Laser speckle imaging to improve clinical outcomes for patients with trigeminal neuralgia undergoing radiofrequency thermocoagulation

Matthias Ringkamp, MD, Matthew Wooten, BS, Benjamin S. Carson Sr., MD, Michael Lim, MD, PhD, Timothy Hartke, BS, and Michael Guarnieri, PhD

Department of Neurological Surgery, Johns Hopkins School of Medicine, Baltimore, Maryland

OBJECTIVE Percutaneous treatments for trigeminal neuralgia are safe, simple, and effective for achieving good pain control. Procedural risks could be minimized by using noninvasive imaging techniques to improve the placement of the radiofrequency thermocoagulation probe into the trigeminal ganglion. Positioning of a probe is crucial to maximize pain relief and to minimize unwanted side effects, such as denervation in unaffected areas. This investigation examined the use of laser speckle imaging during probe placement in an animal model.

METHODS This preclinical safety study used nonhuman primates, *Macaca nemestrina* (pigtail monkeys), to examine whether real-time imaging of blood flow in the face during the positioning of a coagulation probe could monitor the location and guide the positioning of the probe within the trigeminal ganglion.

RESULTS Data from 6 experiments in 3 pigtail monkeys support the hypothesis that laser imaging is safe and improves the accuracy of probe placement.

CONCLUSIONS Noninvasive laser speckle imaging can be performed safely in nonhuman primates. Because improved probe placement may reduce morbidity associated with percutaneous rhizotomies, efficacy trials of laser speckle imaging should be conducted in humans.

<http://thejns.org/doi/abs/10.3171/2015.1.JNS14408>

KEY WORDS trigeminal neuralgia; multiple sclerosis; radiofrequency thermocoagulation; laser speckle imaging; preclinical safety study; functional neurosurgery; pain

TRIGEMINAL neuralgia (TGN) is a neuropathic pain syndrome typically affecting patients older than 50 years.¹ In younger patients, the syndrome is frequently associated with multiple sclerosis.^{2,7,17,18} Percutaneous rhizotomies are front-line tools for treating patients for whom microvascular decompression is not indicated.^{11,15,16} Studies have found the procedure to be simple, safe, and cost-effective.^{5,22,23} Yet, anatomical variables can confound precise needle placement. Clinical experience suggests that treatment processes can lead to complications, including hyperalgesia and drug-resistant pain. Improved lesioning accuracy may help the neurosurgeon minimize complications.^{10,14,17} In the present study, changes in skin blood flow were produced by antidromic electrical stimulation of the primary afferent fibers in different branches of the trigeminal nerve and the trigeminal

ganglion. Electrical stimulation of nociceptive primary afferents leads to the release of vasodilatory neuropeptides (e.g., substance P and calcitonin gene-related peptide) from their terminals in the skin, leading to an increase in skin blood flow. Following trigeminal nerve stimulation, there is a close association between changes in blood-flow distribution, primarily depending on which branch of the trigeminal nerve is being stimulated.⁶

Changes in skin blood flow can be measured by laser speckle contrast analysis (LASCA) imaging, which allows the assessment of blood flow in real time.¹⁹ The surface illuminated by the laser scatters light, forming a random interference pattern (speckle contrast) consisting of dark and bright areas. When there is movement in the surface, such as red blood cells in a tissue, the speckle pattern changes. A digital-imaging camera in the instru-

ABBREVIATIONS LASCA = laser speckle contrast analysis; ROI = region of interest; TGN = trigeminal neuralgia.

SUBMITTED March 10, 2014. **ACCEPTED** January 28, 2015.

INCLUDE WHEN CITING Published online August 14, 2015; DOI: 10.3171/2015.1.JNS14408.

ment records and quantifies the changes. LASCA imaging is being used in a range of clinical research applications including diabetes, dermatology, neurology, and vascular surgery. It shows promise to be a noninvasive, low-cost imaging method for guiding surgical therapies. It appears reasonable to examine LASCA imaging's use for current neuronavigation strategies. If safety is shown in animal studies, the technique could be investigated for safety and efficacy in humans. However, before the technique can be approved for human studies, safety must be unambiguously explored in animal models. The authors explored the safety of LASCA imaging in primates undergoing stimulation. This report shows that 2 neurosurgeons have successfully used a PeriCam PSI (Perimed Inc.) laser-imaging system in 6 procedures involving 3 nonhuman primates.

Methods

Studies were approved by the Johns Hopkins University Institutional Animal Care and Use Committee, which is an adherent to the guidelines of the Committee for Research and Ethical Issues of the International Association for the Study of Pain (IASP). Animals were monitored daily and postoperatively for signs of distress and pain.

Animals

Macaca nemestrina (pigtail monkeys) used in this study included 2 males weighing 6 and 10 kg, and 1 female weighing 5 kg. All 3 animals were 6 years old. The animals were initially sedated with ketamine/atropine (20 mg/kg). An intravenous catheter was placed and anesthesia induced with a pentobarbital bolus (10 mg/kg). A continuous infusion of dextrose (5%) was administered to maintain hydration. Electrocardiography was used to monitor heart rate, and supplemental doses of pentobarbital (5 mg/kg) were administered when heart rate increased > 10% in response to mildly painful stimuli. A rectal probe was inserted to monitor body temperature, which was maintained using water-jacketed heating pads. The animal's cheek was closely shaven. Under fluoroscope guidance, the stimulation probe was inserted through the foramen ovale into the trigeminal ganglion. The probe was used as a cathode for the following electrical stimulation. A 22-gauge needle was placed subcutaneously behind the ipsilateral ear to serve as a return electrode. Electrical stimuli were delivered from a constant-current pulse generator (Digitimer Ltd.) at 1 Hz, and the electrical intensity needed to produce muscle twitch in the masseter muscle was determined. Twitch thresholds below 5 mA suggested proper positioning of the stimulation probe. The animal was then paralyzed with pancuronium bromide (0.1 mg/kg) to avoid stimulus-evoked movement artifacts that would interfere with blood-flow measurements. The animal was then positioned such that half of its face ipsilateral to the stimulated ganglion was perpendicular to the imaging system used to measure blood flow (see below for details).

Electrical stimulation of the trigeminal ganglion was used to increase blood flow to the face. In our initial experiments (n = 2), only a single stimulus paradigm was

used (120 pulses of 0.1-msec duration delivered at 1 Hz at 100-mA intensity), but the position of the stimulation electrode was changed to investigate if different parts of the trigeminal ganglion (V1, V2, and V3) could be stimulated. Stimulation at high intensity was used to ensure activation of a large number of neurons because 1) there are few direct means to monitor the stimulus intensity needed to stimulate nociceptive C-fiber neurons in the trigeminal ganglion, and 2) the stimulus electrode had only a small pointed surface. In the following experiments (n = 2), the effect of pulse number on blood flow was investigated, with trains of stimuli consisting of 2, 4, 8, 16, 32, 64, and 120 pulses (all at 100 mA) so that "pulse number"–response plots could be constructed. In both experiments, we then determined the threshold intensity necessary to produce a noticeable increase in blood flow (120 pulses, 1 Hz). In 1 of these experiments, we created a stimulus intensity response function by delivering 32 pulses (1 Hz) at different stimulus intensities. Similar to our initial experiments, we then repositioned the stimulation electrode to test if different areas of the trigeminal ganglion could be preferentially stimulated. Using the x-ray image after the initial electrode placement as a reference point, the needle was either inserted or removed approximately 2–3 mm at a time, followed by electrical stimulation (120 pulses, 1 Hz) and blood-flow measurements.

Skin blood-flow changes in the face were measured with laser speckle technology using a PeriCam PSI imaging system. Laser speckle technology measures blood flow in perfusion units (arbitrary units), which are collected for each pixel contained in the image. Each pixel, or data point, corresponds to a discrete area (typically about 0.1 mm²) that varies based on the distance of the PeriCam system from the target. In contrast to thermography, which measures changes in temperature, speckle imaging measures changes in blood flow. This system allows for instantaneous, high-resolution visualization of changes in blood flow over large areas. In contrast, comparable laser Doppler flow measurements have much slower data acquisition (taking up to minutes) and allow changes in blood flow to be measured over relatively small areas. In the present study, the region of interest (ROI) was defined by the investigator during off-line analysis, primarily to summarize data for the safety and utility analyses. However, in a clinical setting, such analysis would not be necessary. As shown in Video 1, the surgeon can observe the change in blood flow in real time without data analysis.

VIDEO 1. Clip showing real-time blood-flow changes from trigeminal ganglion stimulation. The upper panel shows the changes in blood flow over time. Units of the y-axis are arbitrary, and the plotted value represents an average of the whole face. Baseline, start, and end of stimulation (100 mA, 16 pulses, 0.1-msec duration, 1 Hz) occurred as indicated. In the lower panel, each image color codes blood flow in a given area, with red being an area of high blood flow and blue being an area of low blood flow. Changes in blood flow corresponding to the regions of the face innervated by the mandibular branch of the trigeminal ganglion are clearly visible approximately 15 seconds after the start of stimulation. Of note, a high speckle signal from below the jaw line could be recorded prior to stimulation, but this signal did not increase with stimulation. Copyright Michael Guarnieri. Published with permission. Click here to view with Media Player. Click here to view with Quicktime.

Prior to stimulation, baseline blood-flow levels were measured for 60 seconds. Following stimulation, blood flow was monitored for 5 minutes or until perfusion levels had returned to baseline levels. After a 2-minute interval, the next stimulation was initiated.

Data Analyzed

Data were collected and analyzed using PIMSoft (Perimed Inc.), which was provided with the imaging system. Speckle images of the side of the face ipsilateral to the stimulated ganglion were acquired at a rate of 1 per second. Two parameters were extracted from the acquired pictures and used for analysis: 1) peak blood flow, and 2) area of increased blood flow.

Peak Blood Flow

To determine peak blood flow in response to electrical stimulation, an ROI encompassing the side of the face stimulated was defined in off-line analysis. The average perfusion value across pixels within this ROI was calculated for each image. A baseline grand mean average was then calculated by averaging these ROI perfusion values across baseline images. To adjust for differences in baseline perfusion and to compare stimulation effects across experiments, this baseline grand mean value was subtracted from every image throughout the subsequent recording. A baseline adjusted average of blood flow was then calculated for every image using the image software, and the highest average value was defined as “peak blood flow.”

Area of Increased Blood Flow

To determine the area showing an increase in blood flow, an ROI was defined in off-line analysis. To reduce the influence of signal variability on area measurements, images captured during the first 5 minutes of recording were down-sampled at a rate of 10:1, creating 1 composite image for every 10 images recorded. The perfusion data of selected composite images from time points of interest (i.e., last 2 composite images prior to stimulation, 1 image with peak perfusion) were then exported to Microsoft Excel for additional analysis. In Excel, the data for a single pixel from a PIMSoft image are pasted in a single cell, i.e., each cell contains the data from 1 pixel. Values from each pixel of the 2 baseline images were averaged to determine the average baseline perfusion value for each individual pixel. In addition, for each pixel, the difference between perfusion values of baseline images 1 and 2 was calculated on a cell-to-cell basis. Then, an average was calculated across the entire image to determine the average perfusion variability and its corresponding SD.

To determine areas of significant perfusion increase due to electrical stimulation, the average perfusion value for each pixel was subtracted from the corresponding value of that pixel in the image showing peak blood flow. If the resulting difference was larger than the average perfusion variability plus 1 SD, the corresponding pixel was judged as showing a significant increase in perfusion. The number of cells fulfilling the above-stated criterion was determined and converted into an area measurement using data provided by PIMSoft.

Results

We performed a total of 9 experiments in 3 pigtail monkeys under conditions that accurately reproduce human therapy. In 6 of the 9 experiments, we were able to increase blood flow to regions of the face by electrically stimulating different regions of the trigeminal ganglion. Examples of such experiments are shown in Videos 1 and 2.

VIDEO 2. Clip showing blood-flow changes from trigeminal ganglion stimulation. The format is identical to that of Video 1. Similar to Video 1, electrical stimulation (100 mA, 16 pulses, 0.1-msec duration, 1 Hz) produced an increase in skin blood flow that became visible within 10–15 seconds after onset of stimulation. The increase in blood flow was restricted to the zone innervated by V3. Copyright Michael Guarnieri. Published with permission. [Click here to view with Media Player.](#) [Click here to view with Quicktime.](#)

As shown in both videos, electrical stimulation produced a striking increase of blood flow in the V3 areas and a more subtle increase in the tongue. In Video 1, it should be noted that the strong signal below the jaw line (i.e., throat, neck, and shoulder region) did not change throughout the recording. The uncharacteristic high signal in that region can be attributed to slight movements of fur hairs that were not shaved during animal preparation.

In each successful case of stimulation, changes in facial blood flow could be observed 10–15 seconds after stimulation onset. After changing the position of the stimulation electrode, different patterns of blood flow were observed within the facial region, suggesting that different neurons within the ganglion were stimulated (see below). By varying the stimulus parameters (pulse number and intensity), we were able to alter the size and intensity of the blood-flow increase.

Effect of Needle Repositioning

In 4 of 6 successful experiments, the pattern of increased blood flow in the facial skin changed following repositioning of the stimulating electrode. An example of such an experiment is shown in Fig. 1, in which still-frame images depict changes in blood flow relative to baseline. In the original needle position (Fig. 1A), increases in blood flow were observed across all areas of the face innervated by the maxillary and mandibular branches of the trigeminal nerve (V2 and V3). After a 6-mm withdrawal of the stimulating electrode (Fig. 1B), stimulation with identical parameters induced blood flow only in the cheek/chin (V3). An additional withdrawal of about 2 mm (Fig. 1C) further reduced the area, showing an increase in blood flow following stimulation.

A different representation of the data from that same experiment is shown in Fig. 2, in which the change in perfusion following electrical stimulation is plotted over time for different electrode positions. Figure 2 (upper panel) illustrates the blood-flow data from the mandibular area (V3), and Fig. 2 (lower panel) shows the corresponding data from the maxillary area (V2). Changes in facial blood flow could be seen almost immediately after stimulation onset, and the increase in blood flow lasted for the duration of the recording. Importantly, the increase in blood flow was different after each repositioning of the stimulation electrode. In the original needle position, blood-flow increases were observed in the max-

FIG. 1. Stimulation-induced blood-flow changes are dependent on the position of the stimulation electrodes. For better visualization of the blood-flow changes, baseline flow values were subtracted. Pictures show change in blood perfusion 10 seconds after stimulation onset. **A:** Blood flow with stimulation electrode at original position. **B:** Effect on blood flow after electrode had been withdrawn by approximately 6 mm. **C:** Effect of electrical stimulation on blood flow after the stimulating electrode had been withdrawn by an additional 2 mm. *Red* indicates an overall increase in blood flow compared with prestimulation baseline values. *Blue* indicates an overall decrease. *Black* indicates no net change.

FIG. 2. Increase in blood flow is dependent on position of stimulation electrode. Changes in blood flow over time are depicted for 3 positions of the stimulation electrode. **Upper:** Blood-flow increase in the mandibular region. **Lower:** Blood-flow changes observed over the maxillary area. Data from upper and lower panels were recorded at the same time. Stimulus parameters were kept constant (120 pulses, 0.1-msec duration, 100 mA) for different electrode positions. Time of stimulation is indicated by arrow. a.u. = arbitrary units.

illary and mandibular innervation territories (blue lines in Fig. 2 [upper and lower panels]). After withdrawing the electrode by approximately 6 mm (red lines in Fig. 2 [upper and lower panels]), the stimulation-induced increase in blood flow was reduced in the mandibular area (Fig. 2 [upper panel]) and lost in the maxillary area (Fig. 2 [lower panel]). In the mandibular area, blood flow was further reduced after the electrode had been withdrawn by approximately an additional 2 mm (green line in Fig. 2 [upper panel]) and, as expected, no changes in blood flow were observed in the maxillary region (green line in Fig. 2 [lower panel]).

Effect of Number of Pulses

Changes to the area of increased blood flow, as well as perfusion intensity, could be induced by changing the number of pulses used for electrical stimulation. As shown in Fig. 3 (upper panel), the size of the area exhibiting an increase in blood flow increased initially with the number of delivered electrical pulses. However, the area size did not increase further when pulse number was increased beyond 32 pulses. Similarly, the maximal perfusion (Fig. 3 [lower panel]) appeared to saturate at higher pulse numbers.

Effect of Stimulus Intensity

In 3 experiments, we investigated the effect of stimulus intensity on: 1) the size of the area with increased blood flow, and 2) the perfusion intensity while the number of delivered pulses was kept constant. As illustrated in Fig. 4, the area of increased blood flow increased with stimulus intensity in a mostly linear fashion.

Discussion

Percutaneous surgery is a primary treatment for TGN in the elderly and in patients with multiple sclerosis.^{3,4,8,9} Clinical outcomes are influenced by variables, including coagulation temperature, coagulation time, and probe location within the trigeminal ganglion.^{12,16,21,24} Positioning of the probe is crucial to maximize pain relief and to

FIG. 3. Effect of pulse number on size of skin area (**upper panel**) and maximal perfusion (**lower panel**). To compare the size of skin areas across different experiments, data were normalized to the largest area of increased blood flow induced by stimulation with 120 pulses. Data were obtained in 2 experiments.

minimize unwanted side effects, such as denervation in unaffected areas.

The primary objective of the study was to test whether laser speckle measurements can be safely used to measure blood-flow changes in the facial skin. The data reported here show that laser speckle technology can be used safely in nonhuman primates in trigeminal-stimulation studies. This procedure appeared to be well tolerated by our animals, and no atypical behavior was observed after recovery from anesthesia. Although muscle contraction could be observed at low stimulus intensities, current intensities of up to 100 mA were used in the experiments to ensure activation of a large number of nociceptive neurons. Although we cannot rule out the possibility that this high stimulus intensity produced neuronal damage, such damage was probably negligible, as blood-flow increases could be produced repeatedly from the same stimulation site.

The data show that trigeminal ganglion stimulation leads to increase in facial skin blood flow that can be visualized in real time using laser speckle technology. It is probable that the skin areas with an increase in blood flow

FIG. 4. Size of skin area with increased blood flow depends on stimulus intensity. Size of area was normalized to the area size induced by stimulation with maximal stimulus intensity ($n = 3$).

reflect and indicate the trigeminal branch(es) stimulated, but recordings of neuronal activity from the trigeminal ganglion/branches would be needed to test this relationship further. Recently, electrophysiological recordings of retrograde sensory and motor action potentials have been used to locate the position of the thermocoagulation probe relative to the different trigeminal nerve divisions.¹³ Such recordings may provide a useful tool to investigate further the relationship between areas of blood-flow changes and innervation territory. Alternatively, in animal studies, one could mark the stimulation site within the trigeminal ganglion/branches (e.g., by producing a small lesion) to investigate postmortem whether the stimulated and marked branch indeed innervated the areas in which an increase in blood flow was seen. Because our tests were planned as survival experiments, such lesions were not produced. Nonetheless, it is probable that the area with an increase in skin blood flow corresponds to the branch stimulated, as the area with an increase in blood flow changed with the position of the stimulating electrode (observed in 4 experiments).

Under the chosen experimental parameters, the speckle imaging technique used was extremely sensitive, as increases in skin blood flow were detected already following approximately 5 pulses (Fig. 3 [upper panel]). In contrast, the speckle imaging technique was not very specific. As seen in Video 1, hair movements from the animal's fur at the neck and shoulder mimicked an area with high skin blood flow. Hair movement, however, is not expected to pose a major problem when imaging the faces of human patients. Specificity of the speckle signal is increased further by considering that the change is occurring in skin areas that are innervated by the stimulated neuronal structure (in this case, facial skin), and that timing of the observed change in speckle signal is closely related to the onset of stimulation.

The results have clinical implications in several aspects. Electrical stimulation of the trigeminal ganglion increases facial blood flow to all regions (V1, V2, and V3) innervated by the trigeminal ganglion, as measured by la-

ser speckle technology. Although it is an important clinical question, in this study, specific efforts to selectively activate V1 and V2 were not made. It is recognized that stimulating V3 is often easier than selectively stimulating the other branches. Selective stimulation of V1 and V2 should primarily depend on the positioning of the stimulation electrode within the ganglion, not the measuring technique used to assess skin blood-flow changes. There is no reason why selective blood-flow changes in V1 and V2 could not be measured with this technology if the stimulation electrode were indeed positioned close to the V1 and V2 branches. After repositioning the stimulation electrode within the trigeminal ganglion, increases in blood flow were observed in different regions of the face that are innervated by different portions of the trigeminal nerve. This finding is particularly encouraging, because selective stimulation should allow us to assess the position of the lesion to be placed in patients. Changes in blood flow following reposition could be seen almost instantly after stimulation onset, potentially quickly providing surgeons with information on needle position.

Conclusions

Monitoring facial skin blood flow with speckle technology was fast and uncomplicated. Therefore, we expect this technology to be easily transferable to the clinical setting. The results from these studies can address safety concerns for an institutional review board application.

Whether the imaging technology can reduce the morbidity in a clinical setting has yet to be determined. It may be particularly useful to couple clinical studies with new tools to measure minimum clinically important differences in pain improvement for patient-reported outcomes.²⁰

Acknowledgment

We gratefully acknowledge Perimed for its efforts to rent equipment for this research.

References

- Anderson WS, James C, Carson BS Sr: Trigeminal, glossopharyngeal, and geniculate neuralgias, in Schmidt RE, Willis WD (eds): **Encyclopedia of Pain**. Berlin: Springer, 2007, p 20
- Bahgat D, Ray DK, Raslan AM, McCartney S, Burchiel KJ: Trigeminal neuralgia in young adults. **J Neurosurg** **114**:1306–1311, 2011
- Bender MT, Pradilla G, Batra S, See AP, James C, Pardo CA, et al: Glycerol rhizotomy and radiofrequency thermocoagulation for trigeminal neuralgia in multiple sclerosis. **J Neurosurg** **118**:329–336, 2013
- Bergenheim AT, Asplund P, Linderth B: Percutaneous retrogasserian balloon compression for trigeminal neuralgia: review of critical technical details and outcomes. **World Neurosurg** **79**:359–368, 2013
- Cheng JS, Lim DA, Chang EF, Barbaro NM: A review of percutaneous treatments for trigeminal neuralgia. **Neurosurgery** **10** (Suppl 1):25–33, 2014
- Drummond PD, Gonski A, Lance JW: Facial flushing after thermocoagulation of the Gasserian ganglion. **J Neurol Neurosurg Psychiatry** **46**:611–616, 1983
- Foley PL, Vesterinen HM, Laird BJ, Sena ES, Colvin LA, Chandran S, et al: Prevalence and natural history of pain in adults with multiple sclerosis: systematic review and meta-analysis. **Pain** **154**:632–642, 2013
- Harries AM, Mitchell RD: Percutaneous glycerol rhizotomy for trigeminal neuralgia: safety and efficacy of repeat procedures. **Br J Neurosurg** **25**:268–272, 2011
- Keravel Y, Gaston A, Ciampi de Andrade D, Mencattini G, Le Guérinel C: [Balloon compression for the treatment of trigeminal neuralgia.] **Neurochirurgie** **55**:197–202, 2009 (Fr)
- Koizuka S, Saito S, Sekimoto K, Tobe M, Obata H, Koyama Y: Percutaneous radio-frequency thermocoagulation of the Gasserian ganglion guided by high-speed real-time CT fluoroscopy. **Neuroradiology** **51**:563–566, 2009
- Koopman JSH, de Vries LM, Dieleman JP, Huygen FJ, Stricker BH, Sturkenboom MC: A nationwide study of three invasive treatments for trigeminal neuralgia. **Pain** **152**:507–513, 2011
- Kouzounias K, Schechtmann G, Lind G, Winter J, Linderth B: Factors that influence outcome of percutaneous balloon compression in the treatment of trigeminal neuralgia. **Neurosurgery** **67**:925–934, 2010
- Lin B, Lu X, Zhai X, Cai Z: Use of sensory and motor action potentials to identify the position of trigeminal nerve divisions for radiofrequency thermocoagulation. **J Neurosurg** **121**:1497–1503, 2014
- Lin MHC, Lee MH, Wang TC, Cheng YK, Su CH, Chang CM, et al: Foramen ovale cannulation guided by intra-operative computed tomography with integrated neuronavigation for the treatment of trigeminal neuralgia. **Acta Neurochir (Wien)** **153**:1593–1599, 2011
- Mallory GW, Atkinson JL, Stien KJ, Keegan BM, Pollock BE: Outcomes after percutaneous surgery for patients with multiple sclerosis-related trigeminal neuralgia. **Neurosurgery** **71**:581–586, 2012
- Mathieu D, Effendi K, Blanchard J, Séguin M: Comparative study of Gamma Knife surgery and percutaneous retrogasserian glycerol rhizotomy for trigeminal neuralgia in patients with multiple sclerosis. **J Neurosurg** **117** Suppl:175–180, 2012
- Mohammad-Mohammadi A, Recinos PF, Lee JH, Elson P, Barnett GH: Surgical outcomes of trigeminal neuralgia in patients with multiple sclerosis. **Neurosurgery** **73**:941–950, 2013
- Montano N, Papacci F, Cioni B, Di Bonaventura R, Meglio M: What is the best treatment of drug-resistant trigeminal neuralgia in patients affected by multiple sclerosis? A literature analysis of surgical procedures. **Clin Neurol Neurosurg** **115**:567–572, 2013
- Peris-Celda M, Graziano F, Russo V, Mericle RA, Ulm AJ: Foramen ovale puncture, lesioning accuracy, and avoiding complications: microsurgical anatomy study with clinical implications. **J Neurosurg** **119**:1176–1193, 2013
- Reddy VK, Parker SL, Lockney DT, Patrawala SA, Su PF, Mericle RA: Percutaneous stereotactic radiofrequency lesioning for trigeminal neuralgia: determination of minimum clinically important difference in pain improvement for patient-reported outcomes. **Neurosurgery** **74**:262–266, 2014
- Roustit M, Millet C, Blaise S, Dufournet B, Cracowski JL: Excellent reproducibility of laser speckle contrast imaging to assess skin microvascular reactivity. **Microvasc Res** **80**:505–511, 2010
- Sivakanthan S, Van Gompel JJ, Alikhani P, van Loveren H, Chen R, Agazzi S: Surgical management of trigeminal neuralgia: use and cost-effectiveness from an analysis of the Medicare Claims Database. **Neurosurgery** **75**:220–226, 2014
- Tang YZ, Jin D, Li XY, Lai GH, Li N, Ni JX: Repeated CT-guided percutaneous radiofrequency thermocoagulation for recurrent trigeminal neuralgia. **Eur Neurol** **72**:54–59, 2014

24. Weng Z, Zhou X, Liu X, Wei J, Xu Q, Yao S: Perioperative pain in patients with trigeminal neuralgia undergoing radio-frequency thermocoagulation of the Gasserian ganglion. *J Craniofac Surg* **24**:1298–1302, 2013

Disclosures

Funds to support this research were received from The Neurosurgery Pain Research Institute at Johns Hopkins. Equipment for this research was rented from Perimed. There are no conflicts of interest.

Author Contributions

Conception and design: Guarnieri, Ringkamp, Carson, Lim. Acquisition of data: Wooten, Carson, Lim, Hartke. Analysis and interpretation of data: Guarnieri, Ringkamp, Wooten, Lim, Hartke. Drafting the article: Guarnieri, Ringkamp, Wooten. Critically revising the article: Guarnieri, Ringkamp. Reviewed submitted version of manuscript: Guarnieri. Approved the final version of the manuscript on behalf of all authors: Guarnieri. Administra-

tive/technical/material support: Ringkamp, Hartke. Study supervision: Carson, Hartke.

Supplemental Information

Videos

Video 1, Media Player. http://mfile.akamai.com/21490/wmv/digitalwbc.download.akamai.com/21492/wm.digitalsource-na-regional/jns14-408_video_1.asx.

Video 1, Quicktime. http://mfile.akamai.com/21488/mov/digitalwbc.download.akamai.com/21492/qt.digitalsource-global/jns14-408_video_1.mov.

Video 2, Media Player. http://mfile.akamai.com/21490/wmv/digitalwbc.download.akamai.com/21492/wm.digitalsource-na-regional/jns14-408_video_2.asx.

Video 2, Quicktime. http://mfile.akamai.com/21488/mov/digitalwbc.download.akamai.com/21492/qt.digitalsource-global/jns14-408_video_2.mov.

Correspondence

Michael Guarnieri, Department of Neurological Surgery, Johns Hopkins School of Medicine, 1550 Orleans St., CRB 2, Rm. 2M51, Baltimore, MD 21231. email: mguarnie@jhmi.edu.