Imaging fusion

To The Editor: We are interested in the technique noted by Kocer et al.1 (Kocer N, Kizilkilic O, Babic D, et al.: Fused magnetic resonance angiography and 2D fluoroscopic visualization for endovascular intracranial neuronavigation. Technical note. J Neurosurg [epub ahead of print December 14, 2012. DOI: 10.3171/2012.11.JNS111355]).

Endovascular intervention is a critical procedure for the treatment of intracranial vascular lesions requiring contrast medium to guide the vascular roadmap. Kocer et al.1 used an imaging fusion technique in combination with MR angiography (MRA) and 2D fluoroscopic visualization for endovascular intracranial neuronavigation in the management of an internal carotid artery cavernous aneurysm with a stent. They demonstrated that the imaging fusion technique successfully reduced the use of the contrast agent, avoiding the potential risk of renal impairment.

We fully agree with their opinion. Actually, this imaging fusion technique provided not only a reduction in contrast use, but also minimized the exposure of radiation to doctors and staff. Moreover, the technique has great potential in application to embolization of arteriovenous malformations (AVMs). Furthermore, it could be applied to aid confidently in the recognition of the feeding artery in microneurosurgery for resection of an AVM.

We also think the technique could have a potential use in the treatment of cerebral AVMs. The 3D MRA-MRI fusion has advantages, such as determination of exact location of the AVM to prevent additional damage during surgical access and to facilitate the procedure, identifying arterial feeders and drainage veins in complex AVMs.

As techniques improve, our ability to use this kind of treatment option, especially in proximal aneurysms, is feasible. The chance of cisternal localization of distal arteries being changed by the microcatheter and guidewire should be kept in mind during navigation. Digital compensation methods are also improving. All dose-reduction techniques in combination with such technology will help and may force us to change our daily practice in the near future.

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Disclosure
The authors report no conflict of interest.

Reference

Response: We would like to give our thanks to Liu et al. for their interest in our technical note.

The authors mentioned that they fully agreed with our opinion and emphasized that the imaging fusion technique could minimize radiation exposure for doctors and staff, and reduce the use of contrast medium. Additionally, they mentioned the potential of this technique in AVMs.

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Two-handed endoscopy

To The Editor: We read with interest the paper by Cutler et al.1 on two-handed endoscopic technique for vestibular nerve sectioning (Cutler AR, Kaloostian SW, Ishiyama A, et al: Two-handed endoscopic-directed vestibular nerve sectioning: case series and review of the literature. Clinical article. J Neurosurg 117:507–513, September 2012). We have used and previously reported a similar two-handed, single-operator endoscopic technique for interhemispheric transcallosal resection of thalamic tumors and subtorcular resection of pineal lesions.2,3 We used a 0° Wolfe endoscope with a mounted rigid suction attachment and channel for intermittent irrigation as described in our papers. As in the technique described by the authors, the suction-mounted endoscope is held in the left hand while the right hand dissects with regular bipolar cautery forceps or resects with an ultrasonic aspirator under endoscopic vision. We had a similar experience with regard to improved magnification, dissection, and illumination. Furthermore, unlike the instrumentation used by the authors, the additional irrigation line in our mounted endoscope facilitated the operative technique.

Through the authors’ experience with vestibular neurectomy, they report that improved maneuverability and light intensity from this two-handed endoscopic technique “virtually eliminates” deficiencies of 2D viewing. However, in our experience, using this technique for more
complex dissection and tumor resection requires a significant learning curve. Movement and light shadow cues from an endoscope do not provide the same visual depth perception and ease of understanding the structural relationships that a microscope allows for when used for complex dissections. We attached a Stealth probe to the endoscope in our technique for intraoperative guidance to compensate to some degree for the lack of stereoscopic vision.

The single-operator endoscopic technique facilitates procedures performed in a variety of patient positions (for example, supine, prone, lateral, park-bench, sitting) with improved maneuverability and positioning comfort of the operator over the traditional microscope. Difficult-to-access and deep-seated tumors that may be firm, vascular, or attached to critical structures can be safely removed with the improved magnification from the endoscope in combination with the bimanual dexterity achieved with the attachments to the endoscope in the two-handed-technique. We agree that the single-operator, two-handed endoscopic-directed approach is both safe and effective for a variety of procedures. The recent progress made in 3D endoscopic devices may further advance this technique.

**Disclosure**

The authors report no conflict of interest.

**References**


**RESPONSE:** No response was received from the authors of the original article.

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**Traumatic head injury**


Traumatic head injury caused a breakdown of the blood-brain barrier and led to the spreading of lymphocytes into brain parenchyma with progression of an inflammatory process in the brain. Sánchez-Aguilar et al.3 performed a clinical trial to investigate the effect of rosuvastatin on inflammation-related cytokine profiles. They found that rosuvastatin significantly reduced the tumor necrosis factor–α level. Moreover, the treatment with rosuvastatin was correlated with a decrease in disability scores and better functional outcome.

Since rosuvastatin belongs to a family of histone deacetylation inhibitors, it may turn on some inflammation-regulated genes.1,2 The changes in gene expression profiles are one of the major issues in statin-treated studies that could be addressed in the future.

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**Disclosure**

The authors report no conflict of interest.

**References**


**RESPONSE:** The relevance of immunological phenomena activated after traumatic brain injury is widely recognized in such a way that therapies approaching this target could be promising.2 Our study of rosuvastatin demonstrated an effect on tumor necrosis factor–α levels and the association between this therapy and a possible reduction in disability. Admittedly, one trial cannot demonstrate all the possible benefits or collateral effects of a new drug’s application. Common problems of trauma studies should be considered (sample size, population heterogeneity, and so forth) in the interpretation of our results.1,3 Moreover, we have measured the cytokine levels in plasma, and so we could be speculating that a measurement in CSF or cerebral tissue would be more exact.3 Gene expression in brain tissue and regulation of leukocyte cell populations are other aspects to consider. We should not forget that statins act not only as regulators of inflammation but also as promoters of neuroplasticity, antioxidation, and improvements in microcirculation.3 All of these possible mechanisms could not be easily translated into clinical trials. However, if we considered the experimental and
clinical evidence, further clinical trials are urgently needed.\textsuperscript{3,7}

\textbf{References}


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\textbf{Disclosure}

The author reports no conflict of interest.

\textbf{References}

Glioma grade

To The Editor: I read with great interest the recent article by Lu et al.1 (Lu J, Ksendzovsky A, Yang C, et al: CNTF receptor subunit α as a marker for glioma tumor-initiating cells and tumor grade. Laboratory investigation. J Neurosurg 117:1022–1031, December 2012). Interestingly, the past few years have seen the identification of novel diagnostic and prognostic markers of gliomas besides ciliary neurotrophic factor receptor subunit–α (CNTFRα).

For instance, KIF14 is a new biomarker with significant prognostic potential. Gliomas tend to demonstrate almost 4 times higher levels of KIF14 than normal brain tissue. More aggressive gliomas tend to express increased KIF14 levels.7 Low Karnofsky Performance Scale (KPS) scores as well as higher tumor grades are typically seen with increasing KIF14 expression. Upregulation of KIF14 correlates with decreased overall survival and poor clinical outcome.

Similarly, microRNA-375 (miR-375) is another emerging biomarker. Gliomas tend to express significantly reduced miR-375 levels in comparison with that in normal brain tissue. Advanced tumor grade is typically seen in gliomas with low miR-375 expression.1 In fact, the miR-375 level is a significant parameter influencing overall patient survival. Another new biomarker is ELTD1. For instance, low-grade gliomas express relatively less ELTD1 than do high-grade gliomas.4 Moreover, ELTD1 expression bears a significant effect on tumor outcome and overall prognosis. Another emerging biomarker of gliomas is SPARC-like protein 1. A close relationship exists between tumor grade and SPARC-like protein 1 expression by the glioma.5

Similarly, recent data suggest that a poor clinical outcome is to be expected in gliomas that co-express matrix metalloproteinase (MMP)–14 and MMP-19. The MMP-14 and MMP-19 levels are typically much higher in gliomas than in normal brain tissue. Low KPS scores are typically seen with either MMP-14 or MMP-19 expression. Individual elevations in MMP-14 or MMP-19 indicate a poor clinical prognosis, which is made worse when both proteins are co-expressed.6 Another emerging marker of gliomas is SATB1. Expression of SATB1 is seen in nearly 63% of all gliomas. More aggressive gliomas tend to express higher SATB1 levels. Not surprisingly, a poor clinical outcome is seen in patients with gliomas that demonstrate high SATB1 levels.2 A positive correlation has been seen between SATB1 expression and Ki 67 expression in gliomas.

The above discussion clearly highlights the emerging diagnostic as well as prognostic markers of gliomas. Hopefully, the next few years will see the increased use of these biomarkers for better management and treatment of gliomas.

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REFERENCES


RESPONSE: We appreciate Dr. Kapoor’s interest in our paper. We examined the expression of CNTFRα and its association with glioma grade and tumor-initiating cells and found that increased CNTFRα expression correlates with tumor grade and is increased in tumor-initiating cells. These findings indicate that CNTFRα expression may have a role in determining clinical grade of gliomas and has a role in tumor-initiating cell maintenance. Because of its expression and role in glioma-initiating cells, CNTFRα represents an attractive therapeutic target for malignant gliomas.

Like CNTFRα, other potential biological markers are associated with glioma grade and survival. These markers have been identified to describe the molecular features of malignant gliomas. Similarly, we describe CNTFRα not only as a marker associated with tumor grade, but also as a marker defining the subset of glioma-initiating cells. It is this subset of glioma cells that may underlie the refractory nature of malignant gliomas to currently available therapeutics.1–3 Consequently, identification of unique tumor-initiating cell markers, including CNTFRα, provides additional and deeper insight into the biology of malignant gliomas, as well as an attractive target for new putative therapeutics.

Diagnosis

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Disclosure

The author reports no conflict of interest.
Pontine hemorrhage


Pontine hemorrhage is a critical neurosurgical event. The disease severity is often dependent on the extent of hemorrhage and whether it ruptures into the ventricle. Lekic et al. conducted a laboratory study to evaluate hematoma consequences, neurobehavioral profiles, and histopathology in a rat model of pontine hemorrhage. They found that stereotactic collagenase injection induced dose-dependent enlargement in pontine hemorrhage volume, neurological deficit, cerebellar edema, and blood-brain barrier breakdown, yet physiological variables were still stable. Importantly, the stereotactic injection technique is very technique dependent. The collagenase was injected using a 27-gauge needle targeting specific setup of coordinates. As we know, the 27-gauge needle is very small and easily banded. Therefore, the accuracy of the puncture target is avoidable and not always in its predicted position. We therefore suggest that MRI monitoring of the puncture trajectory and target is warranted to prevent puncture through the fourth ventricle, which will lead to hydrocephalus and predisposing the rats to earlier death. Moreover, MRI provides longitudinal evaluation of the hematoma volume and associated effect of brain edema on pons.

We therefore agree with the comments from Dr. Hueng’s group and have begun mapping the hemorrhage site with the plan of future brain lesion studies within the brainstem (Fig. 1). Of course, image guidance would help less experienced groups with available resources at hand to expedite the technical modeling of primary pontine hemorrhage. However, image guidance is not absolutely necessary, as we did not need this modality initially to generate this animal model. Nonetheless, MRI would certainly reduce the number of animals required, as rodents can be observed longitudinally over time using multiple simultaneous parameters (for example, brain edema, hematoma expansion, blood-brain barrier rupture, and ventricle size) correlated to mortality, and thus providing invaluable clinical information to further guide clinicians in the evaluation of subsequent patient cohorts.

Importantly, future neurosurgical scientists will ultimately be needed to evaluate the development of hydrocephalus, and we are working on this important pathological condition as well. The strengths of our observations and the future of primary pontine hemorrhage experimental animal modeling therefore rest on the shoulders of investigators using this experimental model in the pursuit of potential treatments for this devastating neurosurgical condition. We thus look forward to and hope to see many studies in the future.

Disclosure
The authors report no conflict of interest.

Reference

Response: We appreciate the comments of Tsai et al. regarding our paper. This primary pontine hemorrhage animal model originated from a widely used approach to study intracerebral hemorrhage in rats. After several technical experience years of modeling intraparenchymal basal ganglia hemorrhage in mice, our group modified this skill toward stereotactic pontine collagenase infusion using rats. Thereafter, we published T1-weighted, T2-weighted, and diffusion- susceptibility-weighted MR images [with and without Gd] of primary pontine hemorrhage in rats, showing precise hematoma localization, perilesional edema, extravascular blood, and blood-brain barrier rupture, and correlated these findings with both gross and histological specimens obtained in the same rodents.

We therefore agree with the comments from Dr. Hueng’s group and have begun mapping the hemorrhage site with the plan of future brain lesion studies within the brainstem (Fig. 1). Of course, image guidance would help less experienced groups with available resources at hand to expedite the technical modeling of primary pontine hemorrhage. However, image guidance is not absolutely necessary, as we did not need this modality initially to generate this animal model. Nonetheless, MRI would certainly reduce the number of animals required, as rodents can be observed longitudinally over time using multiple simultaneous parameters (for example, brain edema, hematoma expansion, blood-brain barrier rupture, and ventricle size) correlated to mortality, and thus providing invaluable clinical information to further guide clinicians in the evaluation of subsequent patient cohorts.

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Acknowledgment

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References


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Fig. 1. Volumetric 3D image reconstructions of a primary pontine hemorrhage (PPH), using T2-weighted MRI data sets. a: Dorsal view. The asterisk indicates the supratentorial region. b: Sagittal perspective of the same animal clearly illustrating the location and relative size of the hematoma. c: Oblique angle (left) illustrating the ability to further maneuver (right) and dissect the 3D data.