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## Editorial

# Can awake glioma surgery be the new standard of care in developing countries?

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Roberts Bartholow's infamous experiment to map functional areas of the human brain in an awake patient in the year 1874 generated not only a lot of controversy among his contemporaries but also resulted in grand mal seizures in the unsuspecting patient Ms. Mary Rafferty. She had, what was termed as an epithelioma that had eroded her skull and exposed dura and brain over a period of 13 months.<sup>[1]</sup> Awake craniotomies in a sense were widely practiced before the introduction of general anesthesia. Awake craniotomy can be defined as an intracranial surgical procedure where the patient is deliberately awake for a portion of the surgery, usually for mapping and resection of the lesion. Pioneering work on cerebral localization included many names such as Otfrid Foerster and later Wilder Penfield.<sup>[14]</sup> The procedure fell out of favor only to experience a resurgence with awake mapping techniques introduced by George Ojemann.<sup>[2]</sup> Conventional glioma surgery is expensive in terms of cost of the equipment, disposables, human resource, etc., as well as the associated length of hospital stay. This still does not include the cost of the expensive imaging required for each glioma case, both before, sometimes during, and after the surgery. The need of sophisticated stereotactic navigation may be beneficial for a greater extent of resection, especially in eloquent locations, which further balloons prohibitive costs in low and middle income countries (LMICs) as the navigation not only requires an investment in the equipment but also requires additional imaging for every patient.<sup>[11]</sup> Intraoperative ultrasound and MRI are other modalities that have been shown to improve resection, but require substantial expenditure.<sup>[10]</sup>

The advantages of awake craniotomy for surgical resection of gliomas have been supported with case series documenting the better extent of resection, lower risk of new deficits, and improved progression-free survival among certain patient sub-groups with both low-grade and high-grade gliomas. A randomized control trial (The SAFE trial) is underway to better answer certain questions regarding the utility of awake craniotomy compared to craniotomy under general anesthesia for glioblastomas. This study will look at important endpoints such as progression-free survival, overall survival, and frequency and severity of adverse effects. The trial is expected to conclude in 2024.<sup>[6]</sup> However, we would recommend caution when interpreting findings from studies that compare outcomes with awake craniotomy for gliomas resection versus historical cohorts. The reason for this is the use of temozolomide more recently which affects survival and the new molecular-based classification of gliomas with differential survival for different varieties.<sup>[7]</sup>

Intraoperative mapping during awake craniotomy has shown significant promise in minimizing postoperative deficits which are independently associated with worse outcomes. Awake craniotomy with intraoperative mapping has been found to be useful in achieving the adequate

extent of resection even in complex low-grade gliomas that several busy neuro-oncology centers do not use the navigation in such cases, with equally good or better results.<sup>[3]</sup>

The cost-effectiveness of awake craniotomy for glioma surgery has been suggested by many authors. The direct cost-benefit from choosing an awake procedure results from the avoidance of general anesthesia decreased hospital stay in both intensive and general care settings and early discharge. There may be an additional cost reduction by avoiding the use of navigation. Eseonu *et al.* showed significant savings with awake procedures with improved outcomes and reduced complication. In their experience, although the operating room cost was higher in the awake craniotomy group (primarily human resource-related), the overall inpatient costs were reduced by an average of 12000 US Dollar (USD) per case.<sup>[4]</sup> The analysis showed that the mean incremental cost per quality-adjusted life-year for the awake craniotomy patients was 82720 USD less per patient than the general anesthesia group.<sup>[8]</sup> The new concept of enhanced recovery after surgery that has been shown to improve both cost and outcomes also recommends awake surgeries whenever feasible.<sup>[4]</sup> There have been no studies evaluating the absolute cost-benefit in a developing country, where the results may not be the same, given the significantly lower cost of human resource and hospital stay.

Mark Bernstein has championed the philosophy of awake craniotomy as a sustainable practice in resource-limited settings through his involvement in teaching the technique in several LMICs.<sup>[9]</sup> Although presently, awake craniotomies for gliomas usually involve inpatient admission in most centers where it is practiced, in certain centers, daycare surgery for gliomas with same-day discharge has been successfully tried and implemented. Turel and Bernstein examined whether such a practice can be extrapolated to underdeveloped countries such as India and according to their estimates, savings of approximately 1000 USD have been demonstrated using such an approach.<sup>[12]</sup> Awake craniotomy also improves the chances of preserving important functions besides basic motor control, such as vision, judgment, and language, allowing patients an early return to work and retaining their livelihood.<sup>[13]</sup> More recently, with reference to the COVID-19 pandemic, the society for neuroscience in anesthesiology and critical care has published guidelines recommending that awake craniotomy may be a suitable option as it also helps reduce the use of advanced personal protective equipment, thus further reducing potential cost. A microphone has been recommended to allow distance to be maintained.<sup>[5]</sup>

This is especially relevant in LMICs like Pakistan, where the per capita income is low, majority of patients are out of pocket payers, and especially in the wake of COVID-19

pandemic, when a large segment of population may be on the verge or below the poverty line. So can awake craniotomies be employed to reduce costs and improve outcomes for gliomas patients in Pakistan? The answer to the latter may only be answered sufficiently once we have sufficient evidence which is at least a few years away. The prior is a more complex question that is influenced heavily by the expense of training individuals in multiple roles to safely perform awake craniotomies at a certain standard. This will ultimately balloon the cost of the procedure at the patient's end unless public health funding can be mobilized. However, one quickly realizes that this is not really saving money but rather drawing it away from other public health needs. The authors feel that awake craniotomy has significant promise that may not be realized in developing countries for the next several years at the very least.

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