

## Use of virtual magnetic resonance imaging to compensate for brain shift during image-guided surgery: illustrative case

John T. Kim, MS,<sup>1</sup> Long Di, BS,<sup>1</sup> Arnold B. Etame, MD, PhD,<sup>1,2</sup> Sarah Olson, BS,<sup>2</sup> Michael A. Vogelbaum, MD, PhD,<sup>1,2</sup> and Nam D. Tran, MD, PhD<sup>1,2</sup>

<sup>1</sup>Department of Neurosurgery, University of South Florida, Tampa, Florida; and <sup>2</sup>Department of Neuro-Oncology, Moffitt Cancer Center and Research Institute, Tampa, Florida

**BACKGROUND** Maximal safe resection is the paramount objective in the surgical management of malignant brain tumors. It is facilitated through use of image-guided neuronavigation. Intraoperative image guidance systems use preoperative magnetic resonance imaging (MRI) as the navigational map. The accuracy of neuronavigation is limited by intraoperative brain shift and can become less accurate over the course of the procedure. Intraoperative MRI can compensate for dynamic brain shift but requires significant space and capital investment, often unavailable at many centers.

**OBSERVATIONS** The authors described a case in which an image fusion algorithm was used in conjunction with an intraoperative computed tomography (CT) system to compensate for brain shift during resection of a brainstem hemorrhagic melanoma metastasis. Following initial debulking of the hemorrhagic metastasis, intraoperative CT was performed to ascertain extent of resection. An elastic image fusion (EIF) algorithm was used to create virtual MRI relative to both the intraoperative CT scan and preoperative MRI, which facilitated complete resection of the tumor while preserving critical brainstem anatomy.

**LESSONS** EIF algorithms can be used with multimodal images (preoperative MRI and intraoperative CT) and create an updated virtual MRI data set to compensate for brain shift in neurosurgery and aid in maximum safe resection of malignant brain tumors.

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**KEYWORDS** virtual MRI; brain tumor surgery; image-guided surgery

Extent of resection is a well-documented prognosticator for both primary and secondary malignant brain tumors.<sup>1-7</sup> Recent technological advances such as intraoperative neuronavigation and brain mapping have facilitated maximum safe resection of brain tumors while preserving neurological function.<sup>8,9</sup> Although intraoperative neuronavigation is one of the most extensively used neurosurgical tools, its reliance on preoperative imaging remains a major limitation because intraoperative brain shift degrades accuracy and precision.<sup>9-12</sup> Hence, innovative approaches that accurately correct for brain shift during neuronavigation could have both a significant and practical impact on maximum safe resection of malignant brain tumors.

Brain shift is an inevitable phenomenon of cranial surgery. Factors such as patient positioning, hyperventilation, gravity, cerebrospinal fluid

egress, perioperative medications, and tumor-specific factors are significant contributors to brain shift.<sup>10,13-16</sup> Further, brain shifts are much more significant close to the cortex compared to subcortical regions.<sup>17</sup> Real-time intraoperative imaging modalities such as ultrasound, CT, and MRI can be applied to mitigate shift. Serial intraoperative MRI (iMRI) has emerged as a gold standard for accurate interrogation and compensation for dynamic shifts in various regions of the brain.<sup>13</sup> However, iMRI is extremely labor intensive, time consuming, resource intensive, and costly, thereby limiting its feasibility to limited number of centers.<sup>10,18</sup>

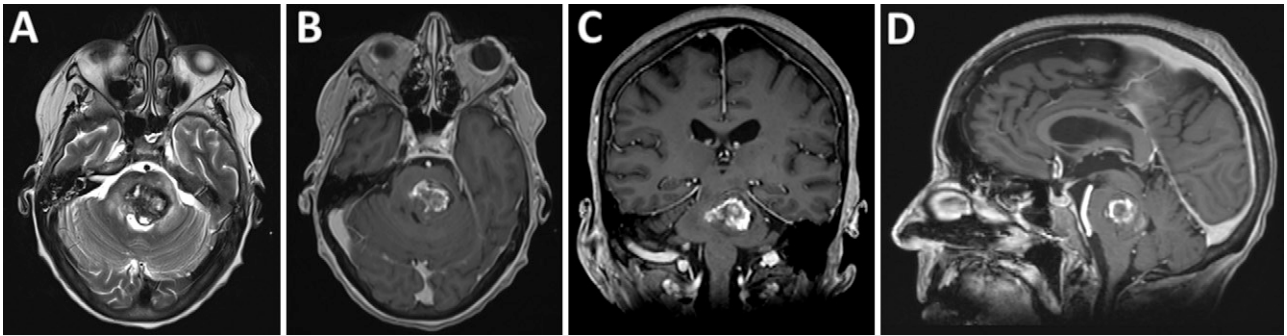
On the other hand, intraoperative CT (iCT) is more common and less expensive, but soft tissue resolution is markedly suboptimal compared to iMRI. Software algorithms that can fuse or transform real-time iCT images into MRI renditions with compensation for

**ABBREVIATIONS** CT = computed tomography; EIF = elastic image fusion; iCT = intraoperative CT; iMRI = intraoperative MRI; MRI = magnetic resonance imaging; RIF = rigid image fusion.

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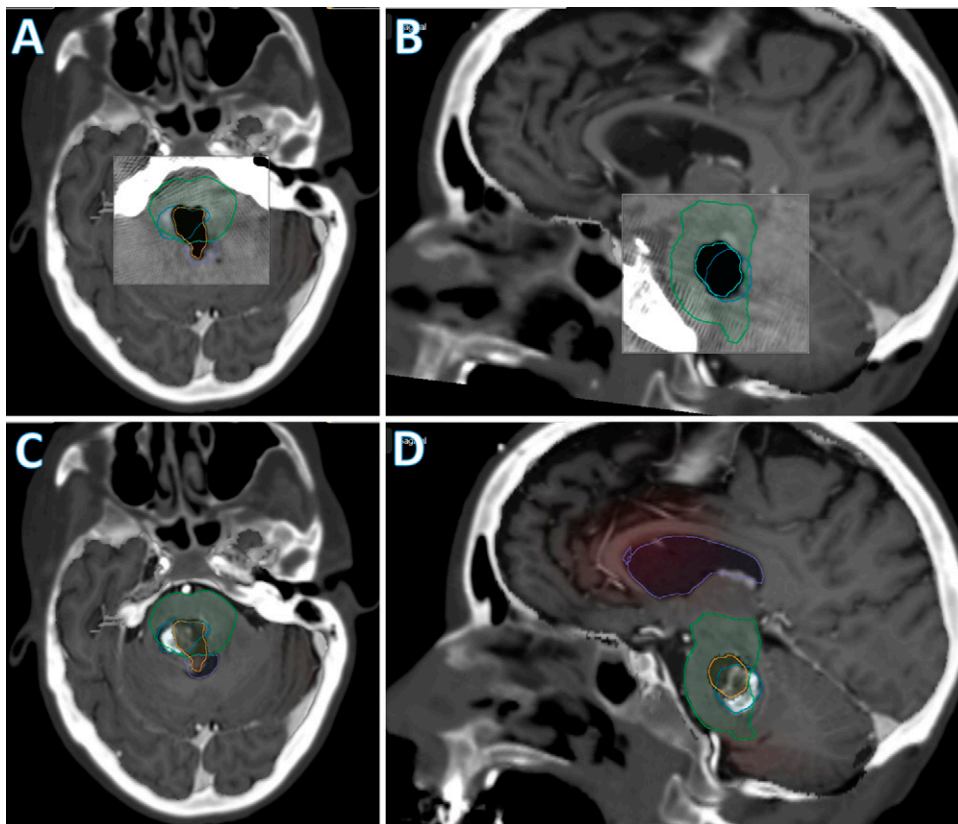


**FIG. 1.** Preoperative axial T2-weighted (A) and axial (B), coronal (C), and sagittal (D) postcontrast T1-weighted images showing pontine hemorrhagic metastasis.

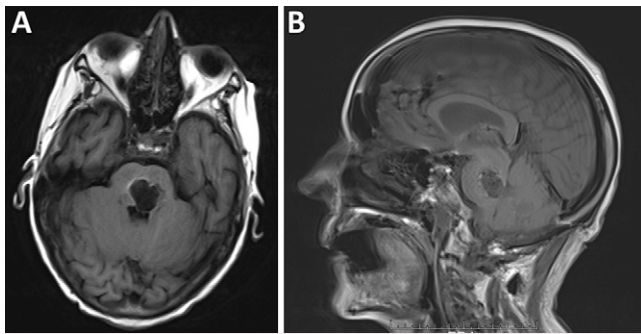
brain shift represent a practical approach to the limitations of widespread applications for iMRI.

A simple method for image transformation is linear or rigid image fusion (RIF). This type of algorithm allows translations, rotations, scaling, and skewness to align the data sets. Traditional neuronavigation is an RIF application, well known to neurosurgeons, involving alignment of image space to physical space using fusion algorithms.<sup>17-19</sup> The relative precision of image fusion is determined by the measured

distance, or Euclidian distance, between defined anatomical landmarks. Thus, smaller Euclidian distances between defined anatomical landmarks in the image space and physical space represent smaller registration errors. However, other factors that contribute to brain shift involve more complex movements that need nonlinear deformations. Therefore, a novel elastic image fusion (EIF) algorithm was developed, and it has been shown to significantly decrease the Euclidean distance for landmarks compared to RIF algorithms.<sup>20</sup>



**FIG. 2.** Intraoperative CT showing surgical cavity (A and B, orange) and virtual MRI demonstrating surgical cavity (orange) and residual tumor volume (C and D, blue).



**FIG. 3.** Axial (A) and sagittal (B) T1-weighted images showing complete resection of the hemorrhagic metastasis.

In this case report, we describe the role of Elements Virtual iMRI Cranial software (Brainlab) that can be used to compensate for brain shift during image-guided resection of a metastatic melanoma in the pontine region. The EIF algorithm uses a finite element model that is based on individual tissue labeling and image-based multirigid fusion optimization between the simulated MRI and the intraoperative scan. This system permits algorithmic renditions of intraoperative CT into virtual MRI for real-time neuronavigation.

### Illustrative Case

A 65-year-old woman presented with dizziness, right hemibody paresthesia, and loss of right-sided proprioception and was found to have a large metastatic melanoma in the pons. She had undergone fractionated stereotactic radiotherapy to the pontine metastasis. Serial imaging of her brain demonstrated progressive enlargement of the pontine tumor with hemorrhagic transformation (Fig. 1). There was increasing compression of the brainstem and fourth ventricle, with early signs of obstructive hydrocephalus. Furthermore, she demonstrated progressive weakness to all extremities and dysarthria. The radiation oncology team determined that she could no longer receive any additional radiation to the brainstem. That opinion, coupled with her progressive neurological symptoms and imaging that showed that the mass and its associated hemorrhage extended close to the pia surface, led to the recommendation for resection of the tumor.

A suboccipital craniotomy and telovelar approach with stereotactic navigation, neuromonitoring, and intraoperative CT was planned for resection of the pontine metastasis. We used Elements Virtual iMRI Cranial software to define anatomical structures on the preoperative MRI study. After positioning the patient and placing the neuromonitoring electrodes, the patient was registered with the preoperative MRI for the IGS. Approximately midway into the decompression, intraoperative CT was performed that showed adequate decompression of the pons. The software was used to perform an EIF between preoperative MRI and the latest intraoperative CT. An updated virtual iMRI data set was generated that displayed an updated three-dimensional visualization of the brainstem and tumor (Fig. 2). Postoperative MRI showed gross-total resection of the pontine metastasis (Fig. 3). The patient demonstrated improvement in neurological symptoms.

## Discussion

### Observations

Brain metastases from melanoma have a very poor prognosis, with an average survival of 3 to 4 months if untreated and up to 1 year with treatment.<sup>21</sup> Survival has been positively correlated with EOR for both glioblastomas and brain metastases from melanoma.<sup>3,4</sup> Therefore, it is imperative to maximize EOR safely while preserving neurological function. To maximize EOR, brain shift must be accounted for accurately, especially in eloquent areas of the brain. In particular, critical brainstem nuclei and neural pathways should be preserved.

The factors that contribute to brain shift involve complex spatio-temporal movements, and the linear transformations used in RIF cannot accurately account for this movement. A retrospective analysis using EIF algorithms on 10 MRI and iMRI data set pairs was shown to significantly decrease the Euclidean distance for landmarks compared to RIF algorithms.<sup>20</sup> The virtual iMRI using EIF software has been validated retrospectively to accurately correct for brain shift distortion of fiber tractography.<sup>22</sup> Furthermore, in a prospective study examining 308 consecutive patients, adjustments of tractography by elastic fusion accurately correlates with intraoperative neuromonitoring.<sup>23</sup> EIF can also be used with different modalities such as intraoperative CT to generate a virtual iMRI data set. Preoperative MRI data that were registered with intraoperative CT data using EIF were prospectively shown to significantly increase the registration accuracy compared to RIF.<sup>24</sup>

The use of virtual iMRI in the brainstem has never been described, nor has the use of EIF with intraoperative CT in the brainstem ever been documented. In such a delicate area, it is imperative to maximize EOR while preserving function. We described the role of virtual iMRI to compensate for brain shift during the surgical resection of a brainstem metastases from melanoma. Postoperative MRI was consistent with complete resection, and there was corresponding improvement in neurological symptoms.

### Lessons

In this case report, we used a commercially available software, Brainlab Elements Virtual iMRI Cranial software, to perform EIF with a preoperative MRI data set that was registered with an intraoperative CT data set. An updated virtual iMRI data set was generated and used to compensate for brain shift and aid in complete resection of the brainstem tumor. This case report highlights the use of multimodal imaging to generate virtual iMRI to display the areas of brain shift during surgery. If further validated, it can prove to be a safe and reliable method to maximize the EOR and improve outcomes in patients with brain tumors. Likewise, compared to the use of intraoperative MRI, it can prove to be a cost- and time-saving alternative.

A limitation of this report is its nonquantitative nature. It was not compared to an RIF algorithm, and the registration accuracy was not measured. A further limitation is that this was only a single case, and future larger studies are needed to validate the benefits and feasibility of virtual iMRI.

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#### Disclosures

Dr. Vogelbaum reported an inventor's share of any royalties or realized net equity in Infuseon Therapeutics, personal fees from Chimerix, grants from Infuseon Therapeutics, Oncosynergy, and Celgene outside the submitted work. No other disclosures were reported.

#### Author Contributions

Conception and design: Tran, Kim, Di, Vogelbaum. Acquisition of data: Tran, Di, Olson, Vogelbaum. Analysis and interpretation of data: all authors. Drafting the article: Tran, Kim, Di, Olson. Critically revising the article: Tran, Kim, Di, Etame, Vogelbaum. Reviewed submitted version of manuscript: Tran, Kim, Di, Etame, Vogelbaum. Approved the final version of the manuscript on behalf of all authors: Tran statistical analysis: Di. Administrative/technical/material support: Di, Olson, Vogelbaum. Study supervision: Tran, Di.

#### Supplemental Information

##### Previous Presentations

This paper was presented in abstract form at the CNS meeting, Austin, TX, October 16–20, 2021.

#### Correspondence

Nam D. Tran: Moffitt Cancer Center and Research Institute, Tampa, FL. [nam.tran@moffitt.org](mailto:nam.tran@moffitt.org).