Developing & Applying a Miniaturized Active Microchip Device

By

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ABSTRACT
Glioblastoma multiforme (GBM) is the most common and aggressive malignant brain tumor. Treatment of GBM is a daunting task with median survival just at 21 months. Methods of localized delivery have achieved moderate success in treating GBM. Depot devices have been limited due to the relatively narrow drug distribution profile they achieve. Convection enhanced delivery has demonstrated that broad distribution is key, but is limited due to uncertain spatial distribution and serious side effects. Miniaturized depot devices, implanted into the tissue surrounding the tumor resection site, could achieve a broad aggregate distribution profile. The capabilities of localized delivery can be enhanced by utilizing microelectromechanical systems (MEMS) technology to deliver drugs with precise temporal control over release kinetics. An intracranial MEMS based device was developed to deliver the clinically utilized chemotherapeutic temozolomide (TMZ) in a 9L rodent glioma model. An activation mechanism based on thermally induced membrane failure was developed and incorporated. The kinetics of TMZ release were validated and quantified in vitro. The safety of implanting the device intracranially was confirmed. The impact of TMZ release kinetics on survival was investigated by comparing the effects of drug release rates and timing. TMZ delivered from the device prolonged animal survival. The results from the in vivo efficacy studies indicate that early, rapid delivery of TMZ from the device results in the most prolonged animal survival. This miniaturized MEMS device holds tremendous potential for the treatment of GBM and related diseases.

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