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Novel Modeling Techniques For Tumor Diagnostics Using Pulsed Laser Sources

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ABSTRACT

In this paper, a two-dimensional transient radiation transport algorithm is developed to analyze short pulse laser transport through a tissue medium having tumors and inhomogeneities imbedded in it. Short pulse probing techniques have distinct advantages over conventional very large pulse width or cw lasers primarily due to the additional information conveyed about the tissue interior by the temporal variation of the observed signal. The distinct feature is the multiple scattering induced temporal signatures that persists for time periods greater than the duration of the source pulse and is a function of the source pulse width, the scattering/absorbing properties and nature of the medium, the location in the medium where the properties undergo changes. A wide range of parameters such as tissue and tumor size, scattering/absorbing properties and phase function of tissues and tumors, tumor location, laser beam diameter will affect the temporal and spatial distribution of the reflected and transmitted optical signals. The goal is to perform a parametric study in order to gain insight about laser-tissue interaction characteristics with the goal to detect tumors.

Keywords: short pulse laser, transient radiative transfer, tumor, tissues, detection

1. INTRODUCTION

The study of short pulse laser radiation transport in strong scattering media has received increasing attention during past few years as a result of its wide applications such as in medical diagnosis,[1-3] thermal therapy, [4] remote sensing,[5,6] laser material processing of microstructures.[7] The analysis of radiation transport through participating media usually neglects the transient effect of light propagation even if the boundary conditions and/or sources that are responsible for the radiative intensity vary with time.[8] Such an exclusion of the transient terms in the radiative transport equations does not result in any practical errors for most engineering problems. This is because the imposed temporal variations are relatively slow when compared with the time scales associated with the speed of radiation light propagation. But with the advent and use of short pulse lasers having pulse width in the order of picosecond to femtosecond range, the temporal dependence of radiative transport must be incorporated. Neglecting this would lead to significant errors in the transmitted and reflected optical signals and has been demonstrated in the past.[9,10]

The propagation of light in optically dense media such as tissues is characterized by multiple scattering. When conventional cw or large pulse width laser sources are utilized to measure the optical signals, the information available is the magnitude of the net attenuation and the angular distribution of the transmitted or reflected signals. For the case of short pulse lasers the signal continues to be observed at large times after the source pulse has been shut off due to the time taken by the photons to reach the detector after multiple scattering in the media. This temporal spread of the scattered signal will provide detailed information about the tissue interior. Thus there is a need to analyze the time-dependant transmitted and reflected signal measurements.

Several numerical models have been developed to simulate time-dependant radiation transport through scattering-absorbing media. Most previous studies have considered the parabolic diffusion approximation,[3,11-16] which is derived from the complete transport equation by neglecting certain time derivative terms in the radiative transport equation. Some of the studies cited have experimentally investigated short pulse laser transport through tissues and have indicated that the parabolic approximation is adequate only for thick tissue samples. Also, these parabolic models do not match most of the available experimental results.[17,18] The commonly used parabolic model also suffers from a major drawback

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in that it assumes infinite speed of propagation of radiation transport through the medium. Also, this approximation cannot accurately account for the change in properties at internal interfaces. Monte-Carlo simulation, which includes finite speed of propagation of radiation transport, has been considered by many researchers but at a great computational expense.[12,19] The Monte-Carlo results have been shown not to match the parabolic diffusion results for tissue samples of smaller thicknesses.[20] The Monte Carlo method in essence being a stochastic method is flexible to handle complex geometrical shapes, but the results obtained always have unavoidable random errors due to practical finite samplings. In contrast, the deterministic methods do not suffer from this defect, and therefore sometimes more preferred. Different deterministic methods such as integral equation formulation,[21,22] radiation element method,[23] and adding-doubling method[24,25] have been used to solve the transient radiative transfer equation. Comparison has also been made between several numerical models such as discrete ordinates method, spherical harmonics expansion, diffusion approximation, two-flux method, and Monte-Carlo simulation for the case of one-dimensional short-pulse laser transport problems.[9]

But the goal of most previous research was only to develop an accurate numerical scheme to solve the transient radiative transfer equation. Most of these papers did not perform any systematic study to analyze short pulse laser transport through tissues with the goal of detecting tumors and inhomogeneities in tissues. There is a critical need for such studies, as variation in tissue, tumor, and laser beam parameters will significantly affect the transmitted and reflected signals. In this paper an accurate solution of the transient radiative transport equation is first obtained using discrete ordinates methods in conjunction with high order upwind piecewise parabolic interpolation scheme. In addition a detailed parametric study is performed to analyze the effects of the variation of scattering/absorbing properties and phase function of tissues and tumors, tumor and detector location on the spatial and temporal distribution of the transmitted and reflected signals.

2. MATHEMATICAL FORMULATION

In this paper the tissue medium is approximated by an anisotropically scattering and absorbing rectangular enclosure in which a tumor / inhomogeneity is imbedded in it (see Fig. 1). The radiative transfer equation (RTE) in a given direction Ω is given by[26]:

$$\frac{1}{c}\frac{\partial I(x,y,\Omega,t)}{\partial t} + \mu\frac{\partial I(x,y,\Omega,t)}{\partial x} + \eta\frac{\partial I(x,y,\Omega,t)}{\partial y} + \sigma_e I(x,y,\Omega,t) = \frac{\sigma_s}{4\pi}\int_{4\pi}\Phi(\Omega',\Omega)I(x,y,\Omega',t)\,d\Omega' + S(x,y,\Omega,t)\,, \quad (1)$$

where I is the intensity ($Wm^{-2}sr^{-1}$), σ_e and σ_s are the extinction coefficient and the scattering coefficient respectively, Φ is the phase function, Ω the direction cosine, c is the velocity of light in the medium, x and y are the spatial coordinates, t is the time, and S is the source term.

The scattering phase function can be represented in a series of Legendre polynomials P_k by:

$$\Phi(\Omega',\Omega) = \sum_{k=0}^{K} a_k P_k[\cos(\Theta)] \quad , \quad (2a)$$

where a_k are the associated coefficients in the expansion and Θ is the scattering angle such that:

$$\cos(\Theta) = \mu\mu' + \eta\eta' + \xi\xi' \quad , \quad (2b)$$

where μ, η, and ε are the directions cosines of the light propagation direction Ω .The pulsed radiation incident on the tissue medium at surface 1 (see Figure 1) is square-shaped pulse with a temporal duration (pulse width) t_p at full width half-maximum (FWHM). The intensity can be separated into a collimated component, corresponding to the incident source, and a scattered intensity. If I_c is the collimated intensity, then I is the remaining intensity described by Eq. (1). The collimated component of the intensity for the square pulse is represented by:

$$I_c(x,y,\Omega,t) = I_0\, e^{-\sigma_e x}[H(t - x/c) - H(t - t_p - x/c)]\delta(\Omega - \Omega_0)\ , \quad (3)$$

where I_0 is the intensity leaving the wall towards the medium, $H(t)$ the Heaviside step function, and $\delta(t)$ the Dirac delta function.

The source function S for the scattered intensity field is then given by:

$$S(x,y,\Omega,t) = \frac{\sigma_s}{4\pi}\int_{4\pi}\Phi(\Omega',\Omega)I_c(x,y,\Omega',t)\,d\Omega' \quad . \tag{4}$$

The associated boundary condition at the surface where the laser beam is incident can be written as:

$$I_0(\Omega,t) = \frac{1}{\pi}\int_{\mathbf{n_s}.\mathbf{\Omega}'>0}\mathbf{n_s}\cdot\Omega' I^{in}d\Omega', \quad \mathbf{n_s}.\mathbf{\Omega}<0 \quad , \tag{5}$$

where $\mathbf{n_s}$ is the unit outward normal vector at the boundary and I^{in} is the intensity coming from the medium toward the laser incident surface. The boundary condition at the other surfaces of the medium can be written in a similar way as Eq. (5).

In the discrete ordinates method, the radiative transfer equation and the associated boundary condition are replaced with a set of equations for a finite number of M directions that cover 4π sr solid angles.[27] The integral terms of Eqs. (1) and (4) are reformulated with the aid of an angular quadrature of order M.

The discrete form of the time-dependent radiative transport equation in the direction Ω_m is then represented as:

$$\frac{1}{c}\frac{\partial I_m(x,y,t)}{\partial t} + \mu_m\frac{\partial I_m(x,y,t)}{\partial x} + \eta_m\frac{\partial I_m(x,y,t)}{\partial y} = -\sigma_e I_m(x,y,t) + \frac{\sigma_s}{4\pi}\sum_{m'=1}^{M} w_{m'}\Phi_{m'm}I_{m'}(x,y,t) + S_m(x,y,t) \quad , \tag{6}$$

where $m = -M,....,-1,\ 1,...,M$, $\{\Omega_m, w_m\}$ defines a quadrature of M discrete directions Ω_m to which the weights w_m are associated.

In this study, the one-dimensional Piecewise Parabolic Advection (PPA) scheme already developed by the authors[28,29] is extended to solve the two-dimensional geometry by using a Strang-type splitting.[30] The left-hand-side of Eq. (6) is treated by the upwind monotonic interpolation methods. PPA scheme is very efficient and produces very small amount of diffusion.[31] These methods have been developed originally to solve Eulerian advection problems.

3. RESULTS

The transmitted and reflected signals are obtained by solving the discrete from of the transient radiative transport equation given by Eq. (6). The base value of optical properties[11] used for tissues are- scattering coefficient ($\sigma_{s,t}$) = 9.8 mm^{-1} and absorption coefficient ($\sigma_{a,t}$) = 0.021 mm^{-1}, whereas for tumors the values used are- scattering coefficient ($\sigma_{s,i}$) = 6.8 mm^{-1} and absorption coefficient ($\sigma_{a,i}$) = 0.022 mm^{-1}. The tumor 1 mm x 1 mm in size is located in the center of the medium having a dimension of 5 mm x 5 mm. A linear forward anisotropic phase function is used to represent the tissue medium and tumor. The laser beam of diameter 1 mm and pulse width (t_p) = 1 ps is incident at x = 0 between y = -0.5 to 0.5 mm (see Figure 1).

Figure 2 shows the effects of the variation of the scattering coefficient of tumor ($\sigma_{s,i}$) on the transmitted signal measured on surface 2 (opposite to the laser incident beam) at a particular time instant. It is observed that with the decrease of the tumor scattering coefficient, the demarcation between tissue and tumor becomes stronger. This is because higher the scattering coefficient higher will be the attenuation of the laser beam as it propagates through the medium and lower will be the magnitude of the transmitted signal. Figures 3 and 4 show the transmitted and reflected signal along surface 2 and 1 respectively at different time instants for base values of optical properties of tissue and tumor. It is observed from the transmitted signals as depicted in Figure 3 that the presence of the tumor is obvious at short time scales. At larger times the multiple scattering effects obscures the spatial details of the transmitted signals. This is consistent with many time-resolved transmittance measurements reported in the literature.[11] This explains that in order to capture the spatial distribution provided by the ballistic photons, time-gating measurements are necessary.[32] On the other hand, it is observed that the corresponding spatial distribution of reflected signal measurements cannot determine the tumor location in the medium.

Figure 5 shows the effect of the tumor location on the transmitted signal measured along surface 2. It is clearly evident from the results that the models could clearly predict the tumor location. The effect of the detector location on the time-resolved transmitted optical signal is depicted in Figure 6. The detector position $y = 0$ corresponds to the tumor center and $y = 1$ mm on the outside of the tumor. The curve obtained on the tumor center ($y = 0$) possesses a lot more early light and is primarily due to the difference in the scattering coefficients between tissue and tumor. The large scattering coefficient of tissues compared to tumor means that the detected early light is not unscattered light. The amount of unscattered light is too small to detect. Figure 7 shows the effect of the phase function on the transmitted signal. The magnitude of the transmitted signal is higher for the case of a highly forward scattered phase function. Thus selection of the appropriate phase function is critical in time-resolved measurements. Figure 8 shows the incident radiation field for the medium at different times.

4. CONCLUSIONS

The paper presents results of spatial and temporal distribution of transmitted and reflected signals for the case of short pulse laser transport through tissues using a two-dimensional transient radiative transport formulation with the goal to detect tumors. A parametric study is performed to analyze the effect of various parameters on tumor detection. The transient radiative transport equation is very sensitive to the optical properties of tissues and tumor as well the nature of the medium. The temporal and spatial distribution of the transmitted and reflected signal can be correlated to the medium properties. The significance of this comprehensive study is that it will provide a guidance tool for the development of time-resolved optical tomography for biomedical imaging of tissues to detect tumors.

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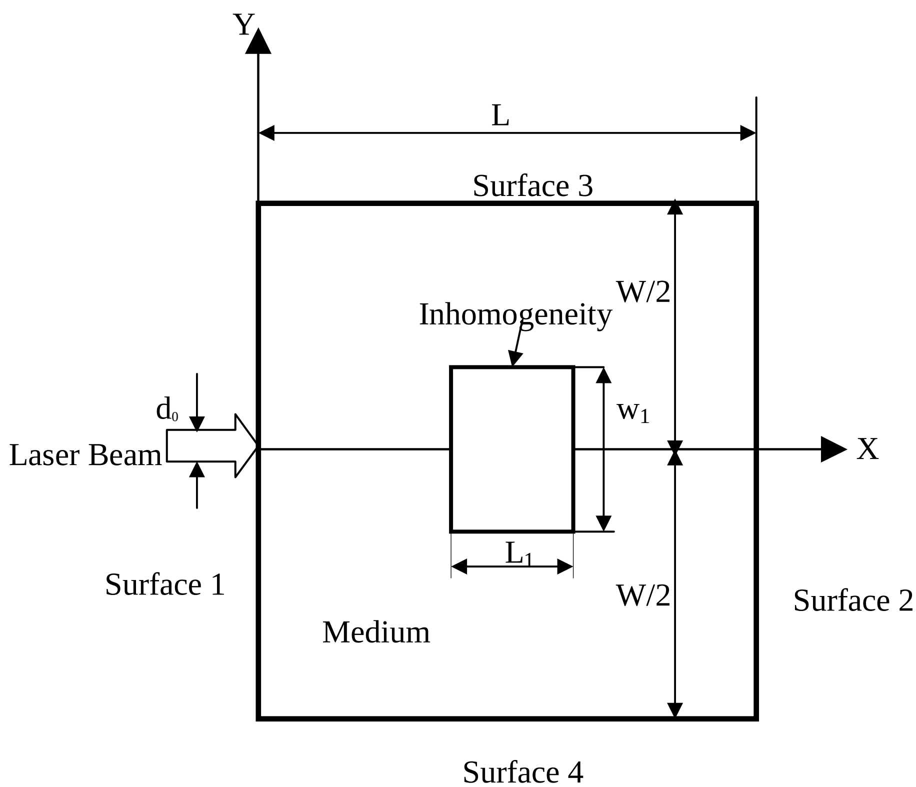

Figure 1. Schematic of the problem under consideration.

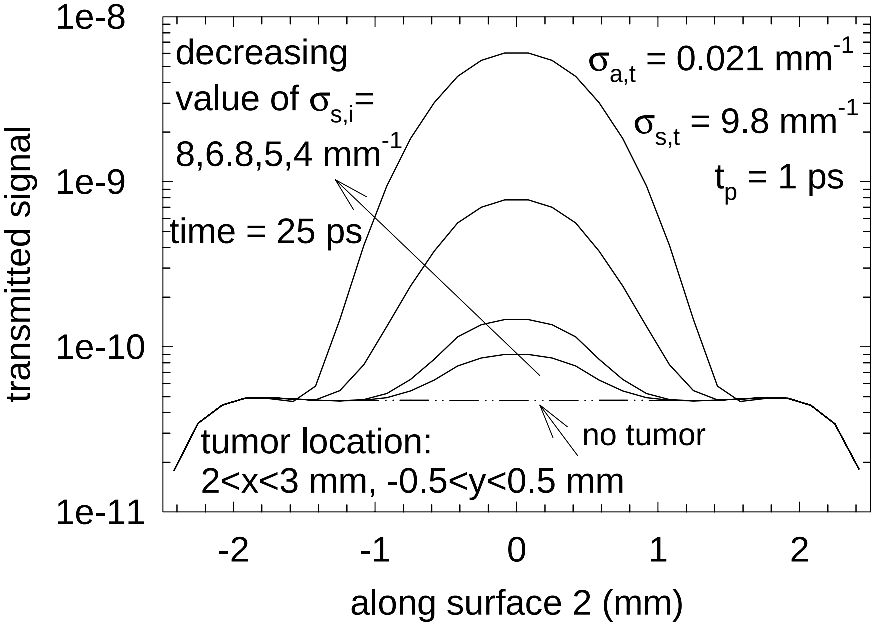

Figure 2. Effect of tumor scattering coefficient on the transmitted signal.

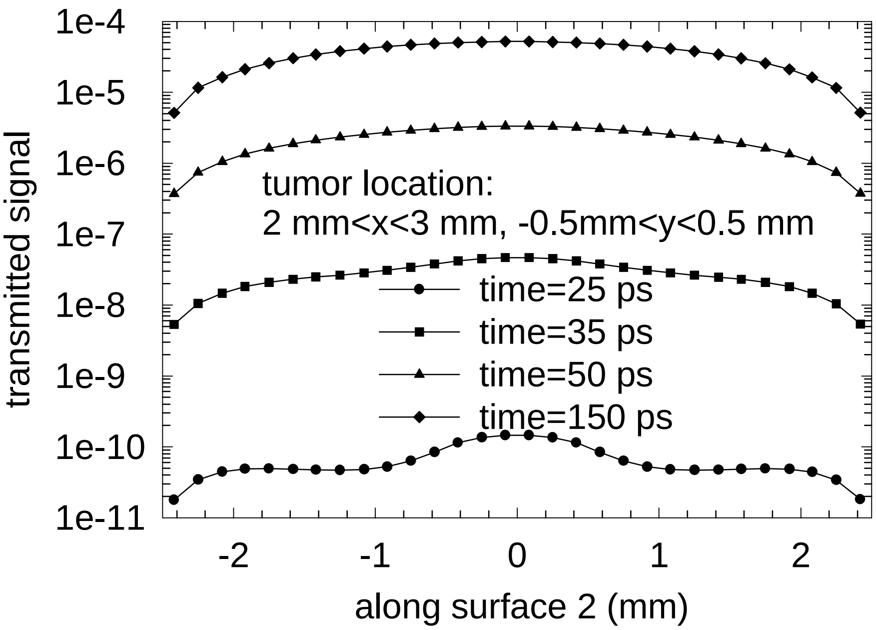

Figure 3. Transmitted signal at various time instants.

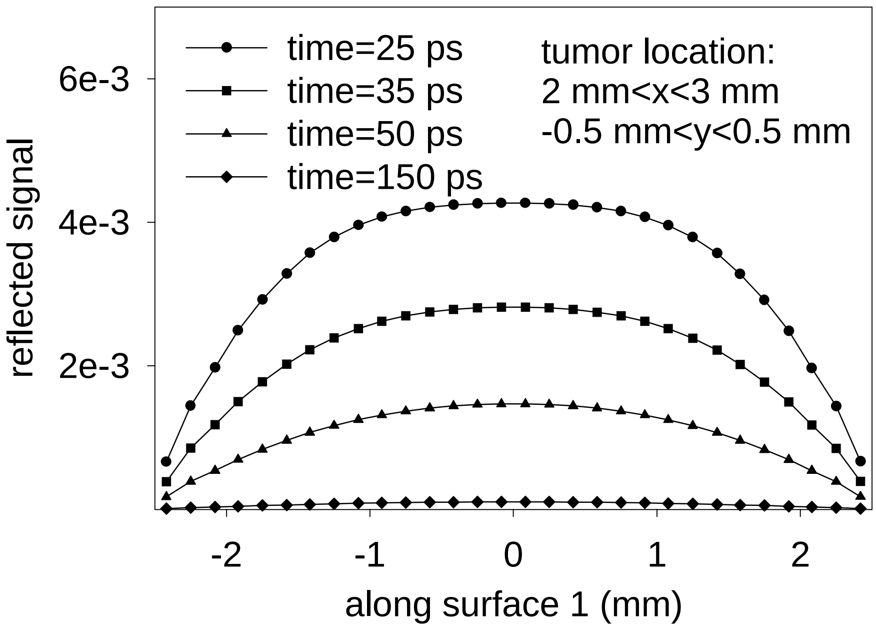

Figure 4. Reflected signal at various time instants.

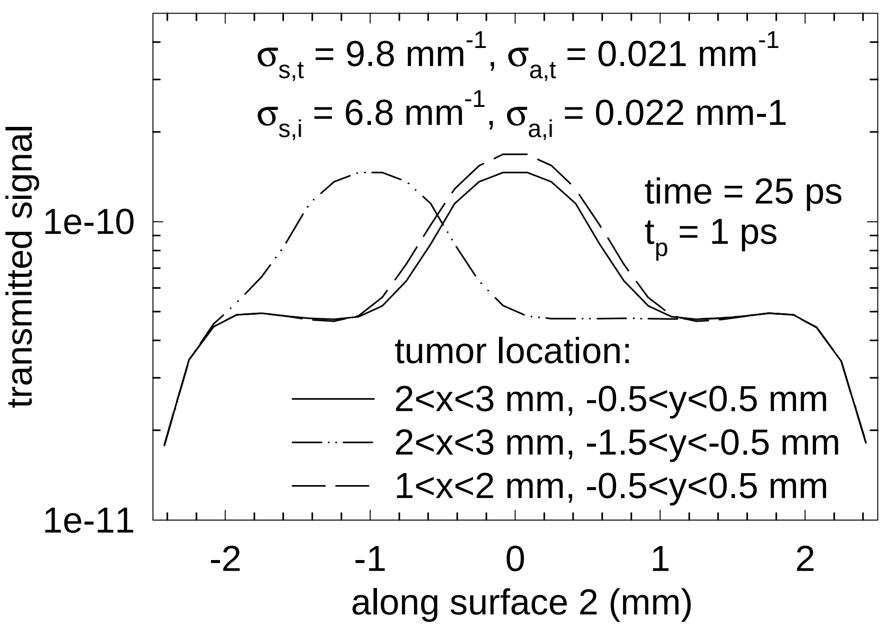

Figure 5. Transmitted signal for various tumor locations.

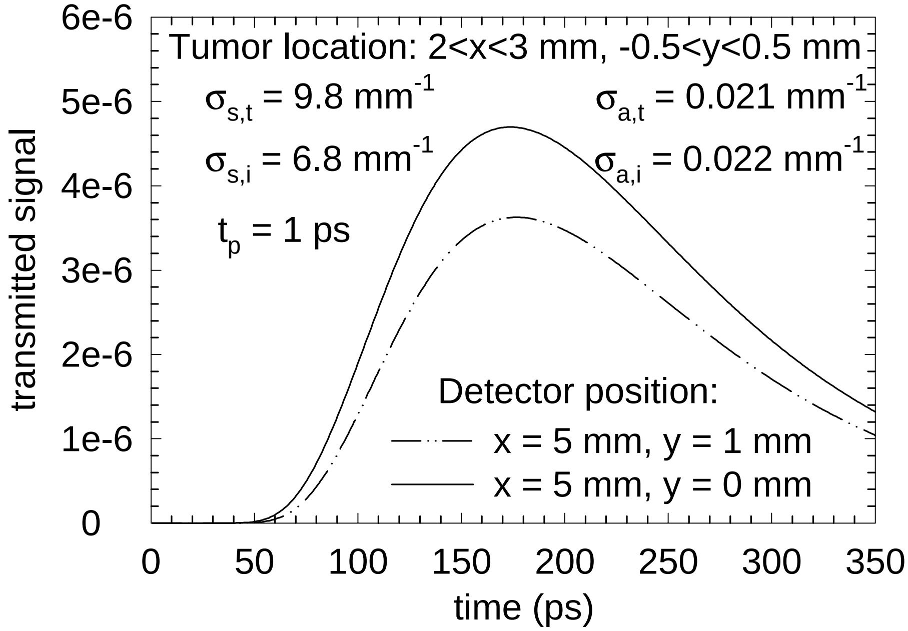

Figure 6. Transmitted signal at various detector positions.

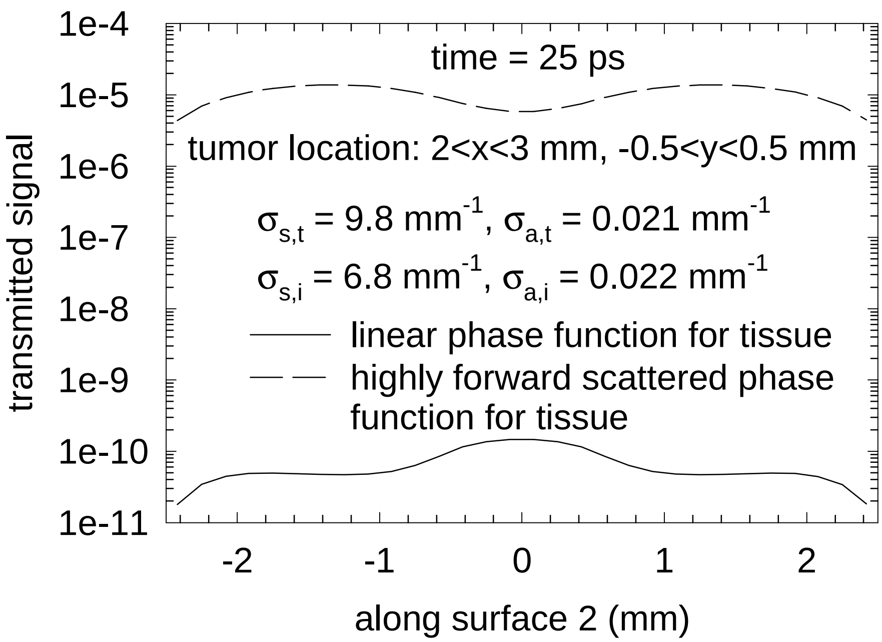

Figure 7. Effect of the phase function on the transmitted signal.

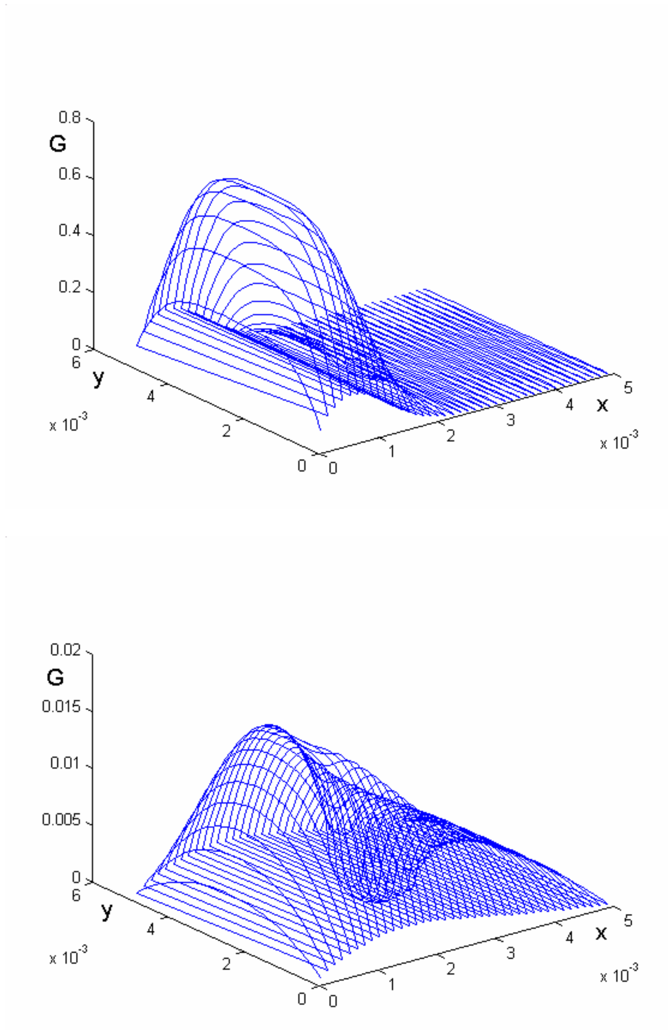

Figure 8. Radiation field in the tissue medium at time = 20 ps and 110 ps.