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Cerebral microcirculation in glioblastoma: A major determinant of diagnosis, resection, and drug delivery

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Abstract

Glioblastoma (GBM) is the most common primary brain tumor with a dismal prognosis. Current standard of treatment is safe maximal tumor resection followed by chemotherapy and radiation. Altered cerebral microcirculation and elevated blood-tumor barrier (BTB) permeability in tumor periphery due to glioma-induced vascular dysregulation allow T1 contrast-enhanced visualization of resectable tumor boundaries. Newer tracers that label the tumor and its vasculature are being increasingly used for intraoperative delineation of glioma boundaries for even more precise resection. Fluorescent 5-aminolevulinic acid (5-ALA) and indocyanine green (ICG) are examples of such intraoperative tracers. Recently, magnetic resonance imaging (MRI)-based MR thermometry is being employed for laser interstitial thermal therapy (LITT) for glioma debulking. However, aggressive, fatal recurrence always occurs. Postsurgical chemotherapy is hampered by the inability of most drugs to cross the blood-brain barrier (BBB). Understanding postsurgical changes in brain microcirculation and permeability is crucial to improve chemotherapy delivery. It is important to understand whether any microcirculatory indices can differentiate between true recurrence and radiation necrosis. LITT leads to peri-ablation BBB opening that persists for several weeks. Whether it can be a conduit for chemotherapy delivery is yet to be explored. This review will address the role of cerebral microcirculation in such emerging ideas in GBM diagnosis and therapy.

Keywords: 5-ALA; EOR; GTR; brain drug delivery; brain tumor; contrast enhancement; indocyanine green; intraoperative MRI; laser interstitial thermal therapy.