Tumor Resection from Eloquent Brain Areas

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Combined use of intraoperative MRI and intraoperative electrical brain stimulation may allow for resection of tumors previously considered unresectable, with a significantly decreased risk of new neurologic deficit, potentially prolonging survival and increasing quality of life.

Brain areas are defined as being eloquent if injuries to these areas result in deficits of neurologic function. The removal of tumors within or adjacent to eloquent brain regions is a complex challenge that requires a multidisciplinary team approach. The benefits of resecting as much tumor as possible to increase survival must be carefully balanced with the risks of compromising neurologic function and decreasing quality of life. The use of intraoperative electrical stimulation for the identification of language and motor areas has greatly facilitated the safe removal of many tumors previously considered inoperable.

“Eloquent cortex” refers to areas on the surface of the brain necessary for language, motor and sensory functions. Examples include the cortical regions of the dominant, generally left, hemisphere inferior frontal lobe, superior temporal lobe and angular gyrus for language function, the bilateral posterior frontal lobes for voluntary movement, the bilateral anterior parietal lobes for tactile sensation and the bilateral medial occipital lobes for vision. An “eloquent brain area” is a region of eloquent cortex and its associated subcortical structures as injury to the latter can also result in loss of function.

Potential Survival Advantage of Less Residual Tumor

While it may appear intuitive that removing more of a benign or malignant primary brain tumor such as a glioma results in longer patient survival, there has never been a randomized, placebo-controlled clinical trial demonstrating this. Numerous retrospective studies, however, suggest a survival advantage in patients who have less residual tumor following surgery. A recent review article identified and analyzed 43 articles on the topic published between 1990-2012. Eleven pertained to low-grade or benign gliomas while 32 addressed high-grade or malignant gliomas. In each of the low-grade articles, there was a survival benefit to greater extent of resection and many of the studies also reported that a greater extent of resection was associated with a decrease in the rate at which low-grade tumors transformed into high-grade tumors. The high-grade tumor articles reported varying degrees of benefit with greater extent of resection, but the overwhelming majority (11 of 14) of the larger studies, defined as those that included 200 or more patients, did show an association between increased extent of resection and increased survival. A later study published in 2014 by authors at SBNI and the National Institutes of Health reported that even patients with recurrent high-grade gliomas survived for longer if they had less residual tumor following surgery. Of the 97 patients enrolled in this study, 38 (39.2 percent) were found to have no gross residual tumor on their postoperative MRI scan. The resection of many of these tumors in an intraoperative MRI-equipped operating suite facilitated the achievement of this relatively high rate of total resection.

The radical resection of brain tumors located within or adjacent to eloquent brain regions can, however, lead to new neurologic deficits. In a retrospective study of 306 patients with glioblastoma tumors, 19 patients (6 percent) acquired new motor deficits and 15 (5 percent) acquired new language deficits versus 272 patients (89 percent) who were free of new deficits following surgery. The median survivals of the three groups were 9.0 months (P < 0.05) and 9.6 months (P < 0.05) versus 12.8 months, respectively. The corresponding two-year survivals of the three groups were 8 percent and 0 percent versus 23 percent, respectively. In a separate study of 88 patients, new motor deficits (P = 0.003) and new language deficits (P = 0.035) were independent predictors of worsened quality of life following glioma surgery. The surgical management of eloquent brain region tumors, therefore, requires a delicate balance between maximal resection and the avoidance of new neurologic deficits.

Need for Highly Skilled Multidisciplinary Team

A highly skilled multidisciplinary team including a neuroanesthesiologist, a neurophysiologist, a neuropsychologist and a neurosurgeon with extensive experience in the intraoperative assessment of language and motor functions is necessary for the accurate identification and anatomic preservation of eloquent brain areas. The resection of tumors located in potential motor function areas can be performed with patients either “awake” under conscious sedation.
or “asleep” under general anesthesia, with the usual practice at Santa Barbara Cottage Hospital being the latter. In contrast, the resection of tumors located in potential language areas requires patients to be awake and interactive. The intraoperative identification of an individual patient’s presumed motor and language regions begins with direct electrical stimulation of the cortex overlying or adjacent to the tumor to be resected. A constant current generator and bipolar stimulating electrodes are used to deliver biphasic square wave pulses with a fixed frequency and duration. Stimulation is generally initiated at a low current setting of 1.5 mA and the current is gradually increased to a maximum of 6 mA until an expected response is initiated. This direct stimulation of the brain is thought to cause the depolarization of neurons within a 5 mm radius of the electrode tips. In motor cortex stimulation, this depolarization leads to electromyographically detected muscle contractions that are monitored by a neurophysiologist. In language cortex stimulation, it leads to speech arrest, inability to name objects shown on flash cards, or inability to read numbers as assessed by a neuropsychologist.

If a stimulated cortical area appears to be functionally silent as evidenced by an absence of muscle contractions or the lack of disruption of a language task, it is generally deemed to be safe for resection. As non-eloquent cortical tissue and tumor tissue are removed and the underlying white matter is exposed, the white matter itself is similarly stimulated, but with a greater maximum current as needed. Again, muscle contractions or the disruption of language functions are closely monitored. If an eloquent cortical or subcortical area is identified, the tissue in this area, even if it contains gross tumor tissue, is generally left undisturbed to avoid the acquisition of permanent neurological deficits. During both motor and language mapping, continuous electrocorticography is used to monitor after-discharge potentials, an indication of subclinical seizure activity.

**Conclusion**

With the combined use of intraoperative MRI and intraoperative electrical brain stimulation, tumors that were previously thought to be unresectable may now be resectable with a significantly decreased risk of experiencing a new neurologic deficit. This in turn may lead to longer survival and increased quality of life for patients.

For an expanded version of this article with footnotes, please visit www.sbni.org. To learn more about the Brain and Spinal Tumor Program or to request an appointment, contact Gary Milgram, Service Line Director, at (805) 569-7550 or gmilgram@sbch.org