

**Case Report**

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**High-resolution intraoperative infrared thermography for the functional imaging and tumor resection maximization of a low-grade glioma: Technical case report****Diego Rodrigues Menezes<sup>1,2</sup>; William Cesar Fiorotti<sup>1</sup>; Lázaro de Lima<sup>1</sup>; Edson da Rocha Constantino<sup>1</sup>; Rafael Teixeira Magalhães Leal<sup>1</sup>; José Alberto Landeiro<sup>1</sup>; Aura Conci<sup>3</sup>; Marcus André Acioly<sup>1,2\*</sup>**<sup>1</sup>Department of Surgical Specialties, Federal Fluminense University, School of Medicine, Niteroi, Brazil.<sup>2</sup>Department of Neurosurgery, Pedro Ernesto University Hospital, Rio de Janeiro State University, Rio de Janeiro, Brazil.<sup>3</sup>Federal Fluminense University (UFF), Niteroi, Brazil.**\*Corresponding Author: Marcus André Acioly**

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**Abstract**

Currently, it is widely recognized the role of the extent of resection on overall and progression-free survival for gliomas surgery. Brain mapping and intraoperative image guidance are generally required to attain such an objective. Infrared Thermography (IRT) has a potential role in the identification of surgical margins, but it has not been consistently assessed in the literature. We aim to demonstrate the use of intraoperative IRT to detect superficial and deep tumoral margins of low-grade glioma, to identify adjacent functional motor cortex, and to maximize surgical resection in a 45-year-old lady with a long history of partial and secondary generalization seizures.

**Keywords:** Infrared thermography; Glioma; Intraoperative imaging.**Abbreviations:** 5-ALA: 5-Aminolevulinic Acid; IRT: Infrared Thermography; MRI: Magnetic Resonance Imaging; FPS: Frame Per Second.**Introduction**

Currently, it is widely recognized the role of the extent of resection on overall and progression-free survival for diffuse gliomas, regardless of the grade [1,3]. To achieve such an objective, functional-guided surgery is generally required [4]. The seminal meta-analysis by De Witt Hamer and colleagues demonstrated that intraoperative brain mapping mainly on local anesthesia in the awake setting was associated with fewer neurological complications and a greater extent of resection for all grades of diffuse gliomas [5]. For glioblastomas, the issue of functional preservation with awake mapping is somewhat controversial [6,7]. Besides brain mapping, intraoperative imaging based on fluorescence guidance by using several tracers has been increasingly used for glioma resection [8,9]. While 5-aminolevulinic acid (5-ALA) has become a new standard for high-grade

glioma surgery, the impact of fluorescein-guided surgery is yet to be defined in terms of contributing to overall survival [8,9]. It is worth mentioning that positive 5-ALA fluorescence rates are rather low in low-grade gliomas, however [10]. Infrared Thermography (IRT) is a non-invasive imaging method used to detect surface temperature through naturally emitted radiation from the body. Regarding its application in brain tumors, IRT has a potential role in the identification of surgical margins, but it has not been consistently assessed in the literature. Herein, we aim to demonstrate the use of intraoperative IRT to detect superficial and deep tumoral margins of low-grade glioma, to identify adjacent functional motor cortex, and to maximize surgical resection.

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### Case report

A 45-year-old lady with a long history of partial and secondary generalization seizures was admitted to our department. She experienced an increase in seizure frequency during the last year. Her physical examination was otherwise normal. Magnetic Resonance Imaging (MRI) revealed an expanding lesion located on the right inferior parietal lobule consistent with low-grade glioma (Figure 1). Surgical resection was then recommended. The patient underwent a right fronto-parieto-temporal craniotomy under mild sedation (dexmedetomidine plus remifentanyl) and local anesthesia (solution of epinephrine, lidocaine, and bupivacaine) to permit intraoperative brain mapping [11]. After dural opening, the FLIR Systems' SC620 thermal camera (FLIR Systems, USA) was brought to the surgical field (30-50 cm) to record tumor thermal profile before tumor resection and during voluntary motor tasks. The camera was attached to a tripod to prevent camera mobilization and positioned perpendicular to the exposed brain for spontaneous and sequential digital imaging. SC620 uses a 640x480 pixels detector with thermal sensitivity of 0.02°C. Before image acquisition, the camera was set with operating room and patient temperature, humidity, and distance from the exposed brain. Surgical lights were redirected from the surgical field during infrared measurements. Spontaneous infrared emissions were taken as baseline images. Then, tumor margins at the cortical surface were outlined with neuro-navigation and ultrasound and a silk thread was placed over the cortex of the affected area. Thermal gradients revealed tumoral hypothermia (range, 1.7 to 3.9°C) in comparison to the surrounding cortex. Sequential digital images were obtained with irrigation-induced hypothermia as described by Gorbach et al. with slight modifications [12]. Uniform irrigation with saline at room temperature caused abrupt hypothermia of the exposed cortex and created a recovery gradient, which can detect tumoral from nontumoral tissues. The effect was most prominent by analyzing the recovery curves (Figure 2). Approximately 140 images were obtained at intervals of 1 second (1 frame per second [fps]) starting 10-15 seconds before irrigation and continued for 1 minute thereafter.

Motor tasks comprised serial finger tapping initiated 10-15 seconds after the beginning of infrared imaging acquisition and lasted 10-15 seconds, also at 1 FPS. Repetitive motor tasks elicited temperature increase in the primary somatosensory cortex mainly dependent on augmented pial vascularization, which was confirmed by mapping (Figure 3). We used bipolar electrodes with a stimulus from 1.5 mA increased to a maximum of 8.0 mA until the neurological function was established. The stimulator device delivered biphasic waves of constant current in 4-s trains at 60 Hz (Leal) [11]. No stimulation-induced seizure was documented. Spatial cognition mapping was additionally performed, but not confirmed with IRT.

Surgical resection was taken to the anatomical and functional boundaries both in cortical and subcortical levels with the help of brain mapping. When resection was deemed complete by the surgical team, the thermal camera was positioned again for spontaneous and sequential infrared imaging using the same protocol. After resection, the temperatures at the tumor bed and the posterior/inferior margins were cooler than the surrounding cortex. Irrigation-induced thermal gradients revealed

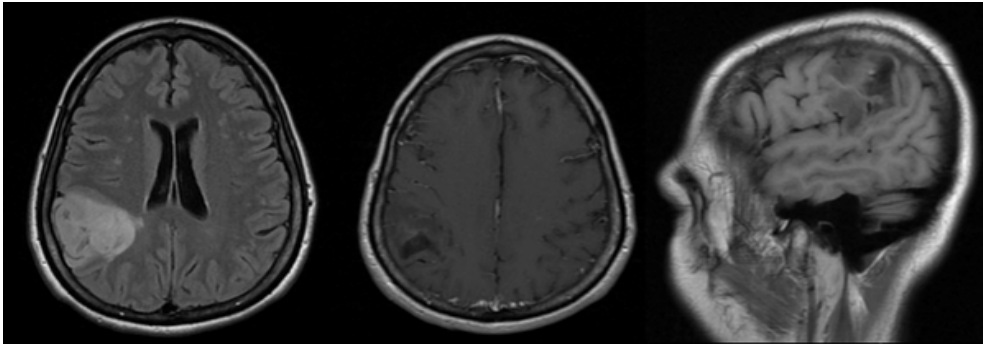
suspicion areas of late temperature recovery in comparison to the exposed cortex (Figure 4). So, some samples were taken from these areas for frozen sections. Histologic examination confirmed residual tumor cells and resection was expanded in such proven areas. The patient experienced an uneventful postoperative recovery with no functional deficits. Postoperative MRI demonstrated complete resection of the tumor. Also, areas of restricted diffusion at the tumor bed were identified without clinical correlates (Figure 5). Histopathological analysis confirmed the diagnosis of an oligodendroglioma WHO grade II. The patient provided informed consent for the publication of this manuscript.

### Discussion

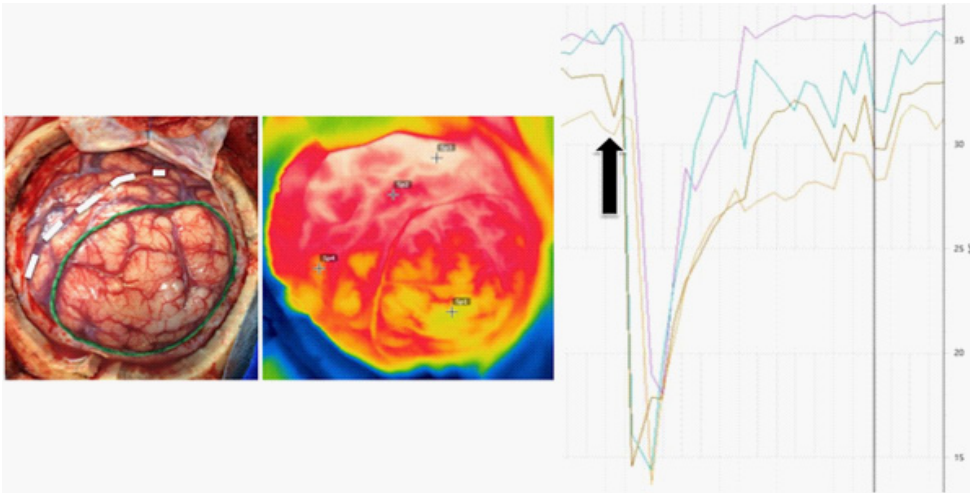
Currently, intraoperative imaging methods mainly include neuronavigation, intraoperative MRI, intraoperative ultrasound, and fluorescence-guided surgery [13,14]. Imaging methods are largely based on the anatomical characteristics of the brain and CNS tumors, while fluorescence methods depend on the degree of contrast uptake by tumor cells [14,15]. The location of relevant functional areas and the dynamic changes in Cerebral Blood Flow (CBF) in tumors and adjacent brain tissue are characteristics not evaluated by any of the abovementioned methods [12,14]. The application of IRT for the analysis of temperature gradients in brain tissue has been previously studied in experimental models and humans [12]. The first intraoperative description of IRT use in brain tumors was made in 1987 by Koga and colleagues [16]. Since then, IRT has been predominantly used for tumor location and prediction of histological diagnosis [12,14,18].

In 2003, Gorbach and colleagues hypothesized that it would be possible to identify cortical activation through the use of high-resolution infrared imaging as a consequence of local changes in CBF induced by increased metabolism due to motor or language tasks. They concluded that the distribution observed in infrared mapping matched perfectly with the complex distribution of the cortical representation obtained with brain mapping. In this way, IRT could be an extremely useful tool for studying intraoperative brain functions. Temperature increase in the functional cortex was generally mild (0.04-0.08°C), though [17].

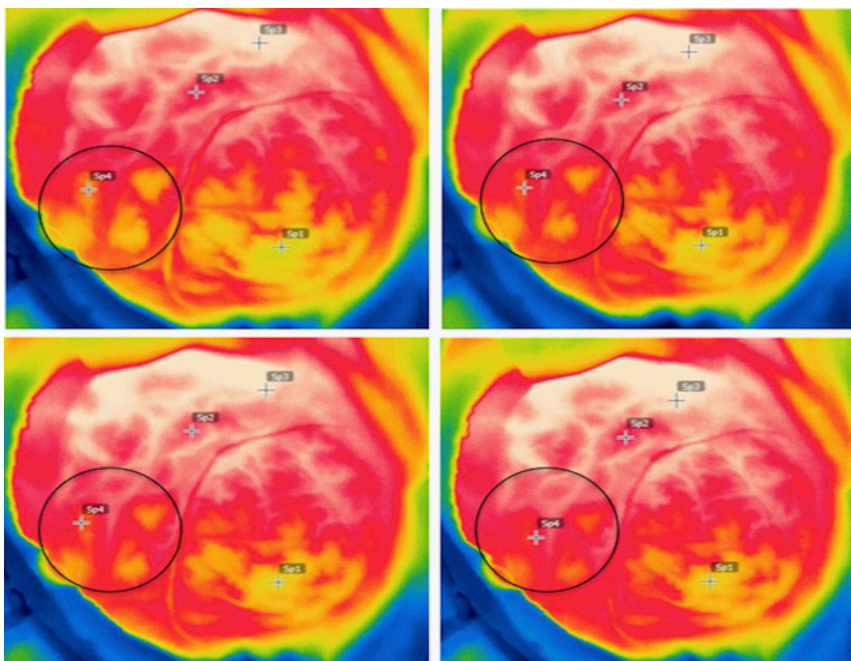
Kateb and colleagues were the first to apply IRT to estimate the degree of tumor resection in a patient with metastatic melanoma. Postoperative MRI revealed subtotal resection, which was not identified in their final thermographic image [19]. Our study is unique since we were able to identify primary somatosensory cortex temperature changes as a result of motor tasks with a greater temperature range than previously demonstrated by using a thermal camera with twice the resolution. Also, surgical resection was expanded by identifying residual tumors in the area of late recovery of the thermal maps after irrigation-induced hypothermia. IRT might have several advantages over the aforementioned intraoperative imaging methods since it is cost-effective, non-invasive, and allows localization of subcortical tumors [18,19].



**Figure 1:** Preoperative neuroimaging showing a right parietal low-grade glioma (left) causing mild anterior displacement of the central area (center and right). There was no contrast enhancement (center).

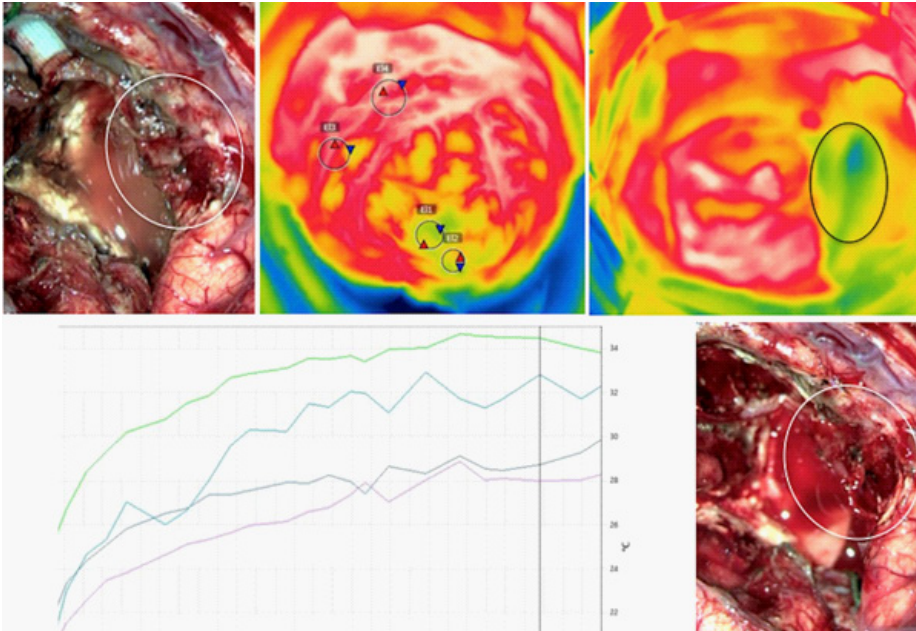


**Figure 2:** Intraoperative photograph of the exposed cortex (left) and the corresponding spontaneous infrared imaging (center). Intraoperative imaging outlined tumor margins with a silk thread. The tumor was marked hypothermic. Irrigation-induced hypothermia (black arrow) caused immediate temperature reduction at all regions, but normal cortical thermal gradients showed a rapid recovery (pink line), while tumor cells demonstrated a gradual and late recovery (yellow line). The central sulcus is demonstrated in the white dashed line.

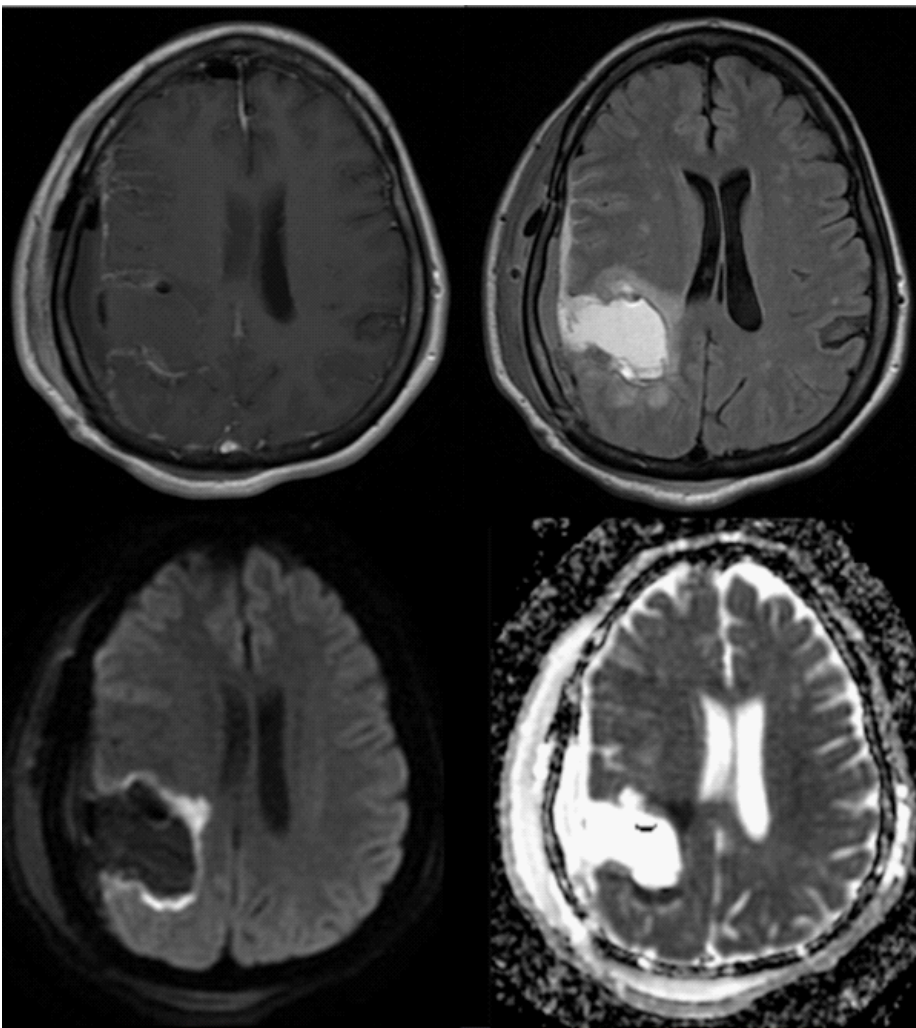


**Figure 3:** Functional infrared imaging during repetitive finger tapping of the contralateral hand (motor task). Four images were chosen to illustrate the intensity increase in the primary somatosensory cortex (black circle) infrared signal. Temperature changes were easily demonstrated on color-coded maps reaching a maximum of 1.1°C after the command was initiated. The distribution between cortical areas of infrared thermal imaging and motor cortex stimulation overlapped confirming the spatial and temporal patterns of cortical representation.





**Figure 4:** Intraoperative photograph from the operating microscope demonstrating the final aspect of the surgical cavity. Thermal maps (graph [pink curve]) showed hypothermic areas (green areas) of delayed temperature recovery at the tumor bed (lower small black circles) and at the posterior/inferior margins (large black circle), which were confirmed as residual tumors by frozen section analysis. Resection was then continued in both areas and the final aspect (lower right) is demonstrated.



**Figure 5:** Immediate postoperative T1-weighted gadolinium-enhanced (upper left), T2-weighted (upper right), diffusion-weighted [lower left (DWI)], and apparent diffusion coefficient map [lower right (ADC)] MR images disclosed complete tumor resection and an ischemic tumor bed without clinical correlates.

## Conclusion

During the last 30 years, intraoperative IRT has been mostly used for diagnostic purposes in brain tumors. The study of the vascular relationships of brain tumors and the impact on the maximization of surgical resection have been poorly addressed in the literature. Our study demonstrates the application of IRT in the detection of surgical margins and functional areas during low-grade glioma resection suggesting its utility as an additional method for maximizing surgical resection while preserving function. Our findings lend support to future investigations in the field.

## Declarations

**Conflict of interest:** All authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements), or non-financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript.

**Ethical approval:** All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

**Informed consent:** Informed consent was obtained from all individual participants included in the study.

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