Strategies for Improving Complete Tumor Resection in Glioblastoma Multiforme (GBM)

Jennifer Ferd, Ahmad Amirshaghaghi, Andrew Tsourkas
Department of Bioengineering, University of Pennsylvania School of Engineering and Applied Sciences

Glioblastoma multiforme (GBM) remains one of the most formidable clinical challenges in neuro-oncology, afflicting patients with a high recurrence rate and a 5-year survival rate as low as 5%. In contrast to other cancers where distant metastases are common, GBM recurrence generally occurs within 1–2 cm of the primary resection cavity. Survival can be improved by increasing the percentage of gross total resection; however, the heterogeneity, similarity of tumor appearance to the surrounding brain parenchyma, and diffusely infiltrative behavior of high-grade gliomas make complete tumor resection challenging to achieve. Current intraoperative navigation technology does not allow surgeons to effectively identify and remove all glioma cells. Phthalocyanine (Pc) and naphthalocyanine (Nc) dyes exhibit intense near-infrared (NIR) absorbance, good photoacoustic (PA) activity, and a good safety profile in human patients. Therefore, they offer a favorable, yet underexplored, option for image-guided surgery. We have proposed to encapsulate hydrophobic Pc and Nc dyes within micelles and use them to differentiate GBM from surrounding healthy tissue. With the development of our nanoparticle-based contrast agent, we will increase GBM detection rate by providing surgeons with the ability to detect deep-seeded tumors by PA and once exposed via an incision, by naked eye. We have optimized the composition and physical-chemical properties of these micelles for maximal accumulation and contrast within an orthotopic model of GBM and have shown accurate delineation of the brain tumor boundary in an orthotopic model of GBM through real-time PA imaging and further assessment following resection and histology.