iPDT for Glioblastoma Multiforme Management: Dosimetric Enhancements

Daniel Molenhuis[1], Carl Fisher[2], Manjunatha Ankathatti Munegowda[3], Arkady Mandel[3], Fynn Schwiegelshohn[4], Vaughn Betz[4], Lothar Lilge[1,2]

[1]Department of Medical Biophysics, University of Toronto, [2]Princess Margaret Hospital, University Health Network, [3]Theralase Inc., [4]Department of Electrical and Computer Engineering, University of Toronto, Toronto, Canada

Lothar.Lilge@uhnresearch.ca

***Abstract*— Median survival for Glioblastoma patients remains at around 15 months after surgery, radiation, and chemotherapy but varies widely between surgeons and centres. Interstitial Photodynamic Therapy (iPDT) mediated by ALA induced PpIX or other photosensitizers is investigated at various clinics. To enable iPDT treatment planning, photosensitizer transport characteristics needs to be known in order to optimize photoactivation. A method using contrast enhanced, functional magnetic resonance imaging, compartment modelling, spatial frequency domain imaging (SFDI) and inductively coupled plasma mass spectrometry (ICP-MS) is proposed to predict and validate the localization characteristics of two photosensitizers in murine Glioblastoma models.**

Keywords—RG2, fMRI, FullMonte, PpIX, Rutherrin, SFDI

I. Introduction

Glioblastoma has a grave prognosis even with radial resection surgery, aggressive radio and chemotherapy, few large multicentre studies report only a 15-18 months median survival.

Talaporfin Sodium mediated PDT was approved of in Japan with a rigid treatment protocol as adjuvant to surgery. The Munich group showed very good results for iPDT, without personalization of the therapy. iPDT personalization should consider anatomy of the tumour, photosensitizer concentrations in the tissue and the tissue's responsivity to the treatment. In this study, a method for predicting the spatial distribution of photosensitizer concentration using PpIX and Rutherrin is proposed to study the presumption that highly dense tumor microvasculature diffuses photosensitizer poorly. A mesoscopic and microscopic validation using SFDI and ICP-MS is ongoing.

II. Material and Methods

A. In vivo Model

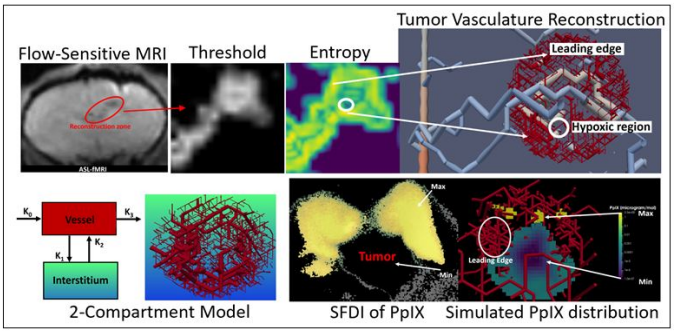
Two orthotopic glioma rat models were used for these studies. RG2 tumors and GSC-30 tumors were injected into the rat neocortex in CDF Fischer and Rag2-/- rats respectively and followed for 10 days and 90 days until reaching an approximate size of 3-4mm in diameter. ALA and Rutherrin were administered IP at 3 mg/kg and 125 mg/kg at 4 hours prior to iPDT and would be given 24 J at 635 nm for PpIX and 600 J at 808 nm for Rutherrin. Quantitative MRI was performed on days -1 Pre- and 11-Day post-tumor injection including DCE and ASL-fMRI. Photosensitizer concentrations were predicted using a two-compartment model and quantified using SFDI for PpIX and ICP-MS for Rutherrin.

B. Predicting Photosensitizer Concentration

DCE maps the interstitial compartment while ASL-fMRI maps both the aberrant vasculature and heterogeneous perfusion. Combined, the mass transfer of photosensitizer is predicted.[1]

III. Results and Discussion

From below figure going from left to right, the first row is a simplified visualization of the tumor vascular compartment reconstruction method using ASL-fMRI. The second row describes the two-compartment model, SFDI drug localization, and *in-silico* PpIX localization.



SFDI identified the localization of PpIX while ICP-MS localization of Rutherrin is ongoing. SFDI shows extravasation of PpIX from the tumor region forming the yellow 'angel-wing' profile surrounding the tumor. *In-silico* mass transfer maps probable PpIX extravasation wherein high concentration regions leak adjacent to the leading edge of the tumor and also remains within the vasculature while minimum concentration is localized at the tumor core. Future work will use this routine for source placement optimization.

IV. References

1. Netti L., et al. *Cancer Res.* 55(22), 5451-8 (1995).

Funding was provided by the Ontario Ministry of Economic Development and Trade through the ORF program RE08-022.