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Pre-operative image-based segmentation of the cranial nerves and blood vessels in microvascular decompression: Can we prevent unnecessary explorations?

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ABSTRACT

Objectives: This study was conducted to validate the accuracy of image-based pre-operative segmentation using the gold standard endoscopic and microscopic findings for localization and pre-operative diagnosis of the offensive vessel.

Patients and methods: Fourteen TN and 6 HS cases were randomly selected. All patients had 3T MRI, which included thin-sectioned 3D space T2, 3D Time of Flight and MPRAGE Sequences. Imaging sequences were loaded in BrainLab iPlanNet and fused. Individual segmentation of the affected cranial nerves and the compressing vascular structure was performed by a neurosurgeon, and the results were compared with the microscopic and endoscopic findings by two blinded neurosurgeons. For each case, at least three neurovascular landmarks were targeted. Each segmented neurovascular element was validated by manual placement of the navigation probe over each target, and errors of localization were measured in mm.

Results: All patients underwent retro-sigmoid craniotomy and MVD using both microscope and endoscope. Based on image segmentation, the compressing vessel was identified in all cases except one, which was also negative intraoperatively. Perfect correspondence was found between image-based segmentation and endoscopic and microscopic images and videos (Dice coefficient of 1). Measurement accuracy was 0.45 ± 0.21 mm (mean $\pm$ SD).

Conclusion: Image-based segmentation is a promising method for pre-operative identification and localization of offending blood vessels causing HFS and TN. Using this method may prevent some unnecessary explorations on especially atypical cases with no vascular contacts. However, negative pre-operative image segmentation may not preclude one from exploration in classic cases of TN or HFS. A multicenter study with larger number of cases is recommended.

1. Introduction

Trigeminal neuralgia (TN) and hemifacial spasm (HFS) are due to a compression of the trigeminal and facial nerves, respectively, usually by a blood vessel. Such neurovascular conflicts most often occur in the cerebellopontine angle (CPA) at the root entry/exit zone close the brainstem [11]. Surgical microvascular decompression (MVD) is a highly efficacious surgical treatment for medically refractory TN and HFS [1–5]. MVD has been performed with the surgical microscope since the technique was first pioneered. The endoscope has quickly become an adjunct to the surgical microscope in MVD [7–19,27,28]. Regardless, preoperative diagnosis of a vascular cause for these pain syndromes is sometimes indefinite and very challenging. It is not uncommon that during MVD, surgeon may not find any obvious artery or vein compressing the nerve.

Interactive intraoperative image guidance is rapidly becoming an indispensable neurosurgical technique [20–23]. Benefits over traditional neuronavigation include optimized craniotomy site positioning and improved approach vectors for reaching deeply seated cranial nerves that minimize cerebellar trauma. Image-guidance has been shown to reduce surgical morbidity while increasing the surgeon's confidence of achieving full

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resection without impinging upon nearby critical structures [24]. Image-guided surgery ensures advanced warning of proximity to important pre-segmented anatomical structures and identifies the full spatial extent of the cranial nerve-compressing vessel interface [25].

The primary objective of our current pilot study was to validate the accuracy of image-based pre-operative segmentation using the gold standard endoscopic and microscopic findings to predict the responsible vascular element. We are actually trying to validate the predictive capability of our navigation system.

2. Patients and methods

2.1. Participants, study size and setting

A total of 14 patients with typical clinical presentations for trigeminal neuralgia (TN) and 6 patients with hemifacial spasm (HFS) randomly underwent image-based pre-operative vascular and neural element segmentation with 3D reconstructions. Patients with atypical clinical presentations, well responsive to the medical managements or those who were medically ill were excluded. Data were prospectively collected and reviewed after approval by the Hospital Institutional Review Board.

2.1.1. Image acquisition

The patients underwent preoperative 3T MRI, which included thin-sectioned 3D space T2, 3D Time of Flight and MPRAGE sequences. Images were reviewed by an expert independent neuroradiologist with 13 years of experience. Imaging sequences were loaded in BrainLab iPlanNet (BrainLab AG, Munich, Germany) and fused for segmentation and pre-operative planning. Individual segmentation of the affected cranial nerves and the compressing vascular structure was performed by a neurosurgeon and was validated intraoperatively. The results were compared with the microscopic and endoscopic findings by two blinded neurosurgeons (Fig. 1).

2.1.2. Data sources

Correspondence between image-based segmentation, and microscopic and endoscopic view of the compressing vascular structure, cranial nerves, major arteries, veins, and venous sinuses was determined by two blinded neurosurgeons.

2.1.3. Study design

This was a randomly selected prospective validation study. Primary endpoints were defined as correspondence between image-based segmentation, and microscopic and endoscopic view of the compressing vascular structure, cranial nerves, major arteries, veins, and venous sinuses.

2.1.4. Statistical methods

Patients' clinical characteristics (age, sex, follow-up length) and compressing vascular structure identity were evaluated using the mean and range for continuous variables and the frequency count for categorical factors. The Sørensen–Dice index was used to compare the correspondence between image-based segmentation and microscopic view and endoscopic view of the compressing vascular structure, cranial nerves, major arteries, veins, and venous sinuses.

3. Results

3.1. Descriptive data

3.1.1. Participants

The mean age was 65 years, and there were 6 male and 14 female patients (see Table 1). Six patients had a diagnosis of hemifacial spasm (HFS), and 14 patients had a diagnosis of trigeminal neuralgia (TN).

3.2. Operative data

All patients underwent retrosigmoid craniotomy and MVD using both microscope and endoscope. In one case with TN, there was also an ipsilateral petrous apex meningioma close to the trigeminal nerve, which was resected before MVD. Compression of the trigeminal nerve by the superior cerebellar artery was responsible in most cases of TN. Compression by anterior inferior cerebellar artery (AICA) and a large vein was responsible for compression in other cases of TN (Fig. 2). In one case, no vascular contact was found (Fig. 3). Based on image segmentation, the AICA was responsible for 5 cases of HFS (Table 1). In one case of HFS, a tortuous ipsilateral vertebral artery was also compressing the facial nerve. Perfect correspondence (Dice coefficient of 1) was found between image-based segmentation, endoscopic and microscopic images and videos (Fig. 2). In other words, intraoperative findings were exactly the same finding that we had predicted by our pre-operative segmentation, even in that case with no vascular compression.

3.3. Accuracy

For each landmark, the error of the neuronavigation system to the anatomy was measured. The mean accuracy measured was 0.45 ± 0.21 mm (mean $\pm$ SD).

3.4. Complications

No perioperative or postoperative complications occurred.

3.5. Clinical outcome

Significant improvement of the spasm was achieved in all cases except one of HFS patients after MVD. Remarkable to complete improvement of the pain was noticed in 12 cases of the TN after MVD. One case of TN showed incomplete pain relief and the last patient, who did not have any obvious vascular compression intraoperatively and was predicted by pre-operative segmentation, did not show any improvement of his pain post operatively. No rhizotomy was performed for this patient.

4. Discussion

Our preliminary study showed that image-based pre-operative vascular and neural element segmentation, especially with 3D reconstruction, is highly informative for both preoperative planning and predicting the vascular agent responsible for trigeminal neuralgia and hemifacial spasm. Microvascular decompression (MVD) is a well-known technique for the treatment of medically intractable hemifacial spasm (HFS) and trigeminal neuralgia (TN). However, because the CPA contains a high density of critical neurovascular structures, MVD confers a risk of postoperative complications, including cerebellar injury (0.45–0.87%), hearing loss (0.8–1.98%) or other cranial nerve damages, and cerebrospinal fluid leakage (1.85–2.44%)[26].

In addition to intraoperative microscope and endoscope navigation of the CPA in MVD surgery, image-based neuronavigation using pre-operatively obtained images is a valuable tool for identification of compressing vessels and other neurovascular structures in the CPA. Refaee and colleagues [6] analyzed the utility of three dimensional steady-state free precession imaging (SSFP) and time-of-flight magnetic resonance angiography (TOF MRA) in identifying the offending vessels in HS. The group found that compared to

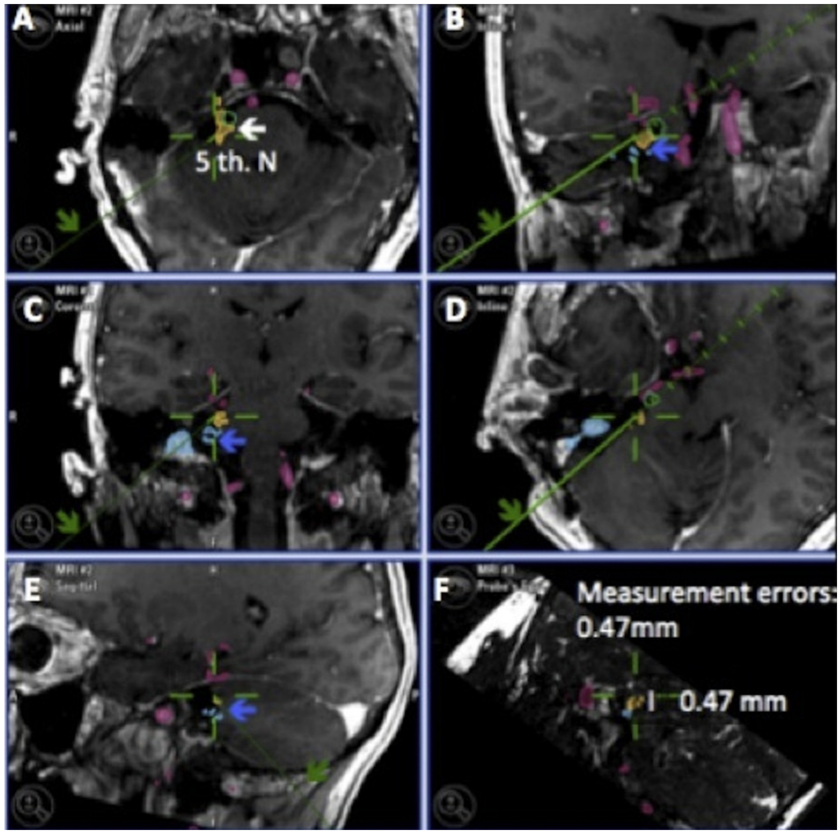

Fig. 1. Pre-operative segmentation with intra-operative validation of the neurovascular structure of a 54 year-old female with a right Trigeminal Neuralgia (case 5). Panel A shows BrainLab probe (green arrow) and Trigeminal nerve (white arrow). Panels B–E show an offending vein, which was the only compressive vascular structure found in this case. Panel F shows our navigation accuracy error. *Abbreviations*: NREZ: nerve root entry zone.

the gold standard of endoscopic visualization, three-dimensional MRI had a 77–83.3% mean accuracy of identifying the offending vessels. While the technique may provide useful information, significant neuroradiological experience is required to interpret the non-segmented images and identify the involved neurovascular structures. Additionally, the technique is limited by the inability of the 3D T2-weighted SSFP technique to distinguish between arteries and nerves. For this reason, 3D TOF images must also be obtained to identify the structures involved in neurovascular conflict.

Image-based neuronavigation provides surgical utility only if the image guidance system data accurately corresponds to the perioperative patient's anatomy. A retrospective review of the literature found that mean neuronavigation accuracies have ranged from 1.8 to 5 mm [33]. Recently, one group has improved on this accuracy with the use of preoperatively acquired 3D digital subtraction angiography (DSA) registered by the facial surface anatomy contained within the data set [34]. The investigators validated their novel neuronavigation technique in a cadaver model, and reported an accuracy of 0.71 ± 0.25 mm (mean ± SE) [34]. This accuracy may be overestimated, as the brain tissue and cerebrovasculature of their cadaver model were relatively anchored in place due to formalin fixation and injection of the vasculature with latex. Thus, the accuracy-degrading complication of perioperative brain shift was largely eliminated. While DSA remains the gold standard for imaging of cerebrovascular pathology due to its superior detection sensitivity and spatial resolution over MR angiography and CT angiography [35], the imaging modality is not without its limitations and risks. Although DSA offers high spatial resolution of the cerebral vasculature, it provides only limited anatomical information about extravascular structures, knowledge of which may minimize surgical morbidity and mortality. Additionally, DSA is a costly and invasive procedure, which confers a risk of permanent neurologic complication in 0.1–0.5% cases [36–40].

Our group achieved a measurement accuracy of 0.45 ± 0.21 mm (mean ± SD), which is improved over previously reported accuracies ranging from 0.71 to 5 mm [33,34]. Additionally, we utilized preoperative thin-sectioned 3D space T2, 3D Time of Flight and MPRAGE Sequences for image acquisition, which are far less invasive procedures than DSA. We fused all of these images and utilized the final fused and segmented image for our intraoperative navigation. Finally, our neuronavigation system was validated in living patients; so, our reported accuracy accounts for the brain shift.

Because locating the main offending vessel pre-operatively can often be challenging, several groups have used 3D image segmentation for preoperative planning in neurovascular conflict cases [29–32]. While these efforts represent important advances in image segmentation, they differ from our study in numerous important ways. First, the raw data used for our image segmentation was obtained from 3T MRI, which included thin-sectioned 3D space T2, 3D Time of Flight and MPRAGE Sequences, which represents a departure from the imaging modalities used by these groups. Second, the accuracy of our image segmentation compared to intraoperative microscopic and endoscopic findings was evaluated by blinded neurosurgeons, whereas the neurosurgeons evaluating the accuracy of the segmented images in the other groups were not blinded. Finally, and most importantly, while the other groups used the image segmentation only for pre-surgical planning, our segmented image data was registered into an intra-op neuronavigation system (BrainLab iPlanNet), utilized, and validated intraoperatively.

Perfect correspondence was found between image-based segmentation, endoscopic and microscopic images and videos,

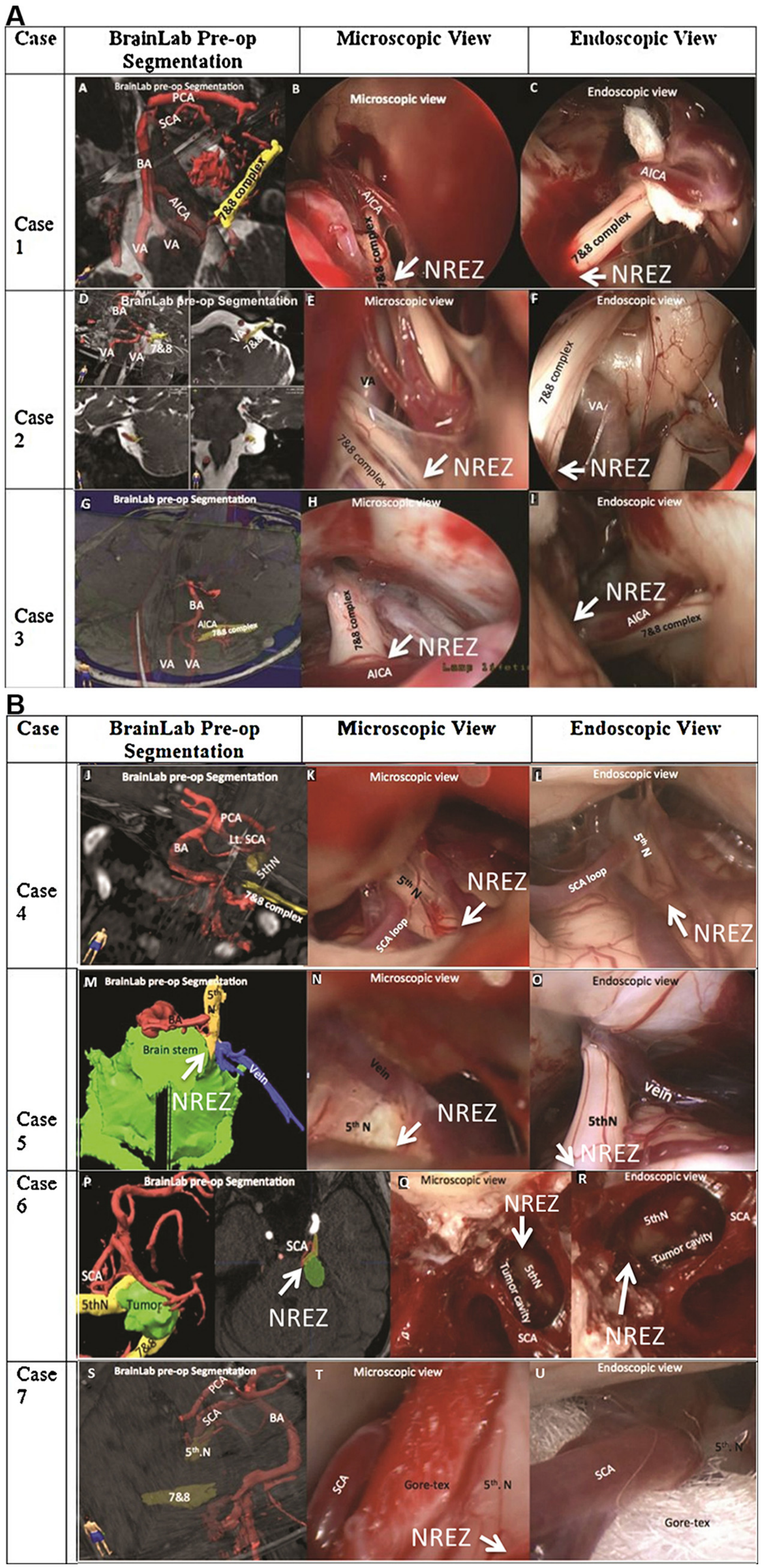

Fig. 2. a Picture series comparison of BrainLab pre-op segmentation, microscopic view, and endoscopic view in three hemifacial spasm cases of our series. A loop of AICA in cases 1 and 3 and a tortuous and elongated VA was the cause of compression of the facial nerve in case 2 are shown here. Abbreviations: NREZ: nerve root entry zone, AICA: anterior inferior cerebellar artery, VA: vertebral artery.

2b Picture series comparison of BrainLab pre-op segmentation, microscopic view, and endoscopic view in four trigeminal neuralgia cases of our series. A loop of SCA in cases 4 and 7, a large vein in case 5, and a loop of SCA and a small tumor were the compressing agents in these cases. *Abbreviations*: NREZ: nerve root entry zone, SCA: superior cerebellar artery.

Table 1
Patients demographic information, presentation, procedure, and etiological finding in three different modalities.

Patients (*n*)	Gender M/F	Age	Presentation	Procedure	Intra-op endoscopic finding	Intra-op microscopic finding	BrainLab segmentation finding	Clinical outcome
6 2 Rt. HFS 4 Lt. HFS	4F 2M	61 ± 7	Cases:	RSA/MVD	Compression by:	Compression by:	Compression by:	Post op:
			1-Rt. HFS	RSA/MVD	- A loop of AICA	- A loop of AICA	- A loop of AICA	Completely spasm free
			2-Rt. HFS	RSA/MVD	- A loop of - AICA	- A loop of AICA	- A loop of AICA	Completely spasm free
			3-Lt. HFS	RSA/MVD	- A loop of - AICA	- A loop of AICA	- A loop of AICA	Completely spasm free
			4-Lt. HFS	RSA/MVD	- A loop of AICA	- A loop of AICA	- A loop of AICA	Completely spasm free
			5-Lt. HFS	RSA/MVD	- RSA/MVD	- A loop of AICA	- A loop of AICA	Completely spasm free
			6-Lt. HFS	RSA/MVD	- A loop of AICA and VA	- A loop of AICA and VA	- A loop of AICA and VA	Partially spasm free
14 5 Rt. TN 9 Lt. TN	4M 10F	65 ± 10	Cases:	RSA/MVD	Compression by:	Compression by:	Compression by:	Completely pain free
			1-Rt. TN	RSA/MVD	- A loop of AICA	- A loop of AICA	- A loop of AICA	Completely pain free
			2-Rt. TN	RSA/MVD	- A loop of AICA	- A loop of AICA	- A loop of AICA	Completely pain free
			3-Rt. TN	RSA/MVD	- A loop of SCA	- A loop of SCA	- A loop of SCA	Completely pain free
			4-Rt. TN	RSA/MVD	- A loop of SCA	- A loop of SCA	- A loop of SCA	Completely pain free
			5-Rt. TN	RSA/MVD	- Compression by SCA and tumor	- Compression by SCA and tumor	- Compression by SCA and tumor	Significant improvement
			6-Lt. TN	RSA/MVD	-A loop of SCA	-A loop of SCA	-A loop of SCA	Completely pain free
			7-Lt. TN	RSA/MVD	- Compression by a large vein in one case	- Compression by a large vein in one case	- Compression by a large vein in one case	Significant improvement
			8-Lt. TN	RSA/MVD	- A loop of SCA	- A loop of SCA	- A loop of SCA	Completely pain free
			9-Lt. TN	RSA/MVD	- A loop of SCA	- A loop of SCA	- A loop of SCA	Completely pain free
			10-Lt. TN	RSA/MVD	- A loop of SCA	- A loop of SCA	- A loop of SCA	Completely pain free
			11-Lt. TN	RSA/MVD	- A loop of SCA	- A loop of SCA	- A loop of SCA	Completely pain free
			12-Lt. TN	RSA/MVD	- A loop of SCA	- A loop of SCA	- A loop of SCA	Partially pain free
			13-Lt. TN	RSA/MVD	- A loop of SCA	- A loop of SCA	- A loop of SCA	Significant improvement
			14-Lt. TN	RSA/MVD	- No vascular compression	- No vascular compression	- No vascular compression	No change in the pain

Abbreviations: rt.: right; lt.: left; RSA: retrosigmoid approach; MVD: microvascular decompression; AICA: anterior inferior cerebellar artery; VA: vertebral artery; SCA: superior cerebellar artery; HFS: hemifacial spasm; TN: trigeminal neuralgia.

suggesting that image segmentation may play a valuable role for identifying offending vessels and other critical neurovascular structures in MVD surgery. This information reassures the surgeon and helps them for detection and localizing the offending vessel, even before the craniotomy and especially when a vein is the only responsible vessel. Therefore, we believe that the use of image-based pre-operative vascular and neural element segmentation, especially with 3D reconstruction and as presented in our series, might prevent unnecessary surgeries for cases with no vascular contacts.

The major limitation of our study was the small number of cases included. The limited number of cases complicates interpretation of our detected true and false negative rate in cases of hemifacial spasm. This drawback is important to note because unlike in cases of trigeminal neuralgia, exploration in the later rhizotomy cannot be performed with favorable postoperative results in cases of hemifacial spasm. Further, our small case number prohibits us from determining if pre-operative image-based segmentation of blood vessels compressing cranial nerves is able to prevent unnecessary surgical explorations. However, it is our hope that the instructive cases presented will inspire further research in this area.

The main question is what to do in cases of intractable classic TN or HFS while the preoperative image segmentation is negative? Can we advise against the exploration based on our current data or we should trust on our clinical information and go ahead with the exploration? Moreover, sometimes just a vascular contact might be the cause of neuralgia and the nerve is not necessarily deformed by compression, and so, might not be well detected by preoperative imaging. Although our single negative preoperative case of TN ended up in a negative intra-operative finding and had a poor clinical result, the number of our negative cases is too few in this case series to be able to draw a robust conclusion. However, based on the study performed by Lee et al. on 257 patients with TN who underwent high-resolution MRI and MR angiography with 3D reconstruction of combined images using OsiriX, the occurrence of TN without neurovascular compression (NVC) was about 28.8% [41]. In 184 of those patients who underwent surgical exploration, imaging findings were highly correlated with surgical findings, with a sensitivity of 96% and specificity of 90% in typical TN [41]. Therefore, they concluded that imaging detects NVC with a high degree of sensitivity. However, a significant number of patients have no NVC. Therefore, trigeminal neuralgia may occur

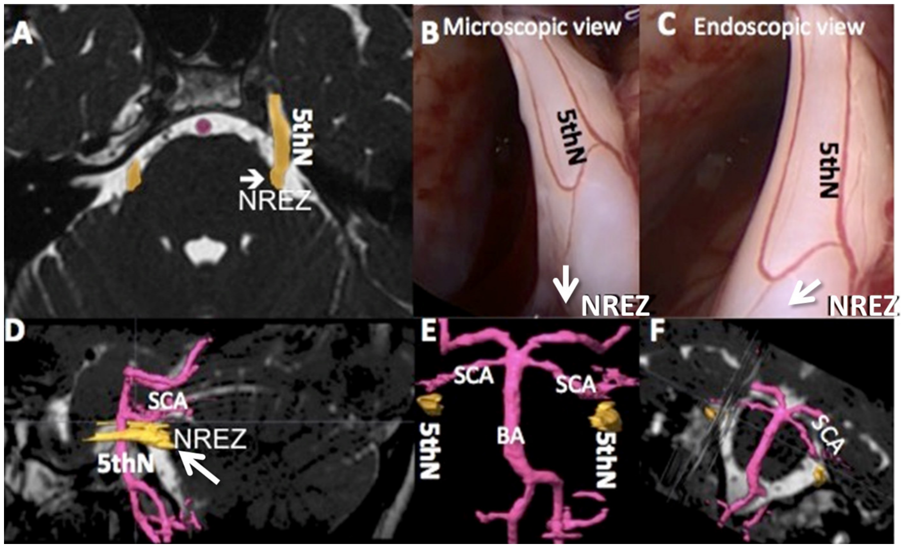

Fig. 3. A 53-year-old male who presented with a two-year history of electrical shock-like left facial pain starting suddenly, lasting for 20 s, and finally, subsiding spontaneously. The pain was only partially responding to multiple related medicines. Pre-operative image-based segmentation did not show any evidence of direct vascular contacts to the trigeminal nerve (panels A, D–F). Intraoperative endoscopic and microscopic explorations also did not show any vascular compression (panels B and C). *Abbreviations*: NREZ: nerve root entry zone.

and recur in the absence of NVC [41]. Moreover, another review of literature revealed that a wide range (4–89%) of TN patients has no demonstrable vascular contact [42–46]. On the other hand, about 17% of the general population manifests NVC of the trigeminal nerve without TN [46]. Putting all of these studies together, we may conclude that a negative pre-operative segmentation may not be a strong indication of not having a typical TN and therefore it may not preclude one from exploration.

The second question remains to be answered is that what the surgeon should do in cases of classic TN, if surgical exploration is also negative to show any NVC, as predicted by pre-operative image segmentations? In a study conducted by Zorman et al. on 125 cases of patients that underwent MVD or partial sensory rhizotomy with the mean duration of follow-up was 26 months (range 6 months–13 years), no compression was seen at the root entry zone in 26 patients [47]. These patients were treated only with partial sensory rhizotomy and the authors reported a 91% success rate of pain relief [47]. Klun reported 178 patients after MVD and 42 patients after rhizotomy with a follow-up period of up to 12 years (mean 5.2 years) [48]. He excluded patients with “atypical pain.” The 5 year-rate of complete pain relief was 84% for both operations [48].

Therefore, we believe that some patients with TN do not manifest NVC at the time of surgical exploration. In these situations, partial sensory rhizotomy (bipolar cautery of the lateral two-thirds of the trigeminal nerve after crushing), may be a reasonable option in cases of classic TN, especially those which are intractable to medical management.

5. Conclusion

Image-based pre-operative vascular and neural element segmentation, especially with 3D reconstruction, is highly informative for both preoperative planning and intraoperative navigation, particularly with neurovascular conflict cases such as trigeminal neuralgia and hemifacial spasm. Moreover, it reassures the surgeons and helps them for early and even pre-operative identification and localization of the offending vessel and other critical neurovascular structures in MVD and HFS surgery, especially when a vein is the only responsible vessel. However, negative pre-operative image segmentation may not be a strong indication of not having a typical TN, and therefore it may not preclude one from exploration. In classic cases with negative surgical exploration, partial sensory rhizotomy may be a viable alternative to surgical exploration. While our number of cases is too small to determine if pre-operative image-based segmentation of blood vessels compressing cranial nerves prevent unnecessary surgical explorations, it is our hope that the instructive cases presented here will inspire further research in this area.

Conflict of interest

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

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