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EDITORIAL - BRAIN TUMORS

Role of intraoperative neurophysiological monitoring during fluorescence-guided resection surgery

Aiming at seemingly complete resection of diffuse gliomas under 5-ALA guidance—Is it safe?

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Acta Neurochirurgica has promoted fluorescence-guided microneurosurgery of central nervous system (CNS) tumours with a number of articles. (a) The peroral 5-ALA (Gliolan/BLUE 400) painting method, introduced by Stummer et al. [19, 22] and now standard in many departments, has been discussed in intracranial malignant gliomas [5, 12, 18–20, 24], metastases [9, 17], meningiomas [3], validity of stereotactic biopsies [25], and differential diagnosis of brain lesions [10, 13]. (b) The age-old intravenous sodium fluorescein, now permanently brought from retinal angiography to microneurosurgery (YELLOW 560) [14], has been introduced in malignant gliomas [1, 16] and in hemangioblastomas [15]. (c) ICG or indocyanine angiography (INFRARED 800), standard in neurovascular microsurgery, has been introduced in various CNS tumours [4, 7, 11, 23]. These examples are just a prelude to the future explosion of targeted visualization of brain tumour tissues and their adjacent brain tissues, based on transcriptomes, signalomes, proteomes, glycomes, and other omes.

Many of us are ardent users of 5-ALA in diffuse grade III–IV gliomas. But, 'Is it safe?' asked Sir Laurence Olivier in *Marathon Man*. Others are suspicious for at least three reasons: (a) pink glioma stain is seen in a somewhat blurred microanatomical landscape (less so with sodium fluorescein), (b) pinkish areas in the resection cavity walls may hide behind thin grayish layers, and (c) pinkish areas may be spotty and diffuse, raising the worry whether they represent glioma tissue only or infiltrated white matter [8] that is still functional, and in the worst case, eloquent white matter tracts.

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So, what is the safety of 5-ALA-guided neuronavigated microneurosurgery of diffuse gliomas when aiming at (a) seemingly complete removal, and (b) preservation of functional connectivity of the adjacent brain tissue [6] (i.e., the optimal removal in terms of possible adjuvant therapies and survival [21])?. Pastor et al. in this issue and Della Puppa et al. in a recent 2013 Acta article [5] report on 36 and 31 gliomas, respectively, in or near eloquent areas, removed using neuronavigation, 5-ALA guidance and intraoperative monitoring (IOM) such as transcranial, cortical and subcortical stimulation mapping, as well as electrocorticography (ECoG), motor evoked potential (MEPs), sensory evoked potential (SEPs) and visual evoked potential (VEPs). Pastor et al. used general anesthesia (propofol + remifentanyl) without muscle relaxant to allow stimulation mapping, while Della Puppa et al. adopted awake surgery in six cases. Why use 5-ALA + IOM in this setting, rather than 5-ALA + 3D navigated ultrasound (US) or intraoperative 3 T magnetic resonance imaging (MRI) (if you can afford one)? Because IOM reflects the connectomic functions to be preserved, while US and MRI reflect the connectomic architecture. A gross total resection (> 98 %) was achieved in 67 % and 74 %, respectively. *IOM warning signs* during removals, as well as neurological worsening or improvement until 3 months, were recorded. These series in their complexities are important reading for neuro-oncological surgeons.

Which IOM warning signs and how grave (> 50 % decrease? total disappearance?)—under general anesthesia without muscle relaxant—would make me interrupt the removal of that particular pinkish area? I try to rely on cortical and subcortical stimulation with electromyography (EMG) responses rather than SEPs, but the ideal setting would be IOM + awake craniotomy [2], the latter not always being applicable.

Conflicts of interest None.

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