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Usefulness of Intraoperative Infrared Thermography in Intracranial Surgeries: Past, Present, and Future

Utilidade da termografia infravermelho em cirurgias intracranianas: Passado, presente e futuro

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Abstract

With the advancement of technology in Neurosurgery, imaging guidance for surgical planning and intraoperative assessment has become relevant. Currently, two major methods of imaging guidance are generally explored in the literature, namely based on imaging and fluorescence. These techniques, however, are not without limitations. Thermal imaging has potentially broad applications in clinical practice, especially for intracranial diseases. Infrared thermography (IT) has been an underestimated tool with few reports on its usefulness during intracranial surgeries. In this article, we aim to provide a brief discussion on the limitations of current intraoperative imaging techniques for intracranial surgeries and to provide an in-depth state-of-the-art review on intraoperative IT (IIT) for intracranial lesions. High-resolution IIT is a non-invasive alternative imaging method that provides real-time estimation of regional cerebral blood flow. For brain tumors, the studies were mostly directed to diagnostic purposes and occasionally for lesion-localization. The use of IIT to address the extent of resection is a potential new application. Clinical data in this issue suggests that IIT might detect residual tumors, occasionally not assessed by other imaging technologies. Thermographic measurements during vascular and epilepsy surgeries comprise an interesting field for future research with potential clinical implications. Further experimental and clinical studies should be addressed to provide technical refinements and verify the usefulness of this noninvasive technology in neurosurgery.

Keywords

- brain tumors
- brain temperature
- imaging
- infrared imaging
- thermography

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Resumo

Com o avanço da tecnologia em neurocirurgia, a orientação do planejamento cirúrgico e da avaliação intraoperatória por métodos de imagem se tornaram extremamente relevantes. Atualmente, dois métodos principais de cirurgia guiada por imagem são geralmente explorados na literatura, ou seja, baseados em imagens e em fluorescência. Essas técnicas, no entanto, apresentam limitações. A termografia infravermelha (TI) tem aplicações potencialmente amplas na prática clínica, especialmente para doenças intracranianas. A TI tem sido uma ferramenta subestimada, com poucos relatos sobre a sua utilidade durante cirurgias intracranianas. Neste artigo, pretendemos fornecer uma breve discussão sobre as limitações das atuais técnicas de imagem intraoperatória para cirurgias intracranianas e fornecer uma revisão aprofundada do estado da arte sobre a TI intraoperatória (TII) para lesões intracranianas. A TII de alta resolução é um método de imagem alternativo não invasivo que fornece estimativa em tempo real do fluxo sanguíneo cerebral regional. Para tumores cerebrais, os estudos foram direcionados principalmente para fins diagnósticos e, ocasionalmente, para localização das lesões. O uso da TII para avaliar a extensão da ressecção é uma nova aplicação em potencial. Os dados clínicos sugerem que a TII pode detectar tumores residuais, ocasionalmente não avaliados por outras tecnologias de imagem. Medidas termográficas durante cirurgias vasculares e de epilepsia constituem um campo interessante para pesquisas futuras com potenciais implicações clínicas. Novos estudos experimentais e clínicos devem ser realizados para fornecer refinamentos técnicos e verificar a utilidade dessa tecnologia não invasiva em neurocirurgia.

Palavras-chave
- termografia
- neurocirurgia
- imagem
- avanços

Introduction

Infrared thermography is a non-invasive real-time imaging technique based on the detection of the emitted electromagnetic radiation coming from an object. Such radiation is converted into temperature color-coded or grayscale images by infrared thermographic cameras, in which different temperatures of body tissues can be interpreted in a localized manner[1] The history of thermal imaging in medical practice started in the 1940s and continued to develop since the 1960s.[2] The detection of cancer was a high priority at that time. The first breast thermography was performed in 1956 by a Canadian surgeon, Dr. Ray Lawson, who observed higher skin temperatures in patients with benign breast tumors and breast cancer (►**Figure 1**).[3,4]

Although thermal imaging has been used in medical practice since the 1950s, its widespread use in the clinical setting is still undetermined and under investigation, except for its application in breast cancer screening.[5] Thermographic profiles have been used to study diverse benign and

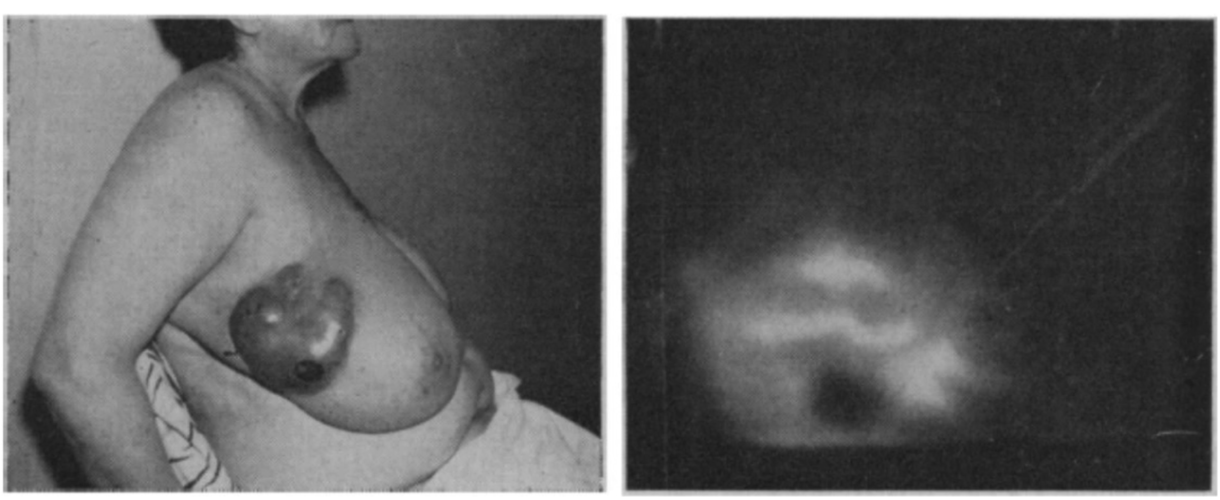

Fig. 1 Patient with advanced breast carcinoma with ulceration (left), demonstrating hyperthermic irregular contours on infrared thermography (right). Adapted from Lawson.[3]

malignant diseases, such as diabetic neuropathy, vascular diseases, thermoregulation, fever monitoring, liver metastatic diseases, and thyroid nodules, among others.[6,7]

Regarding the central nervous system (CNS), thermography has the ability to identify cortical surface temperature as a result of regional cerebral blood flow.[5] In this way, tumor necrosis,[5] low microvascular density,[8,9] vasogenic edema,[10] reduction of cortical metabolism,[11] and the occurrence of cystic lesions[12,13] contribute to lower regional temperature. On the other hand, changes in regional cerebral blood flow after activity-induced tasks during awake surgeries for brain mapping,[14] highly vascularized lesions, namely arteriovenous malformations[9] or some brain metastasis,[5] render thermographic maps of elevated temperature.

Thermal imaging has potentially broad applications in clinical practice, especially for intracranial diseases. Infrared thermography has been an underestimated tool with few reports on its usefulness during intracranial surgeries.[5,9,12,13,15–17] In this article, we aim to provide a brief discussion on the limitations of current intraoperative imaging techniques for intracranial surgeries, especially for brain tumors, and to provide an in-depth state-of-the-art review of intraoperative infrared themography (IIT) for intracranial lesions.

Limitations of Current Intraoperative Imaging Techniques for Intracranial Surgeries

Currently, two major methods of lesion localization and guidance for the extent of resection are generally explored in the literature, namely based on imaging (neuronavigation, intraoperative magnetic resonance imaging [iMRI], and intraoperative ultrasound [iUS]),[18–21] and based on fluorescence (5-ALA, and sodium fluorescein [SF]).[22,23] These techniques, however, are not without limitations.

Neuronavigation loses accuracy intraoperatively over time because of brain deformation, also known as brain shift.[24,25] Cerebrospinal fluid drainage, tissue removal, gravity, tumor localization and size, and brain edema are all well-recognized factors that contribute to intraoperative brain shift.[24,26] Besides brain shift, inaccurate recordings can also limit neuronavigation, especially during surgeries in the lateral or prone positions.[27] In such cases, neuronavigation registration is generally imprecise because of facial distortion and regional deformation on preoperative imaging.[27]

The update of the neuronavigation system with iMRI has been a reliable way to compensate for the effects of brain shift,[24,25] but its use is not widespread worldwide, especially because of the low availability and high costs. Furthermore, infection control, imaging artifacts, and equipment compatibility are always an issue for iMRI.[28–31] iUS has attracted interest for safety, portability, and real-time imaging. Even though iUS has demonstrated high accuracy for lesion location, imaging was deemed suboptimal or of poor quality in up to 8% of the patients.[26] In addition, image quality and the size of the ultrasound transducer are the main limitations of the method.

Regarding fluorescence guidance, tissue overlapping limits the identification of subcortical tumors, since healthy cortex, blood, blood clots, and hemostatic agent's obscure tumor visualization. On the other hand, intraoperative fluorescence enables real-time intraoperative identification of tumor tissue thereby permitting direct visualization of residual tumor.[23,32–34] The seminal paper by Stummer and colleagues in 2006[34] showed a 29% absolute increase in the extent of resection of high-grade gliomas with 5-ALA in comparison to white light. Since then, 5-ALA has been approved in many countries around the world for fluorescence-guided surgery.

SF is the second most used fluorophore, which has recently been given new attention. Even though there is some evidence on the contribution of the extent of resection with fluorescein-guided surgery,[35] its use is still under investigation and not approved for fluorescence guidance brain tumor resection in most countries, because of scanty severe allergic reactions and unspecific staining.[23,32,34] Timing of administration is an essential issue for both 5-ALA and SF. Administering both fluorophores too early might lead to a precocious 5-ALA peak rendering false negative tumor identification or permitting unspecific propagation of SF on edematous brain tissue. Conversely, late administration does not allow effective accumulation of fluorophores. Finally, the low contrast index in low-grade gliomas comprises a crucial limitation of fluorescence.[36]

Usefulness of Infrared Thermography in Intracranial Surgeries

Tumors and Functional Mapping

The first description of the intraoperative application of infrared thermography in brain tumors was made in 1987, in an article in Japanese. Koga et al.[13] studied the thermal microenvironment of six brain tumors (two metastasis and four gliomas). With a low-resolution infrared camera, tumor temperatures were generally cooler than adjacent healthy cortex on thermographic maps, especially for brain metastasis. Cystic and necrotic tumor areas were notably hypothermic, which was confirmed by the help of iUS. In addition, Koga et al.[13] introduced the observation of delayed thermal recovery curves after the cold loading test on those hypothermic areas.

In 2002, Ecker and colleagues expanded the use of infrared imaging for cerebral revascularization surgeries, epilepsy, and cortical brain mapping, in addition to describing thermal characteristics of primary brain tumors by histopathological subtype. Thirty patients were examined with a low-resolution infrared camera (matrix of 256×256 pixels and an accuracy of 0.006°C between pixels). Thus, low- and high-grade gliomas were generally hypothermic in comparison to the adjacent cortex (78% of measurements).[9]

In 2003, Gorbach et al. introduced the identification of cortical functional areas by IIT. The assumption behind this was that thermography was able to identify regional cerebral blood flow changes induced by increased metabolism, because of motor or language tasks during awake mapping.

Twenty-one patients were examined with a low-resolution infrared camera. They concluded that the cortical distribution of the thermographic maps overlaps that obtained with cortical stimulation mapping, thereby comprising a useful tool to study brain function (►**Figure 2**).[14]

In 2004, the same group studied the effects of a brain tumor on the surrounding healthy cortex. Thirty-four tumors comprised their study group. Brain tumors create changes in regional cerebral blood flow, which goes beyond tumoral margins and could be able to improve after tumor resection. Such changes in regional blood flow are made visible by intraoperative infrared thermography rendering temperature differences of about 0.5 to 2.0 °C between the brain tumor margin and the healthy cortex.[15] Tumors of the glial lineage were generally hypothermic, while brain metastasis was consistently hyperthermic. Normalized temperature gradients (the ratio between the coldest and the hottest tumor areas) in brain metastasis were 49% and 40% higher compared to oligodendrogliomas and glioblastomas, respectively. However, the mean temperature gradients may vary depending on the tumor stage, size, location,[15] as well as the occurrence of edema and areas of cystic degeneration or necrosis.

The visualization of these thermal gradients by thermography can be facilitated with the use of isotonic saline solution, at room or cold temperature. With irrigation-induced hypothermia, both the healthy cortex and brain tumor presented temperature reduction, but recovery curves were generally different since brain tumor areas demonstrated a rather delayed curve that lasted 10 to 40 sec longer. Irrigation generated an increase of approximately 10% in the heat gradient, allowing a better visualization of tumor areas.[15]

In 2009, Kateb and colleagues were the first to apply IIT to assess the extent of tumor removal. In a case report, they described a patient with brain metastasis from melanoma. Tumor thermographic maps revealed hyperthermic areas. The resection was deemed complete intraoperatively by the surgical team, however postoperative MRI confirmed subtotal resection (approximately 82%). A retrospective analysis of the three-dimensional thermographic profile indicated the potential location of the residual tumor (►**Figure 3**). It is worth noting that Kateb et al. used a low-resolution thermographic camera (FLIR Systems TCP60 - 320 × 240 pixels and accuracy of 0.06 °C).[5]

Kastek et al. used a high-resolution thermographic camera to report differences in temperature according to diverse regions of interest within the tumor (edema, cyst, and tumor itself) both before and during resection. Six patients were examined with IIT (gliomas, meningiomas, and cystic lung metastasis). Measurements have shown that cystic temperature was 2 °C lower than the surrounding cortex (edema) and 4 °C lower than neoplastic tissue. The magnitude of temperature differences is mainly determined by the histological subtype and degree of metabolic activity. In addition, the authors demonstrated the role of bipolar coagulation and devascularization in reducing tumor temperatures.[12]

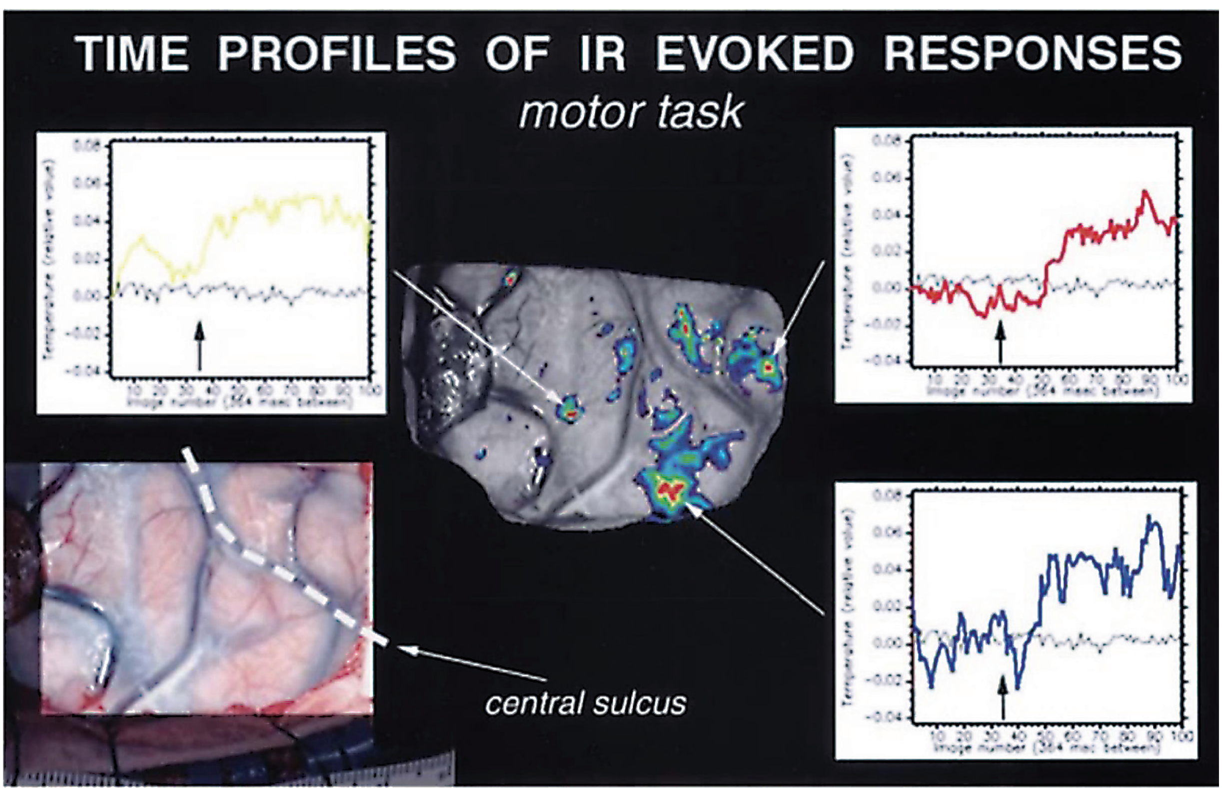

Fig. 2 Surgical microscope (left, bottom) and thermographic (center) images, showing changes in cortical temperature as a function of motor activity. The yellow curve represents the temperature changes during the cold challenge test in the premotor cortex, while the blue graph, is from the primary motor cortex, and the red one, is from the primary sensory cortex. Adapted from Gorbach et al. with permission.[14]

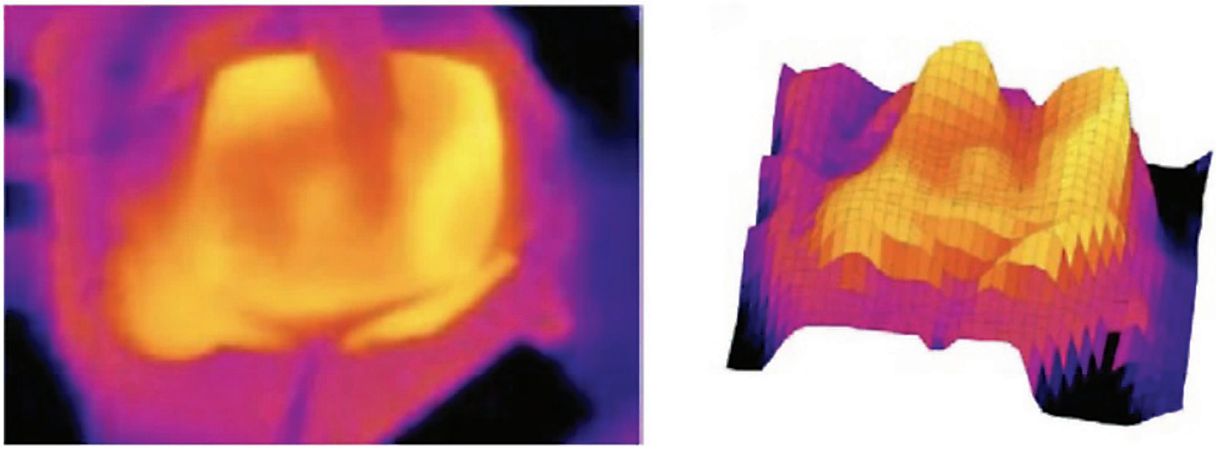

Fig. 3 Intraoperative infrared thermography image (left) of the surgical bed and the three-dimensional thermographic map (right), showing central hypothermia that might suggest the residual tumor detected on postoperative imaging. The black areas might correspond to residual tumors covered by saline or blood clots. Adapted from Kateb et al. with permission (2009).[5]

With these potential applications in mind, we recently started a prospective study in 15 patients with intracranial cortical and subcortical tumors of different histological subtypes to evaluate the usefulness of IIT with a high-resolution thermographic camera for transdural lesion-localization, diagnosis, to assess the extent of resection, and the occurrence of perioperative acute ischemia. Static and dynamic thermographic maps (cold challenge test) were acquired intraoperatively with a high-resolution camera at pre-established time points. Our preliminary results showed that intraoperative thermographic imaging of the exposed dura mater revealed a mixed vascular pattern of meningeal vessels, veins, and cortical arteries. Intra-axial tumors were reliably identified by demonstrating hypothermic areas with high sensitivity and specificity for cortical and subcortical tumors up to 2 cm in depth, which were exacerbated by the cold challenge test.

We also found that dural opening facilitated both the identification of tumors and their neurovascular relations (►**Figure 4**). The analysis of central spot temperatures significantly elucidated histological subtypes. At the end of the surgical resection, there was a consistent rise in the temperature of gliomas and metastasis tumor beds. Residual tumors on imaging were retrospectively evaluated with infrared thermography, presenting a typically delayed temperature recovery curve after the cold challenge test. Acute ischemia was consistently hypothermic, but without clinical deterioration, however (Menezes et al., 2023, submitted).

Vascular Surgery

The application of intraoperative infrared thermography started in 1993 when Okudera and colleagues used a thermographic camera attached to a surgical microscope to study temperature patterns during the resection of an AVM.[37] Thermal imaging permitted real-time noninvasive temperature monitoring of the involved cerebral vessels. At the beginning of the surgical procedure, AVM draining veins was consistently hyperthermic because of arterialization, but progressive occlusion of feeding arteries caused temperature drop to normal levels, especially after the cold loading test (►**Figures 5** and **6**).[37]

Almost ten years have passed since a second study on the field was presented. Watson et al., in 2002, reported their experience using a high-resolution sensitive infrared camera (0.02 °C) to locate cortical function intraoperatively.

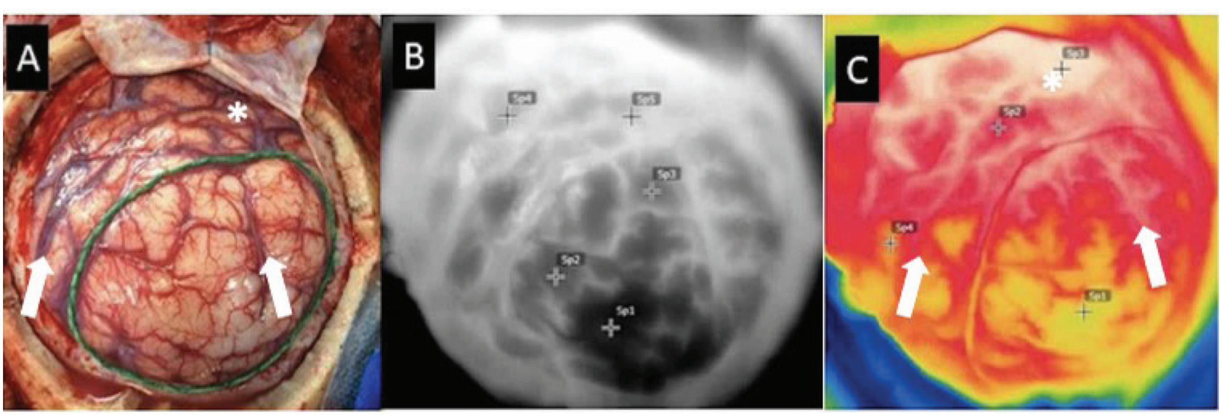

Fig. 4 Intraoperative images during resection of a right temporoparietal tumor (oligodendroglioma WHO grade II). Tumoral area is demarcated with a green cotton thread (**A**). The thermographic maps in black and white (**B**) and color-coded (**C**) reveal higher temperatures in the lateral sulcus (asterisk) and intermediate temperatures in the cortical veins (white arrows). The tumor is consistently hypothermic (yellow area).

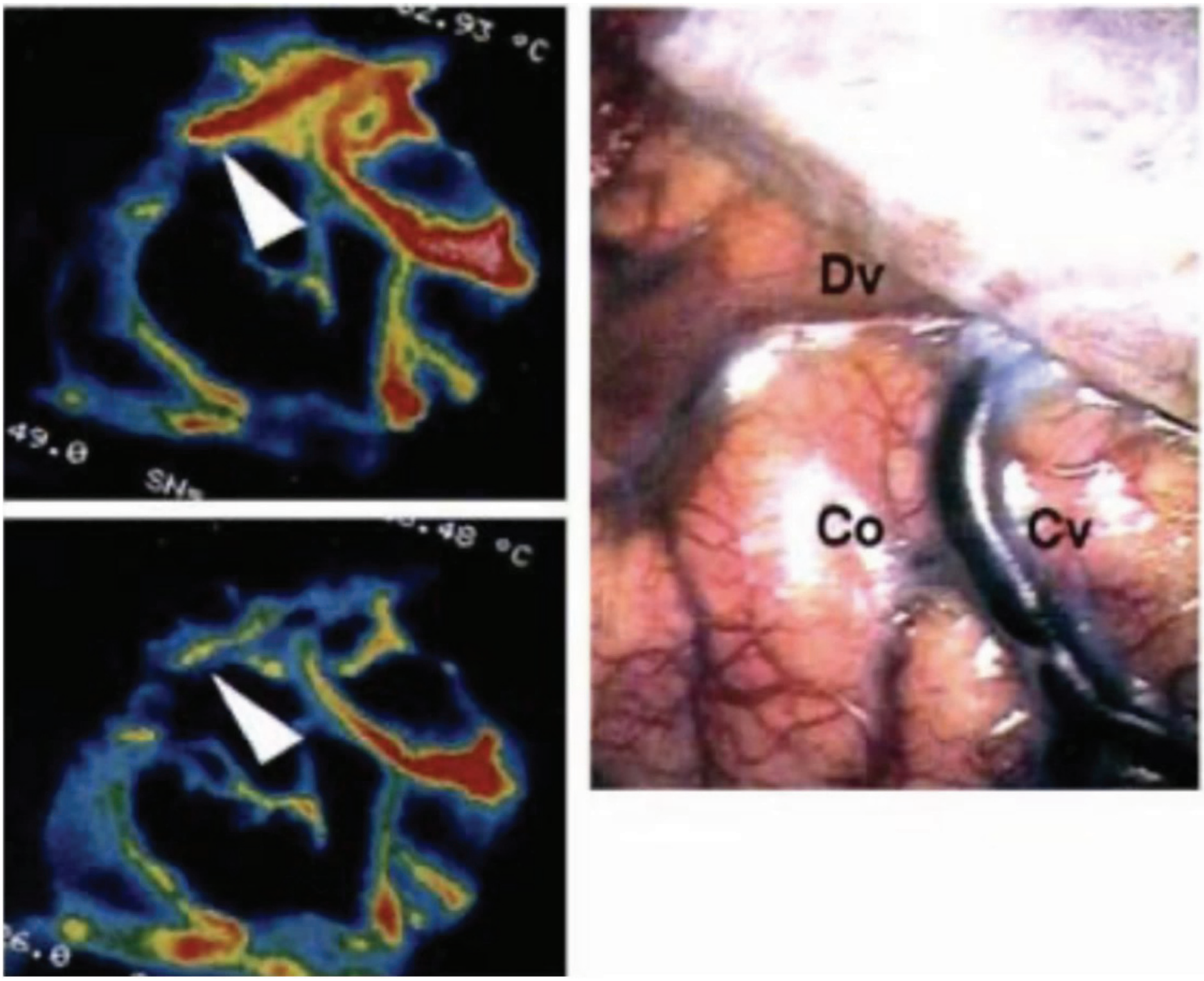

Fig. 5 Intraoperative images of the cortical surface during an arteriovenous malformation resection surgery. The arterialized draining vein (Dv, white arrow) showed a progressive temperature decrease after occlusion of the feeding arteries. Co - cortex; Cv - normal vein. Adapted from Okudera et al. with permission.[37]

They looked at high-resolution images of cerebral vessels and hypothesized that infrared imaging would allow changes in the arterial flow to be seen immediately. Thus, providing a real-time indirect assessment of cerebral perfusion in the vascular territory involved. During surgical procedures that require vascular manipulation, such as brain aneurysms, AVMs, or some tumors, the ability to visualize real-time cerebral blood flow in major vessels and their distribution beds would be beneficial, especially during temporary vascular occlusion.[16]

The next step was provided by Ecker et al., in 2002, showing intraoperative hyperperfusion of the healthy cortex after AVM resection, which was consistent with loss of brain autoregulation. The patency of extra-intracranial bypass for cerebral revascularization was also verified and, additionally, demonstrated an increase in regional cerebral blood flow and indirectly an increase in regional cerebral perfusion. Even though more research is needed to fully define the role of intraoperative infrared imaging for cerebral revascularization, the quantification of increased perfusion can help identify patients who would benefit from a bypass. Such knowledge could have potential implications for detecting cerebral inschemia during brain aneurysm clipping, hemicraniectomy for nondominant stroke, and traumatic brain injury.[9]

Further studies in the field were done by Nakagawa et al.,[38] and Kawamata et al.[39]by using infrared thermography to detect symptomatic cerebral hyperperfusion in patients with moyamoya disease submitted to extra-intracranial bypass for cerebral revascularization. The first study demonstrated that transient neurological symptoms were accompanied by an increase in cerebral blood flow around the anastomosis site, which can be characterized as symptomatic hyperperfusion. Conversely, the results by Kawamata et al. were not optimistic in detecting cerebral hyperperfusion during bypass surgery, since a correlation between intraoperative thermographic changes, and cerebral hyperperfusion was not observed.[39]

Finally, Hwang et al. investigated the role of infrared thermography in studying the steal phenomenon during AVM resection. Through measurements of ocular and perilesional cortical temperatures, the authors demonstrated that ocular temperatures recovered, and perilesional temperature increased. Although such a temperature difference

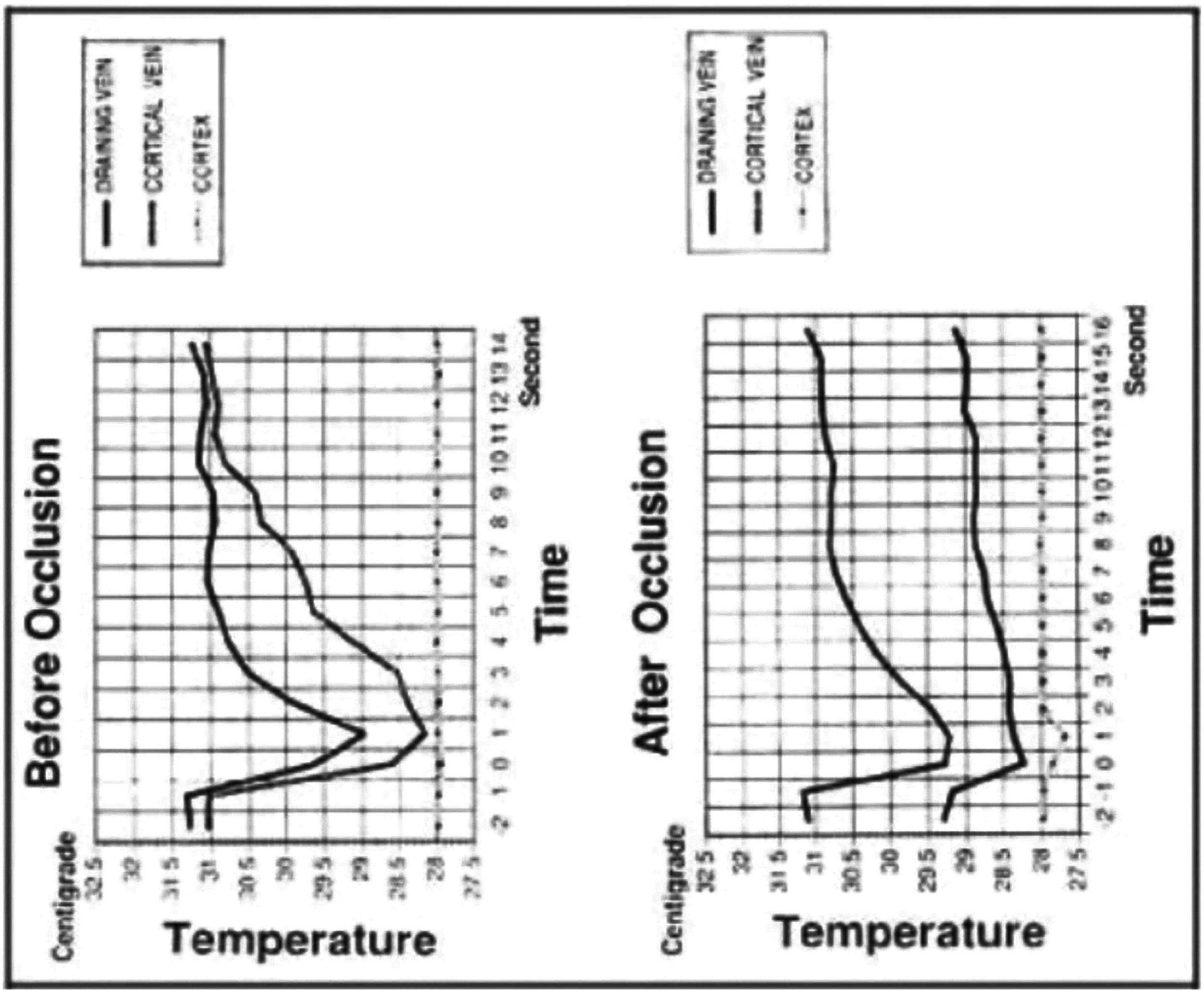

Fig. 6 Temperature recovery curves of the draining and cortical veins, and the exposed cortex obtained after the instillation of cold saline. After occlusion of the feeding arteries (below), the draining vein shows a thermographic recovery profile similar to the cortical vein. Adapted from Okudera et al. with permission.[37]

might be attributed to anesthesia or surgery, the authors deemed thermography to be an efficient tool in identifying the steal phenomenon caused by AVMs (►**Figure 7**).[40]

Epilepsy

The study of seizure foci and their relationship to the adjacent healthy cortex by infrared thermography is sparsely reported in the literature. To the best of our knowledge, only the study by Ecker and colleagues addressed such an issue. In that manuscript, nine patients with intractable extratemporal lobe epilepsy were operated on and had their cortical and lesional thermographic maps measured. Ecker et al. demonstrated highly concordant data between the epileptogenic zone based on preoperative imaging and electrocortigraphic findings and thermal activity. Their results indicated changes in local cortical temperature in the seizure foci, in the way that measurements were generally warmer than the adjacent cortex.[9] No mention is made of absolute thermography values, however. Furthermore, remote, and local hypermetabolic areas caused by seizure activity may not be identified by the method. Therefore, it might not be possible to fully delineate the epileptogenic zones involved in the propagation of seizures.[9]

Conclusion

In the current study, we provided an in-depth overview of infrared thermography for intracranial surgeries. High-resolution intraoperative infrared thermography is a non-invasive alternative imaging method that provides real-time estimation of regional cerebral blood flow. Over the last 30 years, few studies have provided a detailed analysis of thermographic profiles during intracranial surgeries. For brain tumors, the studies were usually directed to diagnostic purposes and occasionally for lesion-localization. Generally speaking, gliomas are consistently hypothermic, both for cortical tumors or the overlying cortex in subcortical tumors, while brain metastases and meningiomas exhibit highly variable thermographic maps that indirectly reveal the grade of tumor vascularization, as well as the presence of edema and cystic degeneration.

For lesion-localization, previous studies and our results demonstrated that infrared thermography allows the

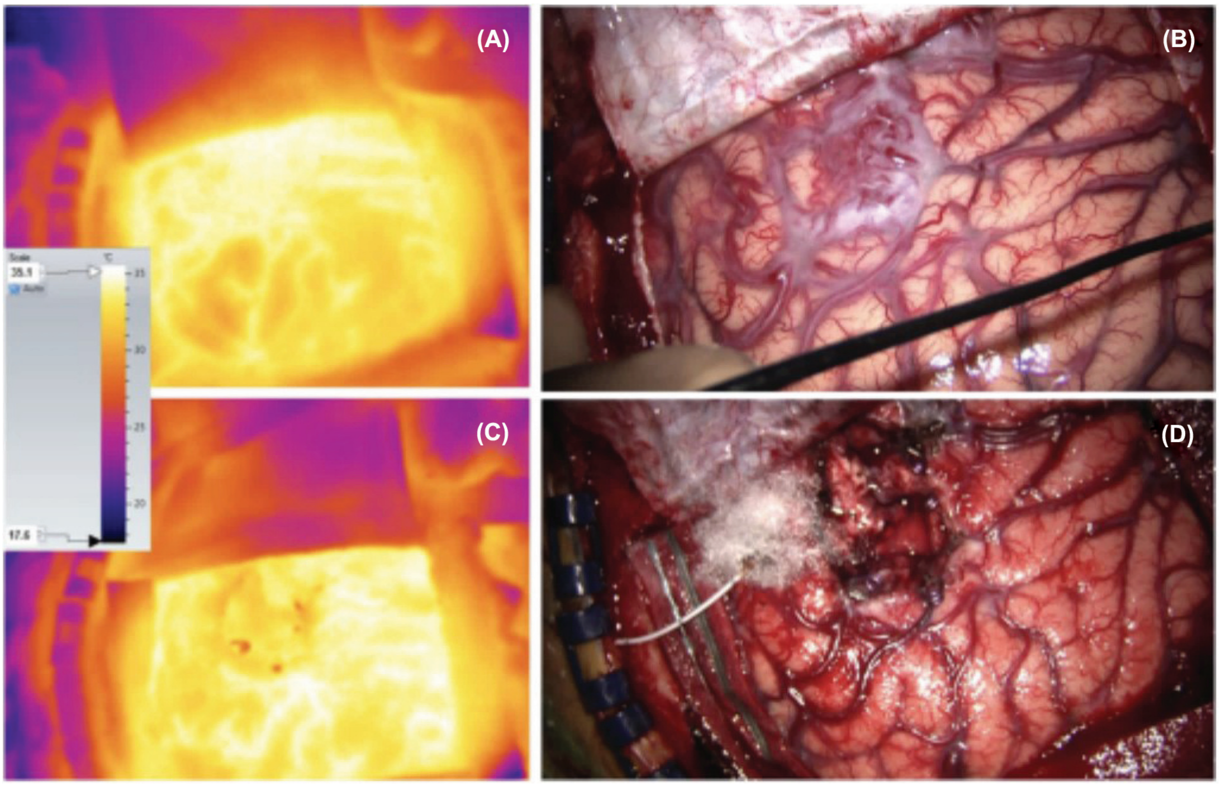

Fig. 7 Thermographic color-coded images (A and C) and intraoperative visual images (B and D) suggest redistribution of blood after AVM resection. Adapted from Hwang et al. with permission.[40]

identification of intracranial tumors of up to 2 cm depth with high sensitivity and specificity. For the assessment of the extent of resection, the literature is scarce. The results obtained by our group suggest a new potential and additional role of infrared thermography since residual tumors revealed nonspecific static and characteristic dynamic thermographic maps. Thermographic measurements during vascular and epilepsy surgeries comprise an interesting field for future research with potential clinical implications. Further experimental and clinical studies should be addressed in order to provide technical refinements and verify the usefulness of this noninvasive technology in neurosurgery.

Conflict of Interest
None declared.

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