Modeling of the Singlet Oxygen Distribution in Photofrin-Photodynamic Therapy of the Plural Cavity

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Introduction: Photofrin-mediated photodynamic therapy (PDT) is used after surgical resection at the University of Pennsylvania to treat the microscopic disease for malignant pleural mesothelioma and to increase survival rate. When Photofrin is exposed to laser light at 630 nm in well-oxygenated tissue, it produces reacted singlet oxygen ($[^1O_2]_{rx}$) that kills cancer cells. As $[^1O_2]_{rx}$ is imperative to PDT efficacy, we use COMSOL Multiphysics to simulate the distribution of $[^1O_2]_{rx}$ on every point of the plural cavity surface that is being treated. The geometry of the pleural cavity was obtained during the surgery using an IR camera–based navigation system (NDI) [1]. The initial Photofrin concentration inside the pleural cavity and the light fluence used for the simulation of $[^1O_2]_{rx}$ were measured during PDT [1, 2].

Use of COMSOL Multiphysics® Software: The NDI acquired volume was imported into COMSOL. The fluence values were also imported as 3D fluence clouds and were assigned to their respective positions (x, y, and z) on the NDI contour. Then, calculation of the equations (1)-(3) was performed in order to simulate temporal changes of oxygen ($[^3O_2]$), and distribution of Photofrin ($[S_0]$), and $[^1O_2]_{rx}$ on the surface of pleural cavity.

$$\frac{d[^3O_2]}{dt}+\left(\xi\frac{\phi[S_0]}{[^3O_2]+\beta}\right)[^3O_2]=g\left(1-\frac{[^3O_2]}{[^3O_2]_0}\right) \quad (1)$$

$$\frac{d[S_0]}{dt}+\left(\xi\sigma\frac{\phi([S_0]+\delta)[^3O_2]}{[^3O_2]+\beta}\right)[S_0]=0 \quad (2)$$

$$\frac{d[^1O_2]_{rx}}{dt}-\left(\xi\frac{\phi[S_0][^3O_2]}{[^3O_2]+\beta}\right)=0 \quad (3)$$

where, light fluence rate, ϕ = 75 mW/cm^2, and initial tissue oxygenation, $[^3O_2]_0$= 40 μM. Table 1 presents the definitions and values of photochemical parameters, ξ, σ, β, δ, and g.

Table 1. Photofrin photochemical parameters [3]

Parameter	Definition	Value
ξ (cm^{2}s^{-1}mW^{-1})	Specific oxygen consumption rate	3.7×10^{-3}
σ (μM^{-1})	Specific photobleaching ratio	7.6×10^{-5}
β (μM)	Oxygen quenching threshold concentration	11.9
δ (μM)	Low concentration correction	33
g (μM/s)	Maximum oxygen supply rate	0.76
$[^3O_2]_0$ (μM)	Initial ground-state oxygen concentration	40

Results: In the ongoing clinical trial, the prescribed light fluence dose for Photofrin-PDT for mesothelioma is 60 J/cm^2. As shown in Fig. 1(a), the magnitude of the delivered fluence changes from 54.5 to 73.6 J/cm^2 on the surface of the pleural cavity.
As $^1O_2$ generation depends in part on the availability of $^3O_2$ in the target tissue, knowing the level of $[^3O_2]$ during PDT is important. Fig. 2 (b) shows the changes of $[^3O_2]$ calculated for ϕ = 75 mW/cm^2 and initial Photofrin concentration of 2.8 μM.

In order to account for the heterogeneity, the initial Photofrin concentration was simulated to change from 0.47 to 11.5 μM in the z direction as shown in Fig. 1(c).

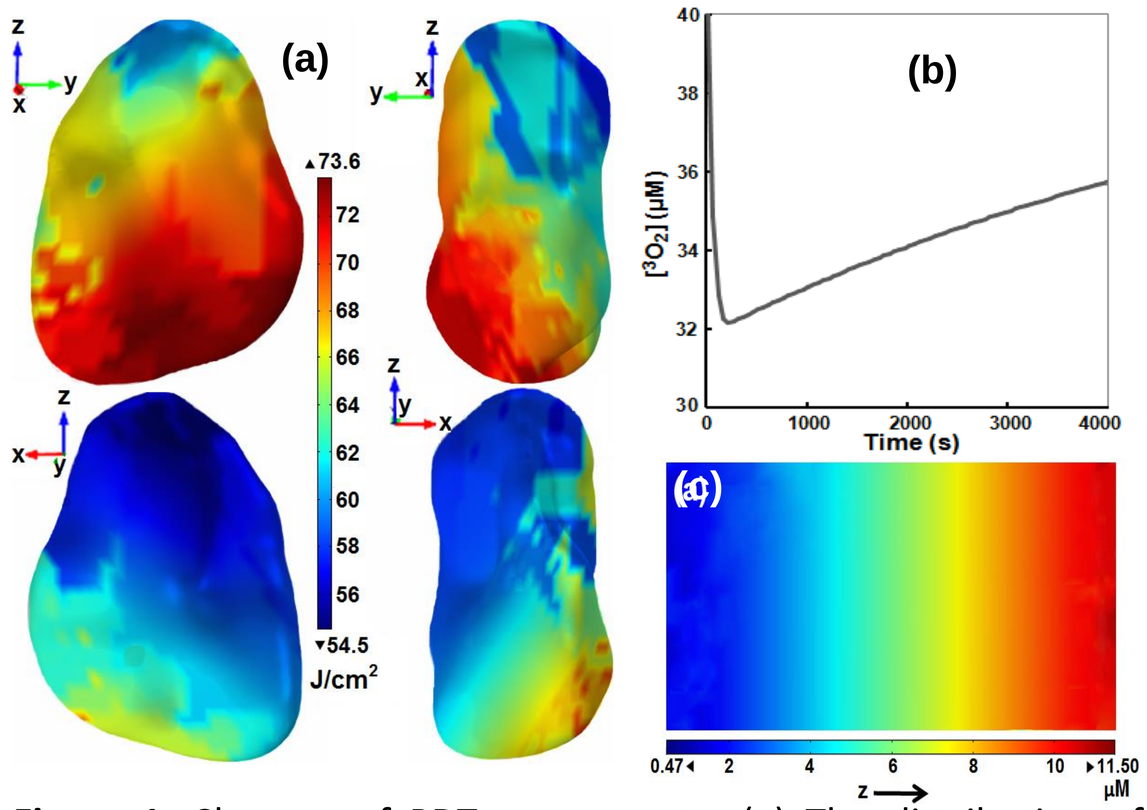

Figure 1. Changes of PDT components. (a) The distribution of light fluence on the surface of pleural cavity. (b) Temporal changes of tissue oxygenation. (C) The changes of Photofrin in the z direction. The color bar shows the different magnitude.

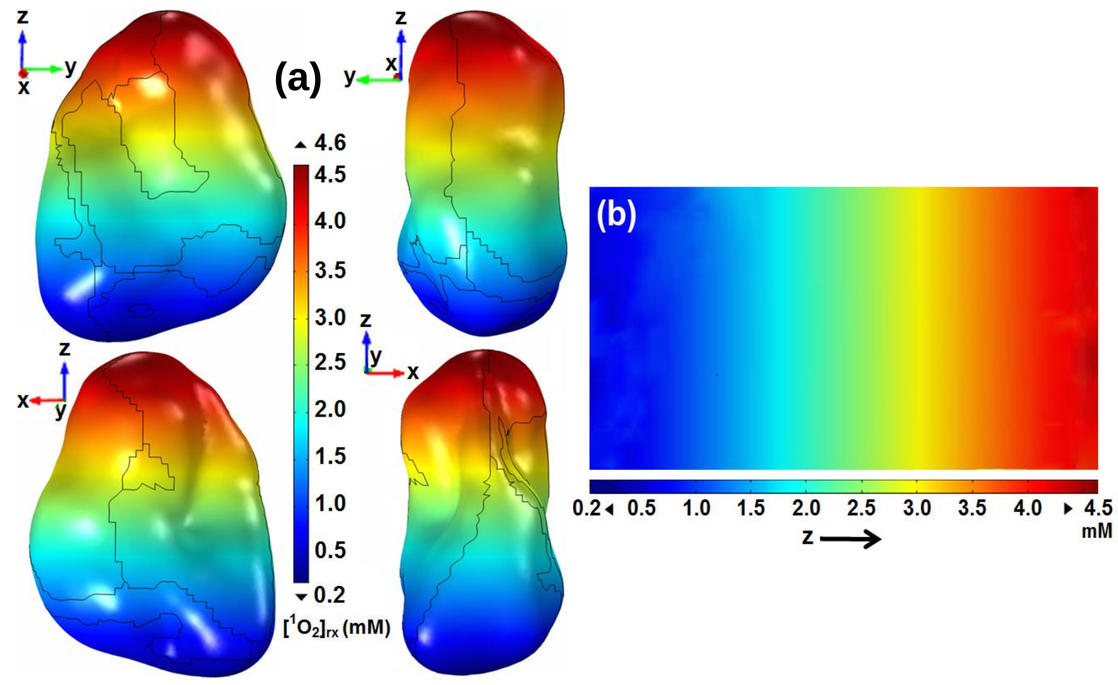

Figure 2. (a) 3D, and (b) 2D $[^1O_2]_{rx}$ distribution on the surface of pleural cavity. The calculations are based on the PDT components in Fig. 1. The color bar shows the different magnitude.

Conclusions: The distribution of $[^1O_2]_{rx}$ during PDT was simulated and mapped on the treated plural cavity by using COMSOL. The final target of this work will be to implement this method in real-time for clinical applications. We believe that *in situ* monitoring of the under- and over- exposed regions to $[^1O_2]_{rx}$ can significantly improve the treatment.

References:

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