Simulation of Intraoperative PDT for Glioblastoma using Monte Carlo Radiative Transport

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Background

Glioblastoma (GBM)

- Highly aggressive, treatment resistant brain tumour
- Diagnosed ~0.004% of people[1]
- 14.6 month median survival rate with standard of care:[1]

Maximal tumour resection → Radiation therapy → Chemotherapy Temozolomide

- > 80% of recurrences occur adjacent to resection edge [1]

Photodynamic Therapy (PDT)

- Kills malignant cells using 630 nm (red) light
- Administered photosensitiser (5-ALA) accumulates in damaged cells

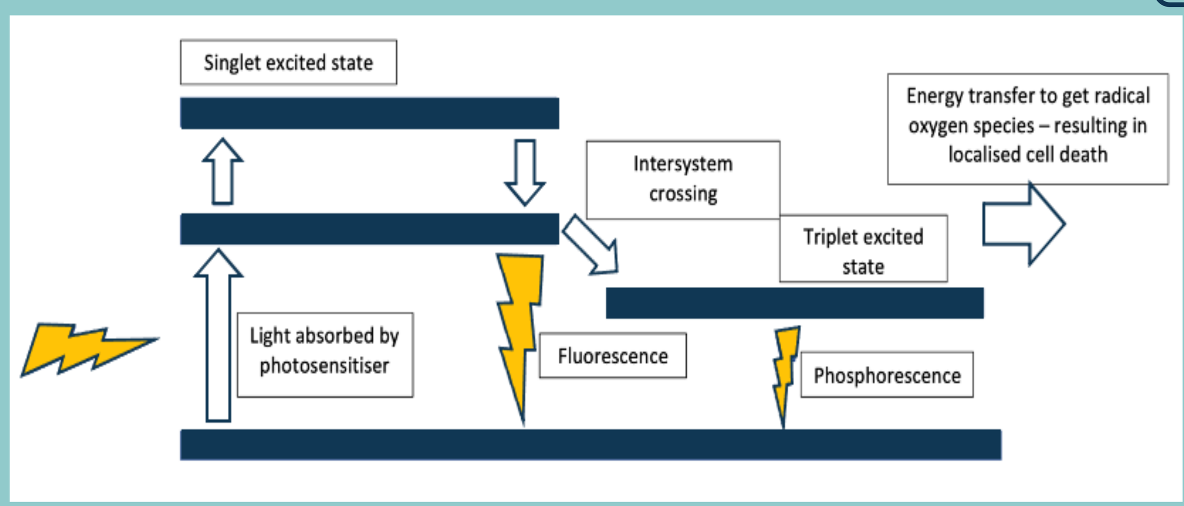


Fig. 1 – Energy level diagram of PDT process

INDYGO Clinical Trial

- Clinical trial at Université de Lille of intraoperative PDT to treat GBM[2]

Maximal tumour resection → PDT → Radiation therapy → Chemotherapy Temozolomide

Fig. 2 - Adapted from Vermandel et al.[1] Surgical setup of INDYGO clinical trial

- Preliminary results show improvement in median survival rate to 23.1 months (cf 14-15mths in historic controls)

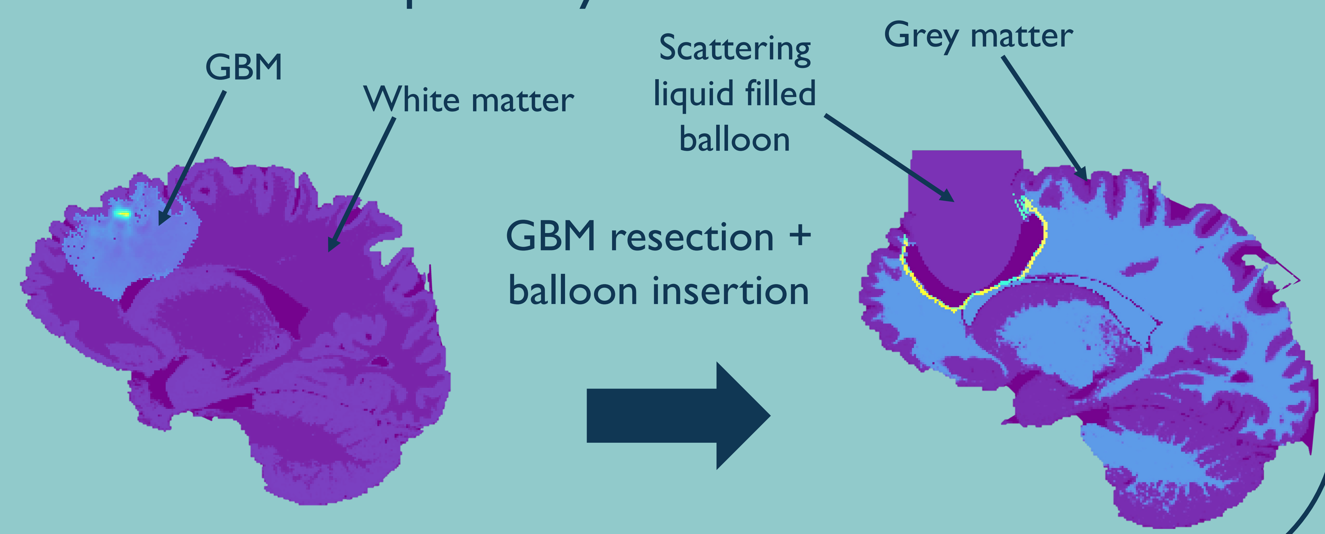
Methods

Monte Carlo Radiative Transport (MCRT)

- Aim to simulate PDT in a brain model with similar setup to INDYGO trial
- MCRT = computational method to predict light distribution in turbid media with specified optical properties
- Simulations run for four initial PpIX concentrations.
- Treatment time = 9.6 min (INDYGO trial treatment time for chosen balloon size)
- Light power = 2 W

Brain Model / Balloon Insertion Simulation

- GBM algorithmically grown in 3D brain[3]
- Python code used to resect GBM and reshape cavity and balloon for insertion



Results / Conclusion

- Initial concentrations > 2.0 μM produced effective cell kill over a 9.6 minute treatment time **(Figs 4a, b)**
- An extended treatment time of 15 minutes resulted in 16 % more cell death with a 2.0 μM concentration suggesting improved treatment outcome **(Fig 4c)**
- Results are a best case scenario
- Next steps:
  - Spatially vary PpIX concentration
  - Add oxygen depletion and recovery
- This will make the simulation more realistic but will likely result in reduced PDT cell kill

Tumour Remaining as a function of Time and Photosensitiser Concentration

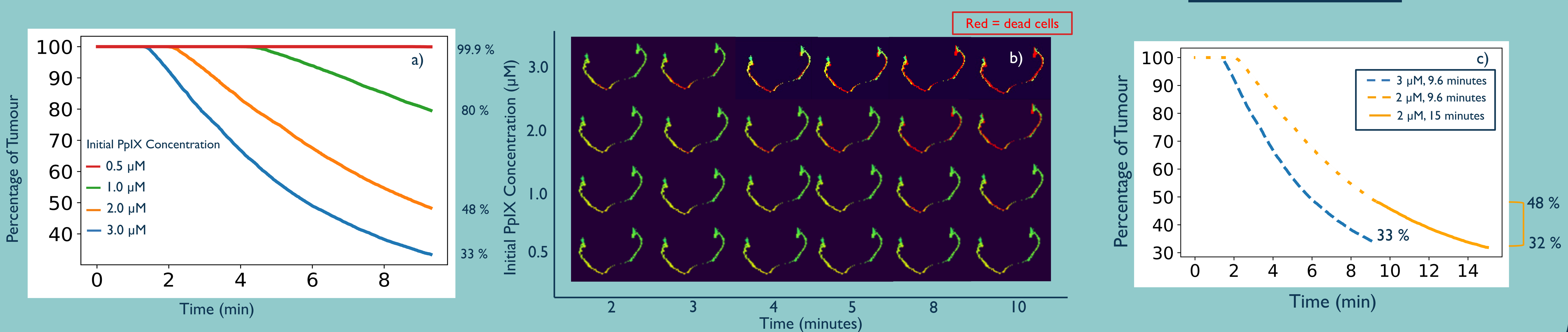


Fig.4 a) Percentage of initial tumour cell remaining over the full treatment time for for different initial photosensitiser concentrations. b) 2D slice of tumour cavity at different times with different initial PpIX concentrations. Red areas show where cell death has occurred. c) Running the 2 μM simulation for 5 minutes longer resulted in 16 % further cell kill

References

1. Cramer, S.W. and Chen, C. C. (2020) Photodynamic Therapy for the Treatment of Glioblastoma. *Front. Surg.* **6**. https://doi.org/10.3389/fsurg.2019.00081
2. Vermandel, M., Dupont, C., Lecomte, F., Leroy, H.A., Tuleasca, C., Mordon, S., Hadjipanayis, C. G. and Reyns, N. (2021) Standardized intraoperative 5-ALA photodynamic therapy for newly diagnosed glioblastoma patients: a preliminary analysis of the INDYGO clinical trial. *J. Neurooncol.* **152**, 501–514. https://doi.org/10.1007/S11060-021-03718-6.
3. Suveges,S.; Hossain-Ibrahim, K.; Steele, J.D.; Eftimie, R.; Trucu, D. Mathematical Modelling of Glioblastomas Invasion within the Brain: A 3D Multi-Scale Moving-Boundary Approach. *Mathematics* **2021**,*9*,2214. https:// doi.org/10.3390/math9182214