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Venous Thromboembolism during Interventional MRI-Guided Stereotactic Surgery

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Abstract

Background/Aims—Interventional MRI (iMRI) allows real-time confirmation of electrode and microcatheter location in anesthetized patients; however, MRI-compatible pneumatic compression devices (PCD) to reduce the periprocedural venous thromboembolism (VTE) risk are not commercially available. Given the paucity of literature on VTE following iMRI surgery, better characterizing patients suffering this complication and the incidence of this event following iMRI procedures is pivotal for defining best surgical practices. We aim to investigate the incidence of postoperative VTE in iMRI procedures without the use of PCD.

Methods—Medical records and operative times of patients were retrospectively reviewed. Patient demographics and mean surgical durations were reported with statistical comparisons via ANOVA and the 2-tailed Student *t* test, an a of 0.05, and the Bonferroni correction. Patients experiencing postoperative VTE underwent an in-depth chart review.

Results—Two out of two hundred ten (0.95%) iMRI procedures resulted in postoperative VTE events. There were statistically significant differences in procedure times between unilateral electrode (157.5 ± 5.7 min), bilateral electrode (193.6 ± 2.9 min), and bilateral gene therapy procedures (467.3 ± 26.5 min). Both patients had longer-than-average operative times for their respective procedures.

Conclusions—The incidence of postoperative VTE is low following iMRI procedures, even without the use of PCD during surgery.

Keywords

Deep brain stimulation; Interventional MRI; Venous thromboembolism; Deep venous thrombosis; Pulmonary embolism

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Introduction

The use of interventional MRI (iMRI) to target deep brain stimulation (DBS) electrodes, as well as gene therapy, allows real-time anatomical confirmation of the electrode and microcatheter tip location in anesthetized patients [1–5]. This iterative scanning technique allows patients who might not otherwise tolerate an awake procedure to undergo stereotactic surgery with outcomes comparable to those of traditional, frame-based procedures [6, 7]. However, MRI-compatible pneumatic compression devices (PCDs) to reduce the risk of venous thromboembolism (VTE) during iMRI are not commercially available and are not used at most centers where iMRI procedures are performed. While there is a growing literature on VTE after spinal surgery [8] or after craniotomy for brain tumor and intracerebral hemorrhage [9], there remains a paucity of literature on VTE after stereotactic neurosurgical procedures in general and there are no reports of VTE after iMRI procedures, which are generally performed on distinctly different patient populations (i.e., movement disorder patients who do not have prolonged postoperative immobilization or hypercoagulable states associated with malignancy). Given that a key variable affecting the VTE risk is the type of neurosurgical procedure a patient is undergoing [10], better characterizing patients who have suffered postoperative deep venous thrombosis (DVT) and/or pulmonary emboli (PE) following iMRI procedures remains pivotal for defining best practices in iMRI surgery.

We retrospectively analyzed a series of iMRI stereotactic neurosurgical cases, focusing specifically on surgical duration, which is a well-known risk factor for the development of VTE. We report our rate of VTE and provide case presentations of the patients in which they occurred.

Methods

Surgical Technique

Detailed reports of operative procedures, equipment, and MRI protocols for children [7] and adults [1, 5] can be found in our previous reports. On the morning of surgery, anesthesia is induced with the patient supine on an MRI table without PCDs. Following induction, the head is fixed in a 4-pin head holder (Malcom-Rand, San Clemente, CA, USA) and RF coils are placed around the patient’s head. An initial high-resolution MRI is acquired, the preliminary targets’ 3-D coordinates are determined in MR space, and trajectory planning is performed. The patient is marked, a coronally oriented incision is made, and 15-mm burr holes are drilled at the locations determined by the trajectory planning. The trajectory guide (Nexframe MR; Medtronic, Minneapolis, MN, USA, before 2010; SmartFrame; MRI Interventions, Irvine, CA, USA, after 2010) is then affixed to the patient’s skull and aligned to the final target using iterative MR scans. Once satisfactory alignment has been achieved, a ceramic stylet and introducer sheath (for DBS cases) or a ceramic microcatheter (MRI Interventions; for gene therapy cases) is slowly advanced to the target. Confirmatory scans are performed to ensure that the device placement is acceptable.

Postoperatively, patients are transferred to the Post Anesthesia Care Unit where they are subsequently moved to a surgical step-down unit. PCDs are utilized for DVT prophylaxis postoperatively, and patients are routinely mobilized the morning after surgery by the nursing staff and/or physical therapy. Chemoprophylaxis for DVT prevention was not used. Patients were on average discharged on postoperative day (POD) 1 with follow-up in the clinic between POD 7 and 10 and again between POD 35 and 49, during which any perioperative complications (such as presentation to an outside facility for VTE) would have been reviewed.

Analysis

University of California, San Francisco (UCSF) hospital system medical records and operative times of patients undergoing iMRI-guided DBS electrode placement and gene therapy infusion were retrospectively reviewed. An in-depth chart review of patients experiencing postoperative VTE was undertaken. VTE events were considered postoperative if they were discovered and presented clinically within the first 30 days after surgery. All aspects of this study are in compliance with the UCSF Committee on Human Research.

Microsoft Excel (Microsoft, Redmond, WA, USA) and Graph-Pad Prism (GraphPad Software, La Jolla, CA, USA) were used for data management, descriptive statistics, and statistical comparisons. Comparisons of means were done using a 2-tailed Student *t* test. An a of 0.05 was chosen for statistical significance. Multiple comparisons were corrected for using the Bonferroni method.

Results

Patient Population

Between April 2004 and August 2015, 188 patients who consented to having their outcomes studied underwent 210 distinct iMRI-guided procedures, including DBS electrode placement or gene therapy, in our functional neurosurgery program. The indications for surgery included Parkinson disease (PD; $n = 158$), dystonia ($n = 24$), Tourette syndrome ($n = 2$), and essential tremor ($n = 1$) (Table 1). Of the patients undergoing DBS, 63.8% ($n = 134$) underwent bilateral electrode placement, while others underwent unilateral placement only (Table 1). There were 187 electrodes placed in the subthalamic nucleus, 132 in the globus palidus internus (GPi), 5 in the centromedian nucleus of the thalamus, and 4 in the ventral intermediate nucleus of the thalamus (1 for essential tremor and 1 for dystonic tremor) (Table 1). One patient with Tourette syndrome had staged bilateral electrode placement in the centromedian nucleus of the thalamus and subsequently developed a unilateral lead infection, requiring removal; this electrode was replaced after the infection cleared. There were also 8 patients who underwent bilateral stereotactic infusions for gene therapy in the putamen (Table 1). The median age at the time of surgery was 57.1 years (range 7.2–77.7; Table 1).

Surgical Durations

The mean "skin-to-skin" surgical duration for all of the procedures was 190.4 ± 4.9 min (range 104–618; Table 2). One-way ANOVA determined that there were statistically significant differences in procedure times between unilateral electrode placement, bilateral electrode placement, and bilateral gene therapy procedures ($F = 198.5$, $p < 0.0001$; Fig. 1).

Of note, individual *t* testing revealed an expected, statistically significant difference between unilateral DBS procedures (mean time 157.5 ± 5.7 min, range 104–341) and bilateral DBS procedures (mean time 193.6 ± 2.9 min, range 138–285, $p < 0.0001$; Table 2; Fig. 1). There was also a statistically significant difference between bilateral gene therapy procedures (467.3 ± 26.5 min, range 380–618) and bilateral DBS procedures ($p < 0.0001$; Table 2; Fig. 1).

Thromboembolic Complications

Our incidence of postoperative VTE in this series of 210 cases was 0.95% ($n = 2$). A detailed description of these patients follows below.

Patient 1—This is a 69-year-old male, former smoker (quit in 1970) with a BMI of 24.1 and a 13-year history of PD who had been well maintained on medical therapy for many years. However, in the year prior to his surgery he had experienced progressively worsening symptoms and wearing-off phenomenon, with significant motor symptom fluctuations including tremor and bradykinesia. He underwent an evaluation for DBS and was found to be a good surgical candidate. His past medical history was significant for depression, an episode of transient global amnesia, mild valvular heart disease, endocarditis, hypertension, and insomnia. His past surgical history included prostate, spine, and shoulder procedures. He had no history of thromboembolic events and his preoperative coagulation studies were normal.

After an uncomplicated surgery lasting 225 min in which DBS electrodes were implanted in bilateral GPi, he began ambulating the morning after surgery and was discharged to his home on the afternoon of POD 1. Over the following 3 days he developed progressive dizziness and cough which culminated in delirium and 6 mechanical falls, the last of which was down a flight of stairs on POD 4. He was brought to the emergency room and was found to have an acute, nonsurgical 8-mm right tentorial subdural hematoma. He was also noted to be short of breath and hypoxic. He was admitted for observation and, because of a persistent need for supplemental oxygen to maintain an oxygen saturation of 92% in the setting of no fever, a CT pulmonary angiogram was performed to rule out pulmonary embolism. The CT revealed an acute lingular segmental pulmonary embolism without radiographic evidence of increased right heart pressures. Subsequent Doppler ultrasound measurements of the lower extremities were negative. Anticoagulation was contraindicated for this patient given the subdural hematoma he had sustained from his fall, so an inferior vena cava filter was placed by interventional radiology with plans to start full anticoagulation 2 weeks later. The patient made an uncomplicated recovery, his inferior vena cava filter was removed, and he was not on anticoagulation at the last follow-up, with normal pulmonary function.

Patient 2—This is a 54-year-old male, nonsmoker with a BMI of 35.8 and an 11-year history of PD. He initially did well with medical therapy but eventually developed motor fluctuations with wearing-off phenomenon. He presented as a candidate for gene therapy delivery via iMRI-guided injection with bradykinesia, rigidity, and a shuffling gait in the medication-off state despite an optimized regimen. His past medical history included hypertension, asthma, and lumbar disc herniation. Prior surgeries included a sinus surgery and refractive eye surgery. He had no history of thromboembolic events and the results of his preoperative coagulation studies were normal.

On POD 1, following an uncomplicated surgery lasting 520 min, the patient experienced severe shortness of breath while ambulating down the hallway. The rapid-response team was called and noted oxygen saturations down to 82% and atrial fibrillation with rapid ventricular response. He remained awake, alert, and hemodynamically stable. He was transferred to the ICU and a STAT CT pulmonary angiogram demonstrated a submassive left main pulmonary artery embolism with lobar/segmental emboli in all lobes of the right lung and radiological evidence of right ventricular enlargement. Subsequent lower extremity ultrasound Dopplers were negative for DVT. Despite a recent intracranial surgery, the patient was immediately started on a heparin drip although no bolus was administered. He was also started on an amiodarone drip for the atrial fibrillation with rapid ventricular response. Within 12 h, the patient had transitioned back to a normal sinus rhythm and the amiodarone drip was stopped. He was slowly weaned off of supplemental oxygen, transitioned to warfarin for 12 months, and discharged on POD 5 with stable vitals and a neurological examination at baseline. At the last follow-up he was off of anticoagulation with normal pulmonary function and exercise tolerance.

Discussion

This case series provides preliminary data suggesting that iMRI-guided stereotactic neurosurgery, despite a prolonged in-scanner time without PCDs, has a low VTE complication rate. While this was not a head-to-head study comparing iMRI and conventional awake stereotactic surgery (during which PCDs are routinely used), it is worth noting that our incidence of 0.95% (210 cases of asleep iMRI surgery) is lower than the 2.5% (121 patients undergoing awake DBS surgery) reported by Baltuch's group in 2009 [11]. However, given the overall increased risk of VTE, adequate postoperative surveillance and prophylaxis are still necessary [12].

The number of iMRI-guided procedures being performed is growing and now includes a significant volume of laser ablations [13] and drug infusion trials for CNS neoplastic disease [14] as well as the DBS and gene therapy procedures in our series. Although the incidence of VTE in these procedures is small even without the use of PCDs intraoperatively, our data suggests that further investigation of individual procedures, especially with regard to surgical duration, may be necessary. Wide statistically significant differences in duration between procedure types in our study (Fig. 1), coupled with the fact that 1 out of 8 gene therapy cases, 1 out of 126 bilateral electrode cases, and 0 out of 76 unilateral electrode patients incurred VTE, may imply a correlation between VTE risk and surgical duration in this population. If so, additional postoperative prophylaxis such as subcutaneous heparin may be warranted. In fact, Baltuch's group reported a 0% incidence ($n = 133$) of VTE in a second group of patients who received subcutaneous heparin [11] approximately 2 h before surgery in the preoperative holding area and then twice daily starting on POD 1. This would, of course, need to be balanced with the risk of intraparenchymal hemorrhage. Although there are currently no MRI-compatible PCD systems commercially available, the growth in the number of iMRI procedures being done may lead to the development of such devices in the future. Some centers have devised ways of using standard PCD systems safely in the MRI environment, but this is quite variable and dependent on the layout of the MRI suite.

The individual patients who suffered postoperative VTE in our series both had longer-than-average operative times for their respective procedures. However, apart from undergoing major surgery, these patients had relatively few risk factors for VTE [15, 16]. Of the known risk factors associated with VTE, one patient had a single additional risk factor (age >40 years) and the other had 2 risk factors (age >40 years and obesity). Additional shared characteristics between the patients included: being male, having a greater than 10-year history of PD with significant bradykinesia, and hypertension. Some data suggest that neurosurgical procedures in general carry an increased risk of VTE [9, 17, 18, 19], and thus these less-established risk factors, as well as other characteristics unique to functional neurosurgical patients, should be investigated in the context of long-duration stereotactic surgery.

The current study does have several limitations. Although the patients were asked about changes in their medical condition and new symptoms at their post-op follow-up visits, they were not systematically asked to fill out a standardized survey that listed specific symptoms such as shortness of breath or leg swelling that might be indicative of VTE. In addition, if they sought care for any new symptoms or conditions in the immediate postoperative period outside of our hospital system, copies of these outside records were usually but not universally included in the UCSF medical records and available for review. Finally, it is possible that some patients suffered a VTE event but had mild symptoms and did not seek medical attention. It is therefore possible that some patients suffered VTE events that were not captured in our analysis. These are all potential shortcomings of a study based on retrospective chart reviews.

Conclusion

Despite the fact that patients undergoing iMRI-guided procedures do not receive mechanical prophylaxis with PCDs like patients do in a traditional operating room, the incidence of postoperative VTE appears to be low. Overall surgical duration and other risk factors need to be investigated in the context of stereotactic neurosurgical patients to guide application of postoperative prophylaxis.

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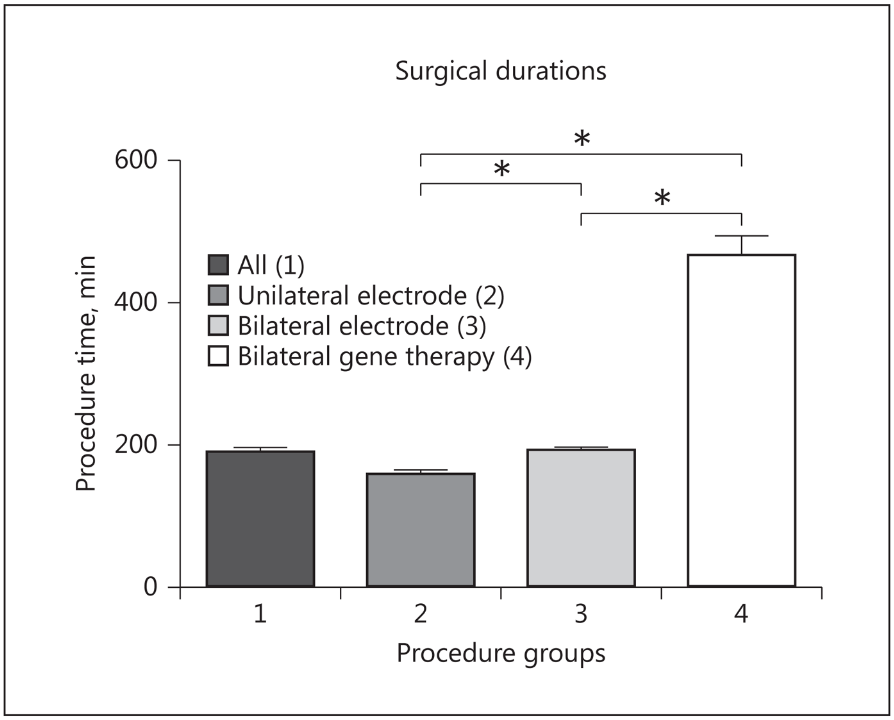

Fig. 1.

Surgical durations. Significant differences in procedure times existed between all groups. * $p < 0.0001$. The initial statistical difference was first assessed with a one-way ANOVA. Individual *t* tests between groups 2 and 3, 2 and 4, and 3 and 4 were all significant. Significance withstood correction with the Bonferroni method.

Table 1

Detailed description of patient characteristics as well as the diagnosis and surgical target at the time of the procedure

Demographics	Value
Patients, *n*	188
Procedures, *n*	210
Bilateral electrode placement, *n* (%)	134 (63.8)
Female sex, *n* (%)	68 (36.1)
Age, years	
Mean	57.1
Median	62
Range	7.2–77.7
BMI	
Mean	25.2
Median	24.1
Range	13.6–69.3
Disease, *n*	
Parkinson	158
Dystonia	24
Tourette syndrome	2
Essential tremor	1
Target, *n*	
STN	187
GPi	132
Thal	5
VIM	4
Pu	16

Gpi, globus pallidus internus; Pu, putamen; STN, subthalamic nucleus; Thal, centromedian nucleus of the thalamus; VIM, ventral intermediate nucleus of the thalamus.

Table 2

Surgical durations

	Patients, *n*	Surgical duration[1], min		
		mean ± SEM	**median**	**range**
All procedures	210	190.4±4.9	176.0	104–618
Bilateral DBS				
All	126	193.6±2.9	189	138–285
Gpi	42	186.1±3.2	186	143–249
STN	81	198.4±4.0	192	138–285
Thal	2	165.0±6.0	165	159–171
VIM	1	171.0±0.0	171	171
Unilateral DBS				
All	76	157.5±5.7	140.0	104–341
Gpi	48	144.1±5.0	136.0	104–270
STN	25	193.6±13.7	169	113–341
Thal	1	127.0	127	127
VIM	2	162.5±34.5	163	128–197
Bilateral gene therapy				
Pu	8	467.3±26.5	448	380–618

DBS, deep brain stimulation; Gpi, globus pallidus internus; Pu, putamen; STN, subthalamic nucleus; Thal, centromedian nucleus of the thalamus; VIM, ventral intermediate nucleus of the thalamus.

[1]Skin-to-skin time.