The study of propagation of a femtosecond laser pulse in the breast tissue

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ABSTRACT— In this paper, the evaluation of time profile of a femtosecond pulse laser propagated through biological tissues is studied. The majority of the biological tissues with a high scattering anisotropy must be considered as turbid media, that their optical responses are complicated. To study the propagation of ultra-short pulse in turbid media, the diffuse equation is used. In this study, the analytical and numerical solution for diffuse equation is investigated. The numerical method is based on Boundary Integral method (BIM), and also, the time evaluation of propagating pulse is studied.

KEYWORDS: femtosecond pulse, scattering, diffuse equation, boundary integral method, biological tissue

I. INTRODUCTION

IN recent years, short pulse lasers are widely used in area of lasers in medicine [1-6]. Recently, ultra-short laser is applied for optical imaging [7-15]. That is because; the temporal distribution of reflected signal is broadened due to multiple scattering of photons into tissues [2, 12]. Thus, the temporal distribution of the reflectance can be used to study the variation of optical properties of the normal or malignant breast tissue, because the optical properties of normal breast tissues vary in malignant progress [13].

The propagation of ultra-short pulse in an optically turbid medium is described by the radiative transfer equation (RTE) [16]. Photon transport in biological tissue can be equivalently modeled analytically by RTE or numerically by Monte Carlo method (MC). However, the RTE is difficult to solve without introducing approximations. A common approximation summarized here is the diffusion approximation. Overall, solutions to the diffuse equation for photon transport are more computationally efficient, but less accurate than Monte Carlo simulations There is not any analytical solution for RTE in the general form. For this reason, the simplified forms of the RTE are investigated which obtained in different approximations such as small-angle RTE and diffuse equation [17]. In the RTE, six different independent variables define the radiance at any spatial and temporal point ($x, y,$ and z from $\vec{r}$, polar angle θ and azimuthal angle φ from direction of $\hat{s}$ and time t). By making appropriate assumptions about the behavior of photons in a scattering medium, the number of independent variables can be reduced. These assumptions lead to the diffuse equation for photon transport. Two assumptions permit the application of diffusion theory to the RTE: first, Relative to scattering events, there are very few absorption events. Likewise, after numerous scattering events, few absorption events will occur and the radiance will become nearly isotropic. This assumption is sometimes called directional broadening. Second, in a primarily scattering medium, the time for substantial current density change is much longer than the time to traverse one transport mean free path. Thus, over one transport mean free path, the fractional change in current density is much less than unity. This property is sometimes called temporal broadening. It should be noted that both of these assumptions require a high scattering medium. Therefore, the diffuse equation is based on multiple scattering.

In small-angle RTE approximation, one can assume that the deviation angle θ of scattered photon from the beam axis is small, so that $\cos\theta \approx 1$. This assuming is accepted for the majority of biological tissues. That is because, these tissues have large anisotropy factor $\left(\langle\cos\theta\rangle \geq 0.9\right)$. By this approximation, the RTE can be simplified and analytically solved.

The Diffuse Equation is used to study of photon propagation into turbid media, but the solution of this equation is difficult, so it should be solved by numerical methods like Monte Carlo method (MC) and Finite Difference Time Domain method (FDTD), which are time-consuming [18-23]. FDTD is a numerical method for modeling computational electrodynamics (finding approximate solutions to the associated system of differential equations). The FDTD method belongs in the general class of mesh-based differential time-domain numerical modeling methods (finite difference methods). The time-dependent RTE or diffuse equation is discretized using central difference approximations to the space and time partial derivatives. The resulting finite-difference equations are solved in either software or hardware in a step manner: the laser fluence in a volume of sample is solved at a given instant in time; and the process is repeated over and over again until the desired transient or steady-state behavior is fully evolved.

MC and FDTD are time consuming and for special application like image reconstruction are not suitable, so a new fast method must be used.

Boundary Integral Method (BIM) can be also used to solve diffusion equation. As this method requires surface tessellation, therefore, computation time is reduced and accuracy of results increases [24]. Diffusion equation in frequency domain has also numerically been solved by BEM [24-27], but that algorithm could only be applied to study propagation of continuum waves in tissues. In this report, we simulate pulse propagation into biological tissues.

As it was previously mentioned, recently, the ultra-short laser is applied for optical imaging. Also, in the optical imagining, to prevent photoablation or other effects that affect on the breast tissue, the value of laser fluence must be low. So, in this paper, a necessitous way to data processing for ultra-short optical imaging is introduced. The method of study of pulse propagation in breast tissue by using analytical method and BIM is presented. In optical imaging and in the range of near infrared spectrum, breast tissue can be assumed as homogeneous phantom defined by specific optical properties [3, 5]. Hence, the propagation of ultra-short pulse inside homogeneous breast tissue is studied. First, the analytical solution of RTE by small-angle approximation is studied and then, the diffused equation is studied by BIM. I obtain appropriate green function to convert diffusion equation to integral form by using the green's second theorem. Next, the surface integral is discretized by using Boundary Element Method (BEM) and the resulting integral is numerically solved [27]. Using this technique, we have calculated intensity and temporal evolution of diffusely reflected pulse from tissue. Furthermore, effects of reduced scattering coefficient on time broadening of diffusely reflected pulse are also studied.

II. REVIEW OF THEORY

A. *Analytical Method:*

The RTE is written in the form [16]:

$$\left(\frac{1}{c}\frac{\partial}{\partial t}+\frac{d}{ds}+\left(a+\sigma\right)\right)J\left(\mathbf{r},\mathbf{s},t\right)= \frac{\sigma}{4\pi}\int_{4\pi} p\left(\mathbf{s},\mathbf{s}'\right)J\left(\mathbf{r},\mathbf{s}',t\right)d\xi \tag{1}$$

where $p\left(\mathbf{s},\mathbf{s}'\right)$ is the phase function of a photon to be scattered from direction $\mathbf{s}'$ into s', ds is an infinitesimal path length, and $d\xi$ is the elementary solid angle about the direction $\mathbf{s}'$. $J(\mathbf{r},\mathbf{s},t)$ is called radiance, and a and σ are absorption and scattering coefficients, respectively. The velocity of light is shown by c.

By applying Fourier transform on Eq. 1:

$$\left(\frac{i\omega}{c}+\frac{d}{ds}+(a+\sigma)\right)J(\mathbf{r},\mathbf{s},\omega)= \frac{\sigma}{4\pi}\int_{4\pi} p(\mathbf{s},\mathbf{s}')J(\mathbf{r},\mathbf{s}',\omega)d\xi \quad (2)$$

where

$$J(\mathbf{r},\mathbf{s},\omega)=\frac{1}{2\pi}\int_{-\infty}^{\infty} J(\mathbf{r},\mathbf{s},\omega)\exp(i\omega t)dt$$

is the spectral radiance. The Eq. 2 is similar to the stationary RTE in a medium with absorption coefficient $\tilde{a}=a+i\omega/c$. If assume that $\mathbf{r}=z\hat{\mathbf{k}}+\mathbf{r}_t$, where $\mathbf{r}_t$ is transverse vector. By integration on transverse vector:

$$J(z,\mathbf{s},\omega)=\int_{-\infty}^{\infty} J(\mathbf{r},\mathbf{s},\omega)d\mathbf{r_t} \quad (3)$$

describes the angular diffused light in direction of z axis, where it can be assumed as following:

$$J(z,\mathbf{s},\omega)= J_b(z,\mathbf{s},\omega)+J_d(z,\mathbf{s},\omega)+\sum_{i=1}^{N} J_i(z,\mathbf{s},\omega) \quad (4)$$

Here $J_b(z,\mathbf{s},\omega)$ is the unscattered intensity and $J_d(z,\mathbf{s},\omega)$ is light multiply scattered by small angle. $J_i(z,\mathbf{s},\omega)$ is the intensity of ith order of scattering. The ith-order of scattering can be assumed as following:

$$\left[\left(1-\frac{n_t^2}{2}\right)\frac{\partial}{\partial z}+(a+\sigma)\right]J_i(z,\mathbf{n}_t)= \frac{\sigma}{4\pi}\int_{4\pi} p(\mathbf{n}_t,\mathbf{n}_t')J_{i-1}(z,\mathbf{n}_t')d\mathbf{n}_t' \quad (5)$$

where $\mathbf{n}_t'$ is unit vector along $\mathbf{r}_t$, in small angle scattering $|\mathbf{n}_t'|<<1$, so $n_z \approx 1-n_t^2/2$.

The $J_d(z,\mathbf{s},\omega)$ is satisfied in RTE:

$$\left[\left(1-\frac{n_t^2}{2}\right)\frac{\partial}{\partial z}+a+\frac{1}{4}\sigma\gamma\Delta_{n_t}\right]J_d(z,\mathbf{n}_t) =\frac{\sigma}{4\pi}\int_{4\pi} p(\mathbf{n}_t,\mathbf{n}_t')J_N(z,\mathbf{n}_t')d\mathbf{n}_t' \quad (6)$$

where $\gamma=2g-1$. The spatial intensity of the source is can be represented by a Gaussian $\frac{P}{\pi\Omega_s}\exp\left(-\frac{n_t^2}{\Omega_s}\right)$ that P and $\pi\Omega_s$ are its power and angular distribution of source, respectively. The detected power $P_{\det}$ of multiply scattered radiation can be described in the following integral:

$$P_{\det}=\int_0^z P(z-z')\exp(-az)dz' \quad (7)$$

It can be shown that the profile of diffused pulse is given by:

$$P(z)\approx\frac{2*W\sigma^3\exp(-az)}{\pi\gamma^2\tilde{a}_t^{\,2}}\ln\left(\frac{\tilde{a}_t z}{8}+1\right)\times \ln\left(\tilde{a}_t\gamma^2 z+1\right) \quad (8)$$

where W is initial power of laser pulse, $\tilde{a}_t=a+\sigma+i\omega/c$. By substitution (9) into (8) and by applying Fourier transform, the temporal profile of pulse is achieved.

B. *Numerical method*

The RTE can be simplified by diffusion approximation. In this approximation, the reduced scattering coefficient must be greater than absorption coefficient, namely $a<<\sigma(1-g)$. Diffused photon into biological tissue Ω with boundary Γ_s, respectively, given by [25]:

$$\frac{\partial}{c\partial t}\varphi(\mathbf{r},t) - D\nabla^2\varphi(\mathbf{r},t) + a\varphi(\mathbf{r},t) = S(\mathbf{r},t) \qquad \mathbf{r}\in\Omega \tag{9}$$

and

$$\varphi(\mathbf{r},t) - 2C_R D\frac{\partial\varphi(\mathbf{r},t)}{\partial n} = 0 \qquad \mathbf{r}\in\Gamma_s \tag{10}$$

where $\varphi(\mathbf{r},t)$ and $S(\mathbf{r},t)$ are, respectively, fluence and the isotropic source term at position $\vec{r}$ and at moment of *t*. The velocity of light is shown by c. The parameter $D = 1/3(a+\sigma')$ is diffusion coefficient, where a and $\sigma' = \sigma(1-g)$ are absorption and reduced scattering coefficients, respectively. σ and *g* are also scattering coefficient and anisotropic factor, respectively. In Eq. 10, $C_R = (1+R)/(1-R)$ where R is Fresnel reflection coefficient.

To solve Eq. 9 with Robin boundary condition (Eq. 10), we can use Green's function [24]. The Green's function of equation (9) in domain Ω can be considered as solutions of the following equation

$$\frac{\partial}{c\partial t}G(\mathbf{r},\mathbf{r}';t,t') - D\nabla^2 G(\mathbf{r},\mathbf{r}';t,t') + aG(\mathbf{r},\mathbf{r}';t,t') = -\delta(\mathbf{r}-\mathbf{r}')\delta(t-t') \tag{11}$$

By applying Laplace transform on *t* in Equation (12) and rearranging the resulting equation, we obtain:

$$\nabla^2\tilde{G}(\mathbf{r},\mathbf{r}';s,t') - \kappa^2\tilde{G}(\mathbf{r},\mathbf{r}';s,t') = \frac{\delta(\mathbf{r}-\mathbf{r}')}{D}\exp(-st') \tag{12}$$

where $\tilde{G}(\mathbf{r},\mathbf{r}';s,t') = L(G(\mathbf{r},\mathbf{r}';t,t'))$, $\kappa^2 = \frac{s}{cD} + \frac{a}{D}$ and ∇^2 operates on $\mathbf{r}$. Next, applying Fourier transform on $\mathbf{r}$ in equation (12) and doing some mathematics results to:

$$g(k,\mathbf{r}';s,t') = \frac{\exp(-i\mathbf{k}.\mathbf{r}')}{D(k^2+\kappa^2)}\exp(-st') \tag{13}$$

where g is Fourier transform of $\tilde{G}$.

Inverse Fourier and Laplace transforms on the green function stated in equation (13) gives the green function as [23]:

$$G(\mathbf{r},\mathbf{r}';t,t') = H(t-t')\frac{c}{\sqrt{(4\pi Dc\,(t-t'))^3}}\times \exp(-ca(t-t'))\exp\left(-\frac{|\mathbf{r}-\mathbf{r}'|^2}{4Dc\,(t-t')}\right) \tag{14}$$

where $H(t-t')$ is Heaviside function.

The intensity of diffused short pulse can be calculated by green function stated in relation (14). Boundary Element Method (BEM) can be used to solve equation (16). In this method the boundary of the sample is first discretized to elements. Then, observation point $\vec{r}$ is located on the surface of tissue and an equation containing fluence at that point is achieved. Locating observation point on different nodes, a system of equations is obtained which gives the fluence at those points. Finally, one can solve that set of equations and calculate the fluence at any arbitrary point inside and outside the sample [27].

III. RESULTS

To verify the numerical method, we use BIM and finite difference method (FDTD) method to study behaviour of reflected pulse. The sample is a semi-infinite slab with $a = 0.02\,\text{mm}^{-1}$, $\sigma = 15\,\text{mm}^{-1}$ and $g = 0.9$ which illuminated by a Gaussian laser pulse with duration of 10 pS, and the reflectance is calculated at distance of 1.014 mm from illuminated point by BIM and FDTD method. The obtained results by FDTD show that by increasing of mesh resolution, they approached to the results obtained by BIM. For example, the peak reflectance at distance of 1.014 mm is achieved $2.10\,\text{mW/mm}^2$ and $2.25\,\text{mW/mm}^2$ by

BIM and FDTD method, respectively, whereas the number of spatial and temporal nodes for BIM and FDTD is 55×35 and 3000×3000, respectively. While the computational time in FDTD is more than four times longer than BIM. So, it can be seen that BIM can be used to simulate pulse propagation into turbid media. For comparison of BIM with Monte Carlo method, the mean distance traversed by photons before exiting the tissues, $\langle ct \rangle$, is calculated as 80.6 mm and 81.6 mm by Monte Carlo method and BIM, respectively, while the computational time for Monte Carlo method is between 4 to 10 hours [28], but BIM takes some minutes. In addition, the numerical results are compared with experimental results reported in [29]. Calba and his colleagues measured the optical depth of ultra-short pulse with duration of 100 fs inside a biological phantom as 17.72, while the value of optical depth is calculated as 18.42 by BIM method.

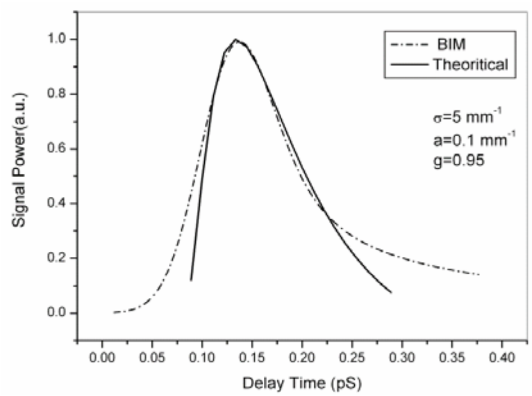


Fig 1. Temporal evolution of reflectance of a pulse originating from a Gaussian source from semi-infinite slab of tissue, Solid line: analytical result. Dashed line: numerical result obtained by using BEM.

After this verification, the accuracy of theoretical method has been investigated. The temporal shape of a Gaussian pulse with duration of 100 fs is calculated by theoretical method and BIM (Fig. 1). The reduced scattering coefficient, σ', and reduced albedo $(\sigma'/(a+\sigma'))$ of sample is 0.25 mm^{-1} and 0.71, respectively. The presented results in Fig. 1 that obtained by theoretical method and BIM have similar trend.

Influence of scattering coefficient on reflected pulse is presented in Fig. 2. Two different value of scattering coefficient are used in theoretical method and BIM. The reduced albedo values are 0.71 and 0.83. The results show that theoretical method can simulate the reflected pulse similar BIM.

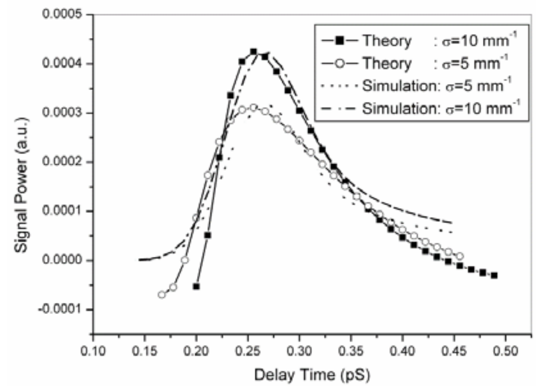


Fig. 2. Temporal evolution of reflectance calculated by using BEM (dash line) and Theoretical method with different value of scattering coefficient (other lines).

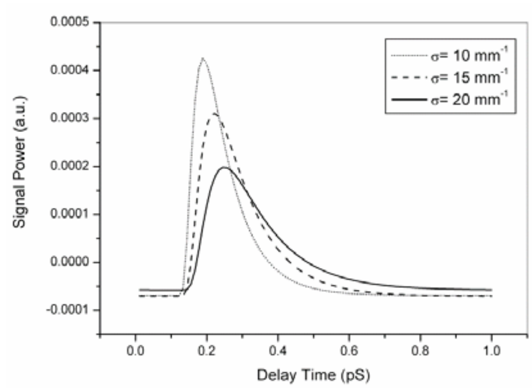
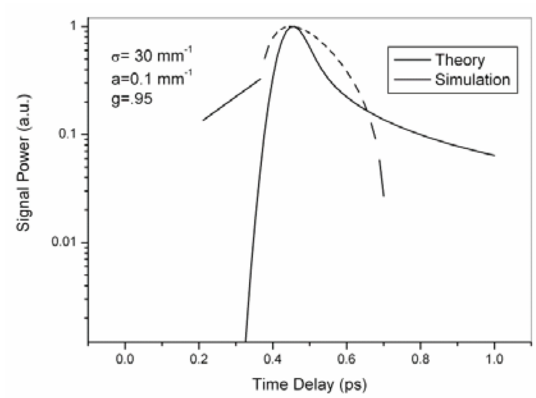
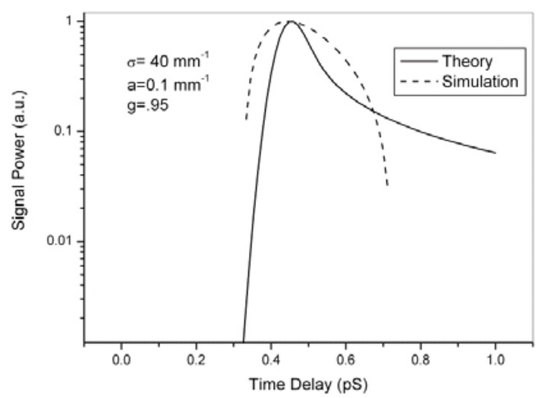


Fig 3. Effect of scattering coefficient on reflected pulse.

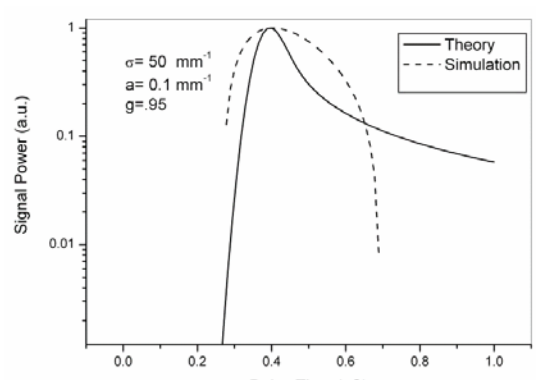
The temporal shapes of reflected pulse for lager value of scattering coefficient are shown in Fig. 3. This graph depicts anomalous style for the peak power of reflected pulse, because we presented in [27] that the peak value of the reflected pulse increases for lager scattering coefficient. That is because by increasing the scattering coefficient, more photons are scattered from the illumination direction, and consequently, the intensity of reflected pulse increases.



(a)



(b)



(c)

Fig. 4. The variation of temporal shape of reflected pulse for different scattering coefficient. a) $\sigma = 30$ mm-1 b) $\sigma = 40$ mm-1 c) $\sigma = 45$ mm-1. Solid line is obtained by BIM simulation and dashed line is results obtained by analytic method. One can see that the broadening of simulated pulse is larger than the analytic calculation. Also, by increasing of scattering coefficient, this discrepancy between simulation and analytical method grows.

As mentioned in review of analytical method, the scattering angle must be small, so for larger scattering coefficient or small anisotropic factor, this method must be inspected. To study this point, the variation of temporal profile of reflected pulse is calculated by theoretical for large value of scattering coefficient, and results have been shown in Fig. 4. The calculated pulse for scattering coefficients of 30, 40 and 50 mm^{-1} by analytical method are compared with those results obtained by BIM.

In these results, the multiple scattering is considered, that is because, the diffuse equation is based on multiple scattering. One can see that the simulated results obtained by BIM differ from the analytical results. That is because for large value of scattering coefficient, the reduced scattering coefficient increases, therefore the diffuse regime governs photons and the scattering angle raises so, the bases of analytical method has been destroyed. The comparison with the BIM simulation demonstrates that the presented analytical method can be used in the case of low-order scattering $(\sigma \leq 10)$ so, this model can only describes small-order scattering (low scattering coefficient and large anisotropic factor), because a smaller anisotropic factor results in greater scattering angles of photons, which is manifested in formation of a slowly decaying trailing edge of pulse caused by long delay times of scattered photons [29]. Figs 3-4 show the proposed analytical method can be applied for tissues with small- order scattering like bladder, brain, kidney and lung. But, the proposed BIM simulation is designed for diffuse regime and can be applied for case of large scattering coefficient.

IV. CONCLUSION

As mentioned in introduction, provide a computational approach to ultra-short optical imaging of breast tissue is the important objective of this study. The optical imaging needs safe and non-ionizing radiation, so the fluence of applied laser must be low. In this study, two different formalisms based on RTE for pulse propagation in biological tissues have been described. First, RTE by small-order scattering was analytically solved; this method is easy to calculation and can be applied for case of low scattering. Then, by this method the variation of temporal shape of short laser pulse in biological tissues has been studied. BIM is applied to solve diffuse equation and the accuracy of this method was compared with Monte Carlo and FDTD methods.

Results show that for case of low scattering coefficient, there is no significant difference between these methods. So for this situation, it prefers to apply analytical method, because this method is faster than BIM and also its algorithm is simpler. The analytical method can be used for mid-IR range, because almost in mid-IR, the value of scattering coefficient of biological sample is small or for case of lung, brain, kidney and bladder in VIS and NIR. But for large value of scattering coefficient, BIM must be used, for example for the most biological tissue in VIS and NIR, BIM is faster than FDTD and Monte Carlo method.

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