PDT for Glioblastoma Multiforme management: dosimetric enhancements

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***Abstract*— Median survival for Glioblastoma patients remains at around 15 months after surgery, radiation and chemotherapy but varies widely between surgeons and centres. Photodynamic Therapy (PDT) mediated by ALA induced PpIX or other photosensitizers is investigated at various clinics. To enable PDT treatment planning photosensitizer transport characteristics needs to be known in order to optimize photoactivation. A method using contrast enhanced, functional magnetic resonance imaging, computational 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 in Japan with a rigid treatment protocol as adjuvant to surgery. The Munich group showed very good results for interstitial PDT (iPDT) but without personalization of the therapy. 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 localization of two photosensitizers is proposed to study the presumption that highly dense tumor microvasculature diffuses photosensitizer poorly. A mesoscopic and microscopic validation routine is also proposed.

II. Material and Methods

A. In vivo Model

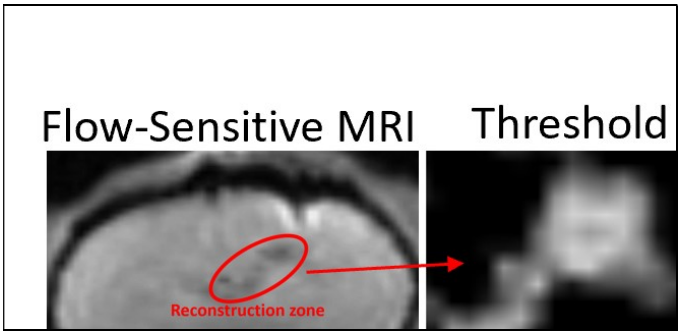
Two orthotopic glioma rat models were used for these studies. RG2 tumors and GSC-30 tumors were injected into the rat neocortex in CDF Fischer and Rag2-/- rats respectively and followed for 10 days and 90 days until reaching an approximate size of 3-4mm in diameter and PDT was performed, Rutherrin and ALA were administered IP at 3 mg/kg and 125 mg/kg at 4 hours prior to iPDT and given 24 J at 635 nm for PpIX and 600 J at 808 nm for Rutherrin for treatment threshold measurements. Quantitative MRI was performed on days -1 Pre-, 3- and 7-Day post-PDT including DCE and ASL-fMRI. Photosensitizer concentrations were predicted using a two-compartment model and quantified using ICP-MS for Rutherrin and SFDI for PpIX.

B. Predicting Photosensitizer Concentration

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

III. Results and Discussion

From left to right a compressed visualization of the method pertaining to tumor vascular compartment creation using ASL-fMRI, SFDI drug localization, and simulation result.



Slices of murine brain tumor is manually extracted following photosensitizer injection. SFDI validates the localization of PpIX while ICP-MS validates the localization of Rutherrin. SFDI shows full extravasation of PpIX from the tumor region forming the yellow 'angel-wing' localization surrounding the tumor. Simulated mass transfer maps the first time point of PpIX localization. High concentration regions leak out adjacent to the leading edge of the tumor while minimum concentration is localized at the central tumor core as indicated by SFDI.

IV. References

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

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