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Technical Notes

Localization of irritative zones in epilepsy with thermochromic silicone

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ABSTRACT

Background: During epilepsy surgery, the gold standard to identify irritative zones (IZ) is electrocorticography (ECoG); however, new techniques are being developed to detect IZ in epilepsy surgery and in neurosurgery in general, such as infrared thermography mapping (ITM), and the use of thermosensitive/thermochromic materials.

Methods: In a cohort study of consecutive patients with focal drug-resistant epilepsy of the temporal lobe treated with surgery, we evaluated possible adverse effects to the transient placement of a thermochromic/thermosensitive silicone (TTS) on the cerebral cortex and their postoperative evolution. Furthermore, we compared the precision of TTS for detecting cortical IZ against the gold standard ECoG and with ITM, as proof of concept.

Results: We included 10 consecutive patients, 6 women (60%) and 4 men (40%). Age ranges from 15 to 56 years, mean 33.2 years. All were treated with unilateral temporal functional lobectomy. The mean hospital stay was 4 days. There were no immediate or late complications associated with the use of any of the modalities described. In the 10 patients, we obtained consistency in locating the IZ with ECoG, ITM, and the TTS.

Conclusion: The TTS demonstrated biosecurity in this series. The accuracy of the TTS to locate IZ was similar to that of ECoG and ITM in this study. More extensive studies are required to determine its sensitivity and specificity.

Keywords: Epilepsy surgery, Infrared thermography mapping, Irritative zone, Thermochromic silicone

INTRODUCTION

The effectiveness of epilepsy surgery depends on the location, resection, disconnection, or safe inhibition of the irritative zone (IZ). This is achieved through a meticulous clinical semiology, analysis of preoperative studies such as video electroencephalogram, magnetic resonance imaging, single-positron emission computed tomography, positron emission tomography (PET), or magnetoelectroencephalography. During epilepsy surgery, the gold standard to identify or corroborate the location of IZs is electrocorticography (ECoG); however, new techniques are being developed to detect those crucial areas in epilepsy surgery, such as infrared thermography mapping (ITM) and even more recently, using thermosensitive and thermochromic materials, which will be describen below.

The human brain has a high metabolic rate with high demands for glucose, oxygen, and blood flow and therefore with high heat production. There are thermal fluctuations during different physiological processes (generation of action potentials, resting potentials, synapses, neurotransmission, etc.) as well as in response to pathological processes such as tumors, cortical malformations, and infections.[13,17]

Infrared thermography in neurosurgery

IT cameras are a low-cost, remote, noninvasive, and real-time diagnostic tool capable of providing structural and qualitative functional information. Multiple studies have been carried out in the experimental field where this technique has been applied as an indicator of greater or lesser physiological activity.[10,11] The IT devices measure the electromagnetic radiation emited by all objects, which are invisible to the human eye, and convert it to temperature, providing a thermal map on a scale of different colors[16] [Figure 1]. Its operation is based on Planck's laws of dark objects. This technology was initially used as a military instrument in the 1960s and since then, it has been used in medical practice in different animal species and for various purposes,[11] one of its first applications being breast cancer.[7,8]

For the ITM to be reliable and reproducible, various factors that can generate temperature differences (ΔT) such as evaporation, differential thermal conduction, and altered surface physical phenomena (emissivity) must be taken into account, which are independent in each tissue, but it is recognized that water vapor is the best absorber of radiation.[16] The absorbance of water can vary by 10% at 100 m and 90% at 10 km. Most devices include software where they make an approximation of this signal loss. In other words, the best way to eliminate these factors is to measure the shortest possible distance so that the data are reproducible and reliable.

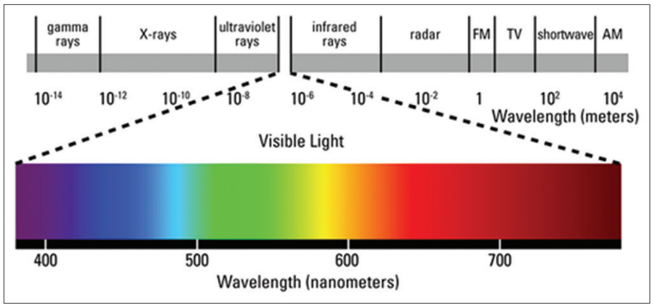


Figure 1: Wavelength spectrum. The spectrum visible to the human eye is very narrow. The infrared spectrum belongs to wavelengths of higher frequency (taken from https://ralcstyle.com/1104).

Some diagnostic techniques for IT currently in use are applied in infectious, inflammatory,[11] tumor,[7,10,13] vascular,[4] traumatic, burns,[12] multiple sclerosis, epilepsy[9,15] diseases, mood disorders, headaches, and neurodegenerative disorders.[17]

It has been described that high-grade gliomas have a lower temperature than the surrounding healthy tissue due to a decrease in the metabolic rate due to edema and necrosis;[10] in other studies with series of various neoplastic pathologies, the limit of the surgical field is decided depending on the results of ITM in real time.

Qualitative thermography and ITM open the possibility of offering the neurosurgeon a tool that gives an anatomical and physiological map with the potential to guide the resection of a lesion.[4] In the world literature, various methods have been described to measure brain temperature, either through the skull or directly on the parenchyma, depending on the pathology to be treated.

There is a relationship between brain temperature, cerebral blood flow, focal brain activity, and the functional state of neurons[17] in patients with epilepsy. It has already been shown in some animal studies that the temperature of the epileptogenic area varies depending on whether the ITM measurement is performed in an interictal or ictal period because the cerebral perfusion will be different depending on whether the focus is active or inactive; likewise, in an area corresponding to cortical dysplasia, the metabolism will be decreased to a greater or lesser extent according to the type of dysplasia, but the center of this is usually an area with low metabolism and therefore with low cerebral perfusion.[5,14,18]

In a study carried out in animals where a record was made with ECoG and correlation of the epileptogenic focus employing IT, an increase in thermal activity was found which was in contrast to the studies carried out by PET using fluorodeoxyglucose where the area epileptogenic was hypometabolic.[4]

Thermosensitive/thermochromic silicone (TTS)

Silicone is a widely used material in different settings of medical practice and its safety in neurosurgery has already been established.[6] In epilepsy surgery, silicone grids with ECoG electrodes are usually placed directly on the cerebral cortex that can be left implanted for periods of several days. Likewise, the catheters of the permanent permanence ventriculoperitoneal shunt systems used in neurosurgery that is used for the treatment of hydrocephalus are made of silicone, to name two very frequent scenarios of neurosurgical medical practice. The TTS responds quickly to the temperature of the surface with which it is in contact with changes in its color [Figure 2], within a response range between 21°C and 38°C.

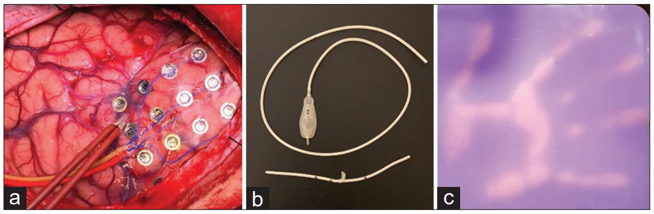


Figure 2: Examples of silicone used in neurosurgery and heat-sensitive silicone. (a) Silicone grids routinely used in electrocorticography; (b) silicone ventriculoperitoneal shunt systems for permanent implantation routinely used in neurosurgery; and (c) change of color according to the temperature of the surface of the thermosensitive/thermochromic silicone. Its basal color at room temperature is purple and changes to pink when heated. Note the high spatiotemporal resolution of the material.

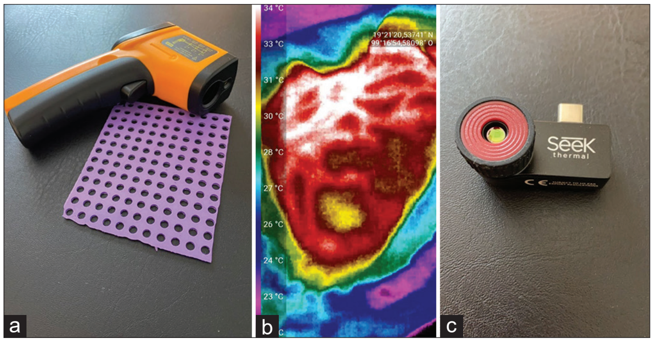


Figure 3: (a) Laser pointer thermometer and silicone grid used in the first stage of the infrared thermography mapping (ITM), in which different sites are recorded through the holes in the silicone grid to establish a coordinate system during the first stage of the ITM. (b) Intraoperative image obtained by the high-resolution thermographic camera that allows obtaining photographs and videos used in the second stage of the ITM. The yellow color shows the irritative area in one of the cases of the series described in this article. (c) Thermography camera that connects to a cell phone and records high-resolution thermography videos and photos.

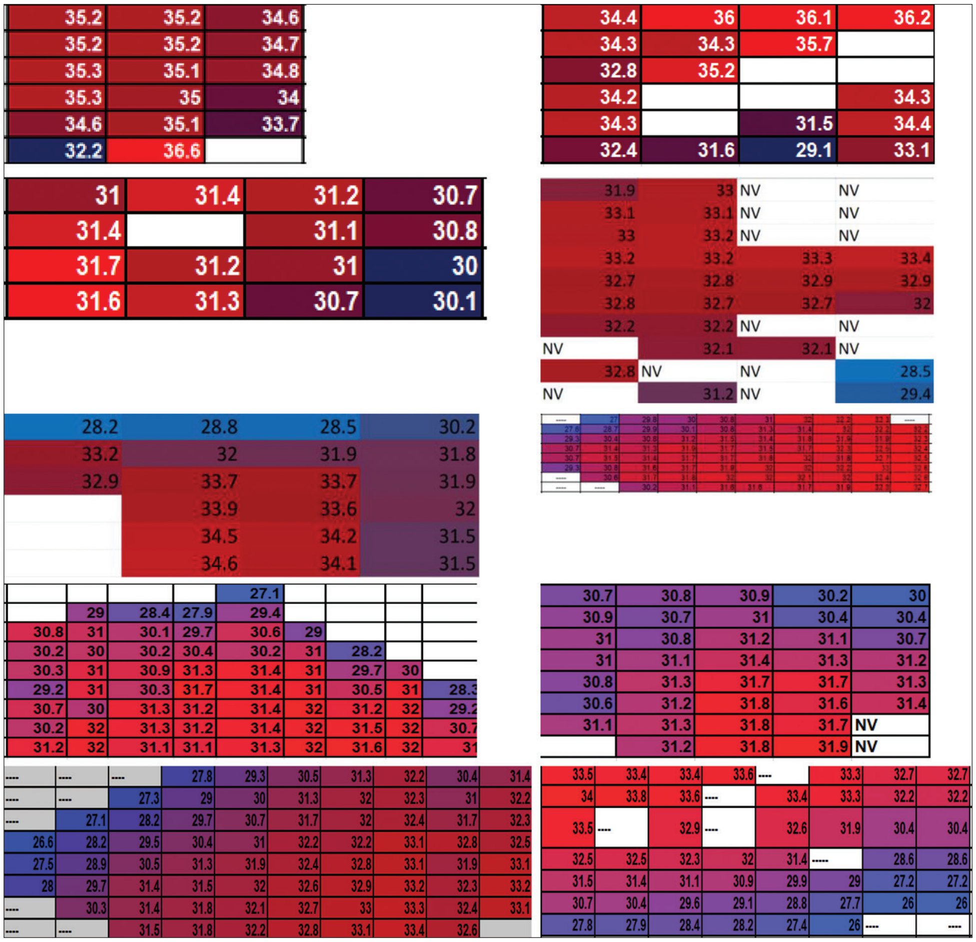
MATERIALS AND METHODS

With prior authorization from the ethics and research committees of our hospital and the signing of the informed consent of each patient, and according with the Helsinki Declaration of 1975, as revised in 2000, we included consecutive patients previously selected by the epilepsy clinic with a diagnosis of drug-resistant unilateral temporal focal epilepsy. We perform craniotomy following the protocol established for ITM,[3] using in the first stage, some silicone grids with perforations with coordinates, through which, using an infrared thermometer with a laser pointer (Floureon (TM), range from -50 to + 380°C), we identified the hypothermic/hypometabolic zones in each case [Figures 3 and 4]. In a second stage of the ITM, we made video filming of the exposed cerebral cortex through another infrared camera (SEEK THERMAL PRO with 320 × 240 thermal sensor, 32° field of view, <9 Hz frame, focusable lens, detection of −40–100°F, captures photos and videos, spot temperature, high-low temperature, threshold mode, nine color palettes, automatic and adjustable control, and four emissivity settings) that converts the temperature measurement to a visible thermographic image [Figure 3b and c], being possible to evaluate the different thermal gradients of the brain, combining the anatomical image with the color palette of the infrared spectrum in real time and storing it on video. All measurements (ΔT, thermocline, temperature recordings, TTS thermic imprint, and ECoG) were interpreted by four independent observers to reduce interobserver (kappa) error. All photos and videos are stored for the future reference.

The third stage of the evaluation of brain metabolism consists of placing the TTS on the brain surface. The TTS shows the observer a thermal imprint of the surface with which it is in contact in a period between 3 and 12 s. Its operating range is between 21 and 38°C. Its basal color is purple and when heated it changes to pink. The coldest areas remain in the basal purple color, allowing different thermal patterns to be identified with the naked eye. After a period of 2–40 s of being in contact with the surface of the brain, eventually, the entire plate of the TTS turns pink by induction of heat, so the reading of the thermal imprint should normally be done before the 20 s of placement. No special filter or light is required to observe the changes and they are easily perceived by any observer [Figure 5]. Once the three stages of the ITM were completed, we performed ECoG to identify the IZs. ECoG consists of placing silicone mesh with electrodes directly on the brain surface to record brain electrical activity during surgery. This allows us to delimit the epileptogenic circuit with greater precision since electroencephalograms have lower sensitivity and specificity than ECoG. Based on the results of the ECoG, the definitive limits of resections or deafferentation in epilepsy surgery are decided. We compared the results obtained by the three methods (ITM, TTS, and ECoG), establishing the ECoG as the gold standard. The samples of the tissues obtained were sent to pathology.[1-3] The purpose of performing the three stages of ITM previously described is to verify the consistency in the identification of hypothermic areas of the brain by the three methods and subsequently compare them with the results of the ECoG.

RESULTS

Ten consecutive cases with surgical criteria for drug-resistant unilateral temporal focal epilepsy were included in our series. Of these, 6 were women (60%) and 4 men (40%). Age ranges from 15 to 56 years, mean 33.2 years. All patients were treated with unilateral functional temporal lobectomy. The mean hospital stay was 4 days. No intraoperative complications were observed and also during the 1st postoperative month. All patients without neurological morbidity were discharged. In all cases (100%), there was consistency in the location of the IZ between the ECoG, ITM, and TTS. All cases were



35.2	35.2	34.6
35.2	35.2	34.7
35.3	35.1	34.8
35.3	35	34
34.6	35.1	33.7
32.2	36.6	

34.4	36	36.1	36.2
34.3	34.3	35.7	
32.8	35.2		
34.2			34.3
34.3		31.5	34.4
32.4	31.6	29.1	33.1

31	31.4	31.2	30.7
31.4		31.1	30.8
31.7	31.2	31	30
31.6	31.3	30.7	30.1

31.9	33	NV	NV
33.1	33.1	NV	NV
33	33.2	NV	NV
33.2	33.2	33.3	33.4
32.7	32.8	32.9	32.9
32.8	32.7	32.7	32
32.2	32.2	NV	NV
NV	32.1	32.1	NV
32.8	NV	NV	28.5
NV	31.2	NV	29.4

28.2	28.8	28.5	30.2
33.2	32	31.9	31.8
32.9	33.7	33.7	31.9
	33.9	33.6	32
	34.5	34.2	31.5
	34.6	34.1	31.5

----	27	29.8	30	30.8	31	32	32.2	32.3	----
27.6	28.7	29.9	30.1	30.8	31.3	31.4	32	32.2	32.2
29.3	30.4	30.8	31.2	31.5	31.4	31.8	31.9	31.9	32.3
30.7	31.4	31.3	31.9	31.7	31.5	31.7	32.3	32.5	32.4
30.7	31.5	31.4	31.7	31.7	31.8	32	31.8	32.7	32.5
29.3	30.8	31.6	31.7	31.9	32	32	32.2	33	32.6
----	30.6	31.7	31.8	32	32	32.1	32	32.4	32.6
----	----	30.2	31.1	31.6	31.6	31.7	31.9	32.3	32.7

				27.1				
	29	28.4	27.9	29.4				
30.8	31	30.1	29.7	30.6	29			
30.2	30	30.2	30.4	30.2	31	28.2		
30.3	31	30.9	31.3	31.4	31	29.7	30	
29.2	31	30.3	31.7	31.4	31	30.5	31	28.3
30.7	30	31.3	31.2	31.4	32	31.2	32	29.2
30.2	32	31.3	31.2	31.4	32	31.5	32	30.7
31.2	32	31.1	31.1	31.3	32	31.6	32	31

30.7	30.8	30.9	30.2	30
30.9	30.7	31	30.4	30.4
31	30.8	31.2	31.1	30.7
31	31.1	31.4	31.3	31.2
30.8	31.3	31.7	31.7	31.3
30.6	31.2	31.8	31.6	31.4
31.1	31.3	31.8	31.7	NV
	31.2	31.8	31.9	NV

----	----	----	27.8	29.3	30.5	31.3	32.2	30.4	31.4
----	----	27.3	29	30	31.3	32	32.3	31	32.2
----	27.1	28.2	29.7	30.7	31.7	32	32.4	31.7	32.3
26.6	28.2	29.5	30.4	31	32.2	32.2	33.1	32.8	32.5
27.5	28.9	30.5	31.3	31.9	32.4	32.8	33.1	31.9	33.1
28	29.7	31.4	31.5	32	32.6	32.9	33.2	32.3	33.2
----	30.3	31.4	31.8	32.1	32.7	33	33.3	32.4	33.1
----	----	31.5	31.8	32.2	32.8	33.1	33.4	32.6	

33.5	33.4	33.4	33.6	----	33.3	32.7	32.7
34	33.8	33.6	----	33.4	33.3	32.2	32.2
33.5	----	32.9	----	32.6	31.9	30.4	30.4
32.5	32.5	32.3	32	31.4	-----	28.6	28.6
31.5	31.4	31.1	30.9	29.9	29	27.2	27.2
30.7	30.4	29.6	29.1	28.8	27.7	26	26
27.8	27.9	28.4	28.2	27.4	26	----	----

Figure 4: Graphs of the measurements with the laser pointer thermometer of the first stage of the infrared thermography mapping. In this color code, the blue tones correspond to the coldest temperature registers and the red to the warmest ones. The presence of cold areas is noticeable, guarded by a radial heating pattern. All measurements are expressed in degrees centigrade. These cold areas coincide with the irritative areas detected by electrocorticography and with the hypothermic areas detected through the thermochromic/thermosensitive silicone in all the cases in this series. NV: Not assessable due to the presence of blood vessels.

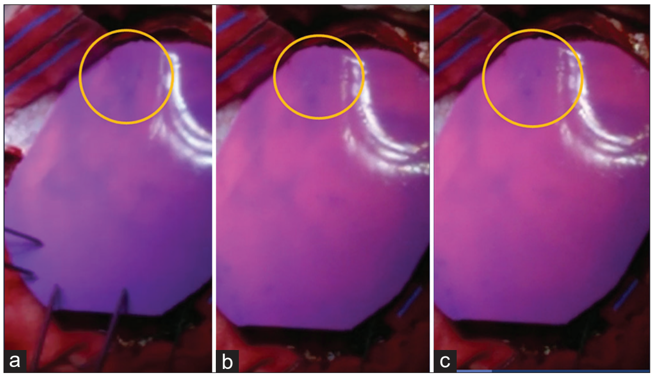


Figure 5: Successive pictures of the changes in the color of the thermosensitive/thermochromic silicone when in contact with the brain surface. (a) At 2.50 s; (b) at 6.15 s; and (c) at 9.15 s. The yellow circle shows the irritative area detected by the electrocorticography. Note how the cooler irritant area remains in the purple basal color, for the silicone that begins to change rapidly (from ~3 s) to the pink color when heated by contact with the rest of the surface of the brain that has a normal temperature, around this zone of abnormal hypothermia.

diagnosed as III-A dysplasia according to the International League Against Epilepsy classification.

DISCUSSION

In neurological surgery, there is always a very delicate balance between the areas of the brain that must be preserved and those that must be removed. This can be even more difficult, if the appearance of healthy tissue is the same as that of diseased tissue to the naked eye, as occurs very frequently in epilepsy surgery since cortical dysplasias are the etiologies most frequently responsible for drug-resistant epilepsy and its gross appearance is indistinguishable from healthy brain tissue. To make surgeries more precise, effective, and safe, we have developed the ITM protocol[1-3] and the TTS that allow real-time assessment of brain metabolism without using stains, contrasts, lights, radiation, or special filters, with a significantly low cost compared to ECoG, which would favor its use in emerging economies like ours. We believe that this facilitates decision-making for the neurosurgeon in real time and could improve surgical results. Our research team has proven the usefulness of these new intraoperative evaluation methods in other pathologies, such as tumor surgery, cavernomas, and abscesses, among others, in addition to their use in epilepsy surgery.[1-3]

In this series of 10 consecutive cases, there were no complications associated with the use of any of the methods described. There was a 100% correlation between ITM, TTS, and ECoG in detecting IZs in drug-resistant temporal lobe epilepsy.

CONCLUSION

The results described in this proof of concept are preliminary. Although we obtained consistency between the three methods to locate IZ in all the cases in this series, it is still necessary to carry out studies with a larger sample to determine its sensitivity and specificity, respecting the current experimentation guidelines in epilepsy surgery, in other neurosurgical etiologies, and in surgery of other organs and systems.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

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Nil.

Conflicts of interest

The principal author participated in the design of the thermochromic silicone and may receive a fee if it is patented and commercialized.

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