



# The Treatment of Glioblastoma: Letter from Russia

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In 1980-1981 the author worked as a nurse at the neurosurgery of the Botkin hospital in Moscow. Patients with glioblastoma (GBM) were routinely operated on, while it was believed by some staff that the treatment was generally useless, just forcing many patients to spend the rest of their lives in bed. The directive to apply the largest possible radical operations for gliomas was issued at the 1959 and especially 1966 Moscow Conferences of Neurosurgeons.[1] Advanced age was not regarded to be an obstacle to the radicalism [2]. Later on, microsurgery, intra-operative imaging and other modern methods lead to a reduction in the surgical morbidity. However, despite extensive research, prognosis has not changed significantly in the past decade [3]. Arguments against resection are based on the invasiveness of GBM, which cannot be totally removed; in addition, there might be a tumor cell spreading due to the operation, new neurological deficits and other complications [4]. Maximum resection using microsurgical techniques as safely feasible is considered standard of care, although the role of surgery has been difficult to define in controlled clinical trials [5]. The evidence is weak in terms of both the number of trials and their robustness [6]. The retrospective design of studies has raised concerns about selection bias [7] that is, some tumors are more respectable than others, and these tumors also may be inherently less aggressive, the impact of surgery possibly being an epiphenomenon [8]. It is often argued that a prerequisite of glioma diagnosis is resection or biopsy, both methods being associated with risk. Of note, intracranial malignancy can be diagnosed in some cases by imaging and "liquid biopsy" [9]. Improvements of preoperative diagnostics must limit indications for the trepanation.

The volume of residual tumor after surgery negatively correlates with the outcome; but it has remained unclear whether the extent of resection improves the outcome or whether tumors amenable to gross total resection have on average less malignant course [5] (Weller et al. 2019). If even surgical outcomes are deemed good, some patients remain with neurocognitive decline or otherwise deterioration of the life quality [10]. Although evidence suggests that surgical excision improves the outcome in most cases, it is often associated with morbidity [11]. There are indications that standard therapy including surgery may be not in a patient's best interests [12]. Without surgery, some patients receiving symptomatic palliative therapy could use the remaining months to complete their tasks. The palliative care increases the number of patients who survive more than 2 years approximately 3-fold compared with those declining the treatment in whole or in part [13]. Existing methods of GBM management are not questioned here. It is important that patients (or caregivers if the patient's thinking capacity is impaired) must be objectively informed about potential benefits and adverse effects of different treatments. Signed informed consent is mandatory for all surgical candidates [14]. Tacit consent must not be supposed, in particular, regarding end-of-life decisions [15]. All the above is of particular importance for the elderly. For aged patients with newly diagnosed GBM, current recommendations include surgery; however, some studies indicated that in patients aged 65 years and older, median overall survival is only

modestly improved or that there is no improvement with resection compared to biopsy [7,16]. Treatment strategies should be balanced against patient-specific factors and quality-of-life concerns [17].

Many patients and their relatives access information on the Internet. The information available online is not monitored [18]. In Russia, media tend to trivialize risks and discomfort associated with surgeries and other invasive procedures. Some medical men on YouTube claim that new techniques enable to radically remove deep GBMs without damaging brain structures: <https://www.youtube.com/watch?v=-0GLCfdMv10>; <https://www.youtube.com/watch?v=l2kSeb92jpY> (accessed February 11, 2024). Unlike other countries, public libraries are rarely used and generally contain no professional medical literature. Medical and scientific libraries are hindered from using by the general public, including even retired doctors, by unfriendly staff and technical difficulties [19]. Some professional publications recommending invasive procedures apply misquoting, for example: "The average life expectancy for malignant gliomas in patients receiving only conservative therapy was 9 weeks - 6.6 months" [20] with references [21-23]. Surgeries are often presented by media as something a priori beneficial, conducive to good convalescence; while side effects, risks and procedural quality are not mentioned. It has been reasonably recommended that medical institutions and professionals must work to produce more reliable content in order to improve the availability of credible health information for patients [18].

Justifications of surgical hyper-radicalism could be heard in private conversations among medics, for example: "The hopelessly ill are dangerous" i.e., may commit reckless acts undesirable by the state. This might be one of the reasons why GBM patients are routinely operated. The training of medical personnel under the imperative of readiness for war has been another motive [24,25]. Finally, the obstacles to the import of drugs and medical equipment should be mentioned. Domestic products are promoted sometimes despite questionable quality and possible counterfeiting. Today, the economical upturn enables acquisition of modern equipment; and scientific research is encouraged by authorities. Under these circumstances, the purpose of this letter was to remind that, performing surgical or other invasive procedures, the risk-to-benefit ratio must be kept as low as reasonably achievable.

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