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COMSOL-based Reactive Oxygen Species Modeling with Deformable Image Registration for Organ-at-Risk Dosimetry in Pleural PDT

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ABSTRACT

Purpose: This study develops an integrated framework combining three-dimensional deformable registration with reactive oxygen species ($[ROS]_{rx}$) distribution calculation in pleural Photodynamic Therapy (PDT).

Methods: Navigation data from 10 clinical cases were processed to reconstruct patient pleural cavity geometries. A deformable registration model based on elastic mechanics was developed to register CT data prePDT (including OARs lung, heart, and esophagus) with the patient lung geometry. Light fluence based on navigation tracking were combined with PS drug map as input to solve macroscopic kinetic equations in COMSOL for $[ROS]_{rx}$ calculation.

Results: Volume-averaged $[ROS]_{rx}$ values ranged from 0.43 to 0.81 mM. Comparison with point measurements showed difference of -28.8% to 18.3% using clinically measured mean $[ROS]_{rx}$. The COMOSOL-simulated mean $[ROS]_{rx}$ was 0.68±0.11 mM compared to the clinical mean of 0.73±0.13mM. Point to point comparisons between COMSOL and clinical results show difference is less than 10%.

Conclusion: [ROS] modeling coupled with deformable registration can provide $[ROS]_{rx}$ distribution on pleural cavities as well as OARs. Comparison with point measurements yield good agreements.

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The results of this poster has since been published in Hongjing Sun *et al*, antioxidants 2026, 15(5), 616.

REFERENCES

1. Hongjing Sun *et al*, antioxidants 2024, 13(12), 1436.

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INTRODUCTION

- Photodynamic therapy (PDT) delivers light-activated reactive oxygen species (ROS) to eradicate microscopic residual disease after resection of malignant pleural mesothelioma (MPM).
- Reacted singlet oxygen concentration ($[ROS]_{rx}$) is a more mechanistically grounded, clinically predictive dosimetric endpoint than light fluence or drug dose alone.
- Conventional dosimetry samples only 8 discrete detector sites — unable to resolve spatial dose heterogeneity or quantify dose to adjacent organs at risk (OARs): lung, heart, esophagus.
- Pre-op CT anatomy and the intra-operative pleural cavity differ substantially after surgical resection, so rigid registration cannot accurately map OAR dose.
- Develop and validate an integrated 3D dosimetry framework in COMSOL Multiphysics that couples a macroscopic photophysical kinetic model with two-stage deformable image registration (DIR) to reconstruct spatially resolved $[ROS]_{rx}$ across the pleural surface and map dose onto registered OAR structures (see Figure 1).

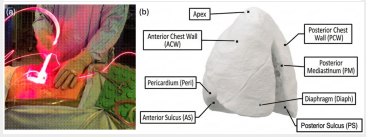

Figure 1. *(a) Intraoperative pleural PDT light delivery. (b) Eight standardized anatomical detector landmarks defining a patient-independent coordinate system.*

METHODS AND MATERIALS

Clinical model inputs

- Light fluence ϕ and Photofrin concentration [S_0] were spatially interpolated across each patient's cavity mesh from detector measurements — both vary markedly across the pleural surface and between patients, motivating fully patient-specific 3D dosimetry rather than uniform-dose assumptions (Figure 2).

Clinical model inputs

- 10 patients received Photofrin (2 mg/kg IV, 24 h pre-op) and 630 nm intraoperative laser light swept across the resected pleural surface, sampled by 8 isotropic detectors with simultaneous IR navigation tracking.
- $[ROS]_{rx}$ computed from a coupled ODE system for ground-state oxygen [$^3O_2$], photosensitizer [S_0], and reacted singlet oxygen (parameters ξ, β, δ, σ, g from Photofrin-PDT fits), solved in COMSOL Multiphysics 6.3 with fluence ϕ and [S_0] as spatially-interpolated input fields.

Geometry Reconstruction & OAR Import

- IR navigation point clouds standardized to a canonical anatomical coordinate system, then converted via spherical-coordinate reconstruction directly into a COMSOL tetrahedral mesh, preserving cavity concavities.

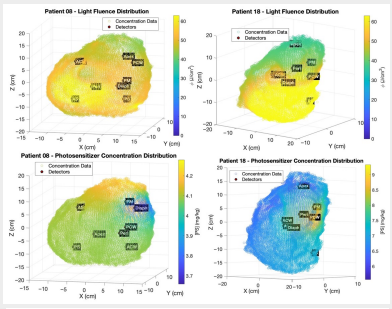

Figure 2. *Light fluence φ (top) and interpolated Photofrin concentration [S_0] (bottom) mapped onto the pleural cavity for two representative patients — marked inter-patient heterogeneity in both quantities.*

- Pre-op CT contours of lung, heart, and esophagus exported as DICOM RT structure sets and imported into COMSOL as solid geometries, discretized into tetrahedral FE domains (Figure 3).

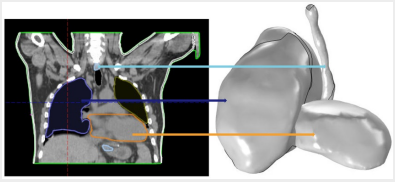

Figure 3. *Coronal CT with contoured OARs — heart, esophagus, lung (left) — and corresponding 3D COMSOL solid geometries (right).*

RESULTS

- The two-stage DIR successfully aligned CT-derived lung geometry to the intraoperative navigation surface despite substantial surgical deformation.
- Post-registration accuracy is consistent with published sub-centimeter benchmarks for FEM-based DIR in thoracic and abdominal applications, confirming boundary alignment sufficient for downstream OAR dose mapping (Figure 4).
- Volume-averaged $[ROS]_{rx}$ ranged from 0.43 mM (Case 12) to 0.81 mM (Case 38) — up to a 1.9-fold variation between patients (Figure 5).

Table 1. *Comparison of COMSOL-simulated volume-averaged $[ROS]_{rx}$ and clinically calculated mean $[ROS]_{rx}$ at discrete detector locations [1] for the ten-patient cohort. Percentage difference quantifies the deviation between the two methods.*

Case No.	COMSOL-Simulated $[ROS]_{rx}$ * (mM)	Clinical $[ROS]_{rx}$ # (mM)	Percentage Difference
08	0.67 ± 0.03	0.64 ± 0.10	4.69%
12	0.43 ± 0.08	0.58 ± 0.23	−26.6%
14	0.71 ± 0.04	0.99 ± 0.17	−28.8%
16	0.77 ± 0.04	0.80 ± 0.18	−3.8%
17	0.67 ± 0.07	0.75 ± 0.10	−10.8%
18	0.72 ± 0.11	0.67 ± 0.14	7.3%
20	0.68 ± 0.08	0.90 ± 0.11	−24.0%
27	0.59 ± 0.06	0.67 ± 0.07	−11.6%
37	0.71 ± 0.09	0.60 ± 0.18	18.3%
38	0.81 ± 0.12	0.70 ± 0.26	15.7%
Mean ± SD	0.68 ± 0.11	0.73 ± 0.13	−6.0%

* Volume-averaged value. # Mean value from clinically calculated $[ROS]_{rx}$ at discrete locations.

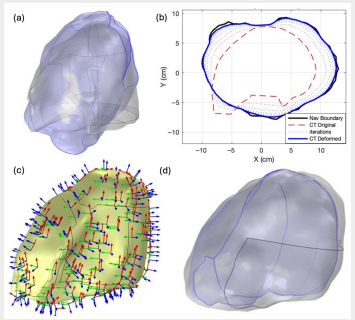

Figure 4. *Registration for a representative patient: (a) initial navigation/CT overlay; (b) iterative boundary convergence (X–Y plane); (c) Stage-2 von Mises stress & displacement field; (d) final registered overlay.*

- The COMSOL-simulated mean $[ROS]_{rx}$ was 0.68 ± 0.11 mM compared to the clinical mean of 0.73 ± 0.13 mM, yielding an overall mean percentage difference of -6%. Individual case differences ranged from -28.8% to 18.3% (Table 1).
- Intra-patient site-to-site differences reached up to 2.4-fold within a single cavity (e.g., Case 38: 0.43 mM at the Apex vs. 1.04 mM at the Posterior Sulcus, Fig.5).
- Focal regions below 0.56 mM [1] Photofrin singlet-oxygen threshold may indicate undertreated residual disease; focal high-dose regions on OAR surfaces may signal risk of off-target photodynamic injury.

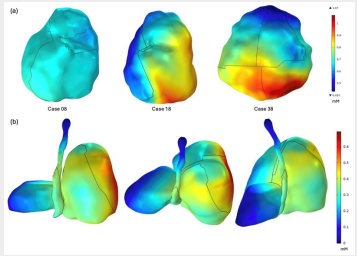

Figure 5. *(a) Cumulative $[ROS]_{rx}$ for three representative cases, each on its own color scale — marked inter-patient heterogeneity. (b) $[ROS]_{rx}$ mapped onto the treated lung and registered OARs (esophagus, heart) from lateral, superior, and posterior views.*

CONCLUSIONS

- First framework to unify 3D $[ROS]_{rx}$ kinetic modeling with FEM-based deformable registration, enabling patient-specific OAR dose mapping in pleural PDT.
- Two-stage DIR aligned CT anatomy to the intraoperative navigation surface with sub-centimeter accuracy, enabling the first patient-specific $[ROS]_{rx}$-to-OAR dose mapping in pleural PDT.
- Establishes a foundation for dose-volume-histogram-based treatment evaluation, OAR safety profiling, and future real-time intraoperative dosimetric guidance.