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A summary of light dose distribution using an IR navigation system for Photofrin-mediated Pleural PDT

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Abstract

Uniform delivery of light fluence is an important goal for photodynamic therapy. We present summary results for an infrared (IR) navigation system to deliver light dose uniformly during intracavitory PDT by tracking the movement of the light source and providing real-time feedback on the light fluence rate on the entire cavity surface area. In the current intrapleural PDT protocol, 8 detectors placed in selected locations in the pleural cavity monitor the light doses. To improve the delivery of light dose uniformity, an IR camera system is used to track the motion of the light source as well as the surface contour of the pleural cavity. A MATLAB-based GUI program is developed to display the light dose in real-time during PDT to guide the PDT treatment delivery to improve the uniformity of the light dose. A dualcorrection algorithm is used to improve the agreement between calculations and in-situ measurements. A comprehensive analysis of the distribution of light fluence during PDT is presented in both phantom conditions and in clinical cases.

Keywords

Photodynamic therapy; navigation system; Photofrin; Pleural PDT

Introduction

PDT is a local treatment aptly suitable to treat malignant, localized tumors such as those observed in malignant pleural mesothelioma (MPM).[1, 2] MPM has no standard treatment and the median survival for diagnosed patients is 6 to 17 months, depending on the disease stage. To treat MPM, PDT is coupled with surgical resection of the tumorous tissue, part of a trend in multi-modal regimes to increase survival rates. The photosensitizer is administered to the patient, followed by a latent period referred to as the illumination time. After the illumination time is fulfilled, debulking surgery is performed, followed by illumination.

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Accurate light dosimetry is imperative to ensure the treatment efficacy. We propose a novel method to guide the PDT treatment in order to achieve uniform distribution of light fluence. This novel method differs from the existing protocols in following aspects: 1) 4D (3D plus time) information of the treatment is obtained using this method by real-time updated unwrapped images; 2) The accumulative light fluence of every single point of the cavity surface being treated is displayed during the guidance, whereas the existing protocol displays light fluence information from a small number of locations.

The pleural treatment program at Penn treats patients with MPM or malignant pleural mesothelioma. Starting 2014, a Phase II Photofrin-mediated PDT protocol was utilized for the IR navigation system. The photosensitizing drug, Photofrin®, is administered 24 hours before irradiation at a dosage of 2 mg/kg using 630 nm laser light at a light dose of 60 J/cm^2. Within the thoracic cavity, the light delivery is continuously administered by a moving point source applied by radiation oncologist or the surgeon. It is at this point in the PDT treatment where real-time dosimetry guidance becomes most critical. As the light source is applied, the knowledge of how well each particular area of the thoracic cavity is being irradiated will make the entire treatment process more effective and efficient and can serve to better personalize treatment delivery. This study is a progress report of our original IR navigation system for Pleural PDT.[3]

2. Methods

2.1 Infrared tracking system

The Polaris® Spectra (North Digital Inc., Waterloo, Canada) system was used as the infrared (IR) camera to track treatment motion in 3D. Passive spherical markers (Fig. 1a) were used for the IR system to track the motion, and the accuracy of the system was ~0.5 mm in 3D. The maximum volume for the system was ~ 205 × 186 × 147 cm^3, which was proper for operations on our patient population (Fig. 1b). Once the positioning wand was inside the working volume, the camera system started to track the position of the laser source. The position data were transferred to a computer using OpenIGTLink [4] at a rate of 20 - 60 Hz and can be displayed and processed by Matlab® (Mathworks, Natick, MA) in real time.

2.2 Modified treatment wand

The procedure of the image-guidance system for pleural PDT is described elsewhere.[5, 6] The modified treatment wand (Fig. 1a) was used in this procedure to complete the image guidance for taking treatment surface contour and for tracking the light source positions during PDT treatment. It was calibrated to locate its tip position by pivoting it around a fixed point (Fig. 1a). Then an optimization algorithm was used to determine the shift between the treatment wand tip and the laser point source. [6] A separate wand with a steel tip was used to locate the detectors on the cavity surface, and also to determine the cavity contour. When the PDT treatment began using the treatment wand, the light fluence distribution on the cavity surface is calculated simultaneously so that the treatment can be guided by the real-time light fluence image to achieve a uniform light fluence on the cavity. To verify the image-guidance procedure, detectors were attached on the cavity surface so that the calculated light fluence can be compared with the measurements at multiple positions.

2.3 Light fluence calculation

One can calculate the light fluence rate (φ) by summing up the direct and the scattering light during pleural PDT. The light fluence rate follows a simple formula for a point source plus a constant for the scatter light, i.e.,

$$\phi=(\frac{S}{4\pi r^2}+g)\cdot \mathrm{CF}, \quad (1)$$

where r is the distance from the point of interest to the laser point source and g is a constant to account for scatter light at a particular light source position, CF is a constant correction factor to match that of the light fluence measurement using a dual-correction method described elsewhere [5]. The value of g is currently a constant for each patient. Two types of calculations were made: (1) Uncorrected light fluence was calculated using directly light only, i.e., $g = 0$ and $CF = 1$; (2) Corrected light fluence using Eq. (1), where the value of CF is determined by a dual-correction method where a proper CF value was applied to minimize difference between calculation and measurement every 30 s and 150 s for local fluence over the last 30 s and the total cumulative fluence over the entire treatment, respectively [5].

The light fluence during pleural PDT treatment was calculated on each point of the reconstructed surface contour, so that 4D (x, y, z, t) information on the contour surface is obtained. For visualization purposes, the 3D light fluence map at any particular time point was unwrapped into a 2D plane, so that the x-axis of the 2D mesh represents the azimuth angle, the y-axis of the 2D mesh represents the height (or z in 3D). This 2D light fluence mesh can be updated in real-time so that it can guide the PDT treatment for uniform light fluence distribution.

3. Results

3.1 Determination of laser source position

Table 1 shows the laser source position determined after each PDT case for x, y, z (in mm) for each patient. The overall shift of the source position was 0.96 ± 1.1 mm.

3.2 Image guidance results in patients

We have monitored the light source position during treatment for 7 patients for Photforin-mediated Pleural PDT using the modified wand (see Table 2). The average %deviations in all detector locations before and after correction are shown as well. For one of the patient (008), we didn't get the location of the detector, thus cannot compare the calculation with the measurements.

Figures 2-7 shows the final results of light fluence distribution for 6 patients. The left panel shows the 2D profiles distribution along with the location of the detectors marked by “x”, the right panel shows the profiles for each horizontal angles, where the dark line is the mean profile and the grey area is the 1σ standard deviation of the mean profile.

4. Discussion and Conclusion

Among 11 patients underwent Photofrin-mediated PDT, we obtained good data in 64% (7/11) patients. Among patients with good data, we can apply a correction introduced previously in 86% (6/7) patients. Among patients with correction, 100% (6/6) get agreement in all sites (Table 2).

An analysis of all 6 patients with corrected light fluence results (Figs. 2 -7) shows that final fluence deviates with prescription with a %St. dev. of 11% with a maximum variation of up to 30% (see Table 3). Notice that largest peak in Figs. 2 - 7 actually corresponding to light fluence at the surgical opening and does not reflect the actual light fluence uniformity on the pleural surface, these large variations of fluence are excluded in the final analysis.

Acknowledgments

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References

1. Pass HI, DeLaney TF, Tochner Z, Smith PE, Temeck BK, Pogrebniak HW, Kranda KC, Russo A, Friauf WS, Cole JW, et al. Intrapleural photodynamic therapy: results of a phase I trial. Ann Surg Oncol. 1994; 1:28–37. [PubMed: 7834425]
2. Pass HI, Tochner Z, DeLaney T, Smith P, Friauf W, Glatstein E, Travis W. Intraoperative photodynamic therapy for malignant mesothelioma. Ann Thorac Surg. 1990; 50:687–688. [PubMed: 2222072]
3. Zhu TC, Kim MM, Jacques SL, Penjweini R, Dimofte A, Finlay JC, Simone CB II, Cengel KA, Friedberg J. Real-time treatment light dose guidance of pleural PDT: an update. Proc SPIE. 2015; 9308:930809.
4. Tokuda J, Fischer GS, Papademetris X, Yaniv Z, Ibanez L, Cheng P, Liu H, Blevins J, Arata J, Golby AJ, Kapur T, Pieper S, Burdette EC, Fischtinger G, Tempany CM, Hata N. OpenIGTLink: an open network protocol for image-guided therapy environment. Int J Med Robot. 2009; 5:423–434. [PubMed: 19621334]
5. Zhu TC, Liang X, Kim MM, Finlay JC, Dimofte A, Rodriguez C, Simone CB II, Friedberg JS, Cengel KA. An IR Navigation System for Pleural PDT. Front Phys. 2015; 3:9. [PubMed: 25995987]
6. Zhu TC, Kim MM, Liang X, Liu B, Meo JL, Finlay JC, Dimofte A, Rodriguez C, Simone CB II, Cengel KA, Friedberg JS. Real-time treatment feedback guidance of pleural PDT. Proc SPIE. 2013; 8568:85680O.

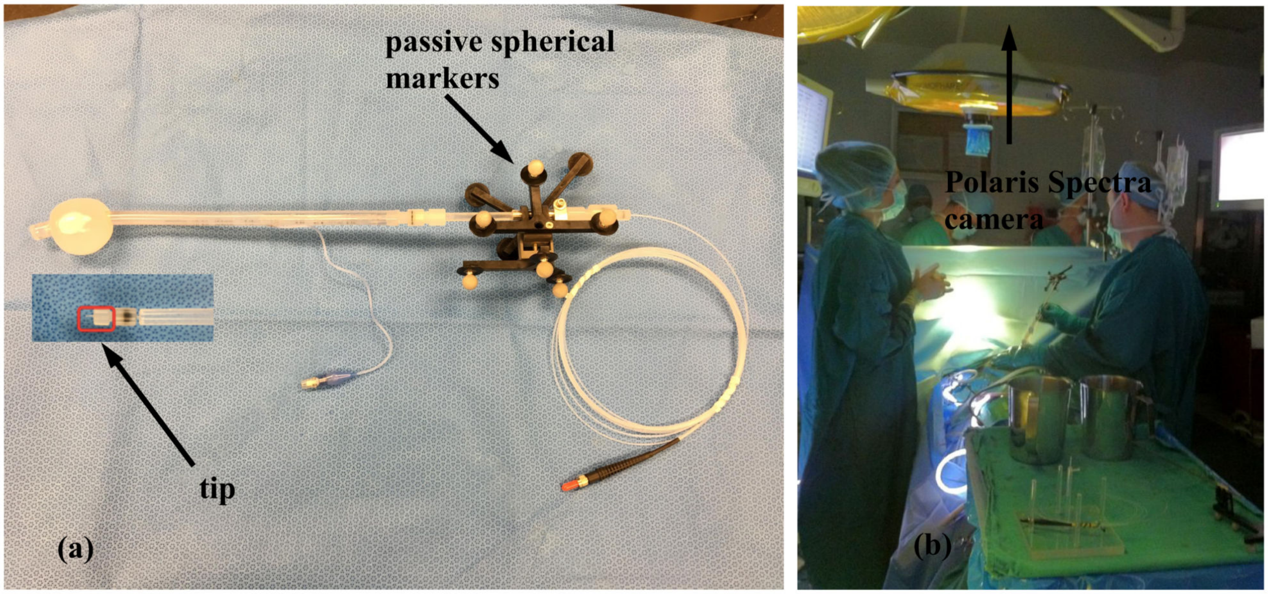

Figure 1.
(a) a modified treatment wand with passive reflective spherical balls mount directly on a plastic rod that leads to the laser fiber tip directly and (b) IR camera to monitor movement of a point in a 3D volume (205×186×147 cm^3) in OR.

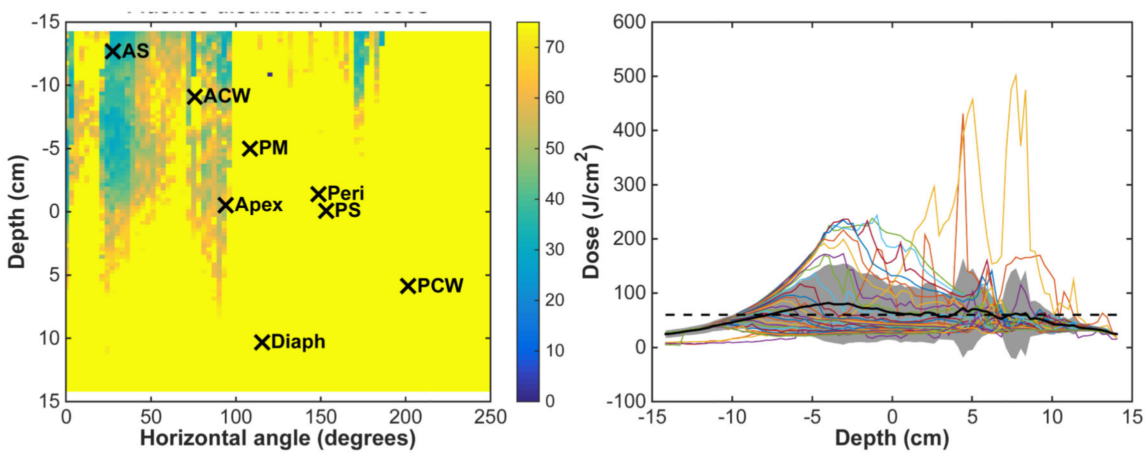

Figure 2.

Corrected light fluence at the end of treatment for patient 012 in Photofrin-mediated pleural PDT. The final light fluence should be 60 J/cm^2.

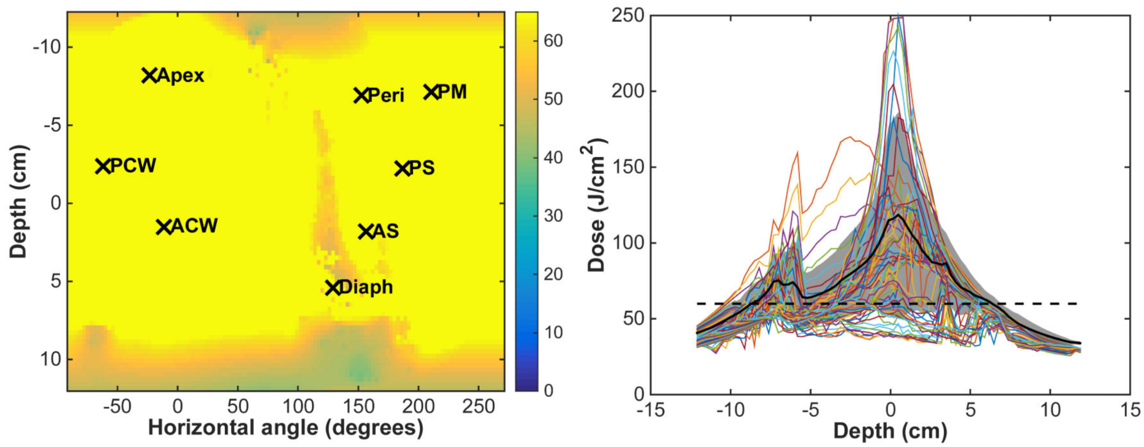

Figure 3.

Corrected light fluence at the end of treatment for patient 014 in Photofrin-mediated pleural PDT. The final light fluence should be 60 J/cm^2.

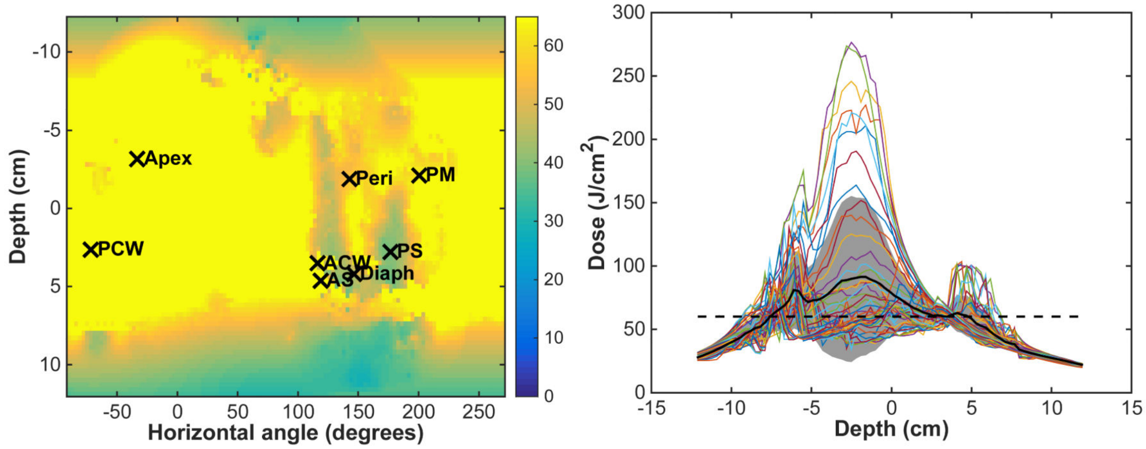

Figure 4.

Corrected light fluence at the end of treatment for patient 016 in Photofrin-mediated pleural PDT. The final light fluence should be 60 J/cm^2.

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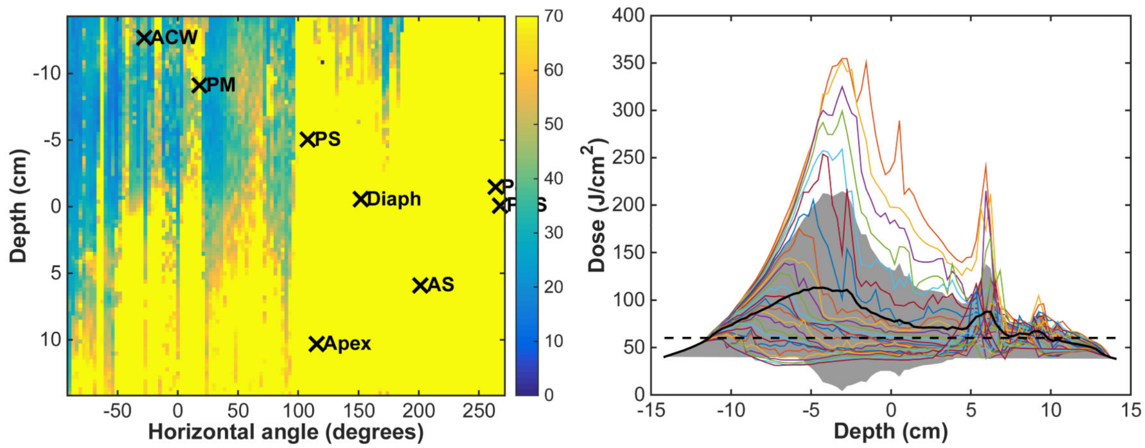

Figure 5.

Corrected light fluence at the end of treatment for patient 017 in Photofrin-mediated pleural PDT. The final light fluence should be 60 J/cm^2.

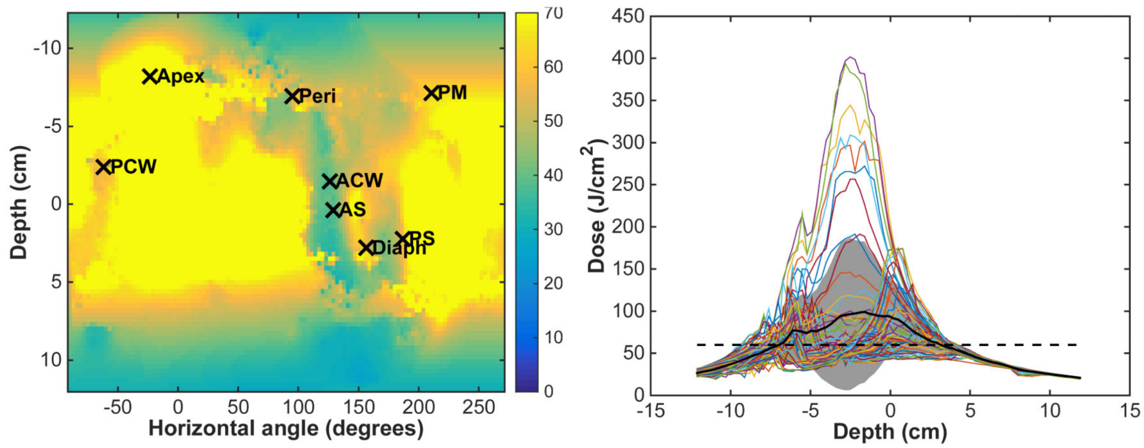

Figure 6.

Corrected light fluence at the end of treatment for patient 018 in Photofrin-mediated pleural PDT. The final light fluence should be 60 J/cm^2.

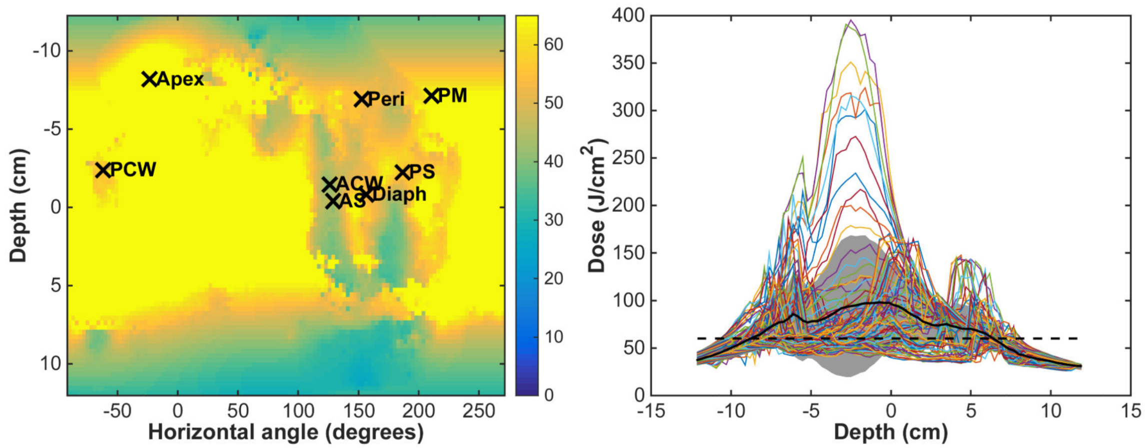

Figure 7.

Corrected light fluence at the end of treatment for patient 020 in Photofrin-mediated pleural PDT. The final light fluence should be 60 J/cm^2.

Table 1

Laser source positions determined after each PDT case.

Patient No.	Shift x (mm)	Shift y (mm)	Shift z (mm)	Average
008	0.88±0.72	0.98±0.12	-0.52±0.42	0.45±0.84
012	1.27±0.11	-0.17±0.04	-0.46±0.26	0.21±0.93
014	0.70±0.42	0.80±0.78	-0.62±0.45	0.29±0.79
016	-0.28±0.13	-0.92±0.19	-0.53±0.35	-0.58±0.32
017	1.20±0.43	0.51±0.24	-0.75±0.23	0.32±0.99
018	1.64±0.17	0.46±0.27	-0.48±0.35	0.54±1.06
020	-0.68±0.19	0.44±0.20	-0.89±0.24	-0.37±0.72
Average	0.68±0.85	0.30±0.65	-0.61±0.16	

Table 2

Summary of Clinical application for Photofrin-mediated pleural PDT.

Case No.	Without Correction %Deviation ± %st. dev.	With Correction %Deviation ± %st. dev.	Detector Positions	Number of Detectors
008	NA	NA	N	--
012	66.5±17.5	13.9±9.1	Y	8
014	72.5±16.9	14.5±16.5	Y	8
016	68.8±11.2	14.6±9.4	Y	6
017	55.0±19.1	14.9±6.10	Y	8
018	76.3±13.4	10.0±7.4	Y	8
020	84.2±10.2	15.4±11.5	Y	8
Average	**74.8±7.4**	**13.7±2.1**		

Table 3

Summary of Profile uniformity during Photofrin-mediated pleural PDT

Case No.	% Standard deviation	% Variation of st. dev
012	6.8%	49%
014	11.2%	13.3%
016	9.3%	15.2%
017	15.7%	51.3%
018	13.3%	27.7%
020	10.0%	24.5%
Average	**11.0 %**	**30.0 %**