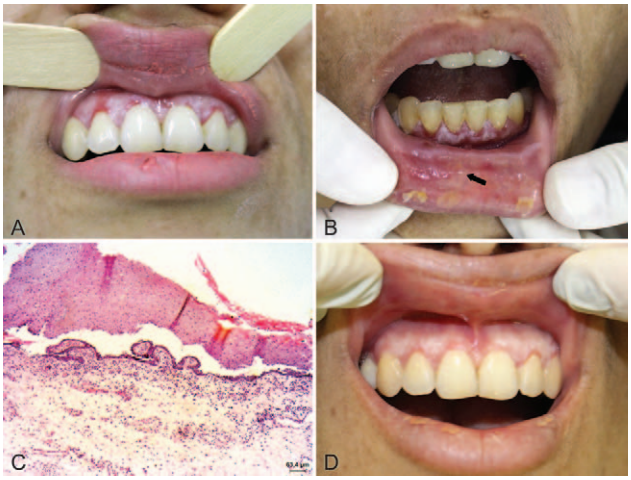

FIGURE 1. Ulcers, erosions, and white plaques involving the (A) upper gingiva and (B) labial mucosa. The black arrow indicates an adequate perilesional location for incisional biopsy. (C) Histopathologic features: stratified squamous epithelium with intraepithelial cleft, persistence of the basal layer, and unspecific chronic inflammatory infiltrate in the lamina propria (hematoxylin and eosin). (D) Seven months follow-up showing significant improvement of the oral lesions.

the buccal and labial mucosae, dorsal, and ventral aspects of the tongue, lower and upper gingiva, and hard palate (Fig. 1A and B). The mucosa was fragile and easily broken when manipulated. Incisional biopsy of a nonulcerated area adjacent to an ulcer was performed (Fig. 1B, black arrow). The microscopic analysis exhibited an intraepithelial cleft containing loose acantholytic cells and persistence of the basal layer. The underlying connective tissue presented mild and unspecific chronic inflammatory infiltrate (Fig. 1C). The final diagnosis was pemphigus vulgaris. In order to manage the patient's signals and symptoms, it was prescribed prednisone 30 mg/d and the she was referred to a reference center. At the 7-months follow-up visit, she reported the dermatologist increased the prednisone dose to 60 mg/d and prescribed methotrexate 12.5 mg/wk. The oral lesions showed significant improvement (Fig. 1D) and the patient has been treated and monitored.

The diagnosis of PV is based on the identification of its clinical manifestations and confirmation through biopsy.[1] In patients with severe pain that hamper the immediate incisional biopsy, the Tzanck smear can also orientate the initial diagnosis of the PV due to the presence of the acantholytic epithelial cells, also called Tzanck cells.[4] It is useful to differentiate PV from mucous membrane pemphigoid but the incisional biopsy is mandatory for the diagnosis of PV.[5]

The election of the anatomical site for the incisional biopsy is the main step of the procedure. It is not uncommon that inexperienced dental or medical professionals choose robust erosive, ulcerative, or bullous areas once they are naturally highlighted. However, in erosions and ulcers, the roof of the blister is already lost and the remaining basal layer of the epithelium could easily be detached from the connective tissue due to the constant attrition of the mucosae surfaces. The blister clinically represents an already broken epithelium that would be easily lost from the piece of biopsy. Once these elementary lesions provide little information or even obscure the actual features of the disease, erosion, ulcer, and blister must not be chosen for the incisional biopsy of a potential PV. In our patient, the professional who previously aimed at diagnosing our patient probably performed the biopsy in a white plaque (Fig. 1A and B) that is somewhat common in PV patients with lesions healing and showing up continuously. As expected, these areas were not contributory for the diagnosis and the prescribed treatment was not effective. The perilesional sites are the most indicated option for incisional biopsy because they still retain the epithelial integrity at that moment but already are affected by the autoimmune reaction. Moreover, these sites usually exhibit only a mild inflammatory infiltrate once there is not broken tissue yet. On the other hand, it is essential that the clinician is aware that the tissue will break during the surgical procedure, so the careful manipulation of the tissue is primordial.

Pemphigus vulgaris is potentially fatal and the oral lesions usually are the first manifestation of this disease. The presented patient reinforces the importance of an adequate incisional biopsy for the early diagnosis and management of this severe vesiculobullous disease.

REFERENCES

1. Kuriachan D, Suresh R, Janardhanan M, et al. Oral lesions: the clue to diagnosis of pemphigus vulgaris. *Case Rep Dent* 2015;2015:593940
2. Rosebush MS, Anderson KM, Rawal SY, et al. The oral biopsy: indications, techniques and special considerations. *J Tenn Dent Assoc* 2010;90:17–20
3. Oliver RJ, Sloan P, Pemberton MN. Oral biopsies: methods and applications. *Br Dent J* 2004;196:329–333
4. Aytekin S, Göktay F, Yaşar Ş, et al. Atypical Tzanck smear findings in pemphigus vulgaris. *Cytopathology* 2016[Epub ahead of print]
5. Baican A, Chiorean R, Leucuta DC, et al. Prediction of survival for patients with pemphigus vulgaris and pemphigus foliaceus: a retrospective cohort study. *Orphanet J Rare Dis* 2015;10:48

Multimodal Neuronavigation in Microsurgery Resection of BrainStem Tumors

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Background: Microsurgery is a common treatment of brainstem tumors. However, misdirection, vascular damage, nerves injuries, paralysis, even death are all well-known complications, and the risk of adverse events is more likely in less experienced operators. This study was aimed to validate the accuracy of multimodal neuronavigation during microsurgery resection of brainstem tumors.

Methods: Ten patients with brainstem tumors underwent preoperative MRI, diffusion tensor imaging, computed tomography, three-dimensional print, and images loaded into the neuronavigation platform were used for its segmentation and preoperative planning. After patients' registration and subsequent surgical exposure, each segmented brain element was validated by manual placement of the navigation probe to the target.

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Results: Preoperative images of the brain matched with three-dimensional print and neuronavigation played important role in all patients. Excellent correspondence between image-based segmentation and microscope view was also evident at the surface of tumors and at the tumor–normal gland interfaces.

Conclusion: Multimodal navigation is a safe and effective method in surgery for patients with brain stem tumors. Our preliminary study is conducted to encourage for future more research with larger numbers of patients.

Key Words: Brainstem, MRI, neuronavigation, tumor

Brainstem tumors in patients are rare. Treatment options for patients with brainstem tumors still are limited and insufficiently studied.[1] The fundamental aims of brainstem tumor surgery are to completely resect the lesion and minimize the potential for recurrence, while avoiding damage to normal structures.[2,3] The surgical treatment is required for the majority of symptomatic brain stem tumors. The correct diagnosis of the brain stem tumor is necessary. Additionally, the reliable symptoms relief from nerve compression is achieved by surgery. The effectiveness of conventional microsurgical resection in the treatment of brainstem tumor is not well established, the brainstem is very important for our life, so it limits our treatment effectiveness.[4] Advances in brainstem tumor surgery have involved the implementation of intraoperative adjuncts that enable enhanced estimation or visualization of adjacent neural, vascular, and brainstem structure. The methods include intraoperative imaging and navigation, intraoperative MRI, and high-resolution ultrasound.[5] But these techniques each have limitations and are not widely available. Lumpish fluoroscopic and radiation exposure equipment limit the application for the surgical guidance. The utility of intraoperative MRI is also hampered by its deficiencies that include added time to the operative procedure, high cost, and inability to find small tumorous fragments.[6,7] In addition, ultrasound guidance is limited by the obvious learning curve required to recognize the anatomic structures in the images received. In recent years, dimensional, high-resolution ultrasound has been applied in clinic service, but its images are still comparatively noisy with weak definition of soft-tissue components. Therefore, rich experience with the ultrasound images must be necessary for describing the images.[8] The current study was aimed to investigate the accuracy of image-based segmentation in localization of tumor structures linked with frameless stereotactic navigation during operation and to investigate the feasibility and benefits of this method.

METHODS

Study Size and Design

This was a prospective study, and the primary aims were defined as correspondence preoperative segmentation of the tumor and tumor–normal gland interfaces with the intraoperative microscope and micro-Doppler findings; meanwhile, we would verify the multimodel neuronavigation have better value in brain tumor's resection.

A total of 10 patients with brain stem lesions were enrolled in this study at a single institution from January 2012 to June 2016 (Table 1). These patients underwent preoperative MRI, diffusion tensor imaging (DTI), computed tomography (CT), and three-dimensional (3D) print. An independent neuroradiologist reviewed these images. Before the operation, in order to get the details of the tumors and the normal tissues, we also made the patient's cranial 3D print solid model by the CT and MRI data. Meanwhile, the imaging sequences were loaded in BrainLab iPlanNet neuronavigation platforms for segmentation and making preoperative planning. Image-based preoperative neural element (brain stem and other tissues) segmentation with 3D reconstruction was performed for every patient. These fused multiimages and their segmentations were applied intraoperatively during the real-time navigation. Data were collected and reviewed after approval by the Institutional Review Board.

Preoperative Patient Registration

Before the operation, we inputted the patient's all the images into the BrainLab neuronavigation system. The registration was based on surface matching covering the skull base and calvaria. Subsequently, after registration and surgical exposure, each segmented neural element was verified by manual placement of the navigation probe directly on that object.

Intraoperative Navigation

For the tumors, we checked their location against the neuronavigation data set by placing the probe at the proper part of the surgical field before and after resection of the lesion, checking again around the tumor in some patients was helpful.

Data Sources

Correspondence of preoperative segmentation of the surface of the tumor and tumor–normal gland interfaces with the intraoperative microscope and micro-Doppler findings was determined by the surgeons during surgery and screen shots were captured and recorded. The extent of brain stem tumor resection and success of localization of the tumor were determined by the surgeons during surgery. An independent neuropathologist determined the tumor pathology.

Statistical Methods

We evaluated characteristics of patients' clinic and tumor (sex, age, presenting symptoms, pathology, induction of anesthesia to incision time, incision to surgery end time, induction to surgery end time) by using the frequency count for the categorical factors and the mean and range for continuous variables. We determined the accuracy of the preoperative segmentation and intraoperative navigation in localization of the tumor, normal brain stem with respect to the direct microscope and micro-Doppler findings.

TABLE 1. Demographic and Clinical Information of Ten Patients Who Underwent Image-Guided Microsurgery

Number of Patients	Male/Female	Primary Presentation	Clinical Outcome: Death/Survival	Radiological Outcome Total/Subtotal Resection	Complication	Pathology
5	3/2	Body lack of power	1/4	1/4	Hemiplegia (3/5)	Glioma
3	2/1	Headache	0/3	2/1	None	Cavernous hemangioma
1	0/1	Headache	0/1	1/0	None	Ependymoma
1	1/0	Fever	0/1	1/0	Poor healing of incision	Encephalopyosis

RESULTS

There were 6 male and 4 female patients and the mean age was 48.6 years. The most common presenting symptom was the body lack of power in 6 patients (60%), headache in 3 patients (30%), fever in 1 patient (10%). Tumor pathology outcome showed that 5 patients (50%) had glioma, 3 patients (30%) had cavernous hemangioma, 1 patient (10%) had ependymoma, 1 patient (10%) had encephalopyosis (Table 1).

The mean time from completion of anesthesia induction to incision was 29.8 minutes (range 15–46 minutes), time from incision to the completion of operation was 315.6 minutes (range 230.5–390.8 minutes). There was no massive bleeding or significant changes in patients' vital signs. In all patients, registration to the neuronavigation systems was satisfactory. We placed the neuronavigation probe over the fixed bony landmarks at each stage, and any misregistration was ruled out. The accuracy of the presented study was $1.19 + 0.22$ mm (mean+SD). After fusion of all preoperative images on BrainLab iPlanNet navigation planning software and preoperative 3D print, the detail of the lesion, and tumor–normal gland interfaces are all clearly visible (as is evident in Figs. 1 and 2).

DISCUSSION

Our preliminary study reveals that image-based preoperative neural and brain element segmentation, including multimodel images fusion 3D reconstruction and print, is amply informative for both preoperative planning and intraoperative guidance of microsurgery. Preoperative 3D segmentation and print can help the operator to understand the relationship of the tumor to surrounding structures of nerves and blood vessels. In some neurosurgery operation, 3D reconstruction of imaging data during operation was reported by Wolfsberger et al,[9] which found that the image-based reconstructed picture correlated adequately with the intraoperative view. 3D print can provide the clearly constructure of the brain and the tumor, especially the brain stem, the tumor's size, the exactly location of the tumor and the boundary between tumor and normal tissue.[10]

Neuronavigation plays a central role in modern neurosurgery, which can provide operatative utility if the image guidance system data is accurately conformity to the intraoperative patient's anatomy.[11] A study[12] found that mean neuronavigation accuracies have ranged from 1.8 to 5 mm. Recently, another study[13] has reported advanced accuracy by using preoperative digital subtraction angiography. The novel navigation technique reported an accuracy of 0.71 ± 0.25 mm in a cadaver model. They maybe overestimate the accuracy. Because the cadaver models' brain tissue and cerebral vasculature were relatively anchored in place by using formalin fixation and injecting latex into the cerebral vasculature. So it largely eliminated the degrading accuracy because of intraoperative brain shift. Digital subtraction angiography offers high spatial resolution of the brain vasculature, but it is an invasive and costly procedure and provides little anatomical information about extravascular structures. Moreover, it has permanent neurologic complication risk in 0.1% to 0.5% patients.[14]

Our result found that image-based brain tissue 3D segmentation was found to have good accuracy. Additionally, 3D reconstruction and print technology could improve the accuracy for tumor resection. In addition, it was wonderfully informative preoperatively and could improve the surgeons' vigilance for preventing normal brain stem and neurovascular injury during operations. But the tumor's total resection rates were not only dependent on the technology, but also relied on the lesion's pathology from Table 1, which released that the total resection rate of cavernous hemangioma was 66.7%, while glioma was 25%.

Advanced imaging technology by improving the spatial resolution has highly improved preoperative visualization of the brain tissues. These advanced imaging schemes like ultrasound imaging, MRI, DTI, and 3D reconstruction sequences can demonstrate small anatomic structures,[15–17] which can provide very informative information before surgically treating a tumor or other lesions of the brain stem. In addition, DTI can show the brain fibers tracks.[18,19] We can get the relationship between the brain tissue and the fibers. We could know that whether the fibers were damaged or intact , and from which we can predict the degree of difficulty in surgury and the clinical outcomes.[19] In the present study, we upload the images into the neuronavigation system, merge them together, segment the brain tissues and the tumor. Meanwhile, we use them in real time during the surgery to minimize damage to normal tissue structure. It can be seen that our method's major advantage is these images' actual clinical application in the operating room and inside the skull.

In our study, the major limitation was the small number of patients. The sample size restricts the interpretation of complication rates in patients, just as the recognition how frequently image-based segmentation aids in the identification of the patient's critical structures. We hope the presented significative patients here will inspire further study in this domain. Image-based preoperative brain tissue element segmentation with 3D reconstruction and 3D print is a promising surgical guidance tool, which may also play an important role in training and instruction.

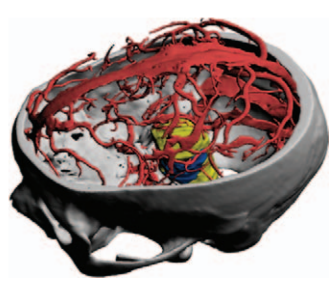

FIGURE 1. A 60-year-old man presented with hemiplegia, headache. His brain MRI with gadolinium showed a brain tumor. Preoperative three-dimensional print showed the relationship between tumor and normal brainstem, and vessel. And we can see the tumor's projection on the skull, which can help us to make the operative plan.

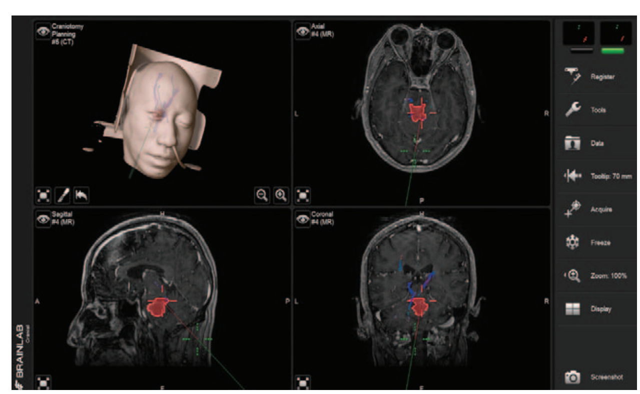

FIGURE 2. Intraoperative neuronavigation shows the multimodel images fusion with computed tomography and MRI with axial, sagittal, and coronal images. We can see the whole anatomy three-dimensional image on the left upper side. The quasicircular tuomr was delineated by red linellae and some of the brain stem fibers were damaged by the tumor. The straight line was used to measure the distance between the tumor and the skin.

CONCLUSIONS

Multimodal images fusion technology can guide the operators' microsurgery by neuronavigation which allows for highly surgical precision and visual accuracy. Image-based preoperative normal brain tissues and tumor element segmentation, especially with 3D reconstruction and 3D print, have highly preoperative information and could help inexperienced surgeons to avoid unnecessary injury during operations. It also could provide reassurance to senior surgeons. Although the number of patients is not enough to determine if preoperative image-based segmentation of brain structures reduces the patients' complication rates, we hope that the neoteric preliminary study is inspiring for future prospective validation of neurosurgery with larger numbers of patients.

REFERENCES

1. Clark KN, Ashford JM, Pai Panandiker AS, et al. Cognitive outcomes among survivors of focal low-grade brainstem tumors diagnosed in childhood. *J Neurooncol* 2016;129:311–317
2. Baussard B, Di Rocco F, Garnett MR, et al. Pediatric infratentorial gangliogliomas:a retrospective series. *J Neurosurg* 2007;107(4 suppl):286–291.
3. Zhang S, Wang X, Liu X, et al. Brainstem gangliogliomas:a retrospective series. *J Neurosurg* 2013;118:884–888.
4. Mortini P, Bailo M, Spina A, et al. Cyst-cisternal shunting for cystic multirecurrent brainstem epidermoid: case report and literature review. *Acta Neurochir (Wien)* 2016;158:1197–1201
5. Jane JA, Thapar K, Alden TD, et al. Fluoroscopic frameless stereotaxy for transsphenoidal surgery. *Neurosurgery* 2001;48:1302–1307
6. Gerlach R, du Mesnil de Rochemont R, Gasser T, et al. Feasibility of Polestar N20, an ultra-low-field intraoperative magnetic resonance imaging system in resection control of pituitary macroadenomas: lessons learned from the first 40 cases. *Neurosurgery* 2008;63: 272–284
7. Vitaz TW, Inkabi KE, Carrubba CJ. Intraoperative MRI 1 for transphenoidal procedures: short-term outcome for 100 consecutive cases. *Clin Neurol Neurosurg* 2011;113:731–735
8. Arita K, Kurisu K, Tominaga A, et al. Trans-sellar color Doppler ultrasonography during transsphenoidal surgery. *Neurosurgery* 1998;42:81–85
9. Wolfsberger S, Neubauer A, Bühler K, et al. Advanced virtual endoscopy for endoscopic transsphenoidal pituitary surgery. *Neurosurgery* 2006;59:1001–1009
10. Li Y, Jiang Y, Ye B, et al. Treatment of dentofacial deformities secondary to osteochondroma of the mandibular condyle using virtual surgical planning and 3-dimensional printed surgical templates. *J Oral Maxillofac Surg* 2016;74:349–368
11. Stieglitz LH. How reliable is neuronavigation? *Praxis* 2016;105:213–220
12. Stieglitz LH, Fichtner J, Andres R, et al. The silent loss of neuronavigation accuracy: a systematic retrospective analysis of factors influencing the mismatch of frameless stereotactic systems in cranial neurosurgery. *Neurosurgery* 2013;72:796–807
13. Stidd DA, Wewel J, Ghods AJ, et al. Frameless neuronavigation based only on 3D digital subtraction angiography using surface-based facial registration. *J Neurosurg* 2014;121:745–750
14. Kaufmann TJ, Huston J, Mandrekar JN, et al. Complications of diagnostic cerebral angiography: evaluation of 19,826 consecutive patients. *Radiology* 2007;243:812–819
15. Li F, He Q, Huang C, et al. High frame rate and high line density ultrasound imaging for local pulse wave velocity estimation using motion matching: a feasibility study on vessel phantoms. *Ultrasonics* 2016;67:41–54
16. Benjamin P, Zeestraten E, Lambert C, et al. Progression of MRI markers in cerebral small vessel disease: sample size considerations for clinical trials. *J Cereb Blood Flow Metab* 2016;36:228–240
17. Zhukov VY, Goryaynov SA, Ogurtsova AA, et al. Diffusion tensor imaging tractography and intraoperative neurophysiological monitoring in surgery of intracranial tumors located near the pyramidal tract. *Zh Vopr Neirokhir Im N N Burdenko* 2016;80:5–18
18. Andrade CS, Figueiredo KG, Valeriano C, et al. DTI-based tractography of the arcuate fasciculus in patients with polymicrogyria and language disorders. *Eur J Radiol* 2015;84:2280–2286
19. Jenabi M, Peck KK, Young RJ, et al. Identification of the corticobulbar tracts of the tongue and face using deterministic and probabilistic DTI fiber tracking in patients with brain tumor. *AJNR Am J Neuroradiol* 2015;36:2036–2041

Magnetic Resonance Imaging and Magnetic Resonance Angiography Findings of External Carotid Artery Aneurysm and Coexisting Carotid Body Tumor

Vahit Mutlu, MD[*] and Hayri Ogul, MD[†]

Abstract: Carotid body tumors originate from paraganglionic tissue in the bifurcation of the common carotid artery. Magnetic resonance imaging is a frequently used diagnostic method in the preoperative diagnosis of these tumors and provides appropriate information for surgical planning. In this study, the authors emphasize magnetic resonance imaging and magnetic resonance angiography findings of the external carotid artery aneurysm associated with carotid body tumor. This highlights that the diagnosis of carotid artery aneurysms is essential to avoid accidental injury to the vessel during tumor surgery.

Key Words: Carotid body tumor, external carotid artery aneurysm, MR angiography, MR imaging, vascular anomaly

Carotid body tumors (CBTs) originate from paraganglionic tissue in the bifurcation of the common carotid artery. Magnetic resonance (MR) imaging is a frequently used diagnostic method in the preoperative diagnosis of these tumors and provides appropriate information for surgical planning.[1] The external carotid artery aneurysm associated with carotid body tumor is an extremely rare condition, and recognizing the vascular anomalies accompanying the CBTs is essential to avoid accidental injury to the vessel during tumor surgery.[1] We present a 66-year-old woman with paraganglioma that originated from the left carotid bifurcation and emphasize the MR imaging and MR angiography findings of the external carotid artery aneurysm associated with this tumor.

CLINICAL REPORT

A 66-year-old woman was referred to our radiology department for further examination because of swelling in the left side of the neck

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