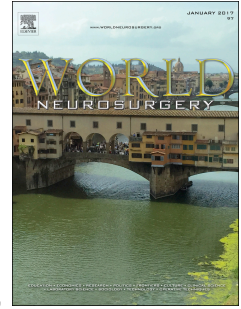


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Awake Surgery for Brain Vascular Malformations and Moyamoya Disease

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37

38 Abbreviations

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40 **AVM** Arteriovenous Malformations41 **DCS** Direct Cortical Stimulation42 **DSA** Digital Subtraction Angiography43 **CTA** Computed Tomographic Angiography44 **ECog** Electrocorticography45 **fMRI** Function Magnetic Resonance Imaging46 **MRI** Magnetic Resonance Imaging47 **MRA** Magnetic Resonance Angiography

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50 Keywords

51

52 Awake surgery, Arteriovenous Malformation, Direct Cortical Stimulation; Neurovascular
53 surgery, Moyamoya, Cavernomas, fMRI

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Abstract

72

73 **Objective** While a significant amount of experience has accumulated for awake procedures for
74 brain tumor, epilepsy and carotid surgery, its utility for intracranial neurovascular indications
75 remains largely undefined. Awake surgery, for select neurovascular cases, offers the advantage
76 of precise brain mapping and robust neurological monitoring during surgery for lesions in
77 eloquent areas, avoidance of potential hemodynamic instability, and possible faster recovery.
78 Additionally, it opens the window for perilesional epileptogenic tissue resection with potentially
79 less risk for iatrogenic injury.

80 **Methods** IRB approval was obtained for a retrospective review of awake surgeries for
81 intracranial neurovascular indications over the past 36 months from a prospectively maintained
82 quality database. We reviewed patients' clinical indications, clinical and imaging parameters,
83 and postoperative outcomes.

84 **Results** 8 consecutive patients underwent 9 intracranial neurovascular awake procedures
85 conducted by the senior author. A standardized "Sedated-Awake-Sedated" protocol was utilized
86 in all eight patients. For the two AVM patients and the three cavernoma patients, awake brain
87 surface and white matter mapping was performed before and during microsurgical resection. A
88 neurological exam was obtained periodically throughout all 5 procedures. There were no intra-
89 operative or peri-operative complications. Hypotension was avoided during the two Moyamoya
90 revascularization procedures in the patient with a history of labile blood pressure. Postoperative
91 imaging confirmed complete AVM and cavernoma resections. No new neurological deficits or
92 new onset seizures were noted on 3-month follow-up.

93 **Conclusion** Awake surgery appears to be safe for select patients with intracranial neurovascular
94 pathologies. Potential advantages include greater safety, shorter length of stay and reduced cost.

95 **Introduction**

96

97 The value of awake surgery has been effectively demonstrated in several surgical specialties
98 including plastic surgery, orthopedic surgery, cardiac surgery, and thoracic surgery, amongst others.¹⁻⁵
99 The benefits of awake procedures in neurosurgery have also become apparent, especially for select brain
100 tumors in eloquent locations, epilepsy surgery and carotid disease.⁶⁻¹⁴ The utility of awake surgery for
101 intracranial neurovascular diseases, however, has not been well established.

102 The potential advantages of awake surgery for select intracranial arteriovenous malformations
103 and cavernomas include more reliable neurological monitoring, more accurate brain mapping and the
104 potential for confidently resecting perilesional epileptogenic tissue with lower risk for neurological
105 deficit. For Moyamoya disease, more robust neurological monitoring and avoidance of hypotension
106 induced ischemia are potential benefits of awake surgery.^{9,13,15-19} The main concerns with awake
107 neurovascular procedures are patient movement, which might jeopardize delicate microsurgical
108 maneuvers, and patient discomfort during long procedures.^{20,21}

109 In this report we present our preliminary experience with awake surgery for highly selected
110 patients with intracranial AVMs, cavernomas and Moyamoya disease. Our aim is to share our rationale
111 and establish the feasibility, and safety of awake surgery for these indications.

112

113

114 **Methods**

115

116 **Data Collection**

117 IRB exemption was obtained for this retrospective case series analysis at Mayo Clinic and
118 Northwestern University. The prospectively maintained neurovascular databases at the Mayo Clinic
119 Hospital and Northwestern Memorial Hospital were queried for patients with intracranial neurovascular

120 pathologies who had undergone an awake craniotomy by the senior author over the past 36 months. The
121 indications for awake surgery were: 1) identification of eloquent cortex (language, motor) in proximity to
122 the pathology or 2) avoidance of hypotension associated with general anesthesia in patients with
123 precarious cerebrovascular reserve. Patients were subsequently stratified into 2 subgroups:

- 124 • Group 1 included Cavernomas and AVMs and
- 125 • Group 2 included patients with Moyamoya disease.

126 The rationale for awake surgery differed between the two groups (see below). Data points
127 selected included clinical indications, clinical presentation, preoperative workup, intraoperative anesthetic
128 and mapping techniques, intraoperative hemodynamic parameters, preoperative and postoperative
129 imaging, intraoperative and postoperative complications, and clinical outcomes. The data points were
130 tabulated and subsequently analyzed.

131

132 **Imaging studies**

133 All patients underwent standard MR imaging (contrast-enhanced T1, GRE, SWI, DWI), MR
134 angiography and digital subtraction angiography (DSA) when indicated. In addition, patients in group 1
135 underwent fMRI sequences and DTI studies for preliminary localization of the functional cortex (motor
136 and language areas) and the corresponding subcortical tracts. The location of the lesion in relation to the
137 fMRI generated functional areas and DTI generated tracts was noted.

138

139 **Preoperative patient preparation**

140 Preoperative evaluation of patients included specific attention to obstructive sleep apnea (OSA),
141 ischemic heart disease (IHD) and previous adverse events related to local anesthesia and sedation. All
142 patients were extensively counseled on the steps of the procedure. Special emphasis was placed on
143 educating them on the portions of surgery where their active co-operation would be required. We were
144 careful to obtain informed consent regarding the nature of awake surgery.

145

146 Technique for anesthetic management

147 The asleep-awake-asleep technique, described previously, was used in all respective surgeries.²²
148 Analgesia was achieved with a combination of a regional scalp block with local anesthetic mixture (6ml
149 of 1% tetracaine is mixed with 30 ml of 1% lidocaine and 1:200,000 epinephrine) and infusion of
150 intravenous remifentanyl (2000 mcg in 50 ml). Sedation was achieved with an infusion of Propofol
151 titrated to clinical effect (10mg/ml). **(Figure 1)** Strategic discontinuation of sedation was employed to
152 ensure that patients were awake and cooperative for the mapping and assessment phases of the surgery.

153

154 Patient Positioning

155 All patients were positioned supine or lateral with close attention to comfort, optimization of
156 venous drainage, and pressure point padding. A Mayfield head fixation device (Integra LifeSciences,
157 Plainsboro, NJ) with pin site local anesthetic infiltration was used for patients in group 1 while a donut or
158 horseshoe device sufficed for those in group 2. Appropriate monitoring devices were placed. Care was
159 taken during draping to allow a direct line of sight between the patient's face, and the anesthesiology and
160 neuro-monitoring teams. Constant periodic reassurance was quintessential for attending to patients'
161 concerns and decreasing their anxiety. Another adopted strategy was playing their favorite music playlist
162 or movie during the operation.

163

164 Awake phase monitoring

165 Patients in group 1 underwent direct cortical stimulation and mapping using an Ojemann cortical
166 stimulator (Integra LifeSciences, Plainsboro, NJ) (1.5-10 ma is delivered by a constant current stimulator
167 in 4-second trains at 60 Hz across 1-mm bipolar electrodes separated by a 5-mm gap), or a grid electrode
168 array. Motor areas were identified with concomitant movement of the face/upper limb/lower limb
169 occurring after cortical stimulation. For language mapping, patients were asked to count numbers from 1
170 to 50, name objects presented as pictures and read words presented on a screen. Speech areas were
171 identified by stimulation-induced speech arrest, errors in naming or word reading for lesions near speech

172 areas. Electrocorticography (ECoG) signals were recorded mainly for Group 1 patients to discern
173 epileptogenic foci from silent brain tissue. Additionally white matter stimulation was used where
174 relevant. Negative responses were seen as cautiously reassuring. Awake procedures for Group 2 were
175 carried out with the main aim of preventing blood pressure lability with general anesthesia. A secondary
176 benefit was the ability to monitor their general neurological status. Hence direct cortical stimulation and
177 mapping was not essential. Monitoring of somatosensory evoked potentials (SSEP) and
178 Electroencephalography (EEG) changes was standard in all patients. Clinical or electrocorticographic
179 seizure activity was suppressed with irrigation of ice-cold Ringer solution over the brain.

180

181

182 **Results**

183 A total of nine awake neurovascular surgeries were performed in eight patients. Demographics
184 and indications for surgery are summarized in **Table 1**. Two patients had arteriovenous malformations,
185 three had cavernous malformations and three patients had Moyamoya disease (bilateral surgeries in one
186 patient). Consequently, group 1 consisted of five awake procedures and group 2 consisted of four
187 procedures. Seven patients were female, and one was male. Age range was 21 to 64 years. All patients
188 were fluent with the English language. No interpreter was needed. All patients underwent postoperative
189 MRI; follow up angiography was performed in addition for patients with AVM or Moyamoya disease.

190

191 **Group 1:**

192 A total of 2 AVM patients were included in group 1; Patient 1 had a grade 2 AVM located in the
193 posterior left temporal lobe and Patient 2 a grade 2 AVM in the right parietal lobe. A total of 3 cavernoma
194 patients were included in this group as well; Patient 3 had a cavernoma located in the right frontal lobe,
195 Patient 4 in the right parietal lobe and Patient 5 had multiple cavernomas. (**Table 2**) All lesions were
196 located in or adjacent to eloquent regions. Patient 2's AVM and Patient 3 and 4's cavernomas were

197 intimately related to the motor area, Patient 1's AVM to the language area and Patient 5's cavernoma to
198 both. Four cases (Patients 1, 2, 4 and 5) presented with seizures and Patient 3 presented with focal
199 neurological deficit. **(Table 2)**

200 All patients underwent successful awake procedures. Smooth transition from asleep to awake
201 phases and back to asleep was achieved in all cases. Motor mapping and language mapping, in addition to
202 ECoG, were accomplished in all patients while in the awake phase. Correspondence between preoperative
203 fMRI and intraoperative awake direct cortical mapping was seen in patients 2, 3 and 4. These three
204 patients had functional cortex in close proximity to lesions. On the other hand, in patients 1 and 5,
205 intraoperative mapping revealed non-functional cortex from a motor and language standpoint surrounding
206 the target lesion. **(Table 3)** Subsequently, both positive and negative mappings allowed strategic
207 dissection around the targeted pathologies and complete resection in all cases. Patient 5 had a perilesional
208 epileptogenic focus detected on ECoG. **(Table 3)** The involved tissue was consequently removed with
209 non-obvious neurological sequelae. No cases were aborted due to issues with patient comfort or
210 cooperation. There were no adverse events such as noticeable brain swelling, desaturation or vomiting.
211 **(Table 4)** Patients 1, 3 and 4 had one episode of seizure each during the mapping process. All seizures
212 abated promptly with ice-cold Lactated Ringer irrigation.

213 Postoperative courses were uneventful in all patients. No new or worsened deficit was observed.
214 All patients reported positive experiences with the awake procedures and were willing to undergo another
215 awake surgery should the need arise in the future. Follow up imaging consisted of postoperative MRI in
216 cases with cavernomas and follow up angiography in AVM patients. Total resection was achieved in all
217 cases. **(Table 4)**

218

219 **Group 2:**

220 Three patients with Moyamoya disease underwent four awake procedures. Patient 6 underwent
221 bilateral awake indirect bypass three months apart. Imaging demonstrated bilateral disease in all patients.
222 **(Table 2)** Patients were kept hypertensive during surgery, with SBP maintained between 160-190 mmHg.

223 There were no episodes of significant blood pressure fluctuations during surgery in any of the patients.
224 There was no requirement of increasing blood pressure at any point during surgery since no motor nor
225 language deficits were noted during monitoring. Periodic evaluation of contralateral motor movements
226 was carried out during these procedures. No adverse events were noted during surgery. Postoperative
227 course was uneventful without new or worsening deficits. **(Table 4)**

228

229 **Case illustrations**

230 **Case 1 (Patient 1)**

231 A 36-year-old female with a new onset seizure and normal exam was found to have an AVM in
232 the left superior temporal gyrus with evidence of prior hemorrhage on MRI **(Figure 2A-B)**. Angiography
233 showed a Spetzler-Martin grade 2 AVM **(Figure 2C)**. fMRI showed the lesion in close relation to
234 Wernicke's area. Microsurgical resection was chosen after discussion of the options with the patient, as
235 we felt it had the added benefit of mapping and resecting epileptogenic tissue. During surgery, awake
236 language mapping revealed that the perinidal cortex was non eloquent and the AVM was resected along
237 with perilesional hemosiderin laden tissue with aid of ECoG **(Figure 2D-E)**. An intraoperative seizure
238 occurred that was easily controlled with ice-cold Ringer solution. The patient remained intact
239 postoperatively. Postoperative angiography confirmed complete AVM resection. She remained seizure
240 free and without any deficits at one year follow up.

241

242 **Case 2 (Patient 2)**

243 A 56-year-old female presented with left facial partial seizures and upper extremity paresis from
244 a right parietal hematoma within the post central gyrus. **(Figure 3A)** Angiography revealed a Spetzler-
245 Martin grade 2 AVM fed by a right middle cerebral artery branch with a single draining vein to the
246 sagittal sinus, just posterior to the hand knob. **(Figure 3B)** fMRI revealed right sided hand, lip, and tongue
247 sensorimotor activity abutting this area. **(Figure 3C)** Surgical resection was performed with awake

248 cortical and subcortical motor mapping and complete AVM excision was achieved. Post operatively she
249 remained without motor deficits but had an episode of left faciobrachial focal motor seizure that resolved
250 promptly. Postoperative angiography showed no residual nidus and she remained seizure free at 6 month
251 follow up.

252

253 **Case 3 (Patient 6)**

254 A 64-year-old female presented with bilateral upper extremity sensory TIAs, left more than right
255 (**Figure 4A**). Digital subtraction angiography revealed bilateral moyamoya disease (**Figure 4B-C**). Right-
256 sided indirect bypass (encephaloduroarteriomyosynangiosis- EDAMS) was performed with the patient
257 awake to avoid hypotension related to general anesthesia. Adequate blood pressure was consistently
258 maintained during surgery and no adverse intra nor post operative neurological events were observed. She
259 was symptom free at 1-month follow up.

260

261 **Case 4 (Patient 5)**

262 A 21-year-old male presented with intractable seizures and multiple cerebral cavernomas on
263 MRI. (**Figure 5A**) Video EEG determined possible ictal origin from a right frontal or a right temporal
264 lesion. fMRI revealed close proximity of the right posterior frontal cavernoma subcortical motor tracts on
265 DTI. (**Figure 5B-C**) Surgical resection of the right frontal and temporal cavernomas was undertaken with
266 awake cortical and subcortical motor mapping with electrocorticographic recording. (**Figure 5D**)
267 Perilesional hemosiderin stained tissue was resected at both locations safely without any intra- nor post-
268 operative deficits. He was seizure free on baseline dosage of anticonvulsants and was at neurological
269 baseline at 6-month follow up. Follow-up postoperative MRI showed complete resection. (**Figure 5E**)

270

271

272 **Discussion**

273

274 **History of Awake Neurological Surgeries**

275 Initial descriptions of awake brain surgery date back to early 19th century. G. Fritsch, E. Hitzig
276 and D. Ferrier experimented with electrically stimulating the cerebrum of live animals and eliciting
277 specific contralateral movements.^{23,24} In 1874, R. Barthelow followed with the discovery of localized
278 brain functional maps by stimulating a human brain through a skull perforation secondary to an eroding
279 tumor.²⁵ With the start of the 20th century, neurosurgeons recognized the potential of combined awake
280 surgery and brain mapping, especially in epilepsy surgery.^{26,27} O. Foerster was one of the first to map the
281 brain's eloquent areas through direct electric stimulation allowing for functional delineation before the
282 epileptogenic foci were removed.²⁷ Stimulation was noted to have the potential to elicit clinical seizures
283 and auras, thus aiding in the localization of epileptogenic foci.²⁷ In the 1980s, M. Berger and G.
284 Ojemann championed awake procedures and brain mapping for brain tumor surgery.¹⁷ This allowed the
285 meticulous removal of primary brain tumors while preserving eloquent areas and functional status.¹⁷

286

287 **Outcomes of Awake Surgery for Primary Brain Tumors and Epilepsy**

288 A meta-analysis conducted by Brown et al. demonstrated that awake tumor resection, as opposed
289 to general anesthesia, led to a decrease in hospital stay, post-operative neurological deficit and surgical
290 time. Extent of resection was, additionally, notably enhanced.⁹ De Wit Hamer et al. in another meta-
291 analysis demonstrated the added value of intraoperative brain functional mapping for glioma resection.
292 They concluded that intraoperative mapping was associated with less severe neurological deficits and a
293 more extensive glioma resection.²⁸ Millian et al. conducted a systematic review to study the psychological
294 sequela of awake surgery on patients. The majority of the patients stated that they were well prepared for
295 their surgeries and overall satisfaction after surgery was very high. The majority indicated they would
296 have the procedure performed again if it were indicated, even though up to 30% of them had reported
297 remembering moderate to severe pain during surgery and 14% reported anxiety during surgery.²⁹

298 As for epilepsy surgery, an awake approach may be preferred over general anesthesia for two
299 primary reasons; anesthetic interference with intracranial electrocorticography (ECoG) recordings and the
300 potential benefit of awake cortical functional mapping.^{14,30,31} This in turn has led to possible improved
301 seizure outcomes.¹⁴ To our knowledge there has been no direct comparison of seizure outcomes with
302 awake resections versus non-awake procedures in epilepsy surgery. Though it has been suggested that
303 awake mapping enables more aggressive resection of lesional tissue.³² Moreover, greater extent of
304 resection in lesional epilepsy is known to correlate with improved seizure outcomes.^{33,34}

305

306

307 **Rational and Concerns of Neurovascular Awake Surgery**

308 The benefits of awake procedures for neurovascular indications may be extrapolated from other
309 neurosurgical disciplines, as outlined above, due to the scarcity of existing published data pertaining to
310 awake cranial neurovascular procedures and absence of any randomized trials. These benefits most
311 importantly include the potential for preservation of neurological function, delineating epileptogenic foci,
312 improving the sensitivity of neuromonitoring and mitigating the side effects of general anesthesia. As for
313 moyamoya disease, hemodynamic volatility, a potential sequela of general anesthesia, has been shown to
314 contribute to perioperative stroke in up to 3.8% to 16.9% of cases. There is increased incidence of
315 perioperative stroke in patients who are experiencing TIA preoperatively and may occur after
316 disconnecting collaterals from dura to the brain.³⁵⁻³⁷ The patients in our cohort were experiencing similar
317 preoperative hypotension associated TIAs and neurological deficits. Thus, application of awake
318 procedures in these patients mitigates the volatility of intraoperative blood pressure and may decrease risk
319 of perioperative stroke.

320 The paucity of experience with awake surgery for neurovascular indications reflects several
321 commonly held concerns. The first is concern with patient motion given the delicate needs of vascular
322 micro-neurosurgery and the decreased ability to relax the brain when the patient is conscious. The second
323 is the potential need for burst suppression for temporary occlusion purposes. Awake surgeries do not

324 permit the utilization of burst suppression essential to several neurovascular procedures. Hence, the
325 metabolic state of the brain cannot be altered in an attempt to protect the brain from ischemia during these
326 surgical procedures. A third is the potential for brain swelling particularly as one might expect with large
327 AVMs. Such barriers may not apply in cases involving small AVMs, cavernomas and moyamoya disease,
328 particularly with indirect bypass procedures.

329 When functional mapping is required, awake direct cortical functional stimulation (DCS) remains
330 the gold standard. Throughout the years, several modalities of non-invasive functional imaging, like
331 fMRIs, PET and DTI, have augmented but not yet supplanted this more invasive procedure. These
332 modalities remain limited by suboptimal sensitivity and specificity in localizing brain function when
333 compared to DCS functional mapping.³⁸⁻⁴⁰ The hemodynamics of vascular lesions, moreover, add to the
334 uncertainty of fMRI imaging. The area of functional cortex may be overestimated secondary to an
335 increase in flow.⁴¹⁻⁴³

336

337 **The Literature on Awake surgery for AVM, cavernoma and Moyamoya disease**

338 Pubmed was queried using the following terms: awake neurovascular, awake cavernoma, awake
339 arteriovenous malformation, awake moyamoya, awake versus general anesthesia, functional mapping
340 cavernoma, functional mapping AVM, and functional mapping Moya Moya. Our search yielded 285
341 results of which, 19 publications were relevant to our literature review. The current published literature
342 pertaining to awake neurovascular procedures is limited to small case series and case reports^{16,41,44-60}.
343 Seven of these publications^{41,44-48,51} encompassed a total of 33 patients who underwent awake AVM
344 surgery and eleven of these publications^{16,49,52-60} encompassed 32 patients who underwent awake
345 cavernoma surgery. **(Table 5)** To the best of our knowledge, there have been no reported cases on awake
346 Moyamoya disease revascularization surgery. One case report, however, has been reported on an awake
347 STA-MCA bypass for hemodynamic insufficiency related to vertebral and right ICA occlusion. The
348 indication for awake surgery in this case was to avoid any hypotension induced by general anesthesia⁵⁰.

349 Earlier attempts at awake AVM procedures, as outlined by Burchiel et al., involved awake
350 surgical functional mapping, followed by resection at a later date under general anesthesia.⁴⁴ Gabarros et
351 al., on the other hand, kept their patients awake during language functional mapping while subjecting
352 them to general anesthesia for motor functional mapping and subsequent resection.⁴¹ In our cohort, both
353 language and motor functional mapping were performed in the awake phase with subsequent surgical
354 resection of the pathology.

355 Cannestras et al. proposed a classification system of AVMs that relates preoperative language
356 function fMRI findings to theoretic operative choice (between awake or asleep) and postoperative
357 outcome.⁴⁵ They categorized AVM patients into 3 groups; Group 1, low risk, included AVMs which were
358 at least one gyrus removed from areas of language activation, Group 2, high risk, are the AVMs that are
359 intimately associated with language functional areas and Group 3, intermediate risk are the AVMs that are
360 adjacent to functional areas. Group 1 undergo asleep surgery, Group 2 undergo radiosurgery due to
361 proximity and Group 3 undergo awake surgery.

362 We found several reports which included one or two awake procedures for cavernomas. There
363 were two larger reports by Zhou (n=17), who used cortical mapping to locate the primary motor cortex,
364 and Matsuda (n=9), who performed sensory motor and language cortical mapping, as well as sub-cortical
365 mapping during the surgical approach.^{52,58} Matsuda reported two incidents of discovering language areas
366 using sub cortical mapping in the pericavernomatous gliosis. These incidents prevented the full removal
367 resection of gliosis and spared eloquent brain tissue. What is of note in both these studies is that all
368 patients were free of neurological deficits at long-term followup.

369

370 **Patient Selection and Indications**

371 Rigorous selection criteria and an experienced surgical team ensure optimal outcomes for awake
372 cranial neurovascular surgery. General contraindications for awake procedures are uncooperative patients,
373 patients with severe language disabilities (such as frank Wernicke's aphasia), very young patients or
374 patients with significant language barriers. Patient's clinical presentation is also important. Patients

375 presenting with hemorrhage associated with hemiplegia, aphasia or a comatosed state may not be good
376 candidates for awake mapping.⁴¹ Anesthetic contraindications include severe obstructive sleep apnea.
377 Specific relative neurovascular contraindications include large and deep AVMs, posterior fossa
378 cavernomas or AVMs and possibly patients undergoing direct bypasses for Moyamoya disease. (Table 6)

379

380 **Our Cases in Perspective**

381 In Group 1, utilization of intraoperative functional mapping with direct cortical stimulation
382 (DCS) allowed functional delineation of tissue surrounding the AVMs and cavernomas. This permitted
383 the surgeon to more confidently remove the corresponding pathologies. Patients in this group had no
384 permanent neurological deficits postoperatively. Moreover, none of the cases exhibited any postoperative
385 residual pathology on post surgical or follow-up imaging. In Group 2, patients experienced preoperative
386 TIAs and neurological deficits induced by hypotensive episodes, which as mentioned previously, is
387 associated with increased incidence of perioperative stroke. Intraoperative hemodynamic instability also
388 increases perioperative stroke risk. The awake procedure prevented the lability in blood pressure, a
389 potential sequela of general anesthesia, thus averting any cerebral ischemia related events intra-
390 operatively and post-operatively. Moreover, it permitted better intraoperative neuromonitoring in this
391 group of patients by means of more robust serial neurological exams. The postoperative courses of these
392 patients were uneventful. Noted, however, are the intraoperative clinical and subclinical seizures with
393 Group 1 patients. This is a relatively common side effect of direct cortical stimulation. The involved
394 surgeons equated their experience in these 9 cases to other established awake procedures in terms of
395 difficulty and ease of operation. They also noted that the operative times of awake procedures in relation
396 to non-awake surgeries were comparable.

397 Success with this approach requires multidisciplinary collaboration between anesthesia, the
398 neurosurgical and the neuromonitoring team. Operating room nurses play a critical role as well.
399 Seamless communication and a calm intraoperative environment are important for a successful outcome.
400 Music selection and a reassuring environment can make for a very smooth experience for the patient.

401 This is fundamental especially when transitioning from the sedated to the awake and back to the sedated
402 phase.

403

404 **Conclusion**

405

406 Our experience with this cohort adds to the body of literature on awake surgery for intracranial
407 neurovascular diseases and may help clarify new indications and rationale. Awake surgery, including both
408 awake language and motor functional mapping, appears safe for microsurgical resection of select small
409 superficial AVMS, and superficial cavernomas. More robust neurological monitoring, cortical and white
410 matter mapping and aggressive resection of perilesional epileptogenic tissue appear to be important
411 advantages. Awake indirect bypass for MoyaMoya disease also appears safe and may shield the patient
412 from hemodynamic induced ischemia. Moving forward, a larger cohort and randomized controlled studies
413 are suggested to further validate this favorable preliminary experience.

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626 **Figure Legend**

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628 **Figure 1** Visual Schematic of Awake Anesthesia Protocol

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630 **Figure 2A** Axial view GRE MRI sequence demonstrating hemosiderin surrounding the AVM (red circle).

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632 **Figure 2B** Lateral view left carotid artery angiogram demonstrating posterior temporal AVM with venous
633 stenosis (red arrow).

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635 **Figure 2C** Axial view fMRI demonstrating proximity of AVM to language centers (red arrow)

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637 **Figure 2D** Surgeons performing direct cortical stimulation utilizing an Ojemman bipolar

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639 **Figure 2E** Direct cortical stimulation mapping with corresponding legend.

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643 **Figure 3A** Axial T2 Magnetic Resonance imaging of a lateral right Post central gyrus hemorrhage.

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645 **Figure 3B** AP and lateral angiography delineating the right parietal AVM.

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647 **Figure 3C** Axial fMRI demonstrating lip motor function in proximity to the AVM

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651 **Figure 4A** Axial FLAIR sequence Magnetic Resonance Imaging demonstrating areas of hypodensities
652 concomitant with ischemia (String of Pearl sign).

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654 **Figure 4B** AP view angiography demonstrating Moymoya vessel stenosis.

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656 **Figure 4C** Lateral view angiography demonstrating Moymoya vessel stenosis.

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660 **Figure 5A** Axial T2 Magnetic Resonance imaging of the frontal cavernoma.

661

662 **Figure 5B** Axial view T2 fMRI demonstrating proximity of cavernoma to motor area.

663

664 **Figure 5C** Digital tractography imaging demonstrating proximity of the cavernoma to the subcortical
665 tracts.

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667 **Figure 5D** Intraoperative grid array used in DCS functional mapping.

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669 **Figure 5E** Sagittal view Post-operative Follow-up Magnetic resonance imaging demonstrating resolution
670 of the frontal cavernoma.
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Group 1	Age	Sex	Presenting Sx	Pathology	Location	Indication for Awake Surgery
Patient 1	36	F	New Onset Seizure No focal deficit Subjective Speech Impediment Partial seizure with speech arrest	AVM	Posterior left temporal lobe	. Nearby eloquent language function . Evidence of prior hemorrhage, possible cause of intractable seizure . Superficial location
Patient 2	56	F	Partial Seizure; Left face and Left Upper extremity Left partial motor seizures	AVM	Right parietal post central gyrus behind hand knob	. Nearby eloquent motor function
Patient 3	23	F	Several weeks of bilateral motor and sensory symptomatology.	Cavernoma	Right posterior frontal lobe	. Cavernoma anterior to motor area
Patient 4	38	F	Intractable seizure secondary to residual/recurrence of cavernoma. (Prior cavernoma resected asleep)	Cavernoma	Right parietal lobe	. Proximity to motor cortex
Patient 5	21	M	Intractable seizures	Multiple Cavernomas	Right frontal lobe, Right parietal lobe and Left occipital lobe	. Right frontal cavernoma in proximity to subcortical motor fibers . Intractable seizure
Group 2						
Patient 6-1	64	F	Right Upper Extremity Numbness	Moyamoya	Diffuse	. Avoidance of Hypotension . Better Neuromonitoring
Patient 6-2	64	F	Previous right sided encephaloduroarteriomyosynangiosis	Moyamoya	Diffuse	. Avoidance of Hypotension . Better Neuromonitoring
Patient 7	43	F	Intermittent left arm numbness, episodic aphasia and complicated headaches	Moyamoya	Diffuse	. Avoidance of Hypotension . Better Neuromonitoring
Patient 8	41	F	Multifocal ischemic strokes 14 months PTP associated with episodic aphasia and paresthesias	Moyamoya	Diffuse	. Avoidance of Hypotension . Better Neuromonitoring

Table 1 Patient Demographics and Indications for Surgery

Patient 1	-	. Small left temporal AVM with surrounding T2 signal change . Evidence of prior hemorrhage	AVM and or associated hemosiderin possibly intersected the left temporal components of the arcuate fasciculus and the left interior longitudinal fasciculus	Reading paradigm elicited strong activation in the left ventral temporal lobe in extremely close proximity to the AVM, with some areas of activation immediately posterior and others immediately ventral to the AVM	1x1.2 cm superficial left posterior temporal AVM with a single feeder off a temporal MCA branch. The draining vein into the sigmoid sinus was ectatic and stenotic
Patient 2	CT Right posterior fronto-parietal intraparenchymal hematoma CTA Negative	. Resolving hemorrhage in lateral right post central gyrus . Early AV shunting in the region of the previous hematoma with a prominent right frontoparietal cortical vein draining into the superior sagittal sinus	-	Chronic hemosiderin staining and mild volume loss of the right post central gyrus. Right sided hand, lip, and tongue sensorimotor activity abutting this area. Language function not in proximity.	Right post central gyrus micro-AVM fed by middle cerebral artery branch with one superficial draining vein to the sagittal sinus
Patient 3	CT: Right frontal hematoma	. Right frontal cavernoma	Frontal lesion in proximity to motor subcortical fibers	Primary motor cortex posterior to cavernoma	None
Patient 4	-	. Evolving residual or recurrent right parietal cavernoma in close proximity to the motor cortex	-	Activation in the hand region, just anterior to the lesion. No language function within proximity	None
Patient 5	-	. Right frontal lobe 9 mm cavernoma with adjacent parenchymal hemosiderin staining . Right lateral temporal lobe approximately 8 mm cavernoma with a small amount of adjacent parenchymal hemosiderin. . Medial left occipital lobe 1.5 cm cavernoma with adjacent parenchymal hemosiderin staining	Frontal lesion in close proximity to subcortical motor fibers	. Motor: The activation was several gyri away from the area of signal change on T2	None
Group 2					

Patient 6-1	CTA bilateral ICA stenosis and prominent collateralization	MRI bilateral small strokes	N/A	N/A	Bilateral ICA stenosis with collateralization from ECA branches
Patient 6-2	CTA bilateral ICA stenosis and prominent collateralization	MRI bilateral small strokes	N/A	N/A	Bilateral ICA stenosis with collateralization from ECA branches
Patient 7	CTA bilateral M1 stenoses, greater on the left		N/A	N/A	Progression of the disease with greater collateral and hypertrophy of the lenticulostriate
Patient 8	CTA small caliber bilateral internal carotid arteries, extending from the cervical segments to the supraclinoid segments. Nearly complete obliteration of the lumina at the supraclinoid segments. There are extensive lenticulostriate collateral vessels	MRA Bilateral MCA territory cortical and white matter infarcts. Severe, preocclusive stenosis of the supraclinoid internal carotid artery bilaterally	N/A	N/A	Bilateral high-grade supraclinoid carotid artery stenosis. Leash of moyamoya vessels replacing the right supraclinoid carotid artery. Extracranial to intracranial collateral via the left middle meningeal artery supplying the right ACA distribution. Hypertrophy of the right lenticulostriate arterial system.

Table 2 Preoperative Imaging

Patient	ECOG; Yes or No	ECoG Findings	Intraoperative Brain Functional Mapping (Y/N)	Type of Cortical Mapping	Language/Motor Mapping	Intraoperative Direct Cortical Mapping Findings
Patient 1	Yes	No Epileptogenic foci	Yes	Direct Bipolar Stimulation	Both Language and Motor	Cortex around the AVM nidus appeared non functional from a language standpoint (negative mapping)
Patient 2	Yes	No epileptogenic foci	Yes	Direct Bipolar Stimulation	Both Language and Motor	In the post-central gyrus, the sensory cortex for left lip, left tongue, left thumb and index finger were mapped. In the precentral gyrus, the motor cortex for left face and left hand were mapped. Utilizing this information, dissection was initiated within the post central sulcus to address the underlying AVM.
Patient 3	Yes	No epileptogenic foci	Yes	Direct Bipolar Stimulation	Both language and motor	Hand area is one gyrus away from cortical incision
Patient 4	Yes	No epileptogenic foci	Yes	Grid Array	Both language and motor	Left lower face, left mouth and left lower lip were within close proximity from cortical lesion
Patient 5	Yes	Singular frontal epileptogenic focus detected	Yes	Grid Array	Both language and motor	Cortex around frontal cavernoma is quite from a motor and language perspective (negative mapping)

Table 3 Intraoperative Mapping Parameters in Group 1

	Intraoperative Complications	Postoperative Complications	Clinical Outcome/Postop Neurological Deficits	Imaging Outcome
Patient 1	One brief episode of seizure during direct stimulation, treated with cold Ringer solution	None	No seizures. Normal neurological exam No speech impediments	Postop angiogram: Total resection of AVM without residual nidus or AV shunting
Patient 2	None	Transient left facial droop and arm twitching No seizures	Normal neurological exam No speech impediments	Postop angiogram: Complete resection of the AVM without residual nidus or AV shunting
Patient 3	One brief episode of seizure during direct stimulation. Managed with Cold Ringer solution	None	No seizures. Normal neurological exam No speech impediments	Postop MRI: total resection of cavernoma
Patient 4	Brief subclinical seizure episode managed by lactated ringer	None	No seizures. No speech impediments. No new neurological deficit.	Postop MRI: total resection of residual cavernoma
Patient 5	None	None	No seizures. No speech impediment. No new neurological deficit	Postop MRI: total resection of both cavernomas
Group 2				
Patient 6-1	None	None	Normal neurological exam No speech impediments	-
Patient 6-2	None	None	Normal neurological exam No speech impediments	Followup MRI and MRA show no evidence of new onset stroke
Patient 7	None	None	Normal neurological exam No speech impediments	Followup angiogram: good collateral to the underlying brain related to the superior left indirect bypass. Hypertrophied meningeal arteries are seen in relation to this area as well as a brain capillary stain with venous drainage
Patient 8	None	Multiple clinical episodes of ipsilateral hypoperfusion, resolved post HHH therapy	Normal neurological exam No speech impediments	Postoperative angiogram: excellent EC-IC collateralization through indirect bypass

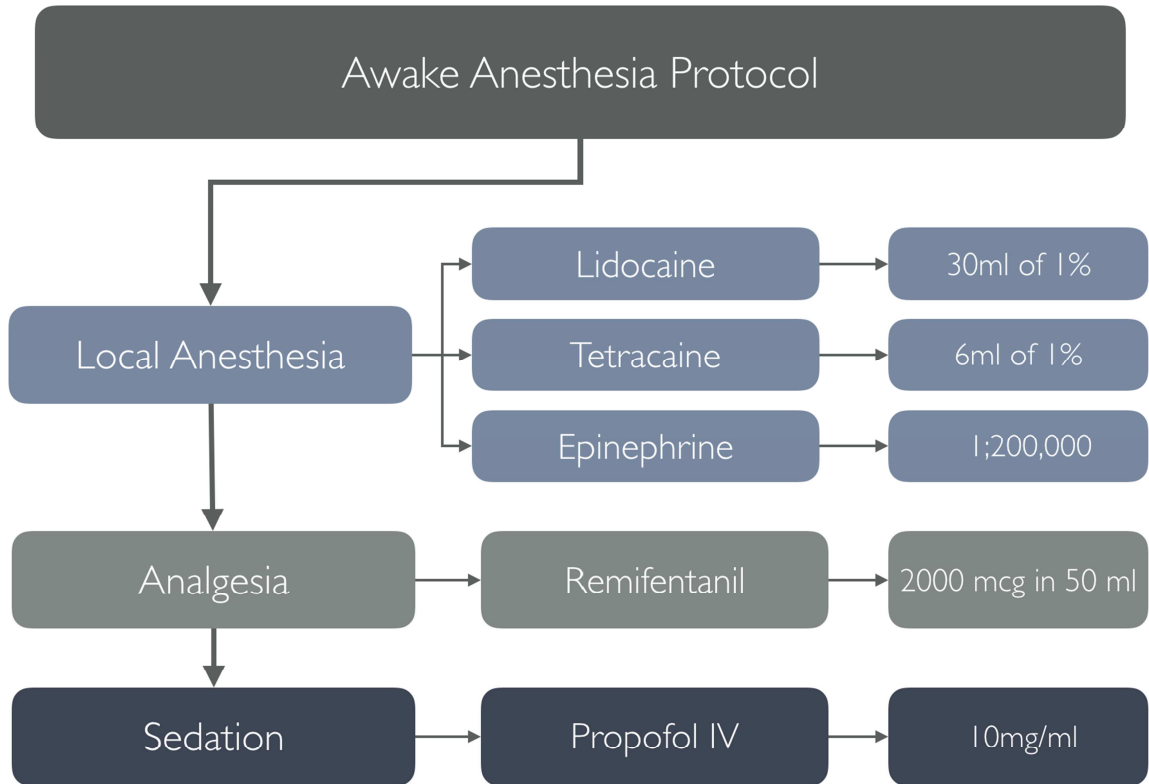
Table 4 Intraoperative and Postoperative Clinical Course

Study	Year	Awake Procedure	# of Patients
Burchiel et al.	1989	AVM	8
Gorecki et al.	1992	AVM	2
Zamorano et al.	1998	AVM	6
Cannestra et al.	2004	AVM	5
Yonekawa et al.	2005	AVM	3
Gabarrós et al.	2012	AVM	5
Gamble et al.	2015	AVM	4
Coppens et al.	2008	Bypass	1
Zamorano et al.	1997	Cavernomas	7
Daffau et al.	2005	Cavernomas	1
Mikuni et al.	2006	Cavernomas	2
Sakurada et al.	2007	Cavernomas	1
Shinoura et al.	2008	Cavernomas	1
Zhou et al.	2009	Cavernomas	17
Leal et al.	2010	Cavernomas	1
Chang et al.	2011	Cavernomas	3
Matsuda et al.	2012	Cavernomas	8
Delion et al.	2015	Cavernomas	2
Joswig et al.	2016	Cavernomas	2

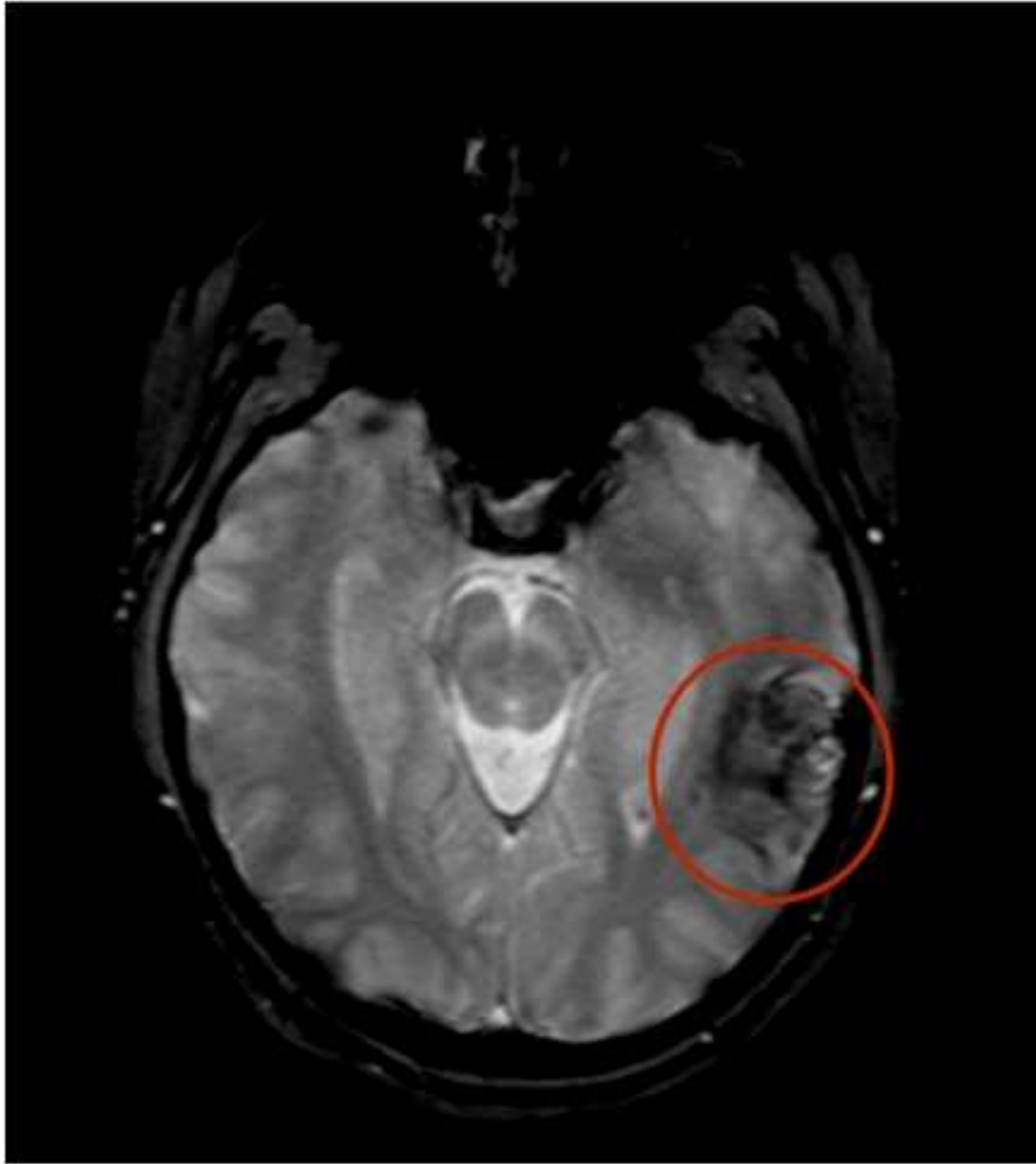
Table 5 Published awake neurovascular surgery cases

Specific Neurovascular Indications for Awake Surgery	General Factors to Consider for Awake Neurovascular Surgery
Most superficial cavernomas	Experienced surgical and anesthesia team
All Moyamoya disease except when direct bypass is needed	Well equipped Center
Superficial small AVMs	Adequate patient cognition
Small unruptured MCA bifurcation aneurysms	Patient willingness and psychological status

Table 6 Specific and General Neurovascular Indications



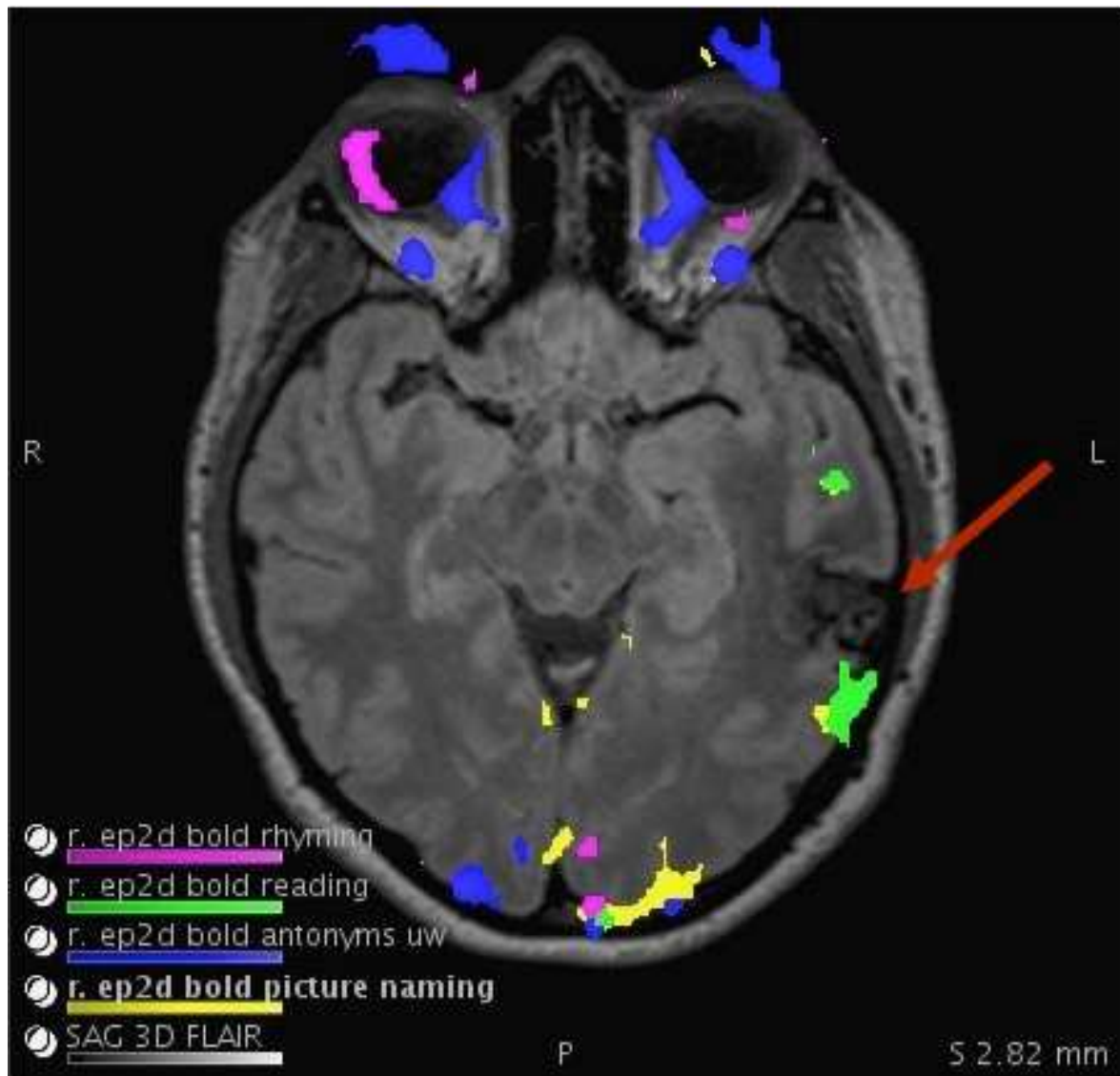
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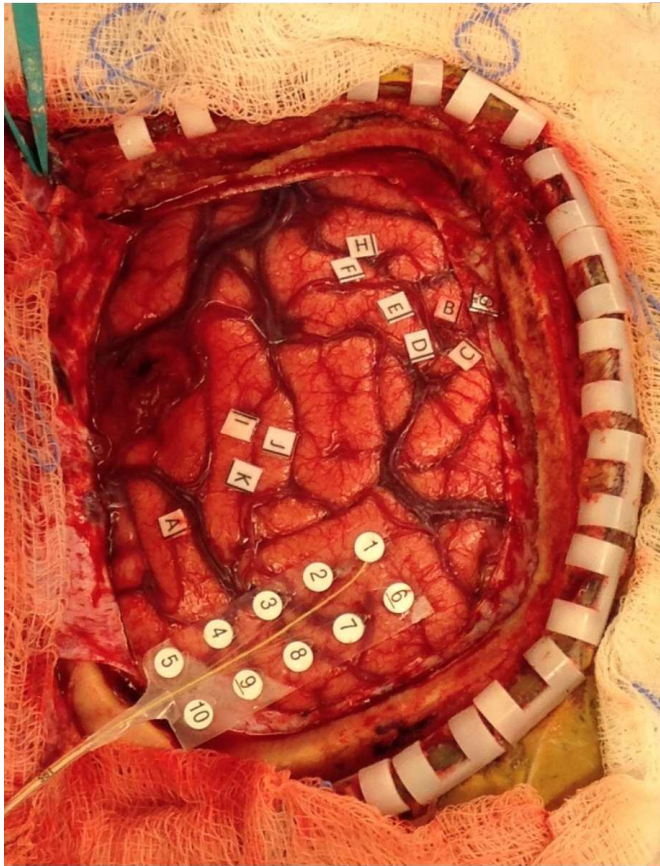
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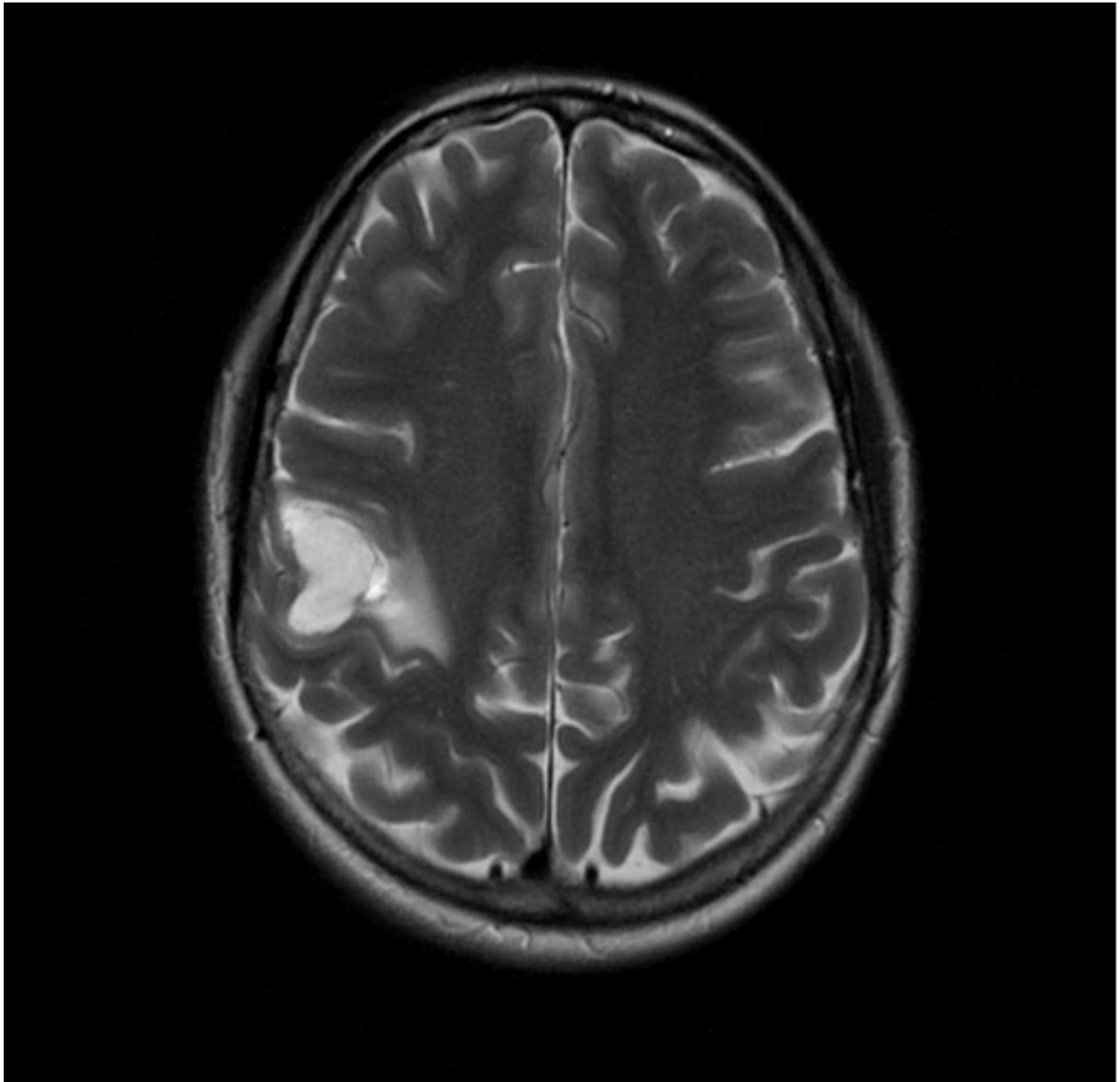


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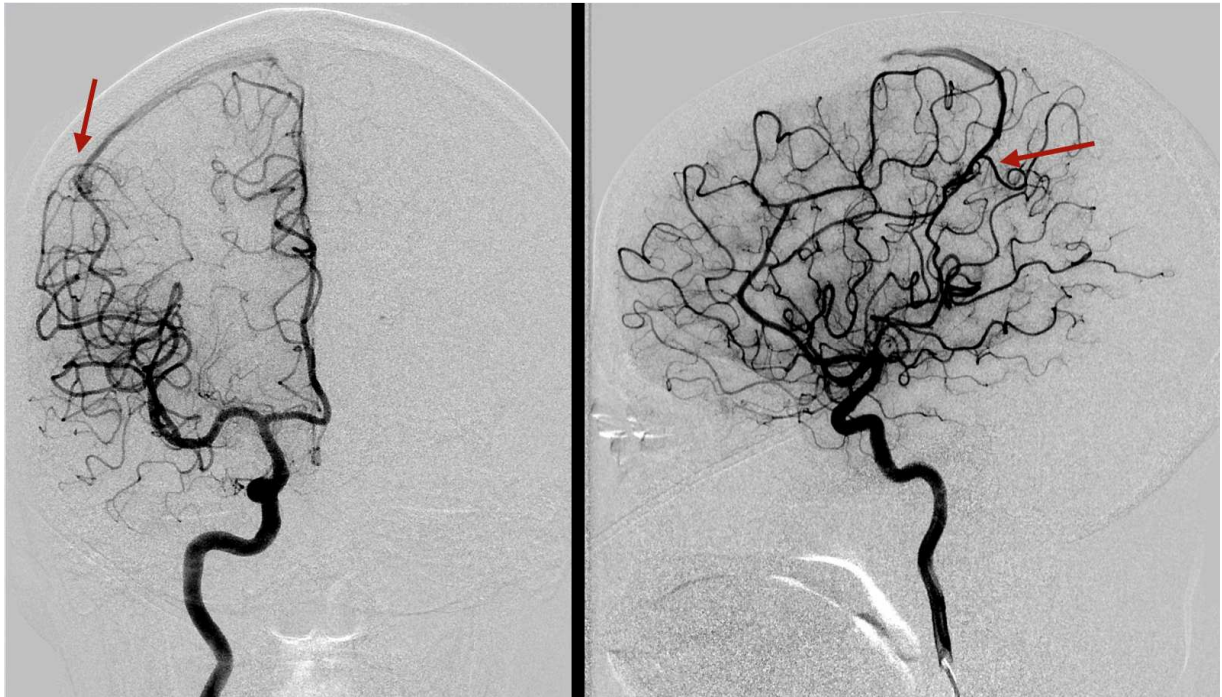


A	Seizure Focus/Dysnomia
B	Tongue Movement
C	Right Thumb Movement
D	Mouth Movement
E	Mouth Movement
F	Mouth Movement
G	Mouth Movement
H	Speech Arrest
I	Dysnomia
J	Anomia
K	Anomia

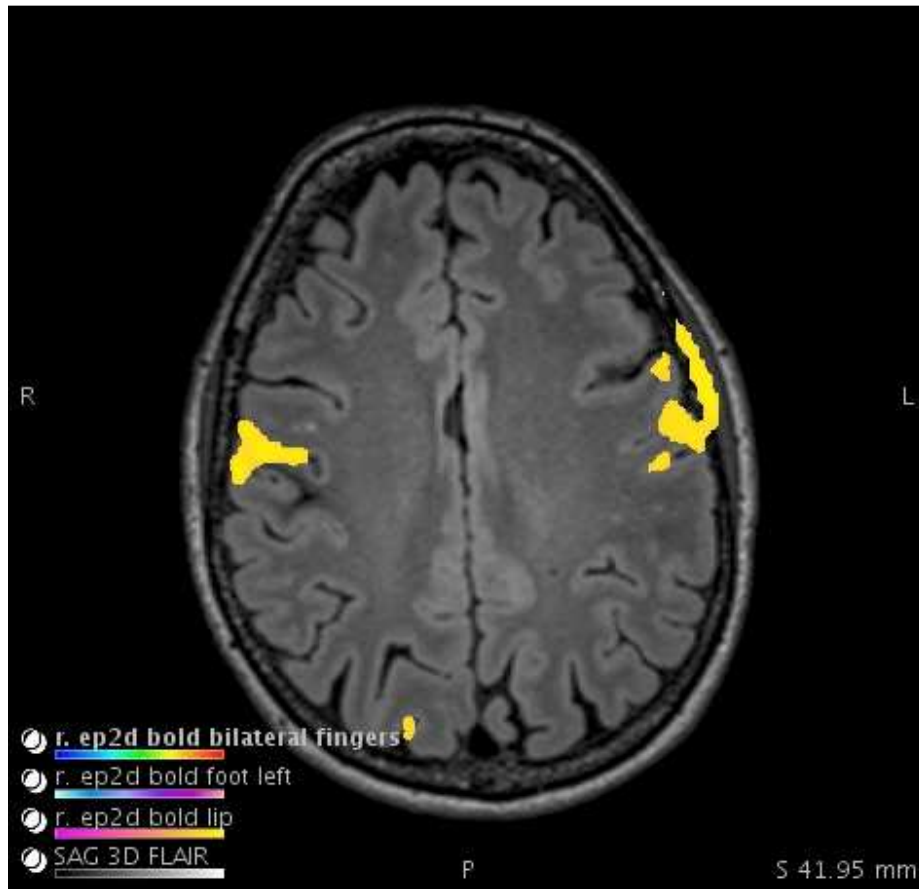
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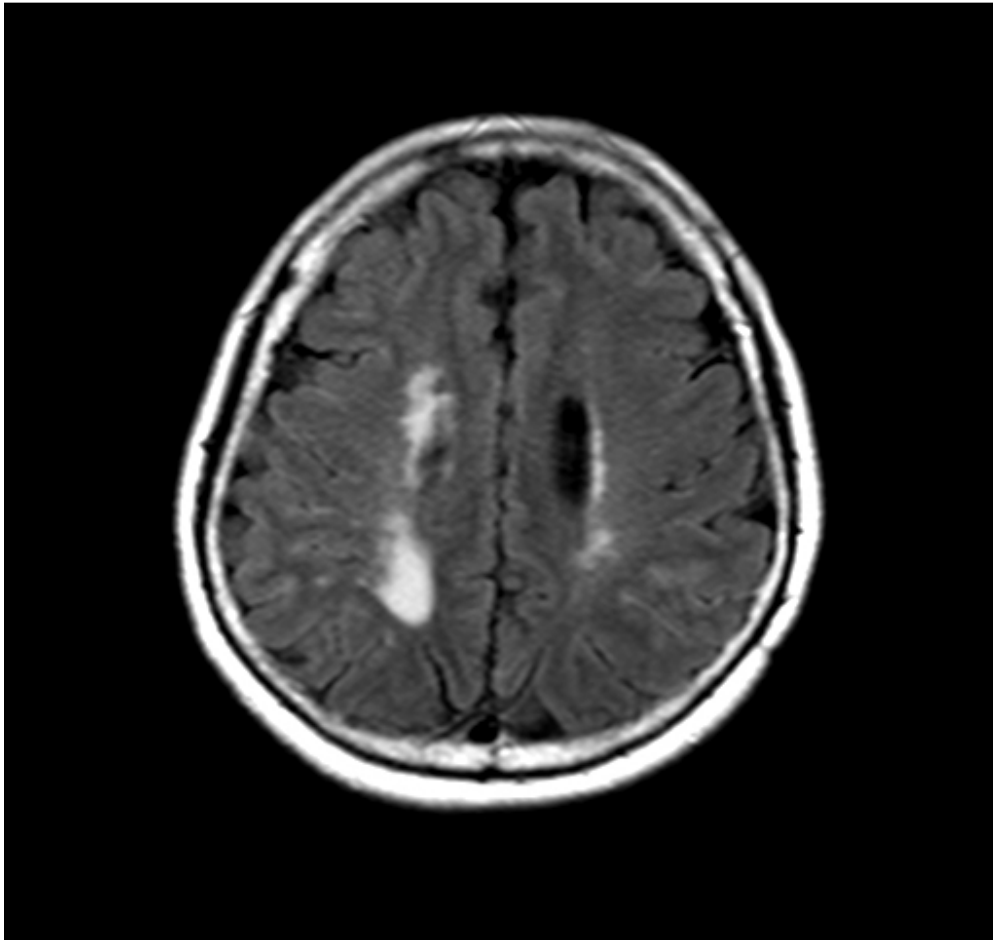


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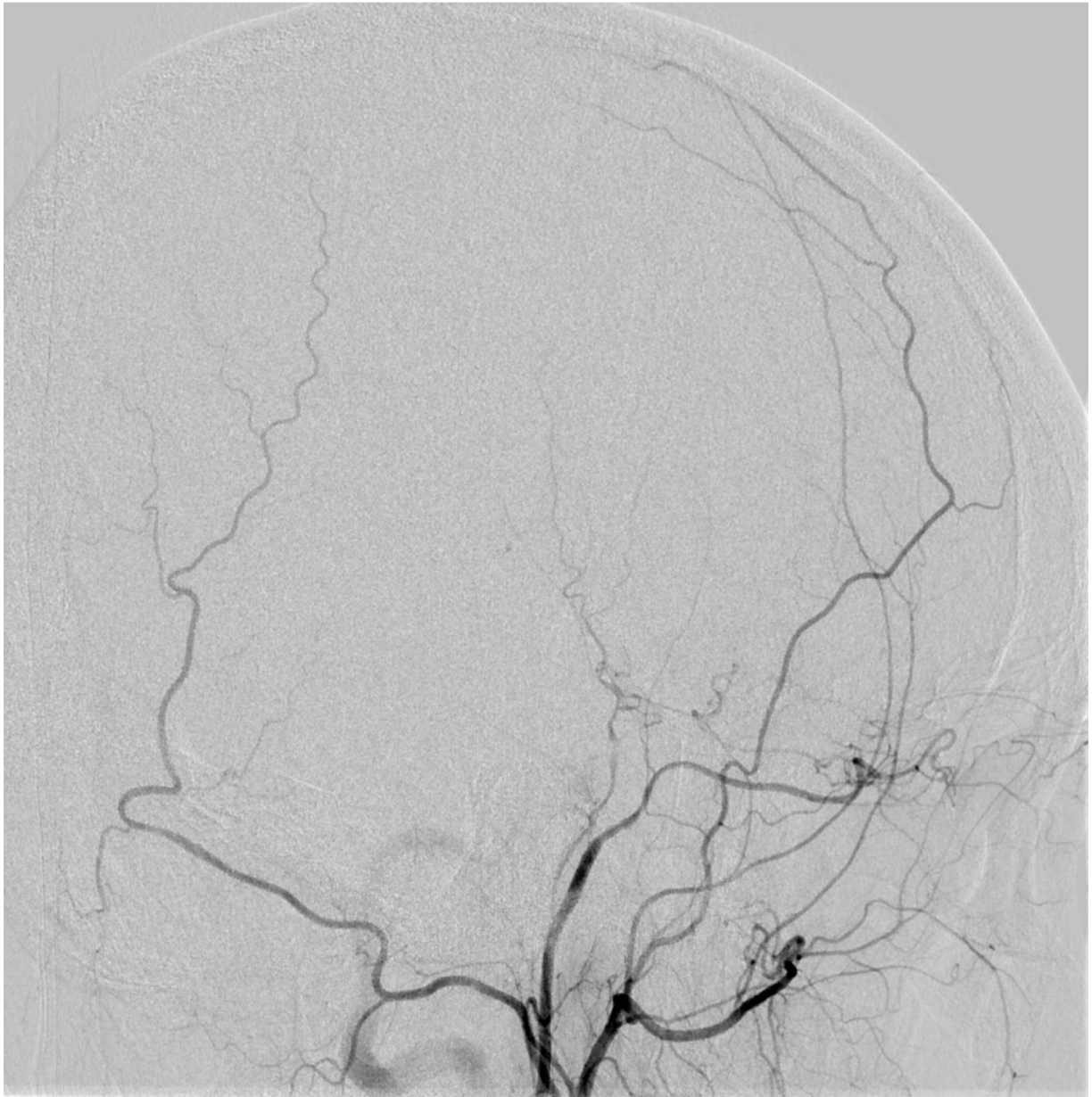
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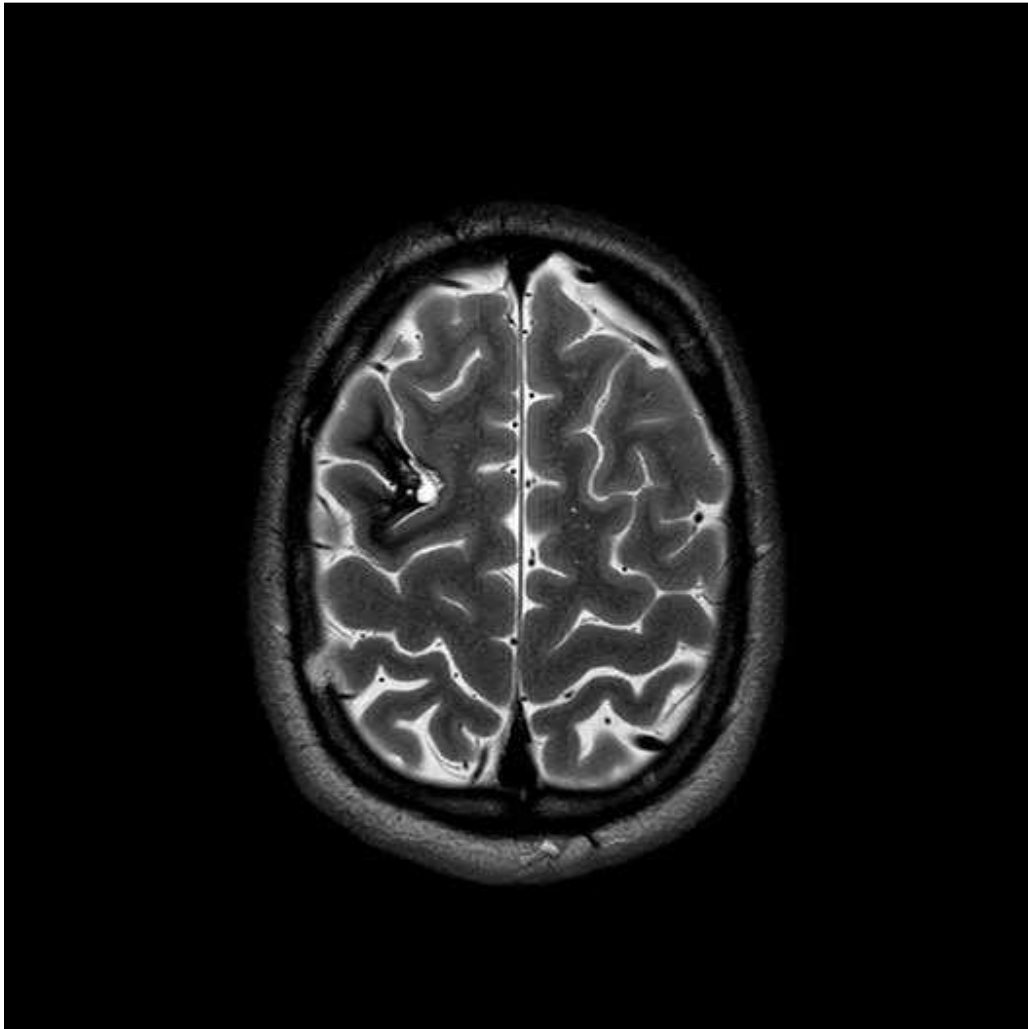
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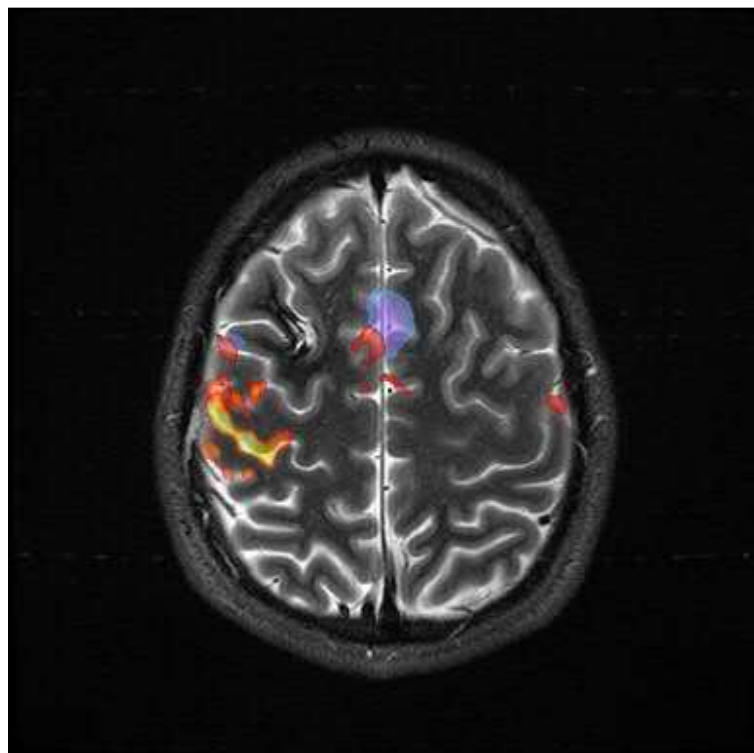


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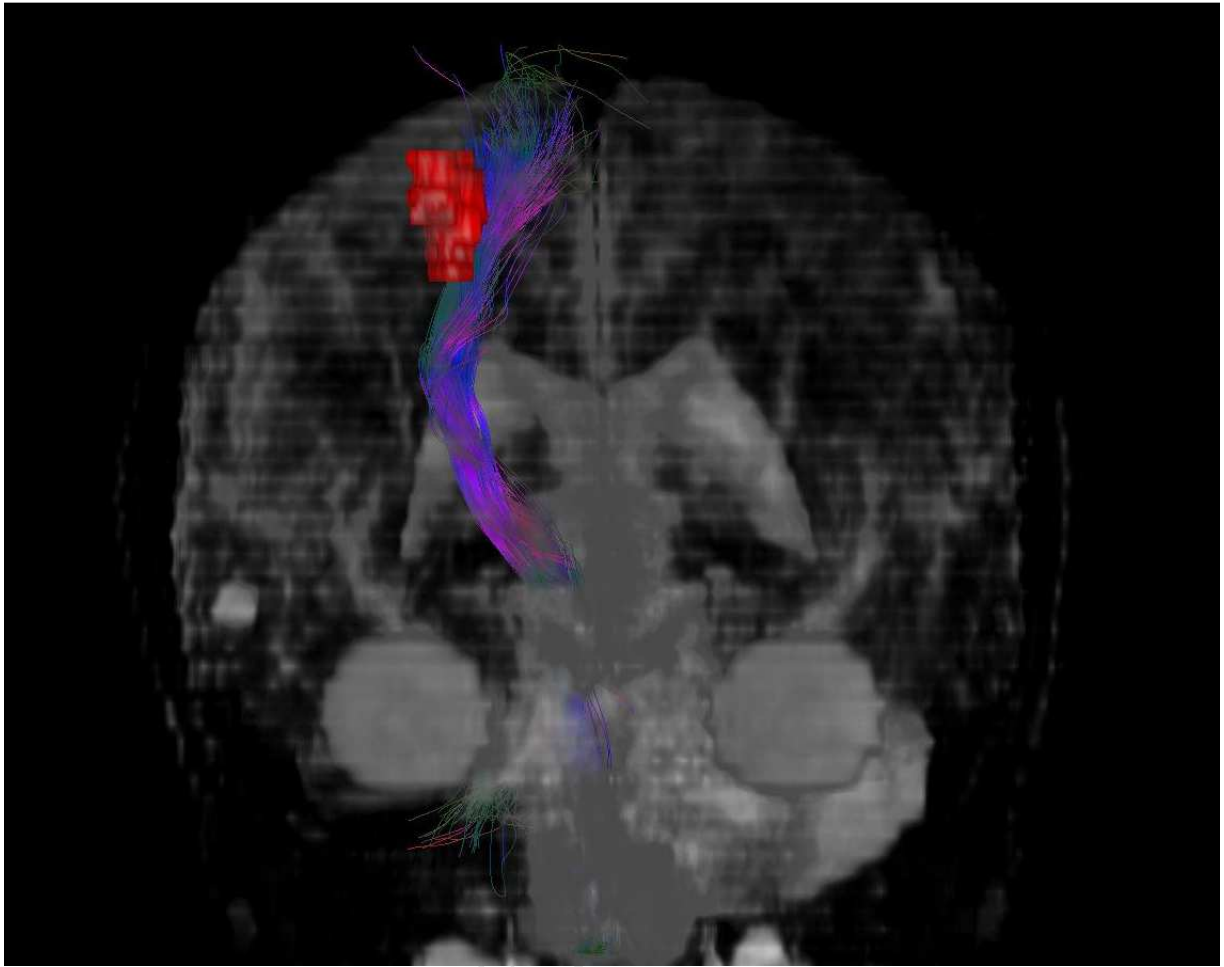


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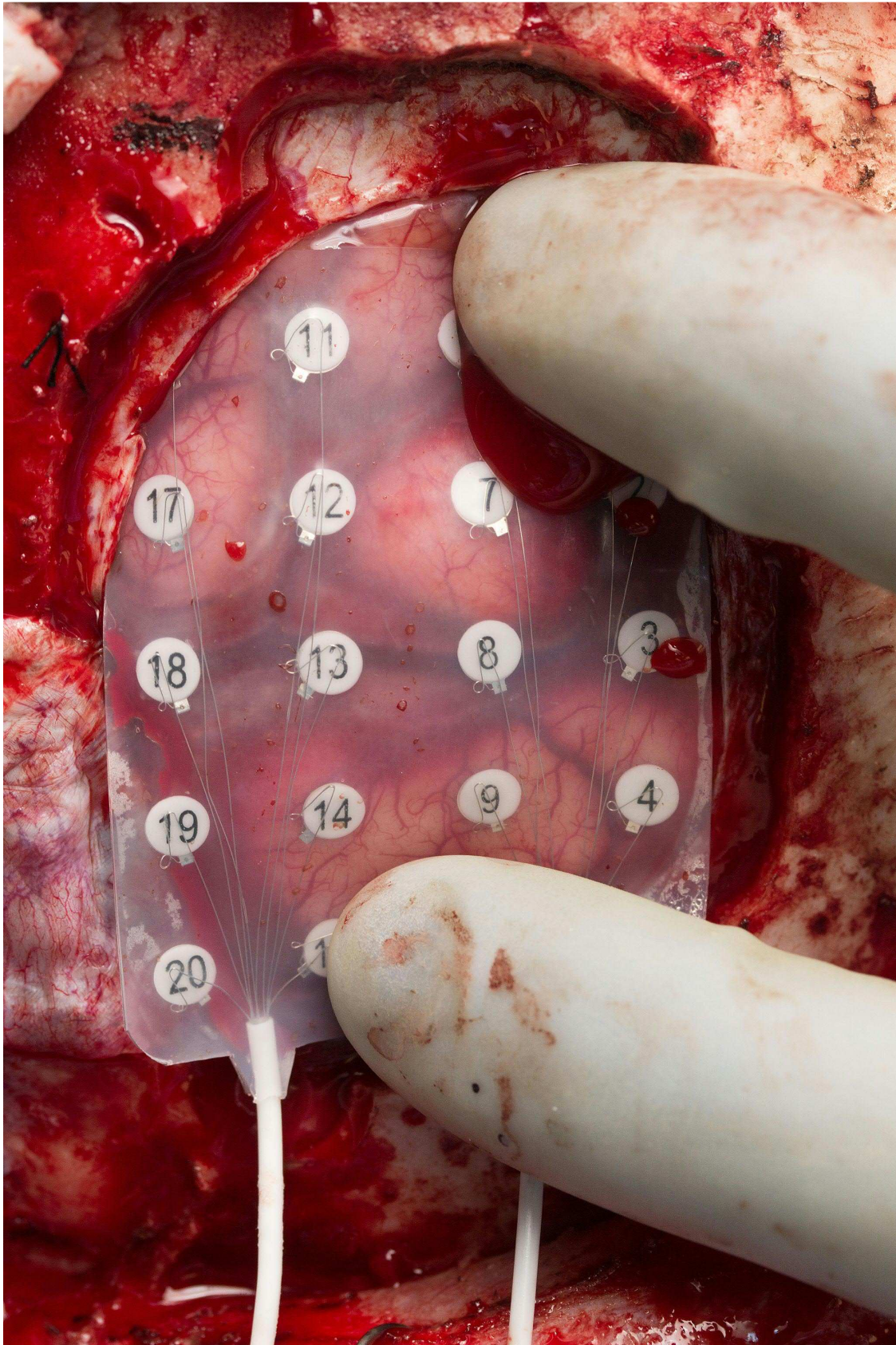
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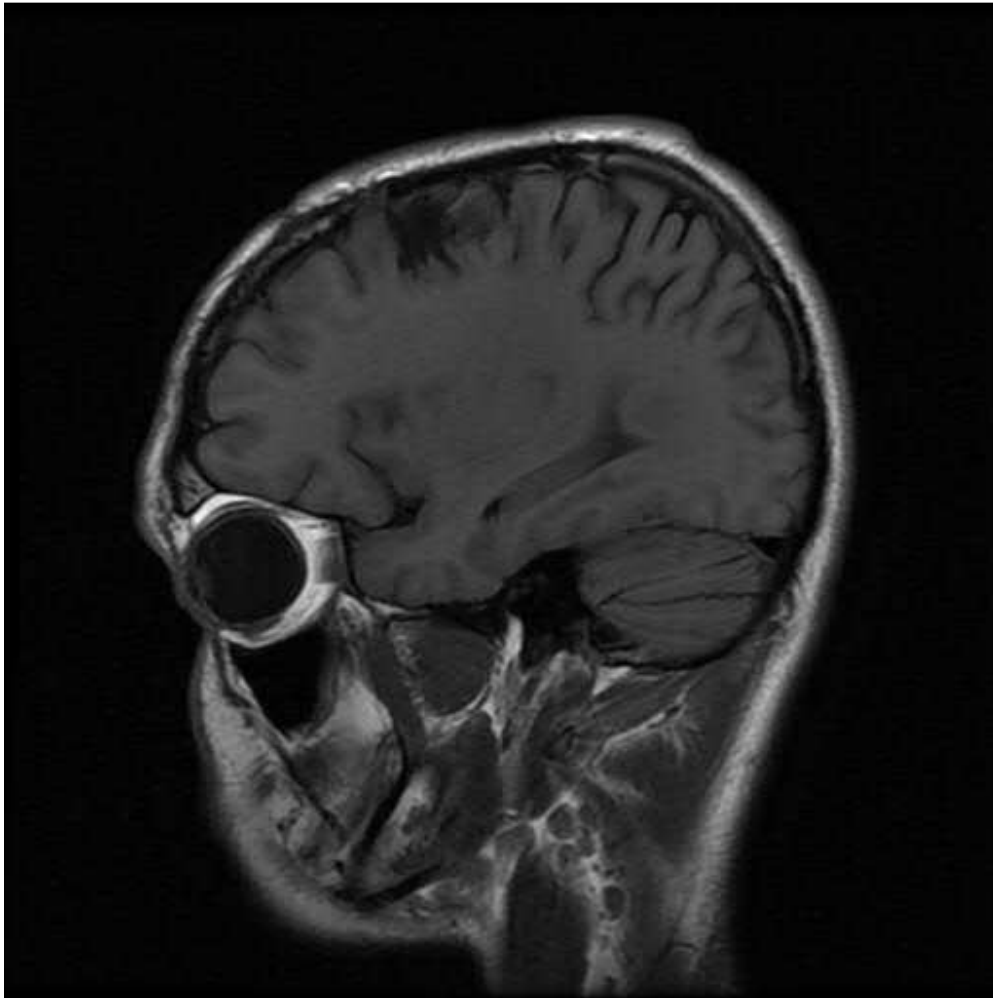


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Highlights

. Awake surgery is an established modality for select neurosurgical procedures, including neurooncology, epilepsy surgery and carotid surgery, but is still not well established for neurovascular indications.

. Hindrances to adopt awake surgery for neurovascular indications include patient motion in a delicate microsurgical procedure, the need for burst suppression and the potential brain edema with large AVMs.

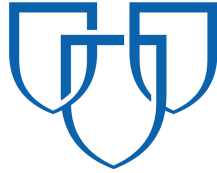
. We present a cohort of awake neurovascular procedures; we are one of the first to implement both awake AVM motor and language functional mapping, and the first to publish an awake Moyamoya procedure.

. With an experienced surgical team and stringent patient selection criteria, awake surgery for neurovascular indications is feasible, efficacious and safe with potentially lower intraoperative and postoperative sequelae.

Abbreviations

AVM Arteriovenous Malformations
DCS Direct Cortical Stimulation
DSA Digital Subtraction Angiography
CTA Computed Tomographic Angiography
ECog Electrocorticography
fMRI Function Magnetic Resonance Imaging
MRI Magnetic Resonance Imaging
MRA Magnetic Resonance Angiography

MAYO CLINIC



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Sincerely,

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