional image of the location and size of tumor by implementing the scanning grid and novel log slope analysis technique. The noise cutoff has been set to 65 percent of the maximum log slope intensity because most of the detected log slope intensity is due to the diffusion nature of NIR laser transport in turbid media and not the presence of inhomogeneity directly underneath the tissue surface. This cutoff value can be adjusted accordingly to detect other lower concentration of inhomogeneity, if present, but with the compromise of some added noise. The white circle at the center of the image represents the location and size of the actual spherical tumor. The reconstructed image, however, is less circular because original scanning grid is not very dense to save simulation time. A three dimensional imaging (3D) of tumor is possible if we collapse two or more 2D images taken from different orientations of the tissue phantom. 3D image reconstruction to further pinpoint the location and size of inhomogeneity will be our next research focus.

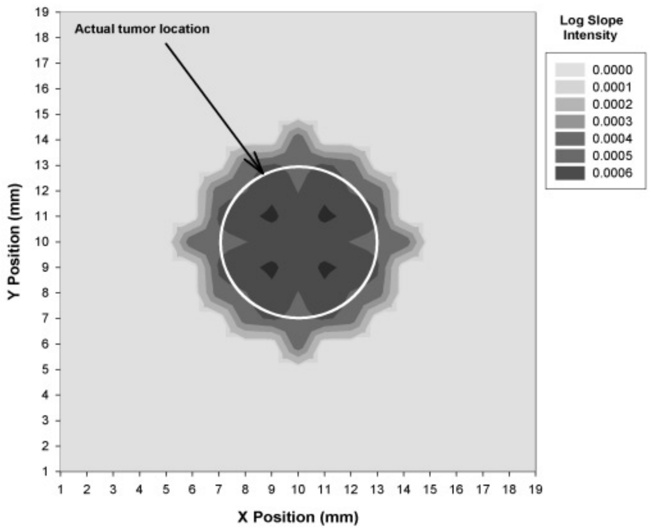

Figure 8. – Two dimensional image of tumor detected.

5. CONCLUSIONS

The experimental and numerical investigation demonstrated that it is viable to utilize decaying log slope analysis as a quick preliminary method to detect region with high absorption in a turbid medium. The absorption effect of the graphite inclusion determines the steepness of the log slope and therefore tells us where it is located base on the v-shape profile. Comparison between Monte Carlo and experimental results indicated that it is flexible to model realistic radiation problems. Manipulation in Monte Carlo simulation allowed us to predict new results and investigate the effectiveness of our technique under different circumstances. Overall investigation revealed that it is possible to detect inhomogeneity under much harsher conditions. The rather large distance between laser and detector positions in the current experimental design resulted in asymmetric v-shape profiles and relatively large affecting region. MC simulation has demonstrated that a tiny detecting probe (i.e laser beam and detector coincide) could improve the accuracy of detecting inhomogeneity. This new method could be applied to optically thick medium which may be out of bound for those which rely on transmitted signal as a source of detection. The two dimensional tumor imaging result has shown that this method may be applied as a biomedical imaging tool for early detection of cancers. The 2D image can be obtained easily and quickly without the need to solve for an inverse problem. The presence of tumor can be easily told by the v-groove profile of the log slopes by scanning the probe over the surface of tissues.

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