The role of secondary motor and language cortices in morbidity and mortality: a retrospective functional MRI study of surgical planning for patients with intracranial tumors

*JED VOSS, B.S.,¹ TIMOTHY B. MEIER, PH.D.,¹ ROBERT FREIDEL, B.S.,¹ BORNALI KUNDU, B.S.,¹ VEENA A. NAIR, PH.D.,¹ RYAN HOLDSWORTH, M.D.,¹ JOHN S. KUO, M.D., PH.D.,² AND VIVEK PRABHAKARAN, M.D., PH.D.¹

Departments of ¹Radiology and ²Neurological Surgery, University of Wisconsin School of Medicine and Public Health, Madison, Wisconsin

Object. Functional MRI (fMRI) is commonly used by neurosurgeons preoperatively to identify brain regions associated with essential behaviors, such as language and motor abilities. In this study the authors investigated the relationship between patient morbidity and mortality and the distance from the tumor border area to functional activations in secondary motor and language cortices.

Methods. Patients with primary or metastatic brain tumors who underwent preoperative fMRI motor and language mapping were selected from a large database of patients with tumors. The lesion-to-activation distance (LAD) was measured in each patient relative to the supplementary motor area (SMA) for motor tasks and the presupplementary motor area (pSMA) for language tasks. The association between LAD and the incidence of deficits was investigated using the Fisher exact tests of significance. The impact of other variables, including age, handedness, sex, and tumor grade, was also investigated. In a subset of patients, logistic regression was performed to identify the likelihood of deficits based on the LAD to primary and secondary regions. Finally, Mantel-Cox log-rank tests were performed to determine whether survival time was significantly related to the LAD to secondary motor and language areas.

Results. A significant association was observed between the LAD to the SMA and the incidence of motor deficits, with the percentage of patients with deficits dropping for those in the LAD > 2 cm group. The relationship between the LAD to the pSMA and the incidence of language deficits was not significant. Logistic regression demonstrated that the LAD to primary sensorimotor cortex does affect the incidence of motor deficits, but that the LAD to SMA does not. Finally, the authors observed no relationship between the LAD to secondary regions and patient mortality rates.

Conclusions. These results demonstrate that the LAD to SMA structures does affect morbidity, although not to the extent of LAD to primary structures. In addition, motor deficits are significantly associated with LAD to secondary structures, but language deficits are not. This should be considered by neurosurgeons for patient consultation and preoperative planning.

(<http://thejns.org/doi/abs/10.3171/2013.2.FOCUS12410>)

KEY WORDS • lesion-to-activation distance • morbidity • tumor • functional magnetic resonance imaging • supplementary motor area • presupplementary motor area

FUNCTIONAL MRI is emerging as an increasingly reliable technique for the noninvasive preoperative localization of eloquent cortex in relation to pathological entities. Functional MRI offers the advantage of spatial localization of language and sensorimotor areas, which allows for noninvasive localization of

neural activity as well as the prediction of postoperative patient deficits based on the proximity of fMRI activation to the margin of intracranial tumors. Previous studies have demonstrated consistent agreement between fMRI and the much more invasive Wada testing for language lateralization, as well as between fMRI and electrocortical stimulation, which has led to an increase in the use of fMRI for routine preoperative assessment of patients with brain lesions.^{2,15} In addition to providing information that can guide tumor resection, the use of preoperative fMRI allows for the investigation of the relationship

Abbreviations used in this paper: fMRI = functional MRI; LAD = lesion-to-activation distance; pSMA = presupplementary motor area; SMA = supplementary motor area.

* Mr. Voss and Dr. Meier contributed equally to this study.

between the mapping of functional areas and tumor location. Several previous studies, including work in our laboratory, have demonstrated that the incidence of language and motor deficits increases as the distance between tumor border and functional activation in primary language and motor areas, respectively, decreases.^{4,8,14,15}

Functional MRI has also proven useful in mapping secondary motor (SMA) and secondary language (pSMA) areas. Generally speaking, resection of the SMA is thought to result in transient motor and language deficits.^{3,11,16} Previous studies have demonstrated the relationship between the overlap of tumor resection and SMA fMRI activity and transient motor and language deficits.^{5,6} However, to our knowledge only one study has investigated the relationship of SMA (or pSMA) fMRI activity to tumor distance and motor and language deficits. In a relatively small sample of patients ($n = 12$), Nelson et al.⁹ demonstrated that the risk of postoperative motor and language deficits was 100% when the distance between the SMA and the tumor was ≤ 5 mm, but 0% when this distance was > 5 mm. In this study, we explore the role of fMRI in predicting morbidity as well as mortality related to tumors encroaching on secondary motor (SMA) and secondary language (pSMA) areas in a large sample of patients with tumors.

Methods

Patient Population

Patients were selected from a database of 423 individuals who received fMRI as part of presurgical planning at the University of Wisconsin Hospital and Clinics between June 1999 and July 2011. Inclusion criteria for this study selected all patients with a diagnosis of primary or metastatic tumors in any lobe of the brain who underwent motor and/or language mapping using fMRI. Demographic information can be found in Tables 1 and 2. Patients gave informed consent according to the study protocol approved by the institutional review board. Patient information was collected from medical records. Any record of preopera-

tive or postoperative weakness (lower extremity, upper extremity, and/or facial) and/or aphasia (Broca, Wernicke, conduction, global, and so on) was included in the analysis as deficits. Mortality information was collected for all patients from medical records that were cross-referenced with the Social Security Death Index. Original data from the Social Security Administration, accessed via <http://stevemorse.org/ssdi/ssdi.html>, which aggregates information from ancestry.com, familysearch.com, familytreelegends.com, genealogy.com, genealogybank.com, newenglandancestors.org, rootsweb.com, and worldvitalrecords.com, were used for query.¹⁰ Patients with no listing in the Social Security Death Index were considered still alive.

Language and Motor Paradigms

The language and motor paradigms used to assess patients are described in more detail elsewhere.^{7,14} In brief, brain activation associated with expressive language was measured with 2 types of word generation tasks: 1) alternating 20-second blocks of antonym word generation and rest, and 2) alternating 20-second blocks of letter word generation task and rest. Similarly, brain activation associated with receptive language was identified with alternating 20-second blocks of text reading and symbol reading. In this task, the patient silently read a short paragraph in the text reading block. During the control or symbols block, the patient was shown a paragraph of symbols and asked to scan and find specific symbols. The symbols block controlled for eye movements during reading, which presumably helped discriminate visual and eye movement-related activity from the true language areas.

Motor activation was determined using a variety of motor tasks, including blocks of unilateral finger tapping, alternative-hand finger tapping, unilateral foot or ankle movement, tongue movement, and lip pursing, all contrasted with blocks of rest. All tasks were not performed by every participant. The task that resulted in the most robust language- or motor-related activation for each patient was selected for analysis.

TABLE 1: Relationship between LAD and patient characteristics for motor and language subsets in patients with intracranial tumors

Characteristic	LAD Group			p Value
	<1 cm	1–2 cm	>2 cm	
motor (SMA) subset				
no. of patients	8	11	33	<0.001
sex (% male)	100	82	64	0.10
handedness (% rt)	100	100	87	0.75
mean age $\pm$ SD (yrs)	31.9 $\pm$ 8.8	41.6 $\pm$ 19.0	48.8 $\pm$ 14.0	0.017
Grade III or IV tumors (%)	67	29	67	0.25
language (pSMA) subset				
no. of patients	4	10	58	<0.001
sex (% male)	100	80	66	0.37
handedness (% rt)	100	88	79	0.99
mean age $\pm$ SD (yrs)	42.2 $\pm$ 12.0	39.5 $\pm$ 13.2	49.1 $\pm$ 15.2	0.73
Grade III or IV tumors (%)	100	50	47	0.61

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TABLE 2: Relationship between patient characteristics and existence of deficits in motor and language subsets in patients with intracranial tumors

Characteristic	No Deficits	Deficits	p Value
motor (SMA) subset			
sex (% male)	72	75	0.99
handedness (% rt)	87	95	0.61
mean age $\pm$ SD (yrs)	44.0 $\pm$ 14.1	45.3 $\pm$ 17.1	0.69
Grade III or IV tumors (%)	61	54	0.73
language (pSMA) subset			
sex (% male)	67	75	0.60
handedness (% rt)	74	91	0.18
mean age $\pm$ SD (yrs)	47.9 $\pm$ 14.8	46.4 $\pm$ 15.7	0.73
Grade III or IV tumors (%)	43	56	0.38

Acquisition and Processing of fMRI Studies

Imaging data were collected using either a 1.5- or 3-T commercial MR scanner (GE Medical Systems) equipped with high-speed gradients. Blood oxygen level dependent–weighted single-shot echo planar images were obtained repeatedly at intervals defined by the repetition time for each patient during task performance. Technical parameters were as follows: FOV 24 cm; matrix 64 $\times$ 64; TR 2000 msec; TE 40 msec (for 1.5 T) or 27 msec (for 3 T); flip angle 85° (for 1.5 T) or 75° (for 3 T); 6-mm coronal plane sections (for 1.5 T) or 5-mm axial plane sections (for 3 T)—spatial coverage was sufficient to provide mapping of the entire cortex. The number of images and length of imaging varied with the paradigm. Imaging duration ranged from 3 to 5 minutes. Additional high-resolution anatomical scans, including 3D volumetric T1- and T2-weighted sequences were acquired as part of the preoperative assessment.

Spatial smoothing was applied to the echo planar imaging data sets by using a full width at half-maximum gaussian kernel of 8 mm for 1.5-T data sets and 6 mm for 3-T data sets. Slice time correction, volume registration, and coregistration with subject-specific anatomical volumes were performed using Analysis of Functional NeuroImages software.¹ Activation was determined by cross-correlation of the time course of the echo planar imaging signal at each voxel with a generalized least-squares fitting algorithm to a smoothed and temporally delayed boxcar reference function modeling the presumed hemodynamic response. This comparison provided a voxel-wise t statistic with which images were thresholded individually to optimize visualization of language or motor areas and overlaid on the coregistered anatomical brain volume maps for each individual patient.

Thresholding was subjectively applied by a trained MRI technologist for each patient, with the intent of optimizing specificity and sensitivity to expected regions of task response. “Specificity” means adjusting threshold to minimize spurious voxels that were considered artifact, for example due to head motion. “Sensitivity” means adjusting threshold to highlight the expected responses at a level that displayed a typical suprathreshold extent. This was subjectively adjusted to localize a particular gyrus

or region, which represented a statistical probability of greatest confidence as indicated by the t-statistical overlay. Often, a compromise threshold was applied to balance the need to highlight an expected response with the concern toward minimizing artifact. For example, in a data set that exhibited significant task-correlated head motion, it may not have been possible to minimize the artifacts while still retaining a sufficient sensitivity to the presumed task-related response. The task-related response magnitudes were also dependent on factors such as the patient’s ability to perform a particular fMRI task, or whether the blood oxygen level–dependent response was compromised by the presence of the tumor. Thus, the threshold was subjectively varied for each individual fMRI study, based on the quality of the data and medical mapping concerns.

Image Analysis and Interpretation

Images used in the analysis were compiled at the time of surgery by a trained MRI technologist and used by the neurosurgical team for presurgical planning. The T1-weighted, T2-weighted, and contrast-enhanced T1-weighted structural images were analyzed using Picture Archiving and Communication Systems (PACS). The shortest distance in any plane (coronal, sagittal, or transverse) from the periphery of the tumor to the border of the area of functional activation corresponding to the SMA and pSMA as well as to primary sensorimotor cortex and primary language cortices (Wernicke and Broca areas) was measured using PACS. Tumor edge was defined as the enhancing margin for tumors that enhanced with contrast or the peripheral margin of the solid portion of the tumor as noted in T2-weighted images. Figure 1 depicts an example of a measurement. When tumor margin was heterogeneous, such as for low-grade tumors, T1-weighted images were used. The LADs were categorized based on classifications from previous studies.^{12–14} These included 1) < 1 cm; 2) between 1 and 2 cm; and 3) > 2 cm.

Statistical Analysis

The Fisher exact tests of independence were used to compare categorical variables of interest. The primary questions of interest were whether there was an as-

FIG. 1. An example of how LAD was measured for this study. This particular image illustrates activation in the SMA in response to a motor task. For this study, similar measurements were performed for secondary motor and language areas.

sociation between the LAD to SMA or pSMA, and the incidence of motor or language deficits, respectively. As a secondary analysis, the effect of the LAD on the existence of postoperative deficits was investigated for patients who had no preoperative deficits. For patients with the relevant information, postoperative deficits were classified as being transient or persistent in nature, and the association between the persistence of postoperative deficits and the LAD to secondary motor and language areas was assessed using Fisher exact tests. Similar Fisher exact tests were performed to compare categorical variables that may confound the relationship between the LAD and deficits, such as the association between LAD and sex, handedness, or tumor grade as well as the total number of patients in each LAD group. The association between the extent of resection, based on postsurgical radiological notes, and the LAD to primary and secondary motor and language regions (with extent of resection being characterized as total or subtotal resection [$\leq 10\%$ residual tumor]; partial resection [$> 10\%$ residual tumor]; or no surgery/biopsy only) was also investigated using Fisher exact tests. The association between the presence of high-grade tumors versus low-grade tumors and the extent of resection was also investigated with Fisher exact tests. Additionally, Fisher exact tests were performed to determine whether the incidence of deficits was associated with sex, handedness, and tumor grade. Chi-square tests were performed to determine whether the number of patients in the LAD group for the motor and language subsets were significantly different. Fisher exact tests were also performed to compare the distribution of patients with preoperative deficits, postoperative deficits, or both pre- and postoperative deficits in each LAD group. Finally, independent-sample Kruskal-Wallis tests were performed to determine if age significantly differed between LAD groups for the language and motor subsets of patients.

Binary logistic regression analyses were performed to determine if the LAD to primary and secondary motor and language areas affected the likelihood of motor and language deficits, respectively. Two models were run. For the subset of patients in the language-deficit analysis, the LAD to primary language regions (Wernicke and Broca

areas) and the LAD to pSMA were included as predictors. For the subset of patients in the motor-deficit analysis, the LADs to sensorimotor cortex and to SMA were included as predictors. Only patients with LAD measures for both primary and secondary regions were included in these analyses.

Mantel-Cox log-rank tests were used to explore relationships between LAD and survival for both the motor (SMA) and language (pSMA) groups. Survival statistics were calculated based on number of months survived from date of diagnosis to date of death. All analyses were done using R statistical software or Statistical Package for the Social Sciences. All tests were considered significant at an alpha of 0.05.

Results

Demographic Data

Of the 423 patients who underwent fMRI for presurgical planning, 52 had tumors encroaching on the secondary motor area and underwent fMRI for motor tasks, and 72 had tumors encroaching on the secondary language area and had fMRI for language tasks. Age, handedness, sex, and tumor grade information for each subset of patients is listed in Table 1.

For the subset of patients included in the motor analyses, a 1-way independent-samples Kruskal-Wallis test found a significant difference in age between the LAD to SMA groups ($\chi^2 = 8.2$ [2 df, $N = 52$]; $p = 0.017$). There were no significant differences in handedness, sex, or the percentage Grade III or IV tumors in LAD to SMA categories ($p > 0.1$). The extent of tumor resection (Table 3) did not vary due to LAD to secondary or primary motor cortices ($p = 0.61$ and $p = 0.67$). Similarly, there was no relationship between the frequency of high-grade tumors (Grade III or IV) and the extent of tumor resection for patients in the language subset ($p = 0.33$). The number of patients in each LAD to SMA group was significantly different ($\chi^2 = 73.0$ [2 df, $N = 52$]; $p < 0.001$).

For the subset of patients included in the language analyses, there was no difference in age between the LAD to pSMA groups ($\chi^2 = 4.1$ [2 df, $N = 72$]; $p = 0.13$). Similarly, there no significant differences in handedness, sex, or the percentage of Grade III or IV tumors in LAD to pSMA categories ($p > 0.1$). The extent of tumor resection did not vary due to the LAD to pSMA ($p = 0.82$); however, the extent of tumor resection did vary due to the LAD to primary language cortices (either Broca area or Wernicke area; $p = 0.037$). This difference was driven by the relationship between the LAD to the Broca area and the extent of resection ($p = 0.005$), whereas the relationship between the LAD to the Wernicke area and the extent of resection was not significant ($p = 0.77$). The frequency of total resection was much higher for patients with LAD > 2 cm to the Broca area compared with the other LAD groups, while the groups ≤ 2 cm included mostly subtotal or partial resections. In addition, there was no relationship between tumor resection and the frequency of high-grade tumors (Grade III or IV) for patients in the language subset ($p = 0.5$). The number of patients in each

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TABLE 3: Information regarding extent of resection and LAD in patients with intracranial tumors

Extent of Resection	LAD Group (%)		
	<1 cm	1–2 cm	>2 cm
motor (SMA) subset			
no surgery/biopsy	0	9.1	9.4
partial	28.6	9.1	34.4
subtotal	42.8	27.3	21.8
total	28.6	54.5	34.4
language (pSMA) subset			
no surgery/biopsy	0	0	7.3
partial	0	33.3	34.5
subtotal	50	33.3	29.1
total	50	33.3	29.1
motor (primary) subset			
no surgery/biopsy	0	11.1	6.7
partial	27.3	22.2	40.0
subtotal	18.2	22.2	26.7
total	54.5	44.4	26.7
language (primary) subset			
no surgery/biopsy	0	12.5	0
partial	57.1	29.2	45.5
subtotal	28.6	45.8	13.6
total	14.3	12.5	40.9
language (Broca) subset			
no surgery/biopsy	0	11.8	3.1
partial	75	23.5	43.8
subtotal	25	58.8	15.6
total	0	5.9	37.5
language (Wernicke) subset			
no surgery/biopsy	0	12.5	4.9
partial	25	50.0	39.0
subtotal	50	12.5	31.7
total	25	25.0	24.4

LAD to pSMA group was significantly different ($\chi^2 = 21.5$ [2 df, $N = 72$]; $p < 0.001$).

Additional Fisher exact tests indicated that patients with and without deficits in both the motor and language analyses did not differ in sex, handedness, or the percentage of Grade III or IV tumors ($p > 0.1$; Table 2). Likewise, Mann-Whitney tests demonstrated that patients with and without deficits did not significantly differ by age for the motor ($Z = 0.39$, $p = 0.69$) and language subsets ($Z = -0.34$, $p = 0.73$).

Table 4 shows the percentage of patients with preoperative only, postoperative only, or both pre- and postoperative deficits for the language and motor subsets. Fisher exact tests found no significant effect of LAD group on type of deficit for the motor ($p = 0.56$) and language subsets ($p = 0.89$).

For patients with information regarding the persistence of deficits, those with postoperative deficits were characterized as being either transient or persistent in nature. There was no significant association between LAD

and the existence of transient versus persistent postoperative deficits for either the motor or the language subsets ($p = 1.0$ in both groups). As seen in Table 4, the majority of postoperative deficits were transient in nature.

Association Between LAD and Deficits

A significant association was found between the LAD to SMA and the existence of motor deficits ($p = 0.04$). Motor deficits were found in 62.5% of the patients in the LAD to SMA < 1 cm group. The percentage of patients with motor deficits was 81.8% in the LAD 1–2 cm group, and dropped to 43.4% in the LAD > 2 cm group (Fig. 2). However, there was no significant association between the LAD to SMA and the existence of postoperative motor deficits in patients who were deficit free prior to surgery ($p = 0.19$). For these patients, 40% in the LAD to SMA < 1 cm group, 33.3% in the LAD 1–2 cm group, and 11.1% of the LAD > 2 cm group had postoperative deficits.

There was no significant association between the

TABLE 4: Distribution of deficit type in patients with motor or language deficits in patients with intracranial tumors*

Deficit	LAD Group (%)		
	<1 cm	1–2 cm	>2 cm
motor (SMA) subset			
preop only	20	44.4	30.8
postop only	60	11.1	38.4
pre- & postop	20	38.5	30.8
persistent postop	0	25.0	16.7
language (pSMA) subset			
preop only	0	25	28.6
postop only	100	50	42.8
pre- & postop	0	25	28.6
persistent postop	0	NA	30.0

* NA = not available.

LAD to pSMA and the existence of language deficits ($p = 0.81$). The percentage of patients with language deficits was 50% in the LAD to pSMA < 1 cm group, 40% in the LAD 1–2 cm group, and 36% in the LAD > 2 cm group (Fig. 2). Likewise, there was no significant association between the LAD to pSMA and the existence of postoperative language deficits in patients who were deficit free prior to surgery ($p = 0.22$). For these patients, 50% in the LAD to pSMA < 1 cm group, 25% in the LAD 1–2 cm group, and 17.8% of the LAD > 2 cm group had postoperative deficits.

Regression Analyses

Binary logistic regression was performed in a subset of 56 patients in the language analyses who had LAD measurements to both pSMA and primary language cor-

tices (Wernicke and Broca areas). Neither the LAD to primary language areas ($\beta = -0.469$, SE 0.395, OR 0.626, $p = 0.235$) nor the LAD to secondary language areas ($\beta = -0.435$, SE 0.535, OR 0.647, $p = 0.415$) significantly affected the likelihood of language deficits.

Binary logistic regression was also performed in a subset of 51 patients in the motor analyses who had LAD measurements to both SMA and primary sensorimotor cortex. This analysis demonstrated that an increase LAD to primary sensorimotor cortex significantly decreased the likelihood of the existence of motor deficits ($\beta = -1.885$, SE 0.609, OR 0.152, $p = 0.002$). In contrast, LAD to SMA did not significantly affect the likelihood of motor deficits ($\beta = -0.317$, SE 0.486, OR 0.728, $p = 0.514$).

Survival Analyses

Mantel-Cox log-rank tests were performed to determine whether survival time significantly related to LAD to secondary motor and language areas. There were no differences in survival rate due to LAD to SMA ($\chi^2 = 3.823$ [2 df, $N = 52$]; $p = 0.148$), nor were there differences in survival rate due to LAD to pSMA ($\chi^2 = 1.281$ [2 df, $N = 72$]; $p = 0.527$).

Discussion

Preoperative fMRI has become a valuable tool for neurosurgeons, guiding patient consultation and resection of intracranial tumors. Although the use of preoperative fMRI has become more prevalent, the relationship between the distance of tumor from fMRI response and the extent of tumor-induced neurological deficits needs to be resolved. Several studies have demonstrated that the proximity of tumors to functional cortical areas as delineated by fMRI is related to postoperative outcome, with the majority of studies focused on the primary motor and language areas.^{4,8,14,15} However, this relationship is probably dependent on the functional brain region being investigated. This is the first study to our knowledge that investigates the relationship between patient morbidity and mortality and tumor distance to secondary motor (SMA) and language (pSMA) areas by using a large database of subjects.⁹

Fig. 2. Graph showing the percentage of patients in the language and motor analyses who have language and motor deficits, respectively. The association between the LAD to SMA and the incidence of motor deficits (black squares) was significant. The association between the LAD to pSMA and the incidence of language deficits (gray diamonds) was not significant.

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As seen in Fig. 2, we found a significant relationship between LAD in the SMA and the incidence of motor deficits. The percentage of patients with motor deficits dropped considerably in patients with LAD > 2 cm, whereas the percentage of patients with deficits in the 1–2 cm and < 1 cm LAD groups was relatively high. Furthermore, this observed difference is unlikely to be a result of demographic differences between these groups; the age, handedness, tumor grade, and sex did not differ between the LAD 1–2 cm and LAD > 2 cm groups. In contrast, there was no relationship between LAD and language deficits for the secondary language area (pSMA), although the percentage of patients with deficits did decrease with increasing LAD.

Several previous studies have demonstrated that lesions to secondary motor and language areas are less severe than lesions to primary regions.^{3,5,6,9,11,16} Our results expand on these studies, and demonstrate that LAD to secondary motor areas (SMA) is associated with motor deficits, with a relatively high incidence of morbidity in patients with LAD < 2 cm. This information should be used by the surgeon to inform patient consultation and resection of tumors near the SMA.

We also investigate the association between LAD and postoperative deficits for patients with no preoperative deficits. Although we found no significant association between these factors, the percentage of these patients with postoperative deficits did decrease as the LAD to SMA or pSMA increases. Unfortunately, the small number of patients who did not have preoperative deficits limits the power of this particular analysis.

Information regarding persistent or transient deficits was limited in this data set. However, for those patients in whom this information was available, we found that the majority of deficits for every LAD group were transient in nature. This is consistent with previous studies in which it has been suggested that deficits resulting from tumors or the resection of tumors in secondary motor and language areas are primarily transient in nature, in contrast to those in primary regions.^{3,5,6,11,16} In this study we also observed a distinction between the effects of primary and secondary regions. We found that decreasing distance between tumors and fMRI activation in primary sensorimotor cortex increased the likelihood of motor deficits, more so than the effect of distance between tumors and fMRI activation in the SMA. In our previous study drawing from the same database of patients, we found that there was a linear decrease in motor deficits with increase in LAD to primary motor cortex.¹⁴ Similarly, for language deficits the highest incidence was observed in the LAD (to primary language areas) < 1 cm group, with a lower incidence of deficits observed in the 1–2 cm and > 2 cm LAD groups. The relationship between the LAD to the pSMA and the incidence of language deficits was not significant.

We also observed no association between the extent of tumor resection and the LAD to secondary motor and language areas. However, we did observe an association between the LAD to primary language cortices, driven by the LAD to the Broca area, and the extent of tumor resection used for patients in this study. Incidentally we found no significant association between the extent of tumor

resection and tumor grade, although it is likely that tumor grade, the use of intraoperative cortical mapping, and other variables are used by neurosurgeons in combination with LAD measurement. The existence of a relationship between the extent of tumor resection and the LAD to primary (Broca area) but not to secondary language areas could reflect more aggressive surgical approaches for tumors near secondary motor and language areas due to the transient nature of postoperative deficits associated with these areas. The data presented here, in conjunction with our previous study, illustrate the relatively greater plasticity of the brain in response to perturbations to secondary motor and language areas in comparison with primary motor and language areas.

Finally, we investigated the relationship between the LAD to SMA and pSMA and the survival rate of patients. No significant relationship existed between survival rate and LAD to secondary motor and language areas. It is possible that the survival rate is primarily driven by other factors, such as tumor grade and patient age.

One methodological issue in the current study that should be considered is the use of subjective thresholding for patient fMRI data. Varying the threshold levels does affect the size of the fMRI activations and thus LAD measures. From a basic science standpoint, it might seem desirable to use a set threshold for every patient's fMRI mapping. However, information regarding the mapping of SMA activity to a hand movement task that does not reach significance at a strict cutoff of 0.05 may still be useful for preoperative planning. The fMRI data used in this study were individually tailored to patients to maximize the information afforded by the fMRI for patient care purposes. In this study we calculated LAD from the same subjectively thresholded fMRI activations that the surgeons used for preoperative planning.

Conclusions

This was the first study, to our knowledge, to investigate the relationship between tumor distance to fMRI responses in secondary language and motor areas and the incidence of language and motor deficits in a large sample. In summary, we found a significant association between the distances of lesions to the fMRI responses in the SMA and the incidence of motor deficits. Whereas the incidence of motor deficits was high in patients with LADs < 2 cm, the incidence dropped considerably for patients with LADs > 2 cm. The relationship between the LAD to the pSMA and the incidence of language deficits was not significant. Logistic regression demonstrated that the LAD to primary sensorimotor cortex does affect the incidence of motor deficits, but that the LAD to SMA does not. Finally, we observed no relationship between the LAD to secondary regions and patient mortality rates. These results demonstrate that the LAD to secondary motor structures does affect morbidity, although not to the extent of the LAD to primary structures. This should be considered by neurosurgeons for patient consultation and preoperative planning.

Disclosure

The authors report no conflict of interest concerning the mate-

rials or methods used in this study or the findings specified in this paper. Research support, including provision of equipment and materials, was provided by a University of Wisconsin ICTR NIH/UL1RR025011 pilot grant from the Clinical and Translational Science Award (CTSA) program of the National Center for Research Resources (NCRR), an RSNA seed grant, a KL2 Scholar Award, and Grant. No. R41 NS081926-01 from the NIH to Dr. Prabhakaran.

Author contributions to the study and manuscript preparation include the following. Conception and design: Voss, Freidel, Kundu, Nair, Holdsworth, Kuo, Prabhakaran. Acquisition of data: Voss, Freidel, Kundu, Nair, Holdsworth, Kuo. Analysis and interpretation of data: all authors. Drafting the article: Meier, Voss, Prabhakaran. Critically revising the article: Meier, Prabhakaran. Reviewed submitted version of manuscript: Meier, Kundu, Nair, Holdsworth, Kuo, Prabhakaran. Approved the final version of the manuscript on behalf of all authors: Meier. Statistical analysis: Meier, Voss, Freidel, Kundu, Nair, Holdsworth, Prabhakaran. Administrative/technical/material support: Nair, Holdsworth, Kuo. Study supervision: Kuo, Prabhakaran.

Acknowledgments

The authors thank M. E. Meyerand for helping with database maintenance and the institutional review board protocol, and C. H. Moritz for helping with data acquisition and creating clinical fMRI reports.

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Manuscript submitted December 15, 2012.

Accepted February 13, 2013.

Please include this information when citing this paper: DOI: 10.3171/2013.2.FOCUS12410.

Address correspondence to: Timothy B. Meier, Ph.D., Department of Radiology, University of Wisconsin–Madison, 1310D Wisconsin Institutes for Medical Research, 1111 Highland Avenue, Madison, Wisconsin 53705. email: tmeier3@uwhealth.org.