Modeling Of Reactive Oxygen Species Distribution In Pleural Cavity Photodynamic Therapy

Hongjing Sun[1], Timothy Zhu[1]

[1]University of Pennsylvania

Abstract

Pleural photodynamic therapy (PDT) represents a promising treatment approach for malignant pleural mesothelioma. However, optimizing treatment efficacy requires accurate prediction of reactive oxygen species ([ROS]rx) distribution, which is challenging due to complex cavity geometries and heterogeneous photosensitizer distributions. This study develops a comprehensive COMSOL Multiphysics model for simulating singlet oxygen generation during pleural PDT using real clinical data from 11 patient cases.

We implemented a macroscopic kinetic model in COMSOL Multiphysics through a system of coupled differential equations governing the dynamics of ground-state oxygen ($[^3O_2]$), photosensitizer concentration ($[S_0]$), and reactive oxygen species ([ROS]rx), as shown in Figure 1 [1]. Key model parameters were experimentally determined: specific oxygen consumption rate ($\xi = 3.7\times10^{-3}$ $cm^2s^{-1}mW^{-1}$), specific photobleaching ratio ($\sigma = 7.6\times10^{-5}$ μM^{-1}), oxygen quenching threshold ($\beta = 11.9$ μM), low concentration correction ($\delta = 33$ μM), maximum oxygen supply rate ($g = 0.76$ μM/s), and initial ground-state oxygen concentration ($[^3O_2]_0 = 40$ μM) [2,3].

The model's input data came directly from clinical cases, including pleural cavity geometry and light fluence (φ) distribution obtained via an NDI navigation system. Navigation data was available for 11 cases (04, 08, 12, 14, 16, 17, 18, 20, 27, 37, 38), providing real patient geometries for our simulations. Previous modeling attempts used randomly oriented, oversimplified geometries that limited clinical applicability [2]. To enable meaningful cross-patient comparisons, we developed a standardized anatomical coordinate system with consistent orientation and landmark positioning, as illustrated in Figure 2. A significant technical improvement was our approach to geometry handling in COMSOL. Rather than using surface interpolation that loses anatomical detail, we developed a method to convert 3D point cloud data directly into COMSOL-compatible format, preserving critical geometric features. This approach maintains the intricate surface details of the pleural cavity essential for accurate light distribution modeling.

Photofrin concentration measurements from clinical samples demonstrated substantial spatial heterogeneity (0.5-4.5 mg/kg) across different cavity regions. Figure 3 illustrates both the concept of photosensitizer gradient effects and the significant inter-patient variability in drug concentrations measured at different anatomical sites. The impact of drug distribution on treatment outcomes is an important consideration in our modeling approach. Our COMSOL simulations for a representative case predicted [ROS]rx concentrations varying from 0.36 to 0.75 mM, as visualized in Figure 4(b). The clinically measured reactive oxygen species values across multiple patients are shown in Figure 4(a), with a mean value of 0.56±0.26 mM. This representative case demonstrates the capability of our modeling approach to identify areas of potentially insufficient photodynamic dose. Similar analyses are being conducted for all 11 clinical cases using the same methodology.

This COMSOL framework enables patient-specific treatment planning and provides a foundation for real-time guidance systems. Ongoing work includes processing all available clinical cases with the improved geometry handling techniques and incorporating complete spatial variation of photosensitizer concentration. This methodology represents a significant advancement in PDT treatment planning, moving from simplified geometric approximations to patient-specific, physics-based models that can guide clinical decision-making.

Reference

[1] Rozhin, Penjweini at al. "Modeling of the Singlet Oxygen Distribution in Photofrin- Photodynamic Therapy of the Plural Cavity." COMSOL Conference 2016.
[2] Ken Kang-Hsin, Wang et al. “Explicit dosimetry for photodynamic therapy: macroscopic singlet oxygen modeling.” Journal of biophotonics vol. 3,5-6 (2010): 304-18.
[3]Timothy C, Zhu et al. “In-vivo singlet oxygen threshold doses for PDT.” Photonics & lasers in medicine vol. 4,1 (2015): 59-71.
[4] Hongjing, Sun et al. “Comprehensive reanalysis of light fluence distribution in pleural photodynamic therapy using standardized anatomical coordinates.” Photochemistry and photobiology, 10.1111/php.14063. 21 Jan. 2025.

Figures used in the abstract

(a)

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

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

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

(b)

Parameter	Definition	Value
ξ ($cm^2s^{-1}mW^{-1}$)	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 ($\mu M/s$)	Maximum oxygen supply rate	0.76
$[^3O_2]_0$ (μM)	Initial ground-state oxygen concentration	40

Figure 1 : Macroscopic kinetic model implemented in COMSOL Multiphysics: (a) System of coupled differential equations governing ground-state oxygen ($[^3O_2]$), photosensitizer ($[S_0]$), and reactive oxygen species (ROS]rx) dynamics; (b) Key model parameters with experime

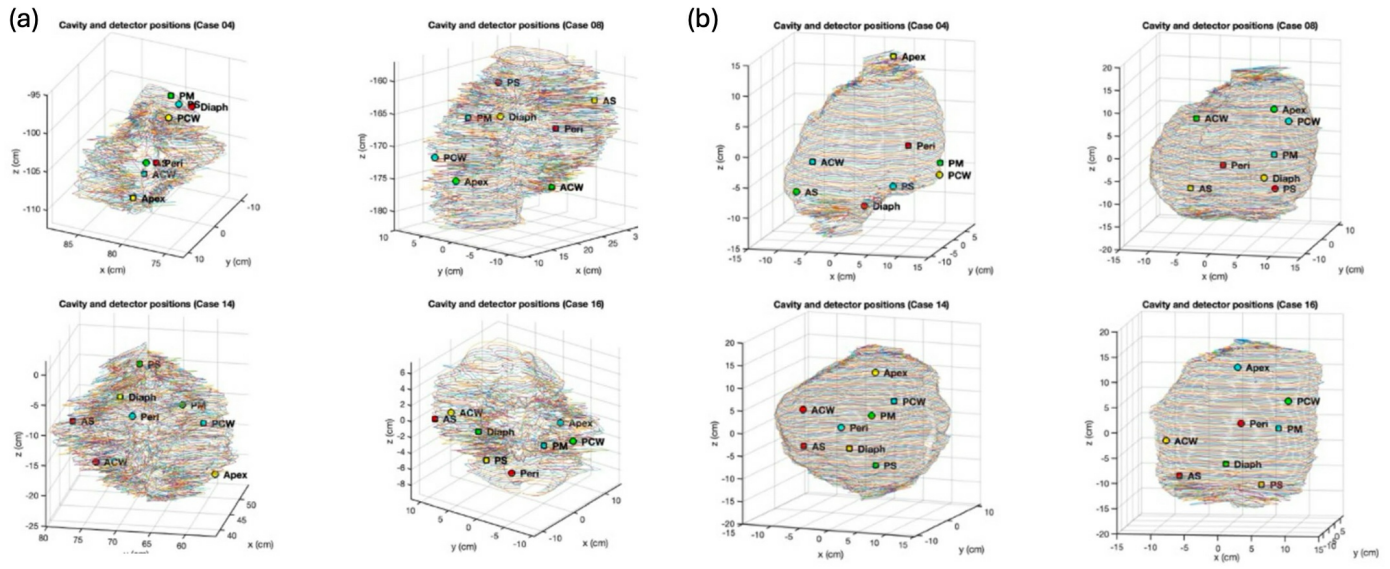

Figure 2 : Implementation of standardized anatomical coordinate system for pleural cavity geometries: (a) Original randomly oriented cavity geometries from four clinical cases in camera coordinates, making cross-patient comparison difficult; (b) The same cases after

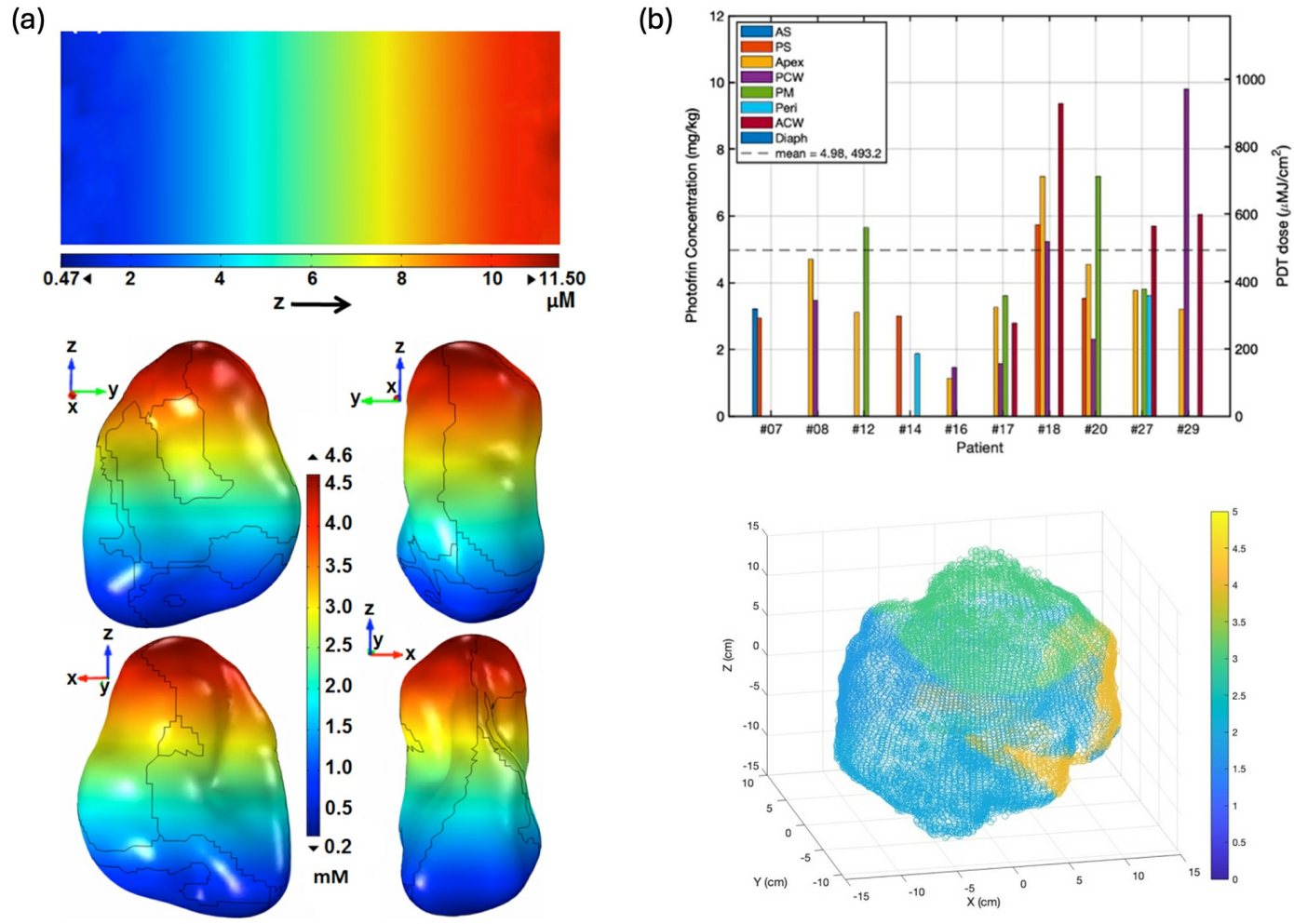

Figure 3 : Impact of photosensitizer distribution on treatment modeling: (a) Illustration of photosensitizer gradient effects in the pleural cavity, demonstrating how concentration varies spatially within the treatment volume; (b) Clinical measurements of Photofrin

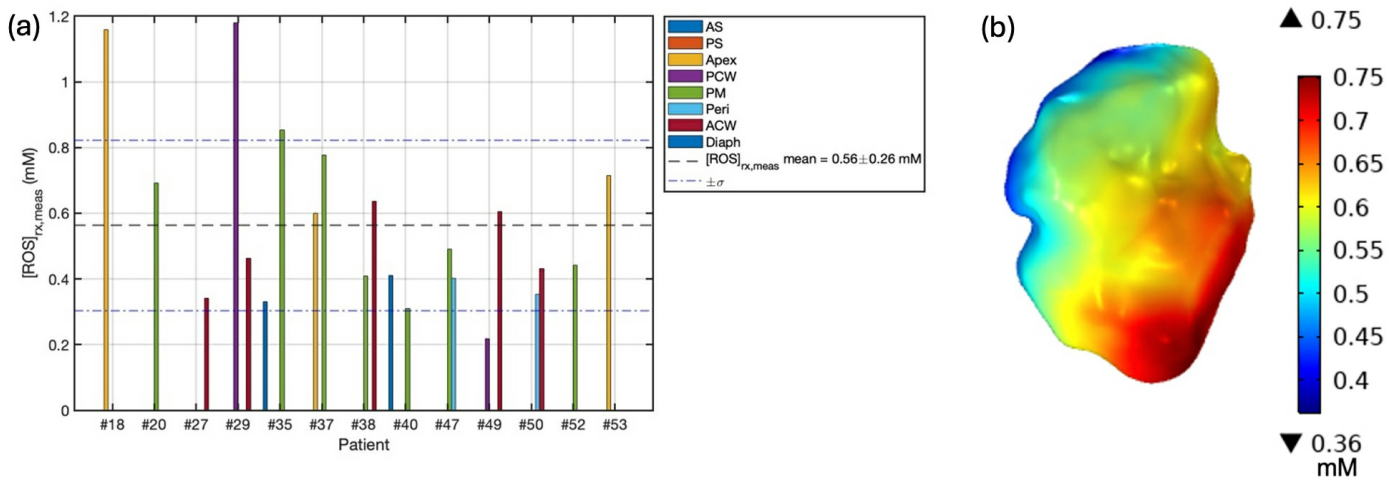

Figure 4 : Reactive oxygen species distribution analysis: (a) Measured [ROS]rx concentrations at different anatomical locations across multiple patients, with a mean value of 0.56±0.26 mM; (b) Three-dimensional visualization of [ROS]rx distribution from COMSOL simul