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Alexander J. Gamble, Sarah G. Schaffer, Dominic J. Nardi, David J. Chalif, Jeffery Katz, Amir R. Dehdashti

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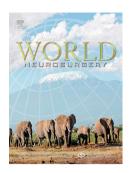
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#### **Abbreviations:**

AVM: Arteriovenous malformation fMRI: Functional magnetic resonance imaging SMG: Spetzler-Martin grade SRS: Stereotactic radiosurgery BOLD: Blood oxygen level dependent

#### **Highlights**:

- Patients harboring Spetzler-Martin grade 2-3 arteriovenous malformations proximal to eloquent speech centers carry unexpectedly higher surgical risks than traditionally recognized.
- Cortical stimulation mapping with wakeful interrogation of language function may provide a means to mitigate these surgical risks while maximizing the chances for a complete and durable obliteration.
- We describe our experience utilizing this technique with the novel addition of subcortical stimulation with continued language assessment throughout the resection.
- Specific to the resection of language arteriovenous malformations, the utility of wakeful mapping has been described in only a few series. Data from these series and our own were compiled in attempts to better characterize the usefulness of the technique in relation to patient outcome, extent of resection and agreement with preoperative functional magnetic resonance imaging.

# Awake craniotomy in arteriovenous malformation surgery; the usefulness of cortical and subcortical mapping of language function in selected patients.

Alexander J. Gamble<sub>1</sub>, Sarah G. Schaffer<sub>2</sub>, Dominic J. Nardi<sub>3</sub>, David J. Chalif<sub>1</sub>, Jeffery Katz<sub>2</sub>, and Amir R. Dehdashti<sub>1</sub>

<sup>1</sup>Cushing Neuroscience Institute, Department of Neurosurgery, Hofstra North Shore-LIJ School of Medicine. North Shore University Hospital, 9th Tower. Manhasset, NY, 11030, USA

<sup>2</sup>Cushing Neuroscience Institute, Department of Neurology, Hofstra North Shore-LIJ School of Medicine. North Shore University Hospital, 9th Tower. Manhasset, NY, 11030, USA

<sup>3</sup>Department of Anesthesiology, North Shore University Hospital, 4 Levitt. Manhasset, NY 11030, USA

#### **Corresponding Author:**

Alexander J. Gamble, DO Cushing Neuroscience Institute North Shore University Hospital, 9th Tower 300 Community Drive Manhasset, NY 11030 Phone: +15167283171 Fax: +15165623026 Email: <u>agamble@nshs.edu</u>

#### Authors

Sarah G. Schaffer, PhD Senior Neuropsychologist Cushing Neuroscience Institute Department of Neurology-Epilepsy 270-05 76<sup>th</sup> Ave New Hyde Park, NY 11040 Phone: +15163257000 Fax: +15163257001 Email: <u>sschaffer1@nshs.edu</u>

Dominic J. Nardi, MD Department of Anesthesiology North Shore University Hospital, 4 Levitt Manhasset, NY 11030 Phone: +15165624887 Fax: +15165621664

#### Email: dnardi@nshs.edu

David J. Chalif, MD Department of Neurosurgery Cushing Neuroscience Institute 300 Community Drive, 9<sup>th</sup> Tower Manhasset, NY 11030 Phone: +15165623070 Fax: +15165623071 Email: <u>dchalif@nshs.edu</u>

Jeffery M. Katz MD Department of Neurology Cushing Neuroscience Institute 300 Community Drive, 9<sup>th</sup> Tower Manhasset, NY 11030 Phone: +15165623064 Fax: +15165622635 Email: jkatz2@nshs.edu

Amir R. Dehdashti, MD Department of Neurosurgery Cushing Neuroscience Institute 300 Community Drive, 9<sup>th</sup> Tower Manhasset, NY 11030 Phone: +15165623026 Fax: +15165623030 Email: adehdashti@nshs.edu

**Key Words:** Awake craniotomy; arteriovenous malformation; language; cortical mapping; subcortical stimulation

#### **Abbreviations:**

AVM: Arteriovenous malformation fMRI: Functional magnetic resonance imaging SMG: Spetzler-Martin grade SRS: Stereotactic radiosurgery BOLD: Blood oxygen level dependent

#### Abstract

#### **Objective:**

Awake craniotomy for removal of intra-axial lesions is a well-established procedure. Few studies however have investigated the usefulness of this approach for resection of arteriovenous malformations adjacent to eloquent language areas. We demonstrate our experience utilizing cortical stimulation mapping and report for the first time, on the usefulness of subcortical stimulation with interrogation of language function during resection of AVMs located near language zones.

#### **Methods:**

Patients undergoing awake craniotomy for AVMs located in language zones and at least 5mm away from the closest fMRI activation were analyzed. During surgery, cortical bipolar stimulation at 50 Hz, with an intensity of 2 mA, increased to a maximum of 10 mA was performed in the region around the AVM before claiming it negative for language function. In positive language site, the area was re-stimulated 3 times to confirm the functional deficit. The AVM resection was started based on cortical mapping findings. Further subcortical stimulation performed in concert with speech interrogation by the neuropsychologist continued at key points throughout the resection as feasible. The usefulness of cortical and subcortical stimulation in addition to patient outcomes was analyzed.

#### **Results:**

Between March 2009 and September 2014, 42 brain AVM resection were performed. Four patients with left sided language zone AVMs underwent awake craniotomy. The AVM locations were fronto-opercular in two patients and posterior temporal in two. The AVM Spetzler-Martin grades were II (2 patients) and III (2 patients). In 1 patient, complete speech arrest was noticed during mapping of the peri-malformation zone, which was not breached during resection. In a second patient who initially demonstrated negative cortical mapping, a speech deficit was noticed during resection and subcortical stimulation. This guided the approach to protect and avoid the sensitive zone. This patient experienced mild post-operative expressive dysphasia that improved to normal within 6 weeks. Complete resection was achieved in all 4 patients. There were no other complications and no permanent neurological morbidity, resulting in good outcome in all 4 patients.

#### **Conclusions:**

Language mapping, both cortical and subcortical during AVM resection may be valuable in a very select group of AVMs in language zones. Defining safe margins and feedback to the surgeon may provide the highest chances of a surgical cure while minimizing the risk of incurring a language deficit.

#### Introduction:

Safe microsurgical resection of arteriovenous malformations in eloquent areas of the dominant cerebral hemisphere can be challenging. Several landmark studies have indicated that most low grade AVMs are best-treated microsurgically as the obliteration rate is very high with low morbidity. (8,9,16,24) In more contemporary AVM literature, there has been mounting evidence that the true surgical risks we quote may not be as straightforward as much of the historical literature has portrayed. Convincing evidence has demonstrated that AVMs in eloquent locations approaching 3cm, and up to 6cm actually represent a group with higher surgical risks not fully appreciated in neurovascular practice. (5,11,17,24) We describe our experience in 4 patients harboring AVMs very close to language cortex. All patients underwent awake mapping and neuropsychological assessment in order to confirm resectability and inform the optimal surgical approach to the lesion. We have also described the use of subcortical stimulation with interrogation of language function throughout the process of microsurgical resection, which to our knowledge has not been reported before. Based upon our experience and careful review of the literature, we believe there exists a subgroup of patients with AVMs near eloquent language cortex in which this approach should be considered.

#### **Methods:**

Between March 2009 and September 2014, 42 patients with brain AVMs were operated on by the lead author (AD). A flow chart depicting the management of these patients is depicted in table 1. Four patients were selected for wakeful resection that harbored AVMs near critical speech areas in the left hemisphere. These 4 patients' demographics and the AVM characteristics are described in Table 2. Eloquent location was first identified anatomically on MRI and then confirmed by fMRI. Patients with unruptured AVMs directly in the language zone where fMRI had shown activity extremely close (<5mm) or within the nidus were not considered for surgery and referred for other non-surgical options. All had preoperative cerebral angiography to better characterize the angioarchitecture of the AVM and if suitable, preoperative embolization was planned. Stereotactic frameless navigation was used to localize the AVM nidus intra-operatively and also correlate the area of cortical mapping to pre-operative fMRI. At surgery, patients were given intravenous sedation and analgesia. The patient was positioned under local anesthetic injection with light sedation. Craniotomy and exposure were carried out with the patient under deeper sedation and the dura was irrigated with local anesthetic before opening. Once the AVM was exposed, sedation was held and the patients were awoken. Cortical bipolar stimulation at a distance of 5mm was performed with the Ojemann Cortical Stimulator (Radionics, Burlington, MA). A biphasic current of 50 Hz, (pulse phase 1ms) with an initial intensity of 2 mA was applied to cortex adjacent to the AVM. During stimulation the neuropsychologist monitored language tasks given to the patient, alerting the surgeon of significant error or arrest of language function. Stimulated areas resulting in dysarthria anomia or alexia, for example, were stimulated three times further to confirm a functional language deficit or "hit". Cortex not associated with language hits were stimulated with increasing intensity to a maximum of 10 mA before being deemed potentially nonessential. We did not necessarily look for a positive response if the perimalformation zone was deemed negative for language activity. The identification of cortex where language function is not located has been demonstrated as effective to guide safe resection of lesions proximal to eloquent speech areas. (23) Upon completion of cortical mapping, patients were kept awake and surgical resection of AVM was pursued. Subcortical stimulation with language interrogation at the same initial and maximal intensities were carried out around the AVM nidus when the anatomy suggested close proximity to eloquent white matter tracts to further define safe margins. Subcortical stimulation was repeated several times during the resection in different directions as the neuropsychologist assessed language function. Patients were examined immediately post resection and then sedated for closure.

#### **Results:**

Each of the 4 patients demonstrated some language activation on fMRI 5-10 mm from the AVM nidus. The AVM locations were frontal-opercular in two and posterior temporal in two. The AVM SMG was II (2 patients) and III (2 patients). Pre-operative embolization was performed in one patient. Cortical or subcortical stimulation influenced the surgical approach in 2 out of 4 cases. These interrogations did not result in a subtotal resection or abortion of the procedure in any case. In 1 patient, significant speech arrest was noticed during stimulation of peri-malformation zone and care was taken to not to breach that specific zone during microsurgical resection. In one patient, some speech arrest was noticed during the subcortical dissection and stimulation. Therefore, the dissection around that specific zone was performed carefully by staying as close as possible to the AVM nidus. In one case significant bleeding during the deeper part of the AVM resection interfered with patient collaboration, and the patient was further sedated. Complete resection was achieved in all 4 patients confirmed by high quality intra-operative and follow-up angiograms. One patient experienced mild post-operative dysphasia that improved to normal within 6 weeks. No seizure was provoked in any patient in this series with the use of cortical or subcortical stimulation.

#### Patient#1:

A 62 year-old female was admitted with a small left frontal intraparenchymal hemorrhage. Investigation revealed a left fronto-opercular AVM (2.5 cm nidus with superficial drainage, SMG II). Middle cerebral artery branches fed the AVM and the draining vein was directed toward the superior sagittal sinus. The fMRI revealed the language zone for nomination of objects to be about 5 mm posterior to the nidus. The patient initially had a slight dysphasia due to the hemorrhage that completely recovered at 4 weeks, and prior to surgery. At surgery, the AVM was exposed and mapping of the perimalformation area was done. No positive mapping was detected around the presumed resection zone. The AVM resection was then carried out under direct language monitoring and subcortical stimulation and the patient's language remained intact during the resection. Post-operative angiogram confirmed complete resection of the AVM and the patient made an uneventful recovery with intact speech.

#### Patient#2:

A 74 year-old male presented with right posterior temporal hemorrhage. The MRI and angiogram revealed an incidental left fronto-opercular AVM (2 cm nidus with superficial drainage, SMG II) shown in figure 1a, b. Multiple small branches fed the AVM from both frontal and temporal MCA tributaries with two superficial draining veins, which drained toward the veins of Trolard and Labbe. The patient recovered completely from hemorrhage and underwent an fMRI showing the closest language zone about 6 mm superior and posterior to the nidus. Both surgery and radiosurgery were offered and the surgical resection was decided upon due to the higher likelihood of immediate cure. At surgery, speech arrest was noted during stimulation of peri-malformation area at 4mA a few millimeters away from the nidus (see figure 1c), allowing for a narrow surgical corridor. Care was taken not to breach the positive zone. The resection was carried out with intermittent subcortical stimulations during which the neuropsychologist assessed his language function. He suffered no neurological deficit and the post-operative angiogram confirmed a complete resection.

#### Patient#3:

A 33 year-old right handed female presented with first onset of seizure. MRI diagnosed a left posterior temporal AVM depicted in figure 2a. fMRI revealed some language activity at slightly less than 1cm around the AVM nidus. The angiogram (figure 2b) confirmed the AVM nidus being about 3.5 cm in diameter, mainly fed by angular and posterior temporal branches of MCA, with superficial venous drainage, (SMG 3). There was an associated intranidal aneurysm and the posterior margin of the nidus was somewhat diffuse. Both interventional and radiosurgical options were offered, but given the opportunity for an immediate cure, surgery was preferred. The patient underwent awake craniotomy, the language mapping was negative around the AVM, however during the resection of the posterior part of the AVM, she presented with intermittent slurred speech and the mapping of subcortical region elicited some further speech arrest. Care was taken to not to breach the normal white matter surrounding that specific zone which was thought to be the arcuate fasciculus. At the end of the resection, her language exam was grossly intact but she made some errors in repetition and nomination of objects. Immediate post-operative exam confirmed a mild dysphasia that had completely resolved by her 6 weeks follow-up. Intraoperative and post-operative angiogram both confirmed complete obliteration.

#### Patient #4:

A 38-year-old right-handed female presented with seizure and a mild right hemiparesis. MRI/MRA showed a 3.8 cm unruptured AVM in the left angular gyrus, (SMG 3) (Fig 3a). fMRI demonstrated language activation at 5mm to the nidus as well as some anterior translocation of language functions (Fig 3b,c). Subsequent cerebral angiogram showed arterial supply predominantly from the left middle cerebral artery with en passage vessels. There were additionally some contributions from the left anterior choroidal artery and the left posterior cerebral artery. Early venous shunting was via a large temporal varix, draining to the veins of Labbe and Trolard (Fig 3d,e). During surgery, stimulation of the area with positive language function on fMRI proximal to the nidus did not result in a noticeable language deficit. Furthermore, no language hits were detected during mapping of peri-malformation zone. The surgery was carried out with intermittent stimulation of the subcortical zone during resection. However, as substantial intra-operative bleeding occurred towards the deep part of the AVM and as all mapping to that point had been negative, it was deemed safer to deeply sedate the patient and place a laryngeal mask airway. The resection was therefore completed without patient cooperation. Postoperative exam revealed normal speech and the patient's baseline mild right-sided hemisensory deficit was unchanged. Intraoperative and postoperative angiogram confirmed AVM total resection (Fig 3f).

#### **Discussion:**

#### Understanding of Surgical Risk and Eloquence

As the number of published series addressing surgical risk in AVM resection has grown, it is evident that the surgical risks for lower grade AVMs were underestimated. It has been demonstrated that resection of grades 1-2 in noneloquent areas resulted in adverse outcomes in 0.6% of the time and as high as 9.5% for AVMs in eloquent brain. (17) Lawton et al, (11) proposed an expanded SMG scale separating the heterogeneous grade III into three distinct subgroups, (3-, 3 and 3+). In their series, the risks for a small/superficially draining lesion in an eloquent location (3-) was 2.9%, a medium/deeply draining/noneloquent lesion (3) carried a risk of 7.1% and a medium/superficially draining/eloquent lesion (3+) harbored a surgical risk of 14.8%. Although this subgroup analysis did not reach statistical significance, the trend was remarkable.

The concept of eloquent proximity as significant factor in surgical morbidity and mortality is supported by several large AVM series. (12,19,24) Furthermore additional factors have been added to grading scales of surgical risk such as an unruptured presentation and diffuse angioarchitecture. (12) The patients presented in this series demonstrate increasing risks as more contemporary and comprehensive prospective grading scales of surgical risk are applied as demonstrated in Table 2.

#### Reluctance to Operate on AVMs in proximity to Eloquent Cortex

In many situations, patients with SMG 2-3 perisylvian AVMs are referred for embolization and/or radiosurgery due to perceived surgical risk, especially when functional investigations reveal proximity to language centers. Unfortunately, a prospective trial comparing SRS to microsurgery in patients with SMG 2-3 AVMs does not exist and would be exceedingly difficult to perform. (20) Regardless of location, surgery has been demonstrated superior in terms of overall risk reduction of future hemorrhage, primarily by means of obliteration rates nearing 100%. %. (5,18,20,26)

In an extensive meta-analysis of 137 studies with 13,698 patients comparing treatment modalities, VanBeijum et al. (26) found complications leading to permanent neurological deficits or death to be 7.4% for surgery, 5.1% for SRS and 6.6% for embolization overall. Obliteration was achieved in 96% after microsurgery, 38% after SRS and 13% after embolization. Although case fatality rates were lower in patients treated by

SRS or embolization, hemorrhage rates during follow up were significantly higher, with the greatest risk being in the radiosurgical cohort. One must consider the surgical cohort's slightly higher mortality rate likely represents a selection bias, as surgery is more often performed in the acute phase, whereas SRS and sometimes embolization are performed in a sub-acute or even delayed fashion.

#### The Limits of Functional MRI and the Usefulness of Awake Cortical Mapping

The widespread adoption of fMRI through the late 1990's and onward confirmed our suspicion that translocation of language function to cortex distant from the AVM nidus regularly occurs. (1,13-15) Furthermore this new tool forced clinicians to reconsider anatomically based assumptions about eloquence and thus, actual SMG. fMRI maps utilized in surgical planning are generated from BOLD signals derived from the difference between oxyhemoglobin and deoxyhemoglobin levels of blood by location, thus giving us a proxy for cortical activity in areas where oxygen is being extracted at a higher rate. BOLD fMRI signals may actually be showing spatial activity "downstream" from active cortex in the venous system. (3) This principal may account for inconsistent correlations between fMRI and intraoperative language mapping that have been reported in tumor, epilepsy and mixed series including AVMs. (7,10,22,25) Lehéricy et al (15) demonstrated that fMRI incorrectly quantified contralateral language reorganization in AVMs with significant flow abnormalities. Language dominance was erroneously right sided in cases of left sided high flow AVMs because of decreased activation volume secondary to derangement of autoregulation, oxygen metabolism, perfusion pressure and blood flow. It is therefore reasonable that fMRI could create a false sense of security in the resection of an eloquently located AVM.

In surgical planning we rely upon the sensitivity of fMRI to identify eloquent cortex as well as its inherent spatial resolution. With regard to vascular lesions, the choice of language tasks employed during fMRI acquisition was shown to be very important when attempting to correlate activations with findings obtained during subsequent awake direct cortical stimulation. Expression tasks best mapped the frontal lobe, with a sensitivity and specificity of 100% and 66% at 5mm resolution. Comprehension tasks best characterized temporal and parietal cortices with a sensitivity and specificity of 96.2% and 69.8% at 10mm resolution. (21) Thus, no false negatives, (a site failing to show activation on fMRI but demonstrating speech arrest with stimulation) were encountered for frontal lesions with a high resolution whereas posterior language areas demonstrated nearly 4% false negatives with half the resolution, (10mm). Given the relatively high sensitivity and specificity of fMRI, positive language activations less than 5mm to or inside the nidus itself represent individuals with a high surgical risk of incurring a speech deficit. Such patients encountered in our practice were referred for other non-surgical options.

In our review of the literature, we found six published series utilizing awake cortical mapping for preservation of function during AVM resection. Only three of these studies specifically addressed language function and the usefulness of mapping. The present series is the first to address the usefulness of subcortical stimulation during resection. Even before the advent of fMRI, Burchiel et al. (2) described the utility of awake cortical mapping in a series of eight patients with AVMs of sensorimotor and language cortex. In 5/7 patients, mapping was considered useful and in one case led to abortion of the procedure. Only one patient suffered a postoperative neurological deficit, which resolved upon follow-up. The approach was next applied to patients undergoing AVM resection and seizure foci for the indication of intractable epilepsy. Unfortunately, the usefulness of mapping for the preservation of language function was not specifically addressed in this series. (27)

A classification system was proposed by Cannestra et al. (4), segmenting AVMs proximal to language cortex into three tiers of surgical risk. Ten patients were considered minimal risk (Group 1), as fMRI activation was at least one gyrus removed from the nidus, and underwent resection under general anesthesia. Five patients were deemed high risk, (Group 2) showing fMRI activation intimate to the nidus and were referred for embolization and/or radiation. The moderate risk group, (Group 3) of five patients showed activation within one gyrus of the nidus without overlap and were selected for awake resection employing both cortical mapping and intraoperative optical imaging of intrinsic signals. As expected, no patients in Group 1 demonstrated a postoperative deficit. Within group 3, despite fMRI findings that suggested a feasible resection, in two patients cortical stimulation and optical imaging showed eloquent cortex enveloping the nidus, halting the resection. The presence of false negatives in two cases between preoperative fMRI and mapping is alarming and raises further questions about the true reliability of fMRI. The other three patients underwent complete resection with two experiencing transient speech deficits that resolved by three months.

Gabarros et al. (6) have recently published series of 12 patients with SMG 3 and 4 AVMs in proximity to eloquent motor [7] or language cortices [5]. Of the 5 AVMs near language areas, all fell within the moderate risk category as defined by Cannestra et al. (4) Awake mapping and resection was deemed useful in all five cases and influenced the surgical approach in two. Mapping limited resection in one patient with a SMG 4 AVM who then received adjuvant SRS and then suffered a hemorrhage one year later resulting in a poor functional outcome. Three out of five patients experienced an improvement in overall function at follow up with good functional outcomes, (mRS $\leq$ 2).

In our series, we deemed cortical and subcortical stimulation instrumental to safe resection in 2/4 patients and did not lead to an abortion of the procedure or a subtotal resection as observed in the other two series. In previous reports, when the AVM was deemed non-resectable by mapping or if a complete resection could not be achieved (e.g. when only partial de-arterialization of the AVM was performed), the patient was referred on to SRS. (3,6) This important intra-operative decision is made if the preservation of language function is the most important goal of the procedure. In regards to the agreement between sites of fMRI activation and speech arrest during cortical mapping, we encountered no false negatives. False positive findings (areas positive on fMRI but not disrupting speech upon cortical stimulation) were encountered in 3/4 patients. One important distinction in our series is that both cortical and subcortical stimulation was performed in all patients while an awake resection was taking place. Previous series have not reported utilizing awake mapping in conjunction with continued cortical and subcortical stimulation during the actual resection. In careful review of the surgical series where awake mapping of language cortex was utilized, it seems that in the majority of cases, resection was performed under deeper anesthetic. The most likely rationale for this is to minimize the stress and discomfort for the patient and the surgeon as well. There are other theoretical factors that may confound the usefulness of wakeful interrogation during AVM resec-

tion. The closure of the arteriovenous shunt could result in hyperemia of adjacent brain, resulting in speech dysfunction and false positives, which could limit the resection. Additionally, given a longer wakeful period, patient fatigue may become an issue.

Sulcal cortex and subcortical white matter that may be quite eloquent are not accessible until the resection has begun. Therefore, we would argue that maintenance of a wakeful state with language interrogation by subcortical stimulation during AVM resection might provide important feedback to the surgeon, possibly enhancing safety. In only one case, at the very deepest part of the resection, significant bleeding was encountered. The decision was made at that point to deepen the sedation and employ the use of a laryngeal mask airway. In the application of this surgical strategy, thorough preoperative discussion with the neuroanesthesiologist is crucial to consider these potential interoperative decisions and managements. Patients must be thoroughly evaluated for comorbidities that may complicate their hemodynamic management. Patients who are felt to be hemodynamically labile or have a problematic airway may not be appropriate candidates for this approach.

We have not applied this approach to any SMG IV AVMs and cannot comment on the usefulness of this strategy in such a patient. It is conceivable to consider that a radiographic SMG IV AVM may indeed map negatively with cortical and subcortical stimulation during the surgery, in disagreement with the preoperative fMRI. This may bring the true SMG down to III, providing the opportunity for complete resection with greater chances of complete language preservation. This claim is mainly theoretical and having no direct experience with this scenario, we cannot advocate for it. We have found three other published series in which a subset of patients with AVM's of language cortex underwent awake cortical mapping in which the authors assessed the usefulness of intra-operative mapping and/or its relation to outcome (Table 3). Upon extraction of these data and combination with our own, 21 patients are represented in total. Cortical mapping or subcortical stimulation (only in the current series) in awake resection was reported to significantly affect the surgical approach in 67% of cases. Fourteen percent of cases resulted in a subtotal resection and complete abortion of the procedure occurred in also 14% of cases. One-third of patients experienced a neurological deficit postoperatively, but this decreased to 9% upon longer-term follow up. If mapping affects the extent of safe resection and only subtotal AVM disconnection can be achieved, further adjuvant treatment may be pursued as discussed previously.

#### **Conclusions:**

Certain anatomical features of AVMs and fMRI activation profiles may identify patients with SMG 2-3 AVMs in close proximity (5mm or more) to eloquent language cortex where awake cortical mapping is a viable strategy to maximize safety of AVM resection. Furthermore, maintenance of a wakeful state during dissection and resection of the AVM may provide valuable information to the surgeon via stimulation of subcortical white matter. We believe this methodology is a reasonable and effective compromise of factors minimizing the risk of neurological deficit while providing the best chance for a durable surgical cure in a very selected group of patients.

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#### **Figure Legends:**

Figure 1:

Radiographic and intraoperative appearance of the AVM in patient 2:

(a): Axial T2 weighted MRI demonstrating a 2cm AVM near Broca's area. (b): Left carotid injection, lateral projection. (c): Intraoperative photograph showing a dilated vein

directly overlying the nidus visualized early in the resection. The gyrus superior to the

AVM (arrow) mapped positive for language.

Figure 2:

Radiographic characteristics of the AVM treated in patient 3:

(a): Axial T2 weighted MRI showing a 3.5cm AVM in the left posterior temporal region.

(b) Preoperative angiogram of left carotid injection, lateral projection.

Figure 3:

Radiographic characteristics of the AVM treated in patient 4:

(a): Axial T2 weighted MRI showing a 3.8cm AVM in the left angular gyrus. (b,c): Func-

tional MRI language map of sentence generation with activations ~5mm to the nidus.

(d,e): A-P and Lateral projections of a left carotid injection demonstrating multiple feed-

ing vessels and a large venous varix. (f) Postoperative lateral left carotid injection show-

ing obliteration of the AVM.

### <u>Tables</u>

Table 1:

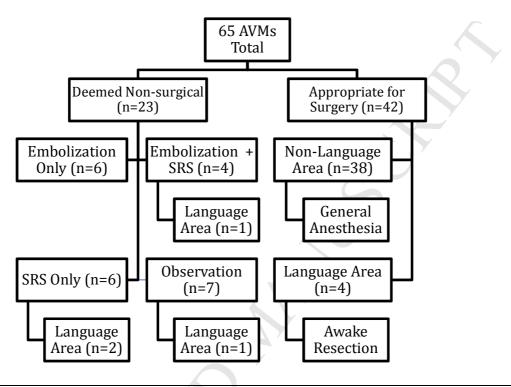


Table 1: Flow chart depicting the management of all AVMs by the lead author from March 2009 – September 2014.

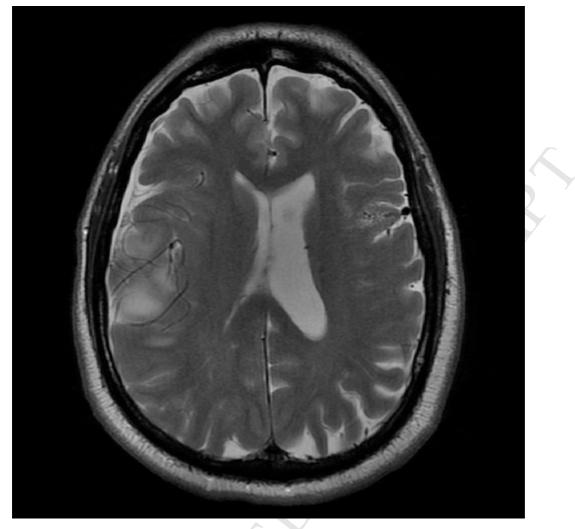
#### Table 2:

| Comparison of Surgical Risk by Model |                           |       |                                     |  |                                   |  |  |  |  |  |  |
|--------------------------------------|---------------------------|-------|-------------------------------------|--|-----------------------------------|--|--|--|--|--|--|
| Age/Sex                              | Location                  | Size  | SMG <sup>a</sup><br>(Surgical Risk) | Modified <sup>b</sup><br>(Surgical Risk) | Supplemental °<br>(Surgical Risk) |  |  |  |  |  |  |
| 62F                                  | Left frontal<br>opercular | 2.5cm | II<br>(0%)                          |  | 4 (40.5%)                         |  |  |  |  |  |  |
| 74M                                  | Left frontal<br>opercular | 2.0cm | II<br>(0%)                          |  | 3 (22%)                           |  |  |  |  |  |  |
| 33F                                  | Left angular<br>gyrus     | 3.5cm | III<br>(2.8%)                       | 3+<br>(14.8%)                            | 3 (22%)                           |  |  |  |  |  |  |
| 38F                                  | Left angular<br>gyrus     | 3.8cm | III<br>(2.8%)                       | 3+<br>(14.8%)                            | 4 (40.5%)                         |  |  |  |  |  |  |

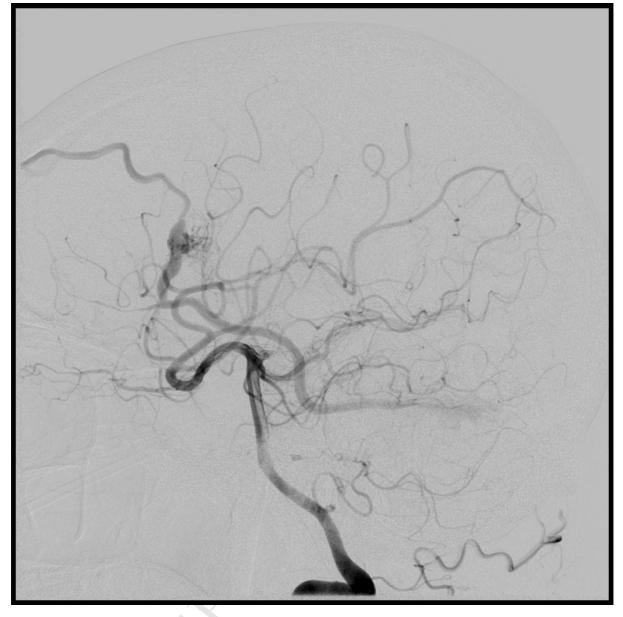
a. Risk of new neurological deficit at an average of one year after surgery. Hamilton and Spetzler, 1994(8) b. Modified grading system; late outcome, new neurological deficit or death. Lawton, 2003 (11) c. Supplemental grading system; late outcome, new neurological deficit or death. Lawton et al. 2010 (12)

#### Table 3:

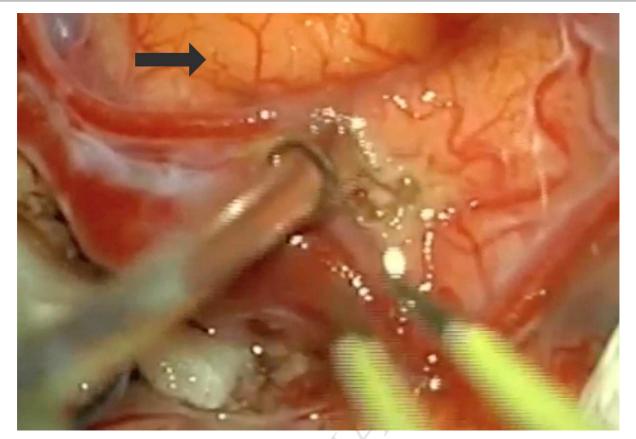
| Series of AVM Resection In Proximity to Language Cortex Utilizing<br>Awake Cortical Stimulation Mapping of Language Function |  |                     |                                      |                      |  |                         |                                      |                                     |  |  |  |
|--|--|---------------------|--------------------------------------|----------------------|--|-------------------------|--------------------------------------|-------------------------------------|--|--|--|
|  | Awake AVM<br>resection with<br>mapping | Affected resection? | Resulted in<br>Subtotal<br>Resection | Aborted<br>Resection | Postoperative<br>Neurological<br>Deficit | Deficit at<br>Follow up | Mapping in<br>agreement with<br>fMRI | Subcortical<br>Stimulation<br>Used? |  |  |  |
| Burchiel et<br>al., 1989<br>(2)  | 7                                      | 5/7                 | 0/7                                  | 1/7                  | 1/7                                      | 0/7                     | N/A                                  | 0/5                                 |  |  |  |
| Cannestra<br>et al., 2004<br>(4)   | 5                                      | 5/5                 | 2/5                                  | 2/5                  | 2/5                                      | 0/5                     | 2 False Negatives                    | 0/5                                 |  |  |  |
| Gabarrós<br>et al. 2011<br>(6)   | 5                                      | 2/5                 | 1/5                                  | 0/5                  | 3/5                                      | 2/5                     | Not Reported                         | 0/5                                 |  |  |  |
| Present<br>Series  | 4                                      | 2/4                 | 0/4                                  | 0/4                  | 1/4                                      | 0/4                     | 3 False Positives                    | 4/4                                 |  |  |  |
| Total  | 21                                     | 67%                 | 14%                                  | 14%                  | 33%                                      | 9%                      |                                      | 4/21 (19%)                          |  |  |  |
|  |  |                     |                                      |                      |  |                         |                                      |                                     |  |  |  |

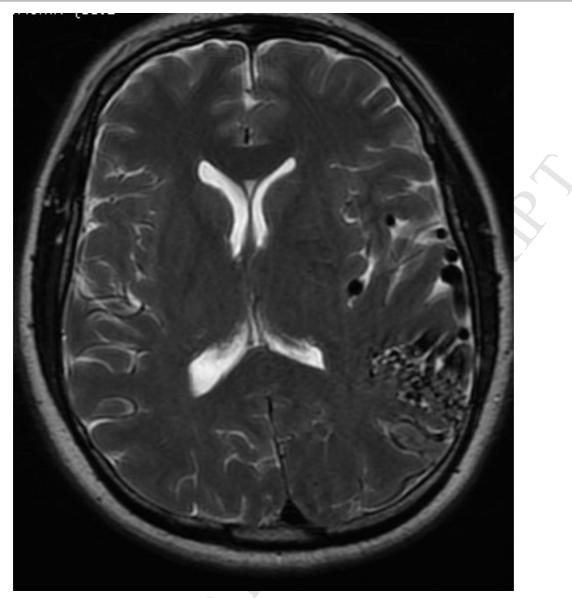




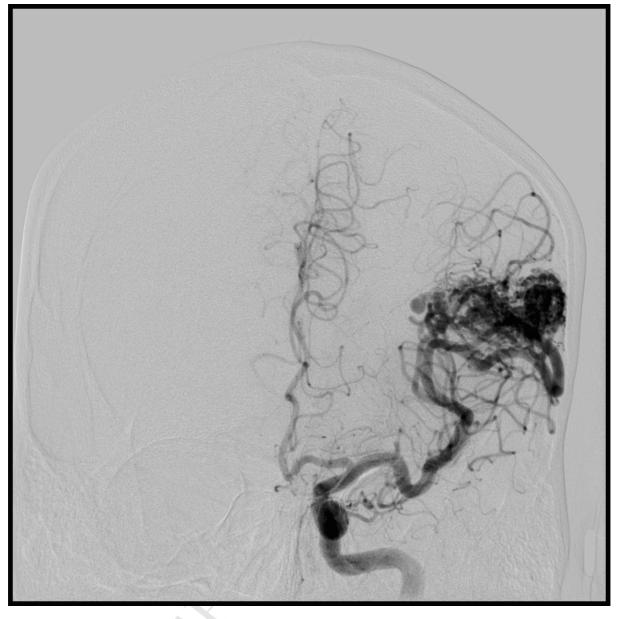




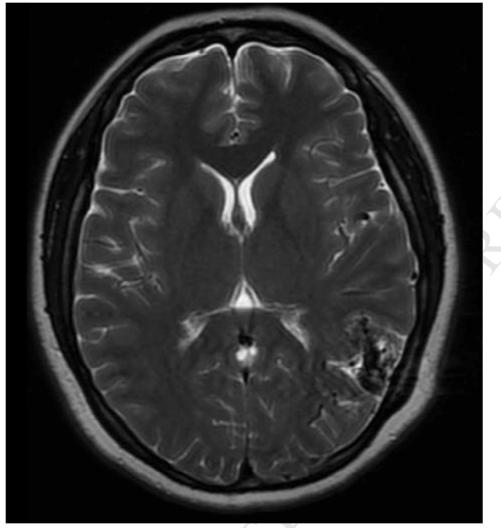




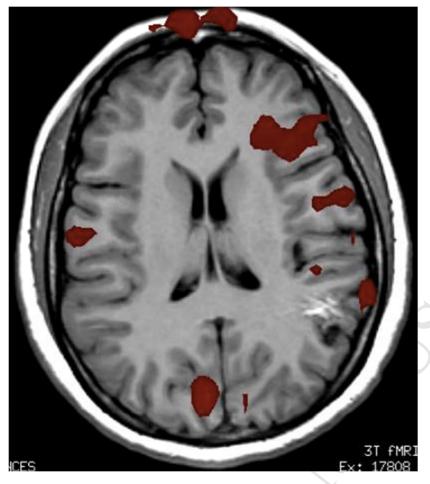


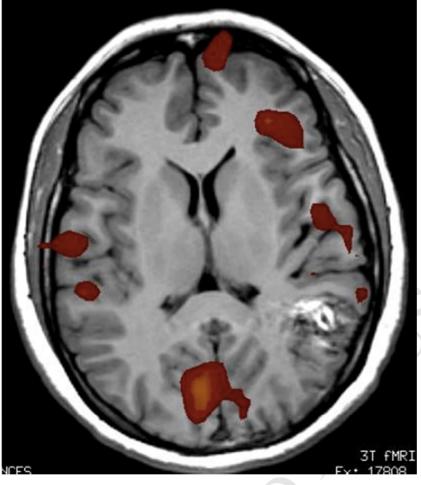






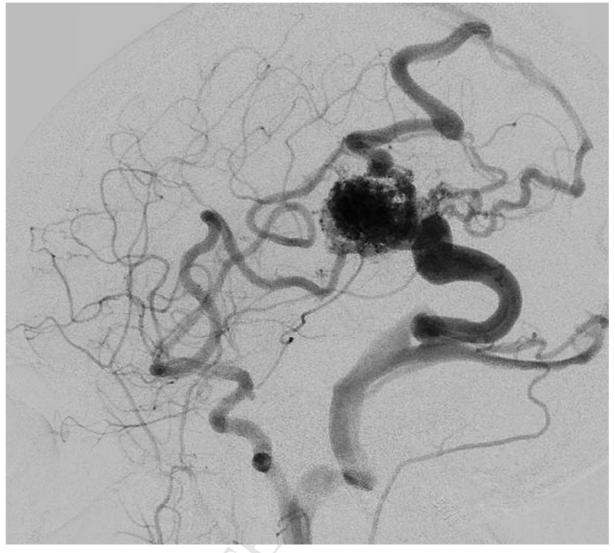




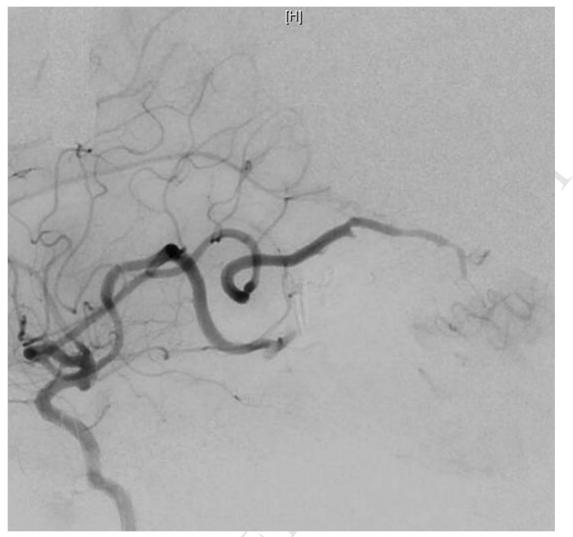














Conflict of Interest Statement

In regards to the manuscript submitted for review to World Neurosurgery: "Awake craniotomy in arteriovenous malformation surgery; the usefulness of cortical and subcortical mapping of language function in selected patients", no author has a conflict of interest to declare.