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Computational Study of a Possible Improvement of Cancer Detection by Diffuse Optical Tomography

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Abstract

In general, malignant tumors manifest an increase of the refractive index compared to the normal tissue which encircles them. So, medical imaging by diffuse optical tomography should take advantage from the emergence of the refractive index as a supplementary contrast parameter. The present paper gives a new computational framework within which theoretical aspect of cancer detection by diffuse optical tomography can be studied. We use radiative transfer theory in a varying refractive index biological tissue. In our previous works, Legendre transform was used as an innovative view to handle the angular derivative terms in the case of uniform refractive index spherical medium. In this paper, we try to extend this technique to modelling near infrared radiation interaction with biological tissue in a rectangular geometry. In biomedical optics, our analysis can be considered as a forward problem solution in a diffuse optical tomography imaging scheme. We consider a rectangular biological tissue-like domain with spatially varying refractive index submitted to a near infrared continuous light source. Interaction of radiation with the biological material into the medium is handled by a radiative transfer model. In the studied situation, the model displays two angular redistribution terms that are treated with Legendre integral transform. Transmitted radiance on the boundary is computed. The model is used to study a possible detection of abnormalities in a general biological tissue. The effect of the embedded non-homogenous objects on the transmitted signal is studied. Particularly, detection of targets of localized heterogeneous inclusions within the tissue is discussed. Results show that models accounting for variation of refractive index can yield useful predictions about the target and the location of abnormal inclusions within the tissue.

Keywords: Abnormal inclusion, biological tissue, diffuse optical tomography, malignant tumor , Legendre transform, varying refractive index

1. Introduction

A special attention in diffuse optical tomography is focused on the development of methods for detection of photons providing the information concerning optical parameters of the explored medium. This gives the targets of localized non homogeneous inclusion arising in tissues due to various pathologies, like tumor formation, local increase in blood volume and other abnormalities (Arridge and Hebden, 1997, Arridge and Schweiger, 1998, Ntziachristos et al., 2001, Hielscher et al., 2002, Cai et al.,2006, Pu et al., 2009). In radiative transfer theory, the most used parameters in modeling Laser radiation interaction with biological tissue is absorption and scattering (Xu et al., 2002, Klose et al., 2008, Klose, 2010, Gantri et al., 2007, Trabelsi et al., 2010, Gantri et al., 2010). However some other studies evoked a significant variation of refractive index of abnormal biological tissues especially in the near infrared range. More precisely, experimental results (Li and Xie, 1996, Das et al., 1997, Ohmi et al., 2000, Lai et al., 2005) showed that the tissue of malignant tumors could manifest an increase of the refractive index which can attain until 10 % of that of a normal tissue which encircles them. So, medical imaging by diffuse optical tomography should take advantage from the emergence of a third contrast parameter which is the refractive index. This drove to the appearance of a big number of numerical and fundamental works in the field of radiative transfer in a varying refractive index biological medium.

While the conventional radiative transfer equation (RTE) has been widely used to study interaction of near infrared radiation with biological media, there exists a number of works dealing with a modified radiative transfer equation in a spatially varying refractive index media (Lemonnier and LeDez, 2005, Liu, 2006, Bal, 2006, Zhang et al., 2009). Some of these papers are interested to varying refractive index biological tissues (Beuthan et al., 1996, Dehghani et al., 2003, Khan et Jiang, 2003, Shendeleva and Molly, 2007, Trabelsi et al., 2009)

In the present paper, our first concern is to contribute to the usability of the radiative transfer theory in a potential optical tomography setting in medical imaging. At this level, studying the effect of refractive index on the transmitted light through a biological rectangular layer should be crucial. This could improve detectability of heterogeneous objects in a typical tomography scheme. However, it is important to note that in a varying refractive index medium, the rays are not straight lines but curves. So even in a rectangular geometry, the varying index radiative transfer equation displays the classical form of the angular derivative terms commonly appearing when dealing with spherical and cylindrical geometries with uniform refractive index (Tsai and Özişik, 1990, Jia et al., 1991, Modest, 2003). This finding gives rise to the use of Legendre transform as a manner for modelling these terms. Although this technique were used by Sghaier et al., 2000 and Trabelsi et al., 2005 in a uniform refractive index spherical domain as an innovative view to handle these terms, it prevails useful in this contemporary problem. This fact is our second concern in this paper. So, we present a computational RTE-based model suitable for basic diffuse optical tomography forward problem with spatially varying refractive index biological medium. We treat angular derivative terms by using the Legendre integral transform technique. We investigate cases concerning optical tomography applications. Results concerning the effect of the refractive index variation on the detected signal are shown.

2. Biophysical model and computational implementation

In this work, the CW regime of radiative transfer in a human biological tissue is described by using a stationary varying refractive index RTE (Ferwerda, 1999, Tualle et Tinet, 2003):

$$\begin{aligned}&\vec{\Omega}.\nabla I(\vec{r},\vec{\Omega}) + (\mu_a(\vec{r}) + \mu_s(\vec{r}))I(\vec{r},\vec{\Omega}) + \frac{1}{n(\vec{r})}\nabla n.\nabla_{\vec{\Omega}} I \\ &- \frac{2}{n(\vec{r})}(\vec{\Omega}.\nabla n)I = S(\vec{r},\vec{\Omega}) + \mu_s(r)\int_0^{2\pi} p(\vec{\Omega},\vec{\Omega}')I(\vec{r},\vec{\Omega}')d\vec{\Omega}'\end{aligned} \tag{1}$$

where $I(\vec{r},\vec{\Omega})$ is the directional energetic radiance at the spatial position $\vec{r}$ and $n(\vec{r})$ is the refractive index distribution. Equation (1) takes into account the fact that the rays are not straight lines but curves. It involves terms that illustrate the expansion or the contraction of the cross section of the tube of light rays in the medium. On the boundary, the radiance is the sum of the external source contribution and the partly-reflected radiance due to the refractive index mismatch at the boundary,

$$I(\vec{r},\vec{\Omega}) = S(\vec{r}_b,\vec{\Omega}) + RI(\vec{r},\vec{\Omega}_{ref}),\ \vec{n}_b.\vec{\Omega} < 0 \text{ and } \vec{n}_b.\vec{\Omega}_{ref} = -\vec{n}_b.\vec{\Omega}$$

where $\vec{r}_b$ is a position on the boundary and $\vec{n}_b$ is an outer normal unit vector. The reflectivity R can be calculated for each direction using Fresnel's relations. For a two-dimensional problem and in Cartesian coordinate system of the x-y plane, the terms due to the refractive index variation can be expressed as

$$\begin{aligned}&\frac{1}{n}\nabla n.\nabla_{\vec{\Omega}} I - \frac{2}{n}(\vec{\Omega}.\nabla n)I \\ &= -\frac{1}{n}\frac{\partial n}{\partial x}(\sin\varphi\frac{\partial I}{\partial\varphi} + 2\cos\varphi\, I) + \frac{1}{n}\frac{\partial n}{\partial y}(\cos\varphi\frac{\partial I}{\partial\varphi} - 2\sin\varphi\, I)\end{aligned} \tag{2}$$

where $\cos\varphi$ and $\sin\varphi$ are the Cartesian coordinates of the unit direction vector in the x-y plane. In fact we assume that the radiance of out of plane directions is negligible. By using notations $\xi = \cos\varphi$ and $\eta = \sin\varphi$, equation (2) displays the classical form of the angular redistribution term commonly appearing when dealing with spherical and cylindrical geometries with uniform refractive index

$$\frac{1}{n}\nabla n.\nabla_{\vec{\Omega}} I - \frac{2}{n}(\vec{\Omega}.\nabla n)I = \frac{1}{2n^2}\left\{\frac{\partial n^2}{\partial x}\frac{\partial}{\partial\xi}[(1-\xi^2)I] + \frac{\partial n^2}{\partial y}\frac{\partial}{\partial\eta}[(1-\eta^2)I]\right\}$$

The angular redistribution terms will be noted

$$D_\xi = \frac{\partial}{\partial\xi}[(1-\xi^2)I] \text{ and } D_\eta = \frac{\partial}{\partial\eta}[(1-\eta^2)I],$$

so the equation above becomes,

$$\frac{1}{n}\nabla n.\nabla_{\vec{\Omega}} I - \frac{2}{n}(\vec{\Omega}.\nabla n)I = \frac{1}{2n^2}\left\{\frac{\partial n^2}{\partial x}D_\xi + \frac{\partial n^2}{\partial y}D_\eta\right\}$$

In our numerical implementation, we use a rectangular domain which is divided into a set of I x J elementary uniform volumes ΔV with a uniform unitary depth. The angular discretization is obtained through a discrete ordinate technique. This yields a set of M discrete directions, $\{\varphi_m, m = 1..M\}$ giving a set of angular discrete direction cosines $\{(\xi_m, \eta_m), m = 1,...M\}$. An orientation depending on the incident ray direction is adopted for each cell. Calculations are done by using integration of equation (1) over an elementary volume ΔV for each discrete direction. This gives

$$\begin{aligned}&\Delta y\xi_m(I_{m,E}-I_{m,W})+\Delta x\eta_m(I_{m,N}-I_{m,S})+\Delta x\Delta y(\mu_a+\mu_s)I_{m,p}\\&+\frac{\Delta V}{2n^2}(\frac{\partial n^2}{\partial x}D_{\xi,m}+\frac{\partial n^2}{\partial y}D_{\eta,m})=\Delta x\Delta y(S_{m,P}+\mu_s w_m p_{mm'}I_{m,p}+\mu_s\sum_{m'=1,m'\neq m}^{M} w_{m'}p_{mm'}I_{m',p})\end{aligned} \tag{3}$$

where $D_{x,m}$ and $D_{y,m}$ are the discrete angular derivative terms at the angular ordinate ξ_m and η_m respectively and w_m is a weighting factor. The discrete term of Henyey-Greenstein phase function is written as

$$p_{mm'} = \frac{1-g^2}{2(1+g^2-2g(\xi_m\xi_{m'}+\eta_m\eta_{m'}))^{3/2}}$$

If the direction cosines are positive, the directional radiances are known on the faces W and S and they are unknown on the faces E and N of the (i,j)-cell and also in the centre P. Therefore, we need two complementary relations to eliminate $I_{m,N}$ and $I_{m,E}$, this can be obtained by using interpolation formula

$$\begin{cases} I_{m,P} = \alpha I_{m,E} + (1-\alpha)I_{m,W} \\ I_{m,P} = \alpha I_{m,N} + (1-\alpha)I_{m,S} \end{cases},$$

where α is an interpolation parameter. Using these relations, equation (3) becomes

$$\begin{aligned}&\frac{\Delta y\xi_m}{\alpha}(I_{m,P}-I_{m,W})+\frac{\Delta x\eta_m}{\alpha}(I_{m,P}-I_{m,S})+\Delta x\Delta y(\mu_a+\mu_s)I_{m,p}\\&+\frac{\Delta x\Delta y}{2n^2}\left\{\frac{\partial n^2}{\partial x}D_{\xi,m}+\frac{\partial n^2}{\partial y}D_{\eta,m}\right\}=\Delta x\Delta y(S_{m,P}+\mu_s w_m p_{mm'}I_{m,p}+\mu_s\sum_{m'=1,m'\neq m}^{M} w_{m'}p_{mm'}I_{m',p})\end{aligned}$$

Theoretically, if we know the solution in the (i,j)-cell, we can do calculus over the cells (i+1,j) and (i,j+1) using the boundary conditions and the following relations:

$$\begin{cases} I_{m,W}(i+1,j) = I_{m,E}(i,j); i = 1,...I-1 \\ I_{m,S}(i,j+1) = I_{m,N}(i,j); i = 1,...J-1 \end{cases}$$

If the direction cosines are both positive, we get the following equation

$$\frac{\Delta y\,\xi_m}{\alpha}(I_{m,i,j} - I_{m,i-1,j}) + \frac{\Delta x\,\eta_m}{\alpha}(I_{m,i,j} - I_{m,i,j-1})$$
$$+\ \Delta x\Delta y(\mu_a + \mu_s)I_{m,i,j} + \frac{\Delta x\Delta y}{2n^2}\left\{\frac{\partial n^2}{\partial x}D_{\xi,m} + \frac{\partial n^2}{\partial y}D_{\eta,m}\right\}$$
$$= \Delta x\Delta y(S_{m,i,j} + \mu_s w_m\, p_{mm}\, I_{m,i,j} + \mu_s \sum_{m'=1,m'\neq m}^{M} w_{m'}\, p_{mm'} I_{m',i,j})$$

Finally, we obtain, the following numerical model:

$$I_{m,i,j} = \left[\frac{\Delta y\xi_m}{\alpha} + \frac{\Delta x\eta_m}{\alpha} + \Delta x\Delta y(\mu_a + \mu_s) - \Delta x\Delta y\mu_s w_m p_{mm}\right]^{-1} \times [\frac{\Delta y\xi_m}{\alpha} I_{m,i-1,j}$$
$$+ \frac{\Delta x\eta_m}{\alpha} I_{m,i,j-1} - \frac{1}{2n_{i,j}^2}\left\{(n_{i,j}^2 - n_{i-1,j}^2)\Delta y D_{\xi,m,i,j} + (n_{i,j}^2 - n_{i,j-1}^2)\Delta x D_{\eta,m,i,j}\right\} \tag{4}$$
$$+ \Delta x\Delta y(S_{m,i,j} + \mu_s \sum_{m'=1,m'\neq m}^{M} w_{m'} p_{mm'} I_{m',i,j})]$$

3. Derivative terms induced by varying refractive index in biological material

As it is explained in [29], we consider the following Legendre transforms:

$$\ell(\frac{\partial}{\partial\xi}[(1-\xi^2)I],s) = \int_{-1}^{1}\frac{\partial}{\partial\eta}[(1-\xi^2)I]P_s(\xi)d\xi$$
$$\ell(\frac{\partial}{\partial\eta}[(1-\eta^2)I],s) = \int_{-1}^{1}\frac{\partial}{\partial\eta}[(1-\eta^2)I]P_s(\eta)d\eta$$

where P_s is the s-th degree Legendre polynomial. According to Sturn-Liouville equation, we can write:

$$\int_{-1}^{1}\frac{\partial}{\partial\eta}[(1-\xi^2)I]P_s(\xi)d\xi = \frac{s(s+1)}{2s+1}[\int_{-1}^{1} I\, P_{s+1}(\xi)d\xi - \int_{-1}^{1} I\, P_{s-1}(\xi)d\xi]$$
$$\int_{-1}^{1}\frac{\partial}{\partial\eta}[(1-\eta^2)I]P_s(\eta)d\eta = \frac{s(s+1)}{2s+1}[\int_{-1}^{1} I\, P_{s+1}(\eta)d\eta - \int_{-1}^{1} I\, P_{s-1}(\eta)d\eta]$$

To obtain derivative terms, we make use o numerical quadrature:

$$\sum_{m=1}^{M} w_m D_{\xi,m} P_s(\xi_m) = \frac{s(s+1)}{2s+1}[\sum_{m=1}^{M} w_m P_{s+1}(\xi_m) - \sum_{m=1}^{M} w_m P_{s-1}(\xi_m)],$$
$$\sum_{m=1}^{M} w_m D_{\eta,m} P_s(\eta_m) = \frac{s(s+1)}{2s+1}[\sum_{m=1}^{M} w_m P_{s+1}(\eta_m) - \sum_{m=1}^{M} w_m P_{s-1}(\eta_m)]$$

The above systems of equations are closed by the obvious relations:

$$\sum_{m=1}^{M} w_m D_{\xi,m} = \int_{-1}^{1} \frac{\partial}{\partial \eta}[(1-\xi^2)I]\,d\xi = 0$$

$$\sum_{m=1}^{M} w_m D_{\eta,m} = \int_{-1}^{1} \frac{\partial}{\partial \eta}[(1-\eta^2)I]\,d\eta = 0$$

So discrete derivative terms in the (i,j)-cell into the medium can be obtained by solving the linear algebraic equations:

$A_\xi \hat{D}_{\xi,i,j} = B_{\xi,i,j}$ and $A_\eta \hat{D}_{\eta,i,j} = B_{\eta,i,j}$, where:

$$A_\xi = \begin{bmatrix} w_1 & w_2 & \cdot\ \cdot & w_M \\ w_1 P_1(\xi_1) & w_2 P_1(\xi_2) & \cdot\ \cdot & W_M P_1(\xi_M) \\ \cdot & \cdot & \cdot\ \cdot & \cdot \\ \cdot & \cdot & \cdot\ \cdot & \cdot \\ w_1 P_{M-1}(\xi_1) & w_2 P_{M-1}(\xi_2) & & w_M P_{M-1}(\xi_M) \end{bmatrix}$$

$$\hat{D}_{\xi,i,j} = \begin{bmatrix} D_{\xi,1,i,j} \\ D_{\xi,2,i,j} \\ \cdot \\ \cdot \\ D_{\xi,M,i,j} \end{bmatrix} \qquad B_{\xi,i,j} = \begin{bmatrix} 0 \\ \frac{2}{3}\sum_{m'=1}^{M} w_{m'} I_{m',i,j}(P_2(\xi_{m'}) - P_0(\xi_{m'})) \\ \cdot \\ \cdot \\ \frac{M(M-1)}{2M-1}\sum_{m'=1}^{M} w_{m'} I_{m',i,j}(P_M(\xi_{m'}) - P_{M-2}(\xi_{m'})) \end{bmatrix}$$

and A_η, $\hat{D}_{\eta,i,j}, B_{\eta,i,j}$ are straightforward by replacing ξ by η. A set of weights are judiciously chosen with an equally spaced distribution of angular ordinates (ξ,η). The matrices A_ξ and A_η must be regular and they are inversed each only once in all the calculation process.

Now, to solve equation (4), we use successive iterations to actualise the implicit internal source term in the right member. So, this gives

$$I^{k+1}_{m,i,j} = \left[\frac{\Delta y \xi_m}{\alpha} + \frac{\Delta x \eta_m}{\alpha} + \Delta x \Delta y(\mu_a + \mu_s) - \Delta x \Delta y \mu_s w_m p_{mm}\right]^{-1} \times$$
$$\left[\frac{\Delta y \xi_m}{\alpha} I^k_{m,i-1,j} + \frac{\Delta x \eta_m}{\alpha} I^k_{m,i,j-1} - \frac{1}{2n^2_{i,j}}\left\{\begin{array}{l}(n^2_{i,j} - n^2_{i-1,j})\Delta y D^k_{\xi,m,i,j} \\ +(n^2_{i,j} - n^2_{i,j-1})\Delta x D^k_{\eta,m,i,j}\end{array}\right\}\right. \tag{5}$$
$$\left. + \Delta x \Delta y(S_{m,i,j} + \mu_s \sum_{m'=1,m'\neq m}^{M} w_{m'} p_{mm'} I^k_{m',i,j})\right]$$

The iteration process is repeated until a convergence criterion is attempted. To improve convergence speed, we use a successive over relaxation method. So the updated value $I^{k+1}_{m,i,j}$ is a linear combination of the iterated value $I^{k}_{m,i,j}$ and the previously computed value,

$$(I^{k+1}_{m,i,j})_{updated} = \rho I^{k+1}_{m,i,j} + (1-\rho) I^{k}_{m,i,j},$$

ρ is a relaxation parameter whose value is usually between 1 and 2. The solution is obtained when the relative discrepancy value,

$$\varepsilon = \left| \frac{I^{k+1}_{m,i,j} - I^{k}_{m,i,j}}{I^{k}_{m,i,j}} \right|,$$

is smaller than a tolerance value. In that case the result is noted $\bar{I}_{m,i,j}$. In all our calculus, we have taken 10^{-8} as a tolerance value. As initial condition, we take a field of null intensities. Also, all our calculations are done in the case of interpolation diamond scheme (α=0.5). If the direction cosines are not both positive, the precedent equations are valid provided that the orientation WESN of cells is done according to the direction of propagation. In all our investigations, the injected power source is assumed to be equivalent to a forward collimated monochromatic point source on the bottom side of the boundary. Results shown below are obtained by using a continuous wave source with a uniform equivalent intensity value of 50 $mW.cm^{-1}$. To present our results, we make use of detected fluence rate which is given in a (i_d,j_d)-detector point on the boundary as

$$\Phi_d = \sum_{m=1}^{M} (1 - R_{m,i_d,j_d}) w_m \bar{I}_{m,i_d,j_d}, \quad \text{with}$$

$$R_{m,i_d,j_d} = \begin{cases} 1 \text{ if } \varphi_m \succ \arcsin\left(\dfrac{n_{air}}{n_{i_d,j_d}}\right) \\ \dfrac{1}{2}\left[\left(\dfrac{n_{i_d,j_d}\cos\varphi_m - n_{air}\cos\varphi_t}{n_{i_d,j_d}\cos\varphi_m + n_{air}\cos\varphi_t}\right)^2 + \left(\dfrac{n_{i_d,j_d}\cos\varphi_t - n_{air}\cos\varphi_m}{n_{i_d,j_d}\cos\varphi_t + n_{air}\cos\varphi_m}\right)^2\right], \text{else.} \end{cases}$$

where

$$\varphi_t = \arcsin\left(\frac{n_{air}\sin\varphi_m}{n_{i_d,j_d}}\right) \text{ and } n_{air} \approx 1.$$

Also, we make use of a normalized detected fluence rate as

$$\Phi_N = \frac{\Phi_d}{1/D \sum_{d=1}^{D} w'_d \Phi_d},$$

where D is the number of the detector points on one side of the boundary and w'_d is a weighting factor from trapezoidal integration rule. In all calculations, we have used 38 detector points on each side. Also, all calculus is carried out by using 16 uniformly distributed discrete directions and a space grid of 121x121cells.

4. Results and discussion

4.1. Model testing: case of continuous varying refractive index medium

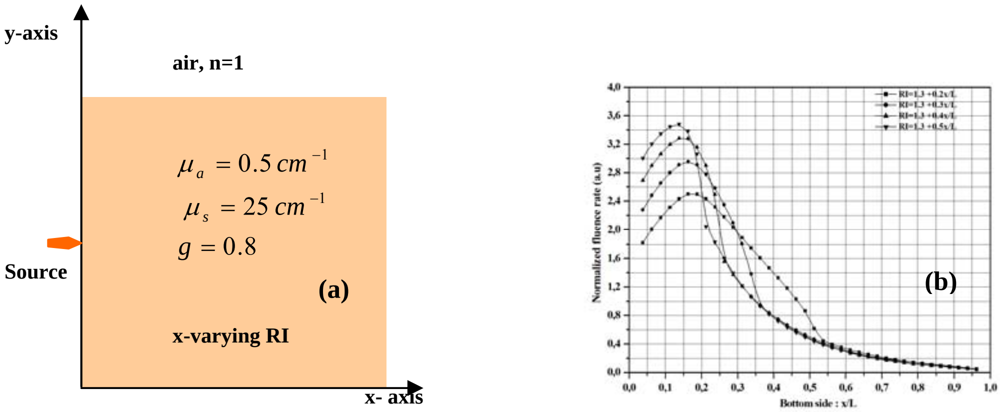

Figure 1. Biological tissue-like medium with a linear continuous x-varying refractive (a) and gradient effect on the detected signal (b)

We study near infrared radiation transport in a rectangular medium exposed to a continuous collimated source which is placed on the left side of the boundary. Figure 1 shows the considered medium, it is assumed to be 2cmx2cm sized with varying refractive index. Within the medium, we consider an x-axis linear varying refractive index with different gradient values. To show the effect of the gradient of refractive index on detected fluence rate, we have used a weakly absorbing and weakly isotropic scattering background medium whose optical parameters are shown in figure1 (a).

Figure1 (b) shows the response of the medium through the detected signal on the bottom side of the boundary. Detected fluence rate curves present a distinguish effect of refractive index gradient in linear case. The transmission zone on the boundary increases with decreasing gradient values. Even though most detected transmission is obtained near by the source, a weak gradient can augment transmitted radiation relatively far from the source while high values of gradient can block transmitted radiation within the medium.

4.2. Second investigation: detection of heterogeneous refractive object

In this investigation, we consider a 2cmx2cm sized background medium containing a circular heterogeneous object. The area of the object is 0.5 cm^2. We limit the analysis to the effect of heterogeneity by the increase of the refractive index only. The background refractive index is taken 1.33. The other optical properties are the same as in the precedent investigation for the background and the object. The geometry of the medium, position of the heterogeneous object and the detected signal on different sides of the boundary are shown in figures 2.

Results are shown for an increase of refractive index by 5% and 10% respectively. There is no significant effect of the object presence on the detected signal on the top side because the object is relatively far from the detectors on that side. Also there is a weak sensible effect of the object presence on the bottom signal. However there is a visible effect of the object on the right side which is the opposite side to the source and where the detectors are relatively near by the object. In such cases, there is an obvious effect of the heterogeneity on the detected signal especially when the refractive index is increased by 10%. The response shows a distinct distortion of the fluence rate curve. It is occurring on the targets where the object is laying exactly. This distortion allows a principled decision on the existence of such object into the medium. These findings highlight the potential of refractive index as a possible detection parameter of a tumor in a surrounding safe tissue.

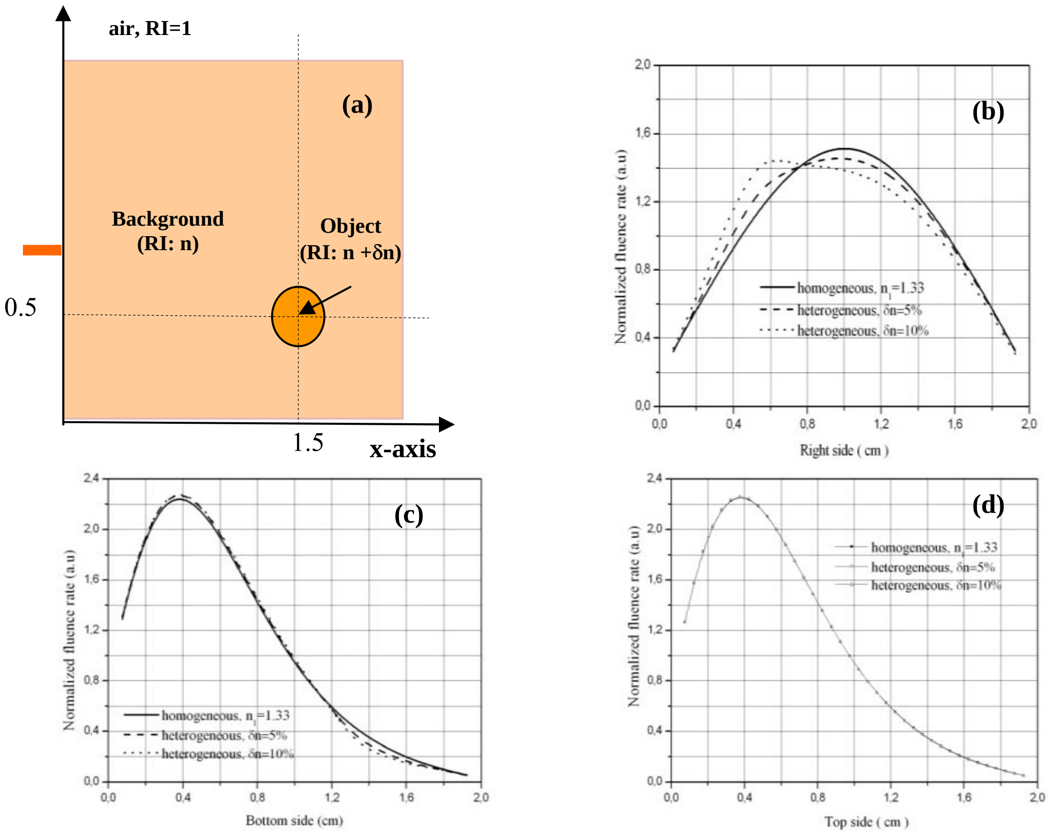

Figure 2. Detection of heterogeneous inclusion by the effect of local refractive index increase: (a) geometry of the considered medium and object, (b) detected fluence rate on the right side, (c) detected fluence rate on the bottom side (d) detected fluence rate on the top side

5. Conclusion

This study attempted to develop a computational way helping in detection of abnormalities in a biological tissue. This should enable predictions of eventual tumor existence when using a diffuse optical tomography scheme. The used model is based on stationary radiative transfer equation including a possible variation of refractive index. In particular, computational technique of Legendre transform is extended to handle angular derivative terms arising by the varying refractive index consideration. The obtained computational model is implemented to investigate some practical situations in DOT setting. Obtained results showed that variation of refractive index can yield useful predictions about the target and the location of abnormal inclusions within the tissue. These findings open prospects for further study of the effect of local refractive variation in time-domain and frequency-domain schemes in diffuse optical tomography.

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