BPD-MA mediated PDT of Spinal Bone Metastases: Determining PDT Threshold Values

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***Abstract*—Spinal bone metastases often present as a diffuse combination of osteolytic and osteoblastic disease. Photodynamic therapy (PDT) is a minimally invasive therapy that has been shown to locally ablate cancer cells within the bony spine. To optimize patient-specific treatment protocols and ensure safety of critical neural structures, the responsivities of the heterogenous tissues to PDT must be known. This work derives a PDT threshold value for the spinal cord using a benzoporphyrin derivative monoacid (BPD-MA) photosensitizer.**

Keywords—Photodynamic therapy, Spinal metastasis model, FullMonte, In silico study

I. Introduction

Spinal metastasis is diagnosed in up to one third of all cancer patients and frequently leads to bone fracture, pain, and neurologic impairment [1]. Photodynamic therapy (PDT) is an emerging treatment option for vertebral bone metastases as demonstrated in a recently completed successful Phase I clinical trial using BPD-MA as the photosensitizer. To further improve PDT efficacy, there is a need for personalized treatment planning whereby light irradiation is optimized based on the anatomy. Such information will direct clinical application with respect to the number, power and interstitial locations of fiber-based diffusers [2]. Critical to safety in this process is knowledge of the photodynamic threshold of the spinal cord. This study aims to derive the spinal cord threshold values of BPD-MA mediated PDT for a preclinical model of spinal bone metastasis using a Monte Carlo simulation and experimentally derived histological data.

II. Material and Methods

A. Animal model

An osteolytic murine model was developed through the intracardiac injection of luciferase transfected human HeLa cervical cancer cells. The animal was treated using BPD-MA mediated PDT (flat-cut optical fiber, 150 mW, 50 J at 690 nm) 14 days after inoculation, and sacrificed after 24 hours [3]. At the time of necroscopy, the region surrounding the PDT treated vertebrae was harvested, fixed in 10% buffered formalin, decalcified and then stained with haematoxcyclin and eosin (H&E) to evaluate cell morphology for quantification of the depth of necrosis.

B. In silico Model

The 3D simulation geometry was constructed with MeshTool based on a segmented murine atlas [4] and assigned tissue optical properties for muscle, bone [5], and spinal cord [6]. As source, a cut-end fiber (200 µm radius, 0.22 NA) was modeled and positioned in the muscle layer above the spinous process. The 3D fluence distribution was computed using FullMonte with 10^8 photon packets [7] and visualized using ParaView 5.6.0.

The photodynamic necrosis threshold for the spinal cord was calculated using $T=2.3\varepsilon CH(r_c)$, where $\varepsilon = 3.3 \times 10^4$ M^{-1} cm^{-1} is the molar extinction coefficient of BPD at 690nm [8], C is the tissue concentration of the photosensitizer (0.065 µg g^{-1} in the spinal cord [9]), and $H(r_c)$ is the fluence at the radius of necrosis.

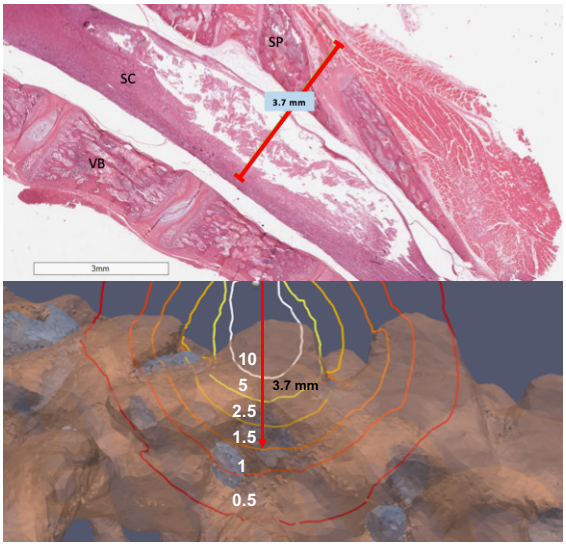

Fig. 1 Top: Histological analysis showing minimum necrotic boundary for the spinal cord. Bottom: Isofluence contours [J/mm^2] overlaying murine Th10 vertebra for irradiation with a cut-end fiber (200µm radius, NA=0.22), located above the spinous process. *SC* spinal cord, *VB* vertebral body, *SP* spinous process.

III. Results and Discussion

The threshold for the spinal cord was calculated to be T ~ 3.5×10^{18} photons cm^{-3} for a necrosis depth of ~3.7 mm and a fluence of ~ 1.5 J mm^{-2} (Figure 1).

Knowledge of the photodynamic necrosis threshold for the spinal cord will minimize chances of spinal cord damage following treatment. Ongoing analysis will resolve BPD-MA mediated PDT threshold values for vertebral bone, surrounding muscle and metastatic tissue in the vertebrae or spinal cord.

IV. References

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Funding was provided by the Canadian Institute of Health Research 125886