Deformable Anatomic Templates Improve Analysis of Gliomas With Minimal Mass Effect in Eloquent Areas

Vinodh A. Kumar, MD*

Jackson Hamilton, MD*

L. Anne Hayman, MD§

Ashok J. Kumar, MD*

Ganesh Rao, MD‡

Jeffrey S. Weinberg, MD‡

Raymond Sawaya, MD‡

Sujit S. Prabhu, MD‡

*Department of Diagnostic Radiology and ‡Department of Neurosurgery, University of Texas MD Anderson Cancer Center, Houston, Texas; §Anatom-*e* Information Systems, Ltd, Houston, Texas

Correspondence:
Vinodh A. Kumar, MD,
Department of Diagnostic Radiology,
University of Texas MD Anderson
Cancer Center,
1400 Pressler St, Unit 1482,
Houston, TX 77030.
E-mail: vakumarmd@yahoo.com

Received, April 18, 2012.
Accepted, May 20, 2013.
Published Online, May 30, 2013.

BACKGROUND: Despite improvements in advanced magnetic resonance imaging and intraoperative mapping, cases remain in which it is difficult to determine whether viable eloquent structures are involved by a glioma. A novel software program, deformable anatomic templates (DAT), rapidly embeds the normal location of eloquent cortex and functional tracts in the magnetic resonance images of glioma-bearing brain.

OBJECTIVE: To investigate the feasibility of the DAT technique in patients with gliomas related to eloquent brain.

METHODS: Forty cases of gliomas (grade II-IV) with minimal mass effect were referred for a prospective preoperative and postoperative DAT analysis. The DAT results were compared with the patient's functional magnetic resonance imaging, diffusion tensor imaging, operative stimulation, and new postoperative clinical deficits.

RESULTS: Fifteen of the 40 glioma patients had overlap between tumor and eloquent structures. Immediate postoperative neurological deficits were seen in 9 cases in which the DAT showed the eloquent area both within the tumor and within or at the edge of the resection cavity. In 6 cases with no deficits, DAT placed the eloquent area in the tumor but outside the resection cavity.

CONCLUSION: This is proof of concept that DAT can improve the analysis of diffuse gliomas of any grade by efficiently alerting the surgeon to the possibility of eloquent area invasion. The technique is especially helpful in diffuse glioma because these tumors tend to infiltrate rather than displace eloquent structures. DAT is limited by tract displacement in gliomas that produces moderate to severe mass effect.

KEY WORDS: Brain atlas, Deformable anatomic templates, Diffusion tensor imaging, Eloquent brain mapping, Functional magnetic resonance imaging, Glioma surgery

Neurosurgery 73:534–542, 2013 DOI: 10.1227/01.neu.0000431479.87160.e2 www.neurosurgery-online.com

Diffuse gliomas (World Health Organization grade II-IV) by their pathological definition and imaging tend to infiltrate brain.[1-7] With resection of gliomas, neurosurgeons must weigh the survival benefits of maximal resection[8] to the risk of permanent neurological deficit[9-12] with sociological and financial implications.[13] Neurological deficit and peritumoral physiology may prevent the localization of eloquent areas with functional magnetic resonance imaging (fMRI) and diffusion tensor imaging (DTI).[14-19] An fMRI may fail to show activity in functioning brain because the presence of glial tumor distorts the neurovascular and metabolic coupling, which produces the blood oxygen level–dependent signal.[14,15] DTI may fail to show functional white matter tracts because edema, tissue compression, and degeneration found in and around gliomas limit the detection of the white matter.[18,19] We have shown that deformable anatomic templates (DAT) can be overlaid on MRIs in 2 and 3 dimensions to assess the normal position of eloquent structures[20] such as those involved in motor and language functions. An initial DAT validation study showed no fitting errors for the hand-motor cortex in normal hemispheres and 83% of tumor-bearing hemispheres with 4 cases of mismatch from up to 10 mm of mass effect.[21]

ABBREVIATIONS: DAT, deformable anatomic templates; **fMRI,** functional magnetic resonance imaging; **DTI,** diffusion tensor imaging

TABLE 1. Nine Surgeries: Eloquent Area in Tumor and in or at the Edge of Surgical Cavity, With New or Worse Deficits[a]

Case	Age, y, and Sex	Histology	Prior Surgery	Prior Chemotherapy or XRT	Relevant fMRI	Relevant DTI
1	46 M	ASTRO	No	None	NA	NA
2	47 M	ASTRO	Yes	None	Hand+^{DAT}	NA
3	35 F	GB	Yes	None	NA	NA
4 (Figure 1)	57 M	AA	No	None	Broca+^{DAT}	Arcuate and CBT+^{DAT}
5 (Figure 2)	69 M	GB	No	None	Hand+^{DAT}	CST+/−
6 (Figure 3)	71 F	GB	No	None	Hand+^{DAT}	CST+/−
7	43 M	GB	Yes	Yes	NA	CST+^{DAT}
8	59 M	AA	Yes	Yes	NA	CST+/−
9	26 M	AO	No	No	Hand+^{DAT}	CST+^{DAT}

Case	Operative Stimulation	Location of Cavity	Preoperative Deficit	New Postoperative Deficits at 0 to 3 mo	Deficits at 3 to 30 mo
1	SSEPs+, DCS+/−	CBT–tongue	None	Yes	NA
2	DCS+^{DAT}	Somatosensory motor gyrus	Yes	Worse, facial droop	Worse
3	NA	Left ventral premotor	None	Yes, speech/motor	NA
4 (Figure 1)	Localized arcuate, Broca, and CBT+^{DAT}	Left ventral premotor; CBT	None	Yes, speech/motor	Worse
5 (Figure 2)	PRASS probe CST+^{DAT}	CST in corona radiata	Yes, sensory	Worse: motor weakness	NA
6 (Figure 3)	SSEPs−, DCS and subcortical+^{DAT}	CST in corona radiata	None	Yes	Worse UE
7	Cortical and subcortical+^{DAT}	CST in corona radiata	None	Yes, UE and LE motor	Worse
8	SSEPs weak, subcortical LE+^{DAT}/UE−	CST	Yes, motor UE and LE	Yes, worse	NA
9	DCS and subcortical Stim + LE and speech^{DAT}; UE−	Subcentral and premotor	Yes, speech	Yes, motor UE and face	Stable at 6 mo

[a]AA, anaplastic astrocytoma (grade III); AO, anaplastic oligodendroglioma (grade III); ASTRO, astrocytoma (grade II); CBT, corticobulbar; CST, corticospinal tract; DAT, within 5 mm of the expected location of the relevant eloquent structure by deformable anatomic template; DCS, direct cortical stimulation; DTI, diffusion tensor imaging; fMRI, functional magnetic resonance imaging; GB, glioblastoma (grade IV); LE, lower extremity; NA, not available or performed; SSEP, somatosensory evoked potential; subcortical, subcortical stimulation with PRASS probe; UE, upper extremity; XRT, radiation therapy; +, positive result; +/−, ambiguous or partially correct results; −, failed to elicit stimulation.

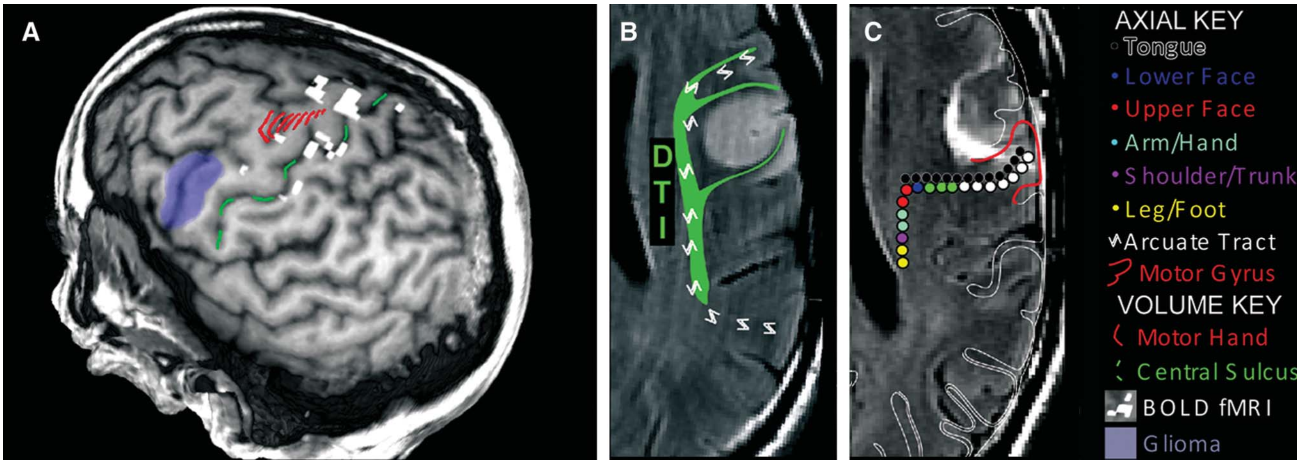

FIGURE 1. *Case 4, Table 1. Intraoperative onset of articulatory speech deficit of an anaplastic astrocytoma.* **A**, *preoperative volume-rendered oblique lateral view of the left cerebral hemisphere shows that the posterior rim of the tumor (blue) invades the opercular part of the motor cortex. Motor hand functional magnetic resonance imaging (fMRI) activation (white pixels) in the central sulcus is shown for orientation and to verify the overlay of the deformable anatomic templates (DAT) motor hand fibers in the center of the motor gyrus (red lines).* **B**, *axial diffusion tensor imaging (DTI; green) demonstrates the arcuate fasciculus and the corticobulbar tract with the superimposed DAT of the arcuate fasciculus (white).* **C**, *postoperative axial DAT shows the close proximity of the resection cavity to the ventral premotor cortex and tongue fibers (black dots), thus explaining the postoperative speech and motor deficits. BOLD, blood oxygen level–dependent.*

The hypothesis for this study is that core eloquent areas can retain all or partial function despite invasion by a diffuse glioma. If this hypothesis is correct and the invasion does not significantly displace these eloquent structures, then DAT of the normal position of structures could provide a useful adjunctive guide for preoperative decision making[22] and interpretation of postoperative deficits. Given the potential limitations of current localization techniques (ie, fMRI and DTI), other adjunctive tools should be used in preoperative evaluation of patient with gliomas. DAT requires only 5 minutes of a technician's time to generate the expected normal position of important eloquent structures in an intuitively understood volume-rendered format. A subset of 40 tumors

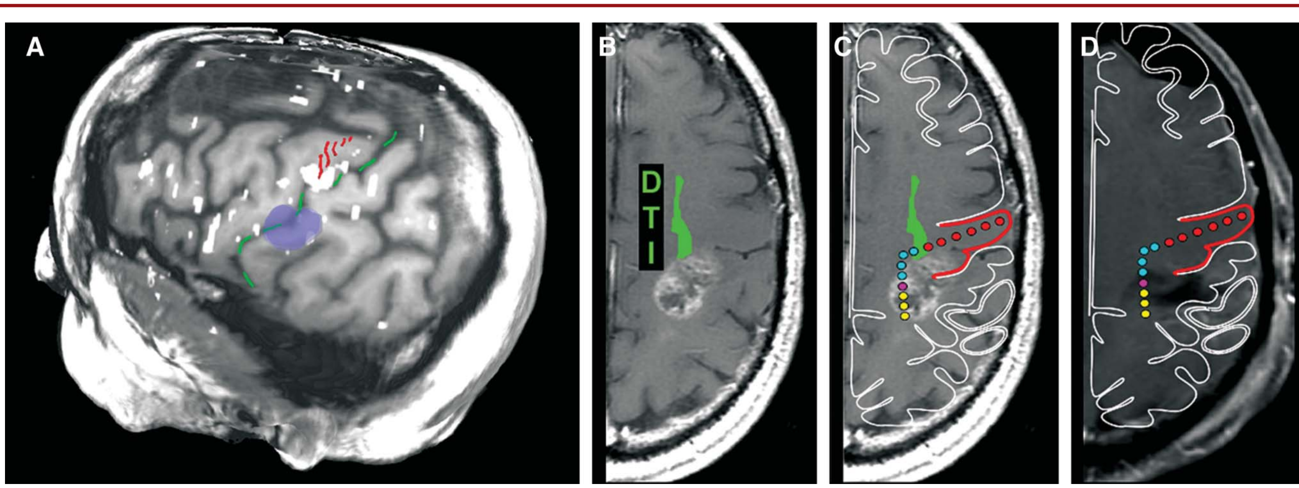

FIGURE 2. *Case 5, Table 1. Deformable anatomic templates (DAT) helped in identifying the close proximity of the leg fibers to the glioblastoma.* **A**, *volume rendering and fitting are similar to those in Figure 1A. The tumor (blue) is mainly deep to the sensory gyrus.* **B**, *axial diffusion tensor imaging (DTI; green) shows the uninvolved corona radiata motor fibers anterior to the tumor. Note that DTI does not show the motor fibers within the enhancing tumor.* **C**, *axial DAT shows the overlay of motor fibers of the lower limb (yellow dots) in the enhancing tumor. It is likely that the motor fibers of the lower limb are within the enhancing wall of the tumor or adjacent impacted brain but still within 5 mm of the normal expected location of the tract as delineated by DAT.* **D**, *postoperative axial DAT shows the close proximity of resection cavity to the lower-extremity motor fibers (yellow dots), which explains the initial postoperative motor weakness.*

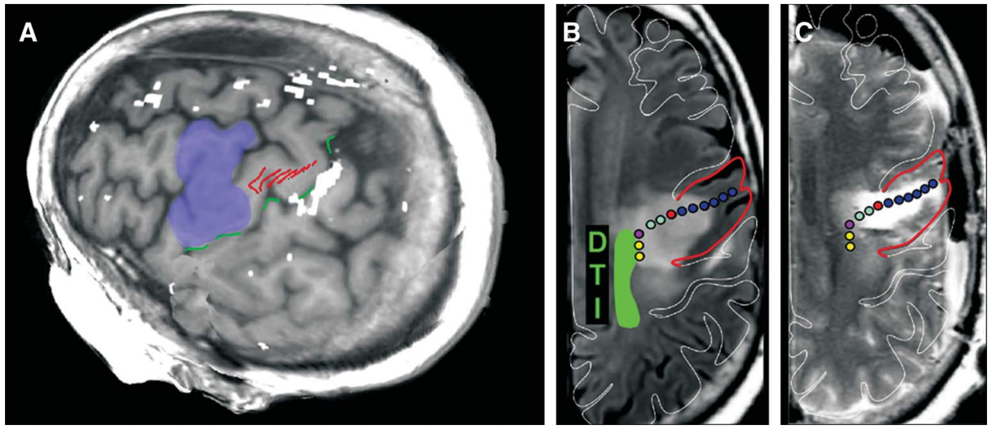

FIGURE 3. *Case 6, Table 1. Removal of glioblastoma caused intraoperative onset of contralateral upper-extremity weakness.* **A**, *volume rendering and fitting are similar to those in Figure 1A. The tumor (blue) expands the motor gyrus.* **B**, *preoperative axial deformable anatomic templates (DAT) shows the overlay of all of the descending motor fibers, but diffusion tensor imaging (DTI; green) shows only those of the lower limb.* **C**, *postoperative axial DAT shows the close proximity of the upper-limb fibers (turquoise dots) to the operative cavity, explaining the postoperative upper-extremity motor deficits.*

prospectively mapped with DAT because of proximity to eloquent structures is presented as a proof of concept. DAT eloquent structures embedded on imaging were correlated to the gold standard of intraoperative operative mapping[9,23,24] and new or worsening postoperative deficits.

PATIENTS AND METHODS

Patient Selection and Medical Record Review

Human studies approval was obtained for an ongoing prospective preoperative and postoperative DAT analysis of gliomas referred by the neurosurgeons at our tertiary referral center because of tumor near eloquent structures. Forty patients were referred from 2010 through 2012. The patient inclusion criteria for this study included diffuse glioma cases (World Health Organization grade II-IV) with minimal mass effect in which DAT showed an overlap between the tumor and an eloquent area. Minimal mass effect gliomas were defined as those that produced < 5 mm of sulcal or midline shift resulting from tumor or edema mass effect. The DAT results were compared when available with the patient's fMRI, DTI, operative stimulation, and new or worsening postoperative neurological deficits.

Imaging Protocol and DAT Analysis of 40 Cases

A standard precontrast and postcontrast brain tumor imaging protocol was performed on a 1.5- or 3.0-T MRI scanner, and the clinically appropriate combination of fMRI and DTI studies was determined by the surgeon and performed before surgery. Postoperative brain MRI was obtained within 24 hours after surgery in all patients. The preoperative and postoperative MRI scans, fMRI, and/or DTI scans were imported into the Anatom-*e* workstation (Anatom-*e* Information Systems, Houston, Texas). The DAT analysis was initially performed in tandem with the Philips iSite PACS (Philips Healthcare Informatics, Foster City, California) or in the intraoperative MRI suite (BrainSUITE, BrainLab, Westchester, Illinois). The results were reviewed by 4 neuroradiologists and a neurosurgeon (V.K., J.H., L.A.H., A.K., and S.P.).

The DAT fitting has been previously detailed.[20] Briefly, a senior neuroradiologist (L.A.H) annotated and manually segmented 1185 color-coded structures on axial MRIs of a normal template brain using domain knowledge across anatomic, radiological, and clinical specialties. The anatomic literature provided detailed neuroanatomy and connections. The radiographic literature provided imaging landmarks and differential diagnosis. Structures that were not visible on conventional MRI were extrapolated within the confines of the anatomically correct framework through the use of anatomic dissections and DTI atlases.[25-27] Information on clinical syndromes caused by damage to a structure was drawn from neurology and ophthalmology literature. Further fine-tuning of the DAT was provided by the use of intraoperative DTI tract generation and intraoperative stimulation.

In approximately 5 minutes, the technician manually embeds the DAT into the patient's MRIs by reslicing, without deforming, the patient's DICOM (digital imaging and communications in medicine) images and then using a simple linear deformation of the DAT to fit the inner table of the patient's cranial vault. Specifically, the anterior cranial fossa was matched to the DAT gyrus rectus and orbital gyri,[20] with variations in brain position from varying skull configurations taken into account.[28,29] The resulting "fit" was evaluated by the distance between the anatomic hand knob and the DAT motor hand fibers in the 3-dimensional volume. The linear deformation alters the DAT to compensate for the patient's head rotation, head tilt, and variations in chin position. It also resizes the DAT to fit the vertical and horizontal dimensions of the patient's brain. The ventricles are not used as landmarks because of wide individual variation. The fitted DAT provided information on the normal location of the eloquent structures, including the arcuate fasciculus, corticospinal tract, language, sensory and motor cortices, and ventral premotor cortex.[20,30,31]

RESULTS

Fifteen of the 40 cases analyzed by DAT had an overlap of tumor and an eloquent area preoperatively. In 9 patients with new

TABLE 2. Six Surgeries: Eloquent Area in Tumor and Outside Surgical Cavity, No Worse[a]

Case	Age, y, and Sex	Histology	Prior Surgery	Prior Chemotherapy or XRT	Relevant fMRI	Relevant DTI
12 (Figure 4)	35 F	AA	No	None	NA	Posterior arcuate−
13 (Figure 5)	24 F	GB	No	None	NA	Posterior arcuate−
14	41 M	OLIGO	No	None	Broca+$^{\text{DAT}}$	Anterior arcuate−
15	54 M	GB	Yes	Yes	Broca+/−; Hand+$^{\text{DAT}}$	CBT−; CST+$^{\text{DAT}}$ arcuate NA
16	56 M	GB	No	None	Hand/Broca+$^{\text{DAT}}$	CBT−; CST+$^{\text{DAT}}$ arcuate NA
17	36 M	Necrosis, prior AE	Yes	Yes	Broca+$^{\text{DAT}}$	Anterior−; posterior arcuate+$^{\text{DAT}}$

Case	Operative Stimulation	Location of Cavity	Resection, %	Preoperative Deficit	New Postoperative Deficits at 0 to 3 mo	Deficits at 3 to 24 mo
12 (Figure 4)	DAT-guided stimulation of arcuate	Left supramarginal gyrus and arcuate	80	None	None	Stable at 16 mo
13 (Figure 5)	DAT-guided stimulation of arcuate	Left supramarginal gyrus and arcuate	90	Yes	Stable	Worse, 6 mo
14	DCS+Broca$^{\text{DAT}}$	Left superior and middle frontal gyrus	60	None	None	Stable at 24 mo
15	DAT-guided stimulation of motor hand/face	Middle frontal gyrus spares CBT/UE CST	95	Yes	Speech improved	Stable at 8 mo
16	DAT-guided localization of face motor	Middle frontal gyrus spares CBT/CST	40	None	None	NA
17	DCS+$^{\text{DAT}}$	Parietal lobe	40	No	Yes, speech	Improved

[a]AA, anaplastic astrocytoma (grade III); AE, anaplastic ependymoma (grade III); ASTRO, astrocytoma (grade II); CBT, corticobulbar; CST, corticospinal tract; DAT, within 5 mm of the expected location of the relevant eloquent structure by deformable anatomic template; DCS, direct cortical stimulation; DTI, diffusion tensor imaging; fMRI, functional magnetic resonance imaging; GB, glioblastoma (grade IV); LE, lower extremity; NA, not available or performed; OLIGO, oligodendroglioma (grade II); SSEP, somatosensory evoked potential; XRT, radiation therapy; UE, upper extremity; +, positive result; +/−, ambiguous or partially correct results; −, failed to localize eloquent areas.

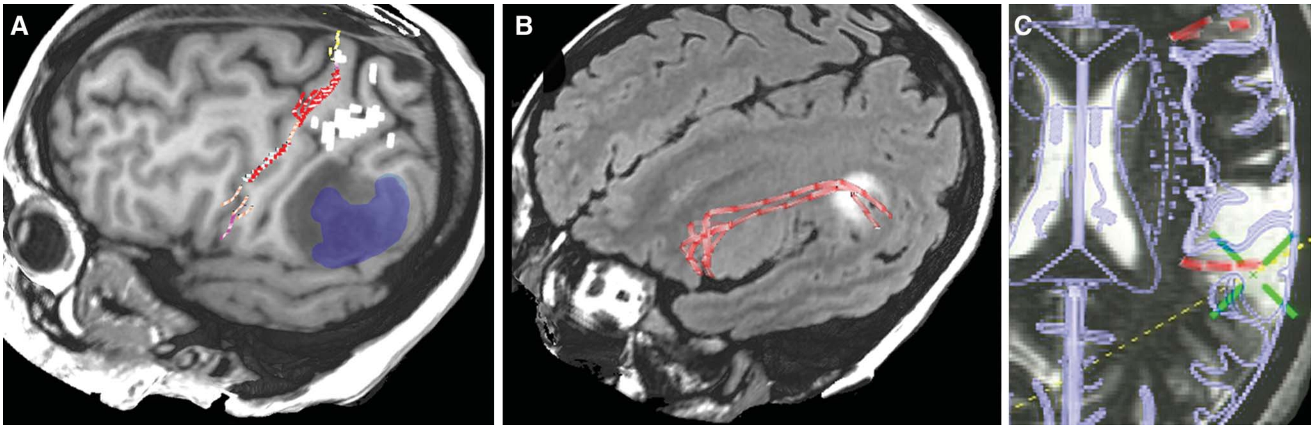

FIGURE 4. *Case 12, Table 2. Deformable anatomic templates (DAT)–guided stimulation prevented a deficit by tailored sparing of tumor-bearing eloquent speech cortex.* **A**, *volume rendering and fitting are similar to those in Figure 1A. The anaplastic astrocytoma invades the left inferior parietal lobule (blue) with a rim of edema.* **B**, *the preoperative volume reconstruction with the DAT overlay shows the normal position of the posterior arcuate fasciculus fibers (red) in the posterior margin the tumor.* **C**, *The axial DAT template shows the excellent match between the location of the arcuate fibers (red) and the location of the operative probe (green cross-hairs) that marks the area at which the patient experienced progressive speech deterioration, and the resection was terminated because the tumor had been successfully removed anterior to the dorsal arcuate fibers. The patient had improving mild hesitancy and word choice alterations when discharged 2 days after surgery, and normal speech was documented for 16 months after surgery.*

deficits immediately after surgery, DAT placed the normal position of the eloquent structures within the tumor and within or at the edge of the resection cavity (Table 1 and Figures 1-3). In 3 of these cases, direct electrical stimulation was inconclusive. All patients had a Karnofsky Performance Scale score of at least 70 and continued with their adjuvant treatments except 1 patient (case 8, Table 1) who had a very significant hemiparesis preoperatively and did not recover after surgery. The deficits were due to the very close proximity of the tumor resection margins to the descending motor tracts in the corona radiata (Figures 2 and 3) in 7 cases and the ventral premotor cortex (motor area of Broca; Figure 1)[31-34] resulting in language deficits in 2 cases. There was excellent agreement between the predicted postoperative deficit by DAT and the actual postoperative deficit in all cases.

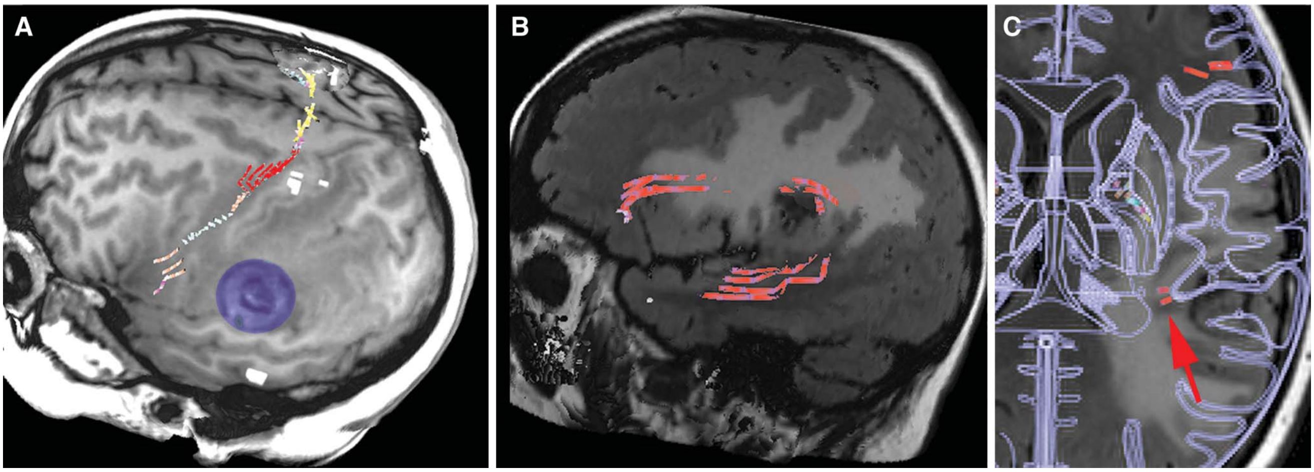

FIGURE 5. *Case 13, Table 2. Deformable anatomic templates (DAT)–guided stimulation–tailored sparing of tumor-bearing arcuate fibers resulted in intact speech at 3 months but dysarthria at 6 months caused by glioblastoma progression.* **A**, *volume rendering and fitting are similar to those in Figure 1A. Glioblastoma (blue) invades the anterior supramarginal gyrus, and extensive peritumoral edema produces minimal mass effect.* **B**, *the preoperative volume-reconstructed image of the DAT shows the normal position of the posterior arcuate fasciculus fibers (red) in the posterior superior margin of the tumor.* **C**, *the preoperative DAT shows the expected normal location of the arcuate fibers (red arrow) in the axial plane that were spared during resection (not shown). An attempted diffusion tensor imaging could not generate the arcuate fiber tract.*

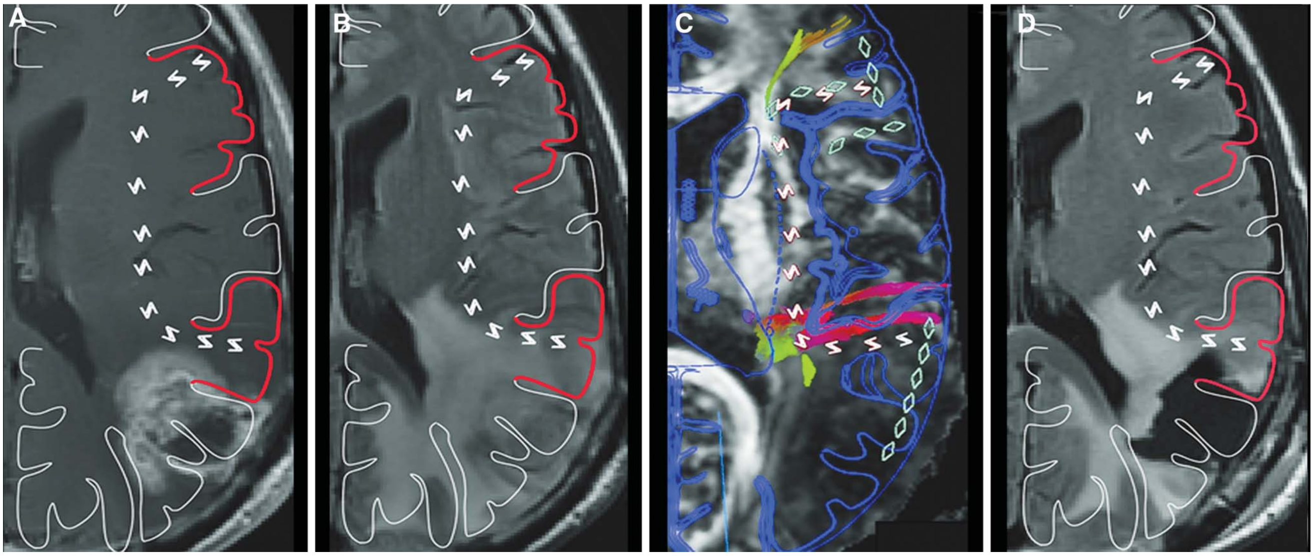

FIGURE 6. *An example of the arcuate tract outside the glioma and outside the surgical cavity with no speech deficits postoperatively. This 50-year-old man with a recurrent left glioblastoma involving the white matter below the superior temporal and angular gyri presented 7 months after the first resection with speech difficulties. The preoperative axial deformable anatomic templates (DAT; white) shows the expected normal position of the arcuate tract in relationship to the contrast-enhancing (***A***) tumor and (***B***) peritumoral edema.* **C**, *note the minimal difference between the DAT (white) prediction of the posterior arcuate and the diffusion tensor imaging (red).* **D**, *DAT (white) shows the arcuate tract ventral to the operative cavity.*

In 6 cases without deficits, DAT placed the eloquent area in the tumor but outside the resection cavity. DAT was useful in identifying subcortical areas of eloquence when preoperative DTI failed at least partially near tumor in all cases (Table 2 and Figures 4 and 5). The DAT overlays helped the surgeon confirm the subcortical tracts by direct electrical stimulation and included the arcuate fasciculus, corticospinal, and corticobulbar tracts. Of the 3 glioblastoma patients, 1 patient was lost to follow-up, 1 patient was stable at 3 months but recurred at 6 months, and 1 patient had improved speech but subsequently died at 8 months. The remaining 3 cases, with grade II and III tumors, remained stable or deficit free up to 24 months.

In the remaining 25 of the 40 referred cases, the tumors were outside an eloquent area by preoperative imaging (Figure 6) and therefore did not meet in the inclusion criteria for this study. In this group, there was agreement on the location of the eloquent structure by all modalities used. Only 2 of the 40 referred patients had deficits secondary to a stroke beyond the surgical cavity with corresponding diffusion restriction matching the DAT corticospinal tract in the internal capsule or corona radiata. One patient had deficits attributable to both resection and pericavity ischemia (case 1). Of note, the DAT predicted the presence or lack of postoperative neurological deficit across all of the histological grades of diffuse glioma. In addition, the following factors did not alter the accuracy of the DAT fit to the patient's images: preexisting chronic surgical cavities (6 cases), all acute surgical cavities, and prior radiation or chemotherapy (4 cases). When fMRI was performed and accurate, it matched DAT in all cases. In our study, DTI often failed near or in tumor, although the tractography that could be generated matched DAT.

DISCUSSION

This study shows that DAT overlays of normal functional anatomy can document eloquent areas that may not always be seen on DTI, fMRI, or intraoperative mapping (Tables 1 and 2) and supports the hypothesis that brain invaded by glial tumor may retain its basic internal structure and function. DAT is especially helpful when preoperative DTI maps fail to give the surgeon useful information.[16,17,19,35] In our study, DTI failed in at least 10 referred cases. DAT was especially helpful in guiding subcortical stimulation for this group. In 3 cases in which the gold standard intraoperative stimulation failed, DAT was correct in predicting the postoperative deficit. This included the motor tract for tongue, which can be difficult to localize by preoperative imaging or operative stimulation. Seven of the 9 postoperative deficits were due to the very close proximity of the tumor and subsequent resection cavity to the subcortical descending motor tracts. This may be due to incomplete display of these tracts by DTI and the complex 3-dimensional anatomy of the descending motor tracts.[36] There is thus a need for additional tools such as DAT to guide the surgeon intraoperatively and to improve localization and preservation of subcortical white matter tracts.

There were limitations to this study. We used a 5-mm margin for minimal mass effect as the standard because several studies have shown that resection within 5 mm of positive operative stimulation puts the patient at high risk of deficit.[23,24,37-39] DAT was able to predict postoperative deficits within this margin of error. Given this 5-mm margin of error, it cannot be ensured that DAT demonstrated the precise location of eloquent structures within enhancing tumor, necrotic tumor, or the tumor edge because of mild displacements from the expected position. The DAT overlays gave the surgeon a better understanding of the "normal" anatomy in these situations to be better informed before surgery. Ultimately, tumor resection in or near eloquent areas represents a risk-to-benefit ratio between maximal tumor resection to improve survival and to prevent neurological deficits. Larger studies are needed to validate the usefulness of DAT.

Upgrades of the DAT over the 3-year course of this study improved the technique, but to demonstrate feasibility, both positive and negative results were needed. The volume-rendered version of DAT added during this study was helpful for understanding complex 3-dimensional anatomy and improving the patient fitting. For variable areas such as the Broca area,[40] DAT now uses probabilistic maps, which need verification. However, DAT cannot determine hemispheric dominance. In development are additional DAT warping techniques that may better take into account structural displacements caused by intracranial masses.

CONCLUSION

This is a proof of concept that DAT supplements preoperative, intraoperative, and postoperative analysis of eloquent areas in close proximity to or within gliomas. The DAT helps the surgeon make a more informative decision by giving the normal position of eloquent structures, which is particularly valuable when other techniques fail, but may be limited by tract displacement and individual variability.

Disclosures

Dr Hayman is the founder and medical director of Anatom-*e* Information Systems, Ltd, Houston, Texas. The other authors have no personal financial or institutional interest in any of the drugs, materials, or devices described in this article.

REFERENCES

1. Diehn M, Nardini C, Wang DS, et al. Identification of noninvasive imaging surrogates for brain tumor gene-expression modules. *Proc Natl Acad Sci U S A.* 2008;105(13):5213-5218.
2. Lu S, Ahn D, Johnson G, Cha S. Peritumoral diffusion tensor imaging of high-grade gliomas and metastatic brain tumors. *AJNR Am J Neuroradiol.* 2003;24(5):937-941.
3. Chen X, Dai J, Jiang T. Supratentorial WHO grade II glioma invasion: a morphologic study using sequential conventional MRI. *Br J Neurosurg.* 2010;24(2):196-201.
4. Mandonnet E, Capelle L, Duffau H. Extension of paralimbic low grade gliomas: toward an anatomical classification based on white matter invasion patterns. *J Neurooncol.* 2006;78(2):179-185.
5. Pallud J, Devaux B, Daumas-Duport C, Oppenheim C, Roux FX. Glioma dissemination along the corticospinal tract. *J Neurooncol.* 2005;73(3):239-240.
6. Stadlbauer A, Buchfelder M, Salomonowitz E, Ganslandt O. Fiber density mapping of gliomas: histopathologic evaluation of a diffusion-tensor imaging data processing method. *Radiology.* 2010;257(3):846-853.
7. Stadlbauer A, Nimsky C, Buslei R, et al. Proton magnetic resonance spectroscopic imaging in the border zone of gliomas: correlation of metabolic and histological changes at low tumor infiltration: initial results. *Invest Radiol.* 2007;42(4):218-223.
8. Sawaya R, Hammoud M, Schoppa D, et al. Neurosurgical outcomes in a modern series of 400 craniotomies for treatment of parenchymal tumors. *Neurosurgery.* 1998;42(5):1044-1055; discussion 55-56.
9. De Witt Hamer PC, Robles SG, Zwinderman AH, Duffau H, Berger MS. Impact of intraoperative stimulation brain mapping on glioma surgery outcome: a meta-analysis. *J Clin Oncol.* 2012;30(20):2559-2565.
10. Sanai N, Mirzadeh Z, Berger MS. Functional outcome after language mapping for glioma resection. *N Engl J Med.* 2008;358(1):18-27.
11. Serletis D, Bernstein M. Prospective study of awake craniotomy used routinely and nonselectively for supratentorial tumors. *J Neurosurg.* 2007;107(1):1-6.
12. Spena G, Nava A, Cassini F, et al. Preoperative and intraoperative brain mapping for the resection of eloquent-area tumors: a prospective analysis of methodology, correlation, and usefulness based on clinical outcomes. *Acta Neurochir (Wien).* 2010;152(11):1835-1846.
13. Whittle IR. The dilemma of low grade glioma. *J Neurol Neurosurg Psychiatry.* 2004;75(suppl 2):ii31-ii36.
14. Holodny AI, Schulder M, Liu WC, Maldjian JA, Kalnin AJ. Decreased BOLD functional MR activation of the motor and sensory cortices adjacent to a glioblastoma multiforme: implications for image-guided neurosurgery. *AJNR Am J Neuroradiol.* 1999;20(4):609-612.
15. Ulmer JL, Hacein-Bey L, Mathews VP, et al. Lesion-induced pseudo-dominance at functional magnetic resonance imaging: implications for preoperative assessments. *Neurosurgery.* 2004;55(3):569-579; discussion 80-81.
16. Bello L, Castellano A, Fava E, et al. Intraoperative use of diffusion tensor imaging fiber tractography and subcortical mapping for resection of gliomas: technical considerations. *Neurosurg Focus.* 2010;28(2):E6.
17. Bello L, Gallucci M, Fava M, et al. Intraoperative subcortical language tract mapping guides surgical removal of gliomas involving speech areas. *Neurosurgery.* 2007;60(1):67-80; discussion 80-82.
18. Bello L, Gambini A, Castellano A, et al. Motor and language DTI Fiber Tracking combined with intraoperative subcortical mapping for surgical removal of gliomas. *Neuroimage.* 2008;39(1):369-382.
19. Henry RG, Berman JI, Nagarajan SS, Mukherjee P, Berger MS. Subcortical pathways serving cortical language sites: initial experience with diffusion tensor imaging fiber tracking combined with intraoperative language mapping. *Neuroimage.* 2004;21(2):616-622.
20. Hayman LA, Kumar VA, Hamilton J, et al. Deformable anatomic templates embed knowledge into patient's brain images, part 1: construction and display. *J Comput Assist Tomogr.* 2012;36(3):354-359.
21. Hamilton JD, Kumar VA, Hayman LA, et al. Deformable anatomic templates embed knowledge into brain images, part 2: validation using functional magnetic resonance imaging of the motor hand. *J Comput Assist Tomogr.* 2012;36(2):280-284.
22. Weksberg DC, Bilton SD, Chang EL. Use of a deformable atlas to identify cryptic critical structures in the treatment of glioblastoma multiforme. *PLoS One.* 2012;7(3):e32098.
23. Kim SS, McCutcheon IE, Suki D, et al. Awake craniotomy for brain tumors near eloquent cortex: correlation of intraoperative cortical mapping with neurological outcomes in 309 consecutive patients. *Neurosurgery.* 2009;64(5):836-845; discussion 345-346.
24. Prabhu SS, Gasco J, Tummala S, Weinberg JS, Rao G. Intraoperative magnetic resonance imaging-guided tractography with integrated monopolar subcortical functional mapping for resection of brain tumors: clinical article. *J Neurosurg.* 2011;114(3):719-726.
25. Nowinski WL, Chua BC, Yang GL, Qian GY. Three-dimensional interactive and stereotactic human brain atlas of white matter tracts. *Neuroinformatics.* 2012;10(1):33-55.
26. Thiebaut de Schotten M, Ffytche DH, Bizzi A, et al. Atlasing location, asymmetry and inter-subject variability of white matter tracts in the human brain with MR diffusion tractography. *Neuroimage.* 2011;54(1):49-59.
27. Peng H, Orlichenko A, Dawe RJ, Agam G, Zhang S, Arfanakis K. Development of a human brain diffusion tensor template. *Neuroimage.* 2009;46(4):967-980.
28. Damasio H. *Human Brain Anatomy in Computerized Images.* 2nd ed. New York, NY: Oxford University Press; 2001.

29. Kretschmann H, Weinrich W. *Introduction in Cranial Neuroimaging and Clinical Neuroanatomy*. 3rd ed. Stuttgart, Germany: Thieme; 2004.
30. Ius T, Angelini E, de Schotten MT, Mandonnet E, Duffau H. Evidence for potentials and limitations of brain plasticity using an atlas of functional resectability of WHO grade II gliomas: towards a "minimal common brain." *Neuroimage*. 2011;56(3):992-1000.
31. Duffau H, Peggy Gatignol ST, Mandonnet E, Capelle L, Taillandier L. Intraoperative subcortical stimulation mapping of language pathways in a consecutive series of 115 patients with grade II glioma in the left dominant hemisphere. *J Neurosurg.* 2008;109(3):461-471.
32. Friederici AD. Broca's area and the ventral premotor cortex in language: functional differentiation and specificity. *Cortex*. 2006;42(4):472-475.
33. Binkofski F, Buccino G. The role of ventral premotor cortex in action execution and action understanding. *J Physiol Paris.* 2006;99(4-6):396-405.
34. Binkofski F, Buccino G. Motor functions of the Broca's region. *Brain Lang.* 2004; 89(2):362-369.
35. Berman JI, Berger MS, Chung SW, Nagarajan SS, Henry RG. Accuracy of diffusion tensor magnetic resonance imaging tractography assessed using intraoperative subcortical stimulation mapping and magnetic source imaging. *J Neurosurg.* 2007;107(3):488-494.
36. Hamilton J, Kumar V, Prabhu S, et al. *Anatomic Considerations for Somatotopic Organization of the Descending Motor Fibers: A Pictorial Essay*. New York, NY: American Society of Neuroradiology; 2012.
37. Ozawa N, Muragaki Y, Nakamura R, Iseki H. Identification of the pyramidal tract by neuronavigation based on intraoperative diffusion-weighted imaging combined with subcortical stimulation. *Stereotact Funct Neurosurg.* 2009;87(1):18-24.
38. Kamada K, Todo T, Ota T, et al. The motor-evoked potential threshold evaluated by tractography and electrical stimulation. *J Neurosurg.* 2009;111(4):785-795.
39. Ganslandt O, Buchfelder M, Hastreiter P, Grummich P, Fahlbusch R, Nimsky C. Magnetic source imaging supports clinical decision making in glioma patients. *Clin Neurol Neurosurg.* 2004;107(1):20-26.
40. Ojemann G, Ojemann J, Lettich E, Berger M. Cortical language localization in left, dominant hemisphere: an electrical stimulation mapping investigation in 117 patients. *J Neurosurg.* 1989;71(3):316-326.

COMMENTS

The authors use a relatively novel approach for establishing eloquent brain involvement, the deformable anatomic template (DAT), to provide proof of principle that brain invaded by glial tumor retains its basic internal structure. DAT is presented as a useful adjunct to established methods for mapping eloquent brain areas. Their experience provides a foundation to explore the clinical applicability of this technique to improve resection accuracy and to reduce functional impairment.

John Boockvar
New York, New York

This study explores the usefulness of deformable anatomic templates (DAT) for estimating functional analysis of preoperative and postoperative magnetic resonance images in 40 cases of cerebral gliomas. In 15 of these cases, the authors found an overlap (invasion) of tumor and eloquent structures (cortical areas, subcortical pathways). In these cases, new postoperative neurological deficit or intraoperative stimulation mapping results validated the DAT maps in cases in which other methods failed to provide valid functional information. The authors conclude that integration of DAT into clinical imaging is complementary to other anatomic and functional data such as diffusion tensor imaging, functional magnetic resonance imaging, and intraoperative stimulation mapping.

It is an intriguing idea to use standardized functional-anatomic data for the analysis of individual clinical images, given the difficulties in obtaining such maps in individual data sets, in particular if (tumorous) pathology is present. Obviously, some tight constraints and prerequisites must be met and some hypotheses have to be accepted before any clinical application of such a method: The linear fitting or nonlinear warping procedures must be highly reliable for any target area of the brain; normal structures must not be displaced significantly by the tumor; if there is overlap of the tumor with some target structures in the standardized data, this means invasion rather than displacement; and the well-known, interindividual anatomic variability, for example, around the central sulcus, should be recognized for the applicability of such standardized maps to individual imaging data. Thus, it is mandatory to critically evaluate results and not to rely uncritically on presumed function. This bears the risk of either intolerable deficits or incomplete tumor removal on the other side.

This technique should be applied as an illustrative adjunct of information for planning and surgical procedures. However, in favor of patient safety and tumor control, the gold standards of surgery in or close to eloquent areas (functional mapping, electrophysiological monitoring) and functional magnetic resonance imaging seem to be indispensable so far. Parallel application of these techniques and the DAT procedure may contribute to further the experience with and necessary validation of this method.

Georg Neuloh
Hans Clusmann
Aachen, Germany