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Hemorrhagic complications seen on immediate intraprocedural stereotactic computed tomography imaging during deep brain stimulation implantation

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ABSTRACT

Background: We present our operative experience of patients with movement disorders who developed intracerebral hemorrhage (ICH), which was identified on intraprocedural stereotactic computed tomography (CT) imaging performed immediately after deep brain stimulation (DBS) lead placement and prior to the implantation of further components of the DBS hardware.

Methods: Patients who underwent DBS lead implantation from January 2009 through December 2017 were included in the present study. Most of the surgeries were performed in a staged fashion. All patients were operated using identical surgical and intraprocedural imaging techniques, and no microelectrode recordings were done. Leksell Stereotactic G frame and neuronavigation software was utilized for all surgeries. Intraprocedural stereotactic CT was performed to confirm the precise position of the implanted DBS lead and to rule out any hemorrhagic complications.

Results: Overall, 222 patients underwent 322 DBS lead implantations during 316 stereotactic procedures. Six patients exhibited early ICH recognized on intraprocedural stereotactic CT performed immediately after DBS lead placement; in addition, two patients developed delayed ICH due to large venous infarction. Four patients with ICH were asymptomatic. The ICH rate was 2.5% per electrode and 3.6% per patient; the permanent deficit rate was 1.2% per electrode and 1.8% per patient. The death rate due to ICH in our cohort was 0.6% per electrode and 0.9% per patient.

Conclusions: Intraprocedural stereotactic CT can not only visualize the implanted DBS lead in the stereotactic space but also rule out early ICH. Identified predisposing factors for development of ICH include patient's age, hypertension, and previous antiplatelet therapy. Careful planning of stereotactic trajectories plays a paramount role in reducing the rate of ICH in DBS surgery.

1. Introduction

Deep brain stimulation (DBS) is an established and accepted treatment modality for patients suffering from intractable movement disorders such as Parkinson's disease (PD), dystonia, or essential tremor (ET) [1,2]. The most feared complication of stereotactic functional neurosurgery is the development of an intracerebral hemorrhage (ICH) caused by the passage of microelectrodes or guiding cannulas for the permanent placement of a DBS lead [3]. The decreased number of passages through the brain parenchyma to the stereotactic target decreases the incidence of possible ICH. Modern stereotactic techniques augmented by neuronavigation devices with the visualization of stereotactic trajectories in three planes help avoid the superficial and intraparenchymal vessels as well the ventricles along a stereotactic trajectory, thereby greatly reducing the ICH rate [4]. Nevertheless, the risk of ICH due to electrode placement has been estimated to be between 0.2% and 5.6% [3]. Not all ICHs are symptomatic, and most are discovered on routine postoperative imaging, usually computed tomography (CT) [5]. The estimated incidence of symptomatic hemorrhagic complications varies between 0.5% and 2.1% [6], suggesting that 0.5%–1.9% of all ICHs due to DBS lead placement are clinically asymptomatic [5].

Intraprocedural stereotactic imaging CT or magnetic resonance imaging (MRI) after DBS lead placement enables the confirmation of proper lead location in the intended stereotactic target and quickly and efficiently rules out the possibility of ICH [3,5]. Recently, intraoperative imaging-guided procedures have gained more validity in DBS surgery. Interventional MRI (iMRI) has emerged as an alternative

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approach for implanting DBS leads under general anesthesia in an elderly patient population [7,8]. iMRI utilizes anatomical targeting without intraoperative electrophysiology and is performed within the bore of an MRI system [7]. The advantages of this approach are shorter surgery time, usually single brain penetration, excellent anatomical targeting, and more importantly, intraoperative detection of ICH [7,9]. Other studies have used MRI-guided and -verified DBS lead placement with immediate postoperative stereotactic MRI, with the Leksell frame in place [3]. We routinely perform intraprocedural stereotactic CT with the Leksell frame in place to check the position of an implanted DBS lead in the intended target and to rule out any ICH before putting patients under general anesthesia to implant further components of the DBS system.

The main goal of the present study was to estimate the incidence of ICH on postimplantation intraprocedural stereotactic CT with subsequent proper management of this complication in affected patients. Moreover, we conducted detailed analysis and grouped all ICHs (acute and delayed) according the their etiology (arterial or venous). Additionally, we aimed to present the clinical outcomes in patients suffering from ICH as well as the potential risk factors in patients before surgery.

2. Methods

The study was a retrospective analysis of DBS procedures performed for movement disorders in the Neurosurgical Department of Postgraduate Medical Center from January 2009 to December 2017. The medical records of patients were reviewed, and data were collected using a standardized protocol. Data collected included demographics and intraprocedural stereotactic CT findings with detailed description of ICH for patients with different types of movement disorders. The study received an Institutional Review Board approval. All patients diagnosed with PD met the clinical criteria of the United Kingdom Parkinson's Disease Society Brain Bank for idiopathic PD [10]. The inclusion and exclusion criteria were based on CAPSIT-PD guidelines [11]. Patients with ET and other forms of incapacitating tremors were diagnosed by movement disorder specialists and referred for DBS after failed pharmacology trials. Patients with different types of dystonia were considered eligible for DBS only after repeated failed botulinum toxin injection sessions or ineffective pharmacological trials. All patients referred for DBS had pharmacologically resistant movement disorders or suffered from levodopa-induced side effects such as incapacitating levodopa-induced dyskinesia or on–off motor fluctuations. All patients and their families were informed about the stereotactic procedures, and they signed written informed consent forms.

The inclusion criteria for the study beside proper diagnosis of an incapacitating movement disorder were as follows: normal MRI findings of the brain without any structural changes, negative history of birth or head trauma, meningitis, and cerebral ischemia. Cognitive impairment, suicidal thoughts, and active psychiatric diseases constituted the exclusion criteria for DBS. The antiplatelet therapy was stopped 10 days before planned stereotactic procedure.

Briefly, DBS lead implantations were performed under local anesthesia for patients suffering from PD, ET, or other forms of tremor. Patients disabled by different forms of dystonia were operated under general anesthesia with propofol. One or two days before the surgery, distortion-free T2-weighed MR images and T1-weighed 3D volumetric contrast-enhanced images for stereotactic trajectory planning were recorded for all patients. Special attention was paid to distortion-free image acquisition, which in most cases, was performed under local anesthesia with the assistance of a treating neurosurgeon and an anesthesiologist. In some cases, imaging was repeated because of excessive head movements during MRI examination. MRI used for image acquisition was 1.5 T magnet (General Electric). In all DBS lead implantations, a stereotactic G frame (Elekta, Instruments, Stockholm, Sweden) was used. After local/general anesthesia, the head frame was secured to the patient's skull, and stereotactic contrast-enhanced CT images with 1.25-mm slice thickness were obtained. These images were then merged with preoperative MRI images using stereotactic surgical planning software (Framelink S7, StealthStation, Medtronic, Minneapolis, MN, USA). This planning software allowed the adjustment to individual patient's anatomy. The anesthesiologist tried to keep blood pressures < 130/80 mmHg during the surgery and < 140/90 mmHg after the surgery. During surgery, patients were placed in the supine position with slight head elevation (approximately 10°–15°). A 14-mm burr hole was drilled at the entry point according to arc and ring settings provided by stereotactic trajectory planning using neuronavigation. To perform intraoperative macrostimulation, the Leksell Neurogenerator (Stereotactic Instruments, Elekta, Stockholm, Sweden) and Leksell macroelectrode with a noninsulated electrode tip of 2 mm in length and 1.5 mm in diameter were used. After the subthalamic nucleus (STN) was located, the electrode (Model 3389, Medtronic, Minneapolis) was implanted for chronic stimulation and secured at the burr hole by a lead-anchoring system. For patients undergoing surgery under local anesthesia, the movement disorders symptoms were assessed through the contacts of the DBS electrode. The depth of the inserted chronic electrode was controlled by lateral fluoroscopic imaging. Microrecording was not performed. The loss of cerebrospinal fluid and possible brain shift were reduced by patient positioning, flooding the burr hole with saline, and placing wet cottonoids around the burr hole.

Immediately after DBS lead implantation, patients were brought to the CT setting where non-contrast-enhanced intraprocedural stereotactic CT images were obtained to assess the exact DBS electrode position and exclude hemorrhagic complication. If no hemorrhagic complication was detected, the implantable pulse generators (IPGs; Soletra, Activa SC 37602/37603, Medtronic, Minneapolis, MN, USA, or Libra, St. Jude) were implanted during the same operative session with the patients under general anesthesia. All IPGs were usually implanted under the clavicle in the chest wall or in the abdominal wall in adolescents with primary generalized dystonia. Delayed CT was not routinely performed at this stage, unless needed. The location of each hemorrhage and time of appearance from implantation procedure was recorded in all cases. Hemorrhage was classified as symptomatic causing a neurological decline, mental status change, or asymptomatic producing no neurological symptoms.

Statistical analysis included the presentation of data as means with range values. Patients who developed hemorrhagic complications were investigated for possible contributing factors such as age at surgery, presence of well-controlled hypertension, and anticoagulation drugs taken before surgery.

3. Results

A total of 322 electrodes were implanted in 222 patients through 316 consecutive procedures. We encountered eight ICHs (four symptomatic and four asymptomatic). The overall ICH rate was 2.5% per electrode and 2.5% per stereotactic procedure. The overall ICH rate per operated patient was 3.6%. In our cohort, most procedures were performed in a staged fashion due to reimbursement regulations, and the number of performed procedures nearly equaled the number of implanted DBS leads (316 procedures and 322 electrodes implanted). In our series, 1.2% of the implanted electrodes were associated with symptomatic ICH, which affected 1.8% patients. Periprocedural death occurred in two (0.9%) patients, which accounted for 0.6% of the implanted electrodes.

To implant these 322 electrodes, we used 343 brain penetrations with macroelectrodes to implant permanent DBS leads. As stated previously, no microrecording was utilized to refine targeting. In our study, 10 patients had > 1 brain penetration with the Leksell macroelectrode (9 patients had 2 passes and 1 patient had 3). In addition, three DBS electrodes were immediately revised after intraprocedural CT due to suboptimal locations. Three PD patients were affected by

Table 1
Distribution of underlying movement disorder diagnosis in 222 patients with description of the numbers of procedures and electrodes in each patient's group affected by Parkinson's disease, tremors and dystonia.

Indication for DBS procedure	Number of procedures	Number of patients	Number of electrodes
Parkinson's disease	258 procedures	186 patients	260 electordes
Dystonia	41 procedures	21 patients	45 electrodes
Tremor	17 procedures	15 patients	17 electrodes
Total	316 procedures	222 patients	322 electrodes

misplaced DBS leads. In all three cases, the electrodes targeting the left subthalamic nucleus (STN) were located just anterior and medial to the stereotactic target, as shown by intraprocedural CT. Immediate revision procedure was performed in 1.3% patients, which corresponded to an immediate revision rate of 0.9% per procedure. Moreover, six patients required revision procedure due to suboptimal clinical effect. The overall revision rate in our series was 2.8% per procedure and 4% per patient.

The most common indication for DBS in the present series was PD. The primary indications with exact numbers of procedures and electrodes implanted are shown in Table 1. Over this 9-year period, there were 186 patients operated due to the diagnosis of idiopathic PD. In this patient group, 252 procedures were performed to implant 260 DBS electrodes. Among the 68 patients with PD scheduled for bilateral surgery, only two had simultaneous implantation of DBS leads, and the remaining procedures were performed in a staged fashion. During the follow-up period, there were six revisions of intracranial electrodes in the PD patient group. Four out of the six revisions performed for suboptimal clinical effect were related to breakage of the DBS lead while two were necessitated due to suboptimal clinical benefit noted over the follow-up period. In three patients, the electrodes had to be replaced due to the breakage of the extracranial part of the DBS lead, and one patient suffered an injury to the left parietal region with subsequent damage to the DBS lead just above the connector. Additionally, two patients required revision of intracerebral DBS leads due to suboptimal clinical benefit in the subsequent months. Two revisions of the DBS leads were done in patients with advanced PD. One lead was found to be placed more medial and was repositioned 2 mm lateral to the original position, while in the other case the DBS lead was found to be anterior, lateral, and superficial to the intended target, the STN. None of the revisions led to any neurological sequel. In all revisions, a new entry point and a new stereotactic trajectory were created. We avoided the use of the previous trajectory to implant a new DBS lead.

The second most common indications for DBS in our series were different dystonic conditions. Overall, 21 patients handicapped by medically incapacitating dystonia were operated. In this patients group, there were six patients diagnosed with Meige syndrome, five with primary generalized dystonia, three with truncal dystonia, and three with tardive dystonia. Additional diagnoses included two patients with cervical dystonia, one with dystonia/mioklonia syndrome, and one with dystonic head tremor. Taken together, in 21 patients, 41 procedures were performed to implant 45 dB electrodes. Two electrodes were reimplanted over follow-up due to the suboptimal clinical benefit and two due to the breakage of the extracranial DBS lead.

The third indication for DBS was ET. There were 11 patients who received unilateral DBS. Additionally, there were two patients with Holmes' tremor, one with tremor due to multiple sclerosis, and one with tremor of unknown origin. One electrode in a patient with ET and one in a patient with Holmes's tremor were reimplanted due to suboptimal antitremor effect in the early postoperative period. Two DBS leads were found located medial to the stereotactic target. Lateral repositioning of the DBS leads by 2 mm resulted in good tremor control. As previously stated, all patients underwent intraprocedural stereotactic CT after electrode implantation with the Leksell Stereotactic G frame in place. Intraprocedural stereotactic CT imaging revealed acute ICHs in 6 patients. Delayed hemorrhagic complications occurred in 2 additional patients due to venous infarctions. In both cases of venous infarction and one unintended minor injury to superficial venous structures, the lesion was noted after dural opening. In the first patient, the mild

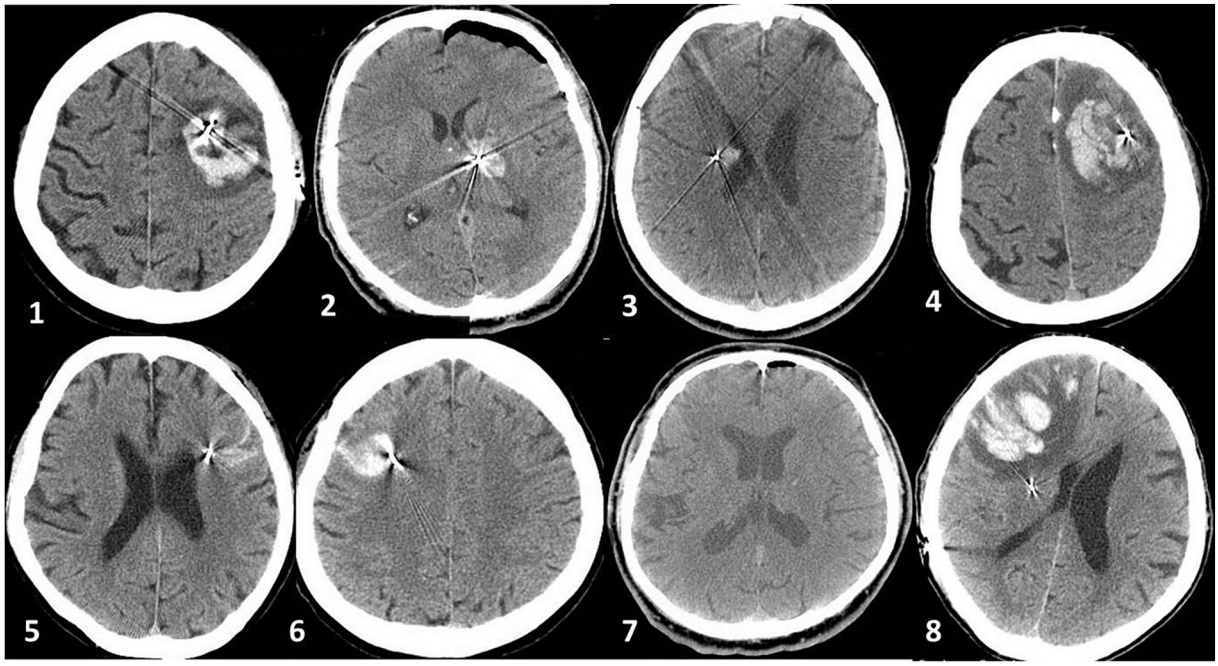

Fig. 1. Axial CT slices in consecutive patients with early hemorrhages (images numbered a,b,c,e,f,g) and with delayed hemorrhages (images numbered d,h) due to venous infarction seen in subsequent CT slices. Different hemorrhages can be seen: image (a) Large left frontal subcortical and bleeding along a DBS lead, image (b) bleeding along stereotactic lead, image (c) small paraventricular bleeding, image (d) Large left frontal delayed hemorrhage due to cerebral venous infarction, image (e) subarachnoid hemorrhage around DBS lead and in the left sylvian fissure, image (f) small right subcortical hematoma, image (g) hematoma along all way of stereotactic trajectory, image (h) large right frontal delayed hemorrhage due to cerebral venous infarction.

Table 2
Detailed patient's data with intracerebral hemorrhagic complications seen on intraoperative CT, indication for a DBS procedure, stereotactic target, localization of an intracerebral hemorrgahe as well clinical outcome are presented. Abbreviations: PSA – posterior subthalamic area, STN – subthalamic nucleus, GPi – globus pallidus interna.

Patient no. (sex)	Age at surgery (yr)	Risk factor	Indication for DBS procedure	Duration of illness (yr)	Side and stereotactic target	Localization of and intracerebral hemorrhage	Neurological deficits	Neurological outcome
1(F)	81	Hypertension, antiplated medications	Essential tremor	34	Left PSA	Large left frontal subcortical and bleeding along a DBS lead	Right hemiparesis and dysartria	Death 2 months after a DBS lead placement due to heart insufficiency
2 (M)	65	Hypertension	Advanced Parkinson's disease	12	Left STN	Large left frontal subcortical and bleeding along a DBS lead, hematoma at the left STN	Right hemiparesis and dysartria	Permanent right sided paresis still present 4 years after surgery Patient wheelchair bound Ambulates with stick small distances
3 (M)	72	Hypertension, antiplated medication	Advanced Parkinson's disease	12	Right GPi	Large right frontal delayed hemorrhage due to cerebral venous infarction	Left mild hemiparesis	Death 5 months after a DBS lead placement due to aspiration pneumonia
4 (F)	61	Hypertension	Advanced Parkinson's disease	13	Left GPi	Large left frontal delayed hemorrhage due to cerebral venous infarction	Dysarthria	Transient dysarthria completely resolved over 6 weeks period
5 (F)	73	Hypertension, antiplated medication	Advanced Parkinson's disease	10	Right STN	Small paraventricular bleeding	No	No neurological deficits
6 (F)	65	Hypertension	Advanced Parkinson's disease	9	Left STN	Large subarachnoid hemorrhage around DBS lead and in the left sylvian fissure	No	No neurological deficits
7 (F)	65	None	Advanced Parkinson's disease	10	Right STN	Small right subcortical hematoma	No	No neurological deficits
8 (M)	73	Hypertension, antiplated medication	Advanced Parkinson's disease	11	Left STN	Hematoma along all way of stereotactic trajectory	No	No neurological deficits

venous bleeding which was stopped with Surgicel resulted in a large left frontal delayed hemorrhage. Eight hours after the stereotactic DBS lead placement, this patient reported difficulty in word finding. The post-operative CT revealed a large, subcortically located hemorrhagic venous infarction (Fig. 1 d). In the second patient with venous infarction, after pia coagulation and introduction of a guiding cannula to the target, we observed venous bleeding from the subdural space anterior to the burr hole; introduction of Surgicel anteriorly completely stopped the bleeding. However, this resulted in a large right frontal delayed hemorrhage (Fig. 1 h). These ICH cases due to venous infarctions were not visible on intraprocedural stereotactic CT. Detailed patients' demographic data are shown in Table 2. All ICHs are visualized in individual patients on axial CT slices in Fig. 1.

Overall, among eight patients with ICH, four were asymptomatic. The remaining four had symptomatic ICH. The first patient with acute symptomatic ICH aged 81 years suffered from long-standing severe ET and had a history of staged bilateral thalamotomy. To control her right-sided postural tremor, we proceeded with the implantation of left DBS targeting the posterior subthalamic area. We utilized the same burr hole previously drilled for left-sided thalamotomy. After DBS lead placement, the patient became restless and developed right hemiparesis. Intraprocedural stereotactic CT revealed bleeding along the stereotactic trajectory. The patient developed right hemiparesis and dysarthria. The patient passed away 2 months after surgery due to progressive heart insufficiency. The second patient was a 65-year-old man who suffered symptomatic ICH and had well-controlled hypertension. Although the anesthesiology team continuously monitored his blood pressure, the patient experienced a hypertensive event during the surgery (peak blood pressure: 190/110 mmHg). Intraprocedural CT revealed a large ICH along the stereotactic trajectory. This patient developed right hemiparesis and dysarthria. The patient's dysarthria improved, but he became wheelchair-bound over the next 4 years. His right-sided hemiparesis improved, and 4 years after ICH incidence, the patient could ambulate using a stick. The third patient who developed delayed ICH was a 72-year-old man with a 12-year history of PD who was scheduled for right GPi DBS. Intraprocedural stereotactic CT visualized the DBS lead in a proper place without any ICH. Twenty-six hours after the surgery, the patient became somnolent; hence, we urgently performed CT, which showed a large hemorrhagic venous infarction in the right frontal region. The patient underwent right frontal craniotomy for hematoma evacuation. After 2 months, he was discharged and was on supportive care. Unfortunately, he developed aspiratory pneumonia and passed away 5 months after DBS. The fourth patient with symptomatic ICH was a 61-year-old woman who developed ICH 8 h after targeting the left GPi word finding difficulties. In this patient, the implantation of the connector and internal pulse generator were postponed for the next day. An urgent CT visualized a large left frontal hemorrhagic venous infarction. The dysarthria resolved completely within 6 weeks. The patient underwent successful contralateral GPi DBS 4 years after the initial surgery and 2 years after bilateral GPi DBS, the patient remains independent in daily living activities and without severe and disabling bilateral dyskinesia.

Four additional patients with ICH identified on intraprocedural stereotactic CT had no neurological deficits. These ICHs resulted in postponing the implantation of DBS hardware in three patients. One patient with bleeding along the stereotactic trajectory experienced a hypertensive event with rise of blood pressure to approximately 180/120 mmHg during targeting of the left STN. Since this patient developed poorly controlled hypertension in the subsequent months, further stereotactic procedures were stopped.

All ICHs resulted in significant prolongation of hospitalization of affected patients. The mean hospital days in patients with all ICHs were 26.3 days (range 7 ± 67 days). For patients with symptomatic ICH, the mean hospital stay was the longest and reached 44.7 days (range, 34 ± 67 days). Patients affected by asymptomatic ICH had a shorter hospital stay than with symptomatic ICHs. In four patients with

asymptomatic ICH, the mean hospital stay was 8.5 days (range, 7 ± 11 days). On the contrary, the mean hospital stay in patients not affected by ICH was 5.4 days (range 3 ± 7 days).

In our series, the strongest predisposing factor for development of ICH was the patient's age at surgery. The mean age of patients who developed ICH was 69.3 years (range, 61–81). Conversely, the mean age of patients who did not develop ICH was 58.9 years (range 12–79). Age was not found to be a determinant of the development of symptomatic or asymptomatic ICH. The mean age of patients with symptomatic ICH (69.7 years [range, 61–81]) was nearly the same as that of patients with asymptomatic ICH (69.2 years [range 61–81]). This observation is supported by the fact that none of the dystonic patients experienced ICH. Of note, patients with dystonia had the lowest mean age at surgery (52.3 years [range, 11–68 years]).

Beside patient's age at surgery, also the strong determinant of ICH was the presence of hypertension in the past. Seven of eight patients suffered from hypertension and were on hypotensive drugs preoperatively. Moreover, two of them experienced uncontrolled hypertensive events during a DBS lead placement.

In addition to the patient's age at surgery, past history of hypertension was also a strong determinant of ICH. Seven of the eight patients suffered from hypertension and were on hypotensive therapy preoperatively. Moreover, two of them experienced uncontrolled hypertensive events during DBS lead placement. Among patients with PD, six out of seven patients with ICH had hypertension in the preoperative period. Out of the 186 PD patients operated during this time period, 35 were on hypotensive therapy before surgery. Six of these 35 patients developed ICH during DBS lead placement. All four PD patients who developed symptomatic ICH were on hypotensive drugs. In addition, five PD patients who were eligible for DBS procedure were excluded from surgery due to poorly controlled hypertension in the preoperative period. Among the ET patients, three patients were on hypotensive drugs preoperatively. Of these, one patient who also had a history of antiplatelet therapy developed ICH. In this patient, the use of a previously made burr hole and trajectory for DBS lead placement may also have contributed to the development of ICH. Among the dystonic patients, only two patients were preoperatively on hypotensive drugs. None of these patients affected by dystonia experienced an ICH event.

Antiplatelet therapy was found to be a predisposing factor in four patients affected by ICH. Two patients with symptomatic ICH and two patients with asymptomatic ICH were on antiplatelet therapy preoperatively. In most patients, the combination of known predisposing factors, mainly hypertension and antiplatelet therapy, contributed to the development of ICH. Four patients with ICH had at least advanced age, history of hypertension and antiplatelet therapy, and longstanding movement disorder; the other three patients had a history of hypertension, while only one patient had normal blood pressure and was not taking hypotensive drugs in the preoperative period.

With respect to the targeted brain region, STN exhibited a correlation with ICH, as observed on intraprocedural stereotactic CT after DBS electrode placement.

On the contrary, delayed hemorrhagic venous infarction occurred in two patients targeting GPi for advanced PD complicated by levodopa-induced dyskinesia. The time course, location, and clinical symptoms developed due to ICH enabled us to grade hemorrhagic complications as arterial bleeding or venous bleeding. We could assess five ICH as the result of an injury to an intracerebral artery and three intracerebral bleedings due to an injury to venous structures (one paraventricular hematoma as a result of possible injury to the deep vein located just lateral to the ventricular wall and two delayed venous infarctions due to injury of the superficial cortical veins).

All patients with ICH were managed in the intensive care unit. Among four patients with symptomatic ICH, one with large venous infarction affecting the right frontal lobe and a coexistent mass effect underwent craniotomy with hematoma evacuation. The DBS hardware was spared during the right frontal craniotomy. The remaining seven patients were treated conservatively. All four patients with symptomatic ICH also required extensive rehabilitation during their prolonged hospital stay at the department of neurosurgery and, subsequently, in the rehabilitation units.

ICH, particularly symptomatic ICH, affected further surgical management. Of four patients, only one who developed transient dysarthria that completely resolved over 6 weeks had all components of the DBS system implanted with an excellent clinical outcome. Two patients had only a DBS lead implanted. One patient died 2 months after DBS lead placement because of heart failure, and another was handicapped because of permanent right-sided hemiparesis still present 4 years after surgery. The fourth patient with large right frontal delayed hemorrhage due to cerebral venous infarction had the entire DBS system implanted but died from aspiration pneumonia 5 months after placement. The clinical outcome for four patients with asymptomatic ICH was more favorable. None of the patients suffered neurological sequel, three had implanted DBS systems at longer follow-up with good clinical outcome, and one patient had no DBS hardware implanted in the ensuing months due to unstable hypertension and previous bleeding in the stereotactic trajectory during DBS lead implantation.

4. Discussion

In this series, we demonstrate the incidence of ICH revealed on intraprocedural stereotactic CT performed after DBS lead placement before implanting further components of the DBS system under general anesthesia. Moreover, intraprocedural stereotactic CT performed after DBS lead insertion allowed to determine the precise location of an implanted lead. With use of commercially available neuronavigation software, the precise location of a DBS lead can be easily determined by merging postoperative CT or MRI images with preoperative MRI images. We repositioned three electrodes during the initial procedure owing to detection of suboptimal location on intraprocedural CT images. All repositioning procedures were performed in three PD patients in whom the target was the left STN. Zrinco et al. also reported a low rate of immediate repositioning due to suboptimal location revealed on intraprocedural MR images. Over the follow-up period, we repositioned six additional DBS leads (two in PD patients, two in patients with primary generalized dystonia, and two in patients with tremor) due to suboptimal clinical response. The additional six DBS leads were replaced due to breakage of the extracranial part of the DBS electrodes.

Moreover, intraprocedural imaging with CT or MRI allows the neurosurgeon to exclude the possibility of the most feared complications of DBS-mainly ICH. The early and timely recognition of ICH in DBS is mandatory for its appropriate management. If bleeding occurs, subsequent surgery is withheld, and the patient is individually managed. The reason for aborting the procedure is that visible bleeding on intraprocedural stereotactic CT or MRI can significantly increase in volume during general anesthesia with possible enlargement of ICH. Our incidence rates of ICH per electrode, per stereotactic procedure, and per patient are comparable to those reported in studies that did not employ microelectrodes for electrophysiological targeting [3,7,9]. Comparable overall hemorrhage rates of 2.4% for electrodes and 3.9% for surgery were reported by Martin et al., who utilized interventional MRI throughout DBS [9]. These patients underwent exclusively image-guided DBS lead placement without microrecording.

Nearly the same overall hemorrhagic rate of 2.4% for electrodes and 3.9% for surgery was reported by Martin et al. who utilized interventional MRI throughout DBS [9]. These patients performed solely image-guided DBS lead placement without microrecording. In the study by Zrinzo et al. including 417 electrodes implanted in 214 patients during 230 consecutive procedures, the total incidence of overall ICH was the lowest at 0.9% [3]. In their study, 0.5% of ICHs were asymptomatic and 0.5% were symptomatic without causing permanent neurological deficits. They performed DBS lead placement without microrecording and

with routine MR-guided and -verified lead verification [3]. Conversely, we utilized intraprocedural stereotactic CT with the Leksell frame. Our ICH rate was not very favorable and comparable to that reported by Zrinzo et al. and other authors who did not use microrecording during functional procedures for DBS lead placement [7–9].

Patient's age has been reported as a risk factor for ICH in several studies. Our results confirmed this observation, and the mean age of our patients with ICH was significantly higher than of those without ICH (69.3 years [range, 81 ± 61 years] vs. 58.9 years [range, 12 ± 79 years]). A multicenter study by Voges et al. involving 1183 patients indicated that even age of > 60 years was a risk factor for ICH [14]. There were two deaths in our series related to ICH in patients whose ages at the time of surgery were 81 and 72 years, respectively. The same observation was noted by Ory-Magne et al., who examined the effect of age on outcome of STN DBS in PD patients [15]. They reported a high bleeding rate of 8.9% and mortality rate of 4.4% among 45 PD patients, and the strongest determinant of ICH was the patient's age [15]. On the contrary, other authors did not find significant correlations between ICH and age [4,16].

The presence of preoperative hypertension was a significant risk factor for developing ICH [4,13,16–19]. Among our eight patients, seven had hypertension and were on hypotensive drugs. All four patients in our study with symptomatic ICH had hypertension preoperatively. Almost all previous studies have postulated that hypertension is a risk factor for ICH [16–19]. In the largest series of 644 patients who underwent lesioning or DBS, Xiawou et al. found that in hypertensive patients, the risk of ICH is 2.5-fold higher than in normotensive patients [20]. In our series, only one patient with small subcortically located ICH had no history of hypertension or antiplatelet therapy.

Some authors found that the diagnosis of underlying movement disorders can have an impact on the rate of postoperative ICH [6]. Sansur et al. suggested that PD diagnosis is associated with increased ICH rate [6]. A similar observation was made by Ellias et al., who reported that patients with PD experienced a three times higher incidence of ICH than patients with ET or dystonia [4]. Our results are in agreement with these results. Seven patients in our series had advanced PD. The oldest patient in our series, who unfortunately passed away, was an 81-year-old woman who suffered from ET. We suggest that it is not the diagnosis per se but rather the patient's age at operation along with concomitant diseases, such as hypertension, heart disease, and diabetic microvascular changes, that contribute to a higher rate of ICH. Moreover, longstanding hypertension induces changes in brain vessels, causing hypertensive encephalopathy, which may contribute to higher ICH rates among elderly patients. This observation is supported by the fact that none of the dystonic patients in our series developed ICH. The mean age of the patients at the time of surgery in the dystonia group was the lowest in this study. Another factor that must be taken into account is that dystonic patients were operated under general anesthesia unlike the PD or ET patients. General anesthesia reduces stress, discomfort, and operative time during DBS surgery, which may also affect the rate of ICH development. The abovementioned factors such as the patient's age, visible MRI changes in the brain white matter, and the type of anesthesia (general versus local) during DBS lead placement may contribute to ICH development. Further studies are required to provide more definitive evidence in this respect.

Another important issue that may play a major role in the development of ICH is careful trajectory planning. We tried to approach all stereotactic targets while avoiding the ventricles and sulcal structures as well as cortical veins. Interestingly, we found immediate ICH only when implanting DBS leads in the STN (five surgeries) or posterior subthalamic area (one surgery). On the other hand, delayed venous infarction affected only PD patients when targeting the GPi. We postulate that the stereotactic target (STN or GPi) itself has no impact on ICH rate, but the location of the entry point has. The exact location of the entry point depends on the preselected stereotactic target. The entry points for STN targeting are usually placed 1.5–1.0-cm anterior to the coronal suture and 3.5–5-cm lateral to the midline depending on the thickness of the lateral ventricles. The entry points for GPi targeting are located more posteriorly, usually at the coronal suture or even 0.5–1.0-cm behind it and 3.5–4.0-cm from the midline. The trajectory for GPi targeting was more perpendicular than for STN targeting. In both targets, usually the trajectory from the entry point to the stereotactic target passed through the middle frontal gyrus. Placing the entry points more posteriorly and medially may damage the cortical veins and cause delayed ischemic venous infarction such as in our two patients with advanced PD who were targeted in GPi. Other authors have suggested that targeting specific nuclei may be associated with a higher risk for ICH, but we speculate that the location of the entry point and careful planning of the stereotactic trajectory while avoiding the sulci and ventricles are the primary contributors to reducing hemorrhagic complication rates in DBS surgery [4].

Our study utilized electrode implantations without applying MER with intraprocedural stereotactic CT verification of implanted leads. The use of MER may be associated with an increased risk of ICH as suggested by some authors [3]. Even the authors, who perform DBS lead implantation with intraoperative MRI guidance in anesthetized patients without the use of MER and MER-guided procedures, found that MER-guided procedures had higher rates of both asymptomatic (2.1% vs. 1.3% per electrode) and symptomatic (1.3% vs. 1.1% per electrode) hemorrhages [9]. We cannot compare these results because we used only macrostimulation without MER to guide placement of our DBS leads. Interestingly, we did not find an increased rate of ICH in 10 patients who had more than one brain pass (9 patients had two brain passes with a macroelectrode and 1 patient had three passes with a macroelectrode prior to final DBS lead implantation). None of these patients in our study developed ICH. All ICHs in our series occurred in patients with single brain macroelectrode penetration including a patient with unstable hypertension who developed hemorrhage along the stereotactic trajectory. This observation may suggest that careful trajectory planning has a greater influence on the rate of ICH than other technical issues (such as use of microrecording technique or not). Another factor that makes it difficult to compare different studies is the wide variability in the number of microelectrodes used in each brain hemisphere, which may vary from one to even five microelectrodes per brain hemisphere. We propose that the microrecording technique, and especially the number of microelectrodes or macroelectrodes passages, should be individualized taking into account several factors like hypertension, past antiplatelet therapy, white matter changes on MRI and brain atrophy, and patient's age.

In our opinion, performing a CT or MR verification of an implanted lead is essential in detecting early ICH. Implementing interventional MR techniques may additionally reduce the risk of bleeding and enhance detection of small intracerebral bleedings due to better visibility that is not obscured by artifacts caused by a permanently implanted DBS lead [9]. Interventional MRI obtained throughout the procedure may visualize true intraoperative bleedings during and after guiding cannula withdrawal prior to introducing a permanent DBS lead, which by producing artifact, may obscure detection of small bleedings and could contribute to underreporting of asymptomatic small hemorrhagic complications [7–9]. Because interventional MRI is performed only in few centers worldwide, in our opinion, another factor which obscures the true incidence of the detection of asymptomatic ICH is the lack of scheduled CT or MRI as part of DBS. Wang et al. in one of the largest patients cohorts including 396 patients with 691 leads implanted found 10 patients with symptomatic ICH [12]. The true incidence of asymptomatic ICH rate in this study was unknown due to lack of CT images in asymptomatic patients for reducing the costs. On the contrary, Park et al. performed two postoperative CT examinations, one intraprocedural after lead implantation and the other 1 day after DBS, in 272 patients who underwent 448 DBS lead implantations [5]. The ICH rate was 2.9% per electrode and 4.77% per patient. Interestingly, only 3

(1.1%) patients demonstrated early ICH and 10 (3.7%) exhibited delayed ICH [5]. This useful study shows us how many asymptomatic hemorrhagic complications escape our attention. Among 13 patients, only 1 required craniotomy with hematoma evacuation and the other 12 demonstrated small ICH without permanent disability [5].

In our study, we recognized early ICH in six patients and two with delayed hemorrhagic venous infarctions. We scanned patients only once immediately after DBS lead placement. Theoretically, rescanning patients 2 or 3 days prior to discharge could reveal a higher incidence of asymptomatic ICH rates than reported in this study and in the world literature [3,6,9,14,19,21]. In our opinion, the advantage of performing immediate intraprocedural CT or MR imaging allows recognition and appropriate grading of a hemorrhagic complication as arterial or venous with its proper management.

5. Conclusion

In our study, the overall ICH rate for DBS implantation (as assessed by intraprocedural stereotactic CT) was 2.5% per electrode and 3.6% per patient. Four ICH patients were asymptomatic. The death rate due to ICH in our study was 0.6% per electrode and 0.9% per patient. The predisposing factors for ICH development in our series were the patient's age, hypertension, and history of antiplatelet therapy. In our opinion, intraprocedural stereotactic CT is also a very good method for precise confirmation of the implanted DBS lead, which is mandatory in functional neurosurgery. The image-verified approach in movement disorders neurosurgery confirms the true incidence of symptomatic and asymptomatic ICH rates and their etiology, which allows for appropriate management.

References

[1] P. Larson, Deep brain stimulation for movement disorders, Neurotherapeutics 11 (3) (2014) 465–474, https://doi.org/10.1007/s13311-014-0274-1.

[2] M.I. Hariz, S. Rehncrona, N.P. Quinn, J.D. Speelman, C. Wensing, Multicentre advanced Parkinson's disease deep brain stimulation group. Multicenter study on deep brain stimulation in Parkinson's disease: an independent assessment of reported adverse events at 4 years, Mov. Disord. 23 (3) (2008) 416–421, https://doi.org/10.1002/mds.21888.

[3] L. Zrinzo, T. Foltynie, P. Limousin, M.I. Hariz, Reducing hemorrhagic complications in functional neurosurgery: a large case series and systematic literature review, J. Neurosurg. 116 (1) (2012) 84–94, https://doi.org/10.3171/2011.8.JNS101407.

[4] W.J. Elias, C.A. Sansur, R.C. Frysinger, Sulcal and ventricular trajectories in stereotactic surgery, J. Neurosurg. 110 (2) (2009) 201–207, https://doi.org/10.3171/2008.7.17625.

[5] C.K. Park, N.Y. Jung, M. Kim, J.W. Chang, Analysis of delayed intracerebral hemorrhage associated with deep brain stimulation surgery, World Neurosurg. 104 (2017) 537–544, https://doi.org/10.1016/j.wneu.2017.05.075.

[6] C.A. Sansur, R.C. Frysinger, N. Pouratian, K.M. Fu, M. Bittl, R.J. Oskouian, E.R. Laws, W.J. Elias, Incidence of symptomatic hemorrhage after stereotactic electrode placement, J. Neurosurg. 107 (5) (2007) 998–1000.

[7] J.L. Ostrem, N. Ziman, N.B. Galifianakis, et al., Clinical outcomes using ClearPoint interventional MRI for deep brain stimulation lead placement in Parkinson's disease, J. Neurosurg. 124 (4) (2016) 908–916, https://doi.org/10.3171/2015.4.JNS15173.

[8] S. Chabardes, S. Isnard, A. Castrioto, et al., Surgical implantation of STN-DBS leads using intraoperative MRI guidance: technique, accuracy, and clinical benefit at 1-year follow-up, Acta Neurochir. 157 (4) (2015) 729–737, https://doi.org/10.1007/s00701-015-2361-4.

[9] A.J. Martin, P.A. Starr, J.L. Ostrem, P.S. Larson, Hemorrhage detection and incidence during magnetic resonance-guided deep brain stimulator implantations, Stereotact. Funct. Neurosurg. 95 (5) (2017) 307–314, https://doi.org/10.1159/000479287.

[10] A.J. Hughes, S.E. Daniel, L. Kilford, A.J. Lees, Accuracy of clinical diagnosis of idiopathic Parkinson's disease. A clinico-pathological study of 100 cases, J. Neurol. Neurosurg. Psychiatry 55 (3) (1992) 181–184.

[11] G.L. Defer, H. Widner, R.M. Marié, P. Rémy, M. Levivier, Core assessment program for surgical interventional therapies in Parkinson's disease (CAPSIT-PD), 14 (4) (1999) 572–584.

[12] X. Wang, J. Wang, H. Zhao, N. Li, S. Ge, L. Chen, J. Li, J. Jing, M. Su, Z. Zheng, J. Zhang, G. Gao, X. Wang, Clinical analysis and treatment of symptomatic intracranial hemorrhage after deep brain stimulation surgery, Br. J. Neurosurg. 31 (2) (2017) 217–222, https://doi.org/10.1080/02688697.2016.1244252.

[13] M. Tonge, L. Ackermans, E. Kocabicak, V. van Kranen-Mastenbroek, M. Kuijf, M. Oosterloo, P. Kubben, Y. Temel, A detailed analysis of intracerebral hemorrhages in DBS surgeries, Clin. Neurol. Neurosurg. 139 (12) (2015) 183–187, https://doi.org/10.1016/j.clineuro.2015.10.017.

[14] J. Voges, R. Hilker, K. Bötzel, K.L. Kiening, M. Kloss, A. Kupsch, A. Schnitzler, G.H. Schneider, U. Steude, G. Deuschl, M.O. Pinsker, Thirty days complication rate following surgery performed for deep-brain-stimulation, Mov. Disord. 22 (10) (2017) 1486–1489.

[15] F. Ory-Magne, C. Brefel-Courbon, M. Simonetta-Moreau, et al., Does ageing influence deep brain stimulation outcomes in Parkinson's disease? Mov. Disord. 22 (10) (2007) 1457–1463.

[16] D.K. Binder, G.M. Rau, P.A. Starr, Risk factors for hemorrhage during microelectrode-guided deep brain stimulator implantation for movement disorders, Neurosurgery. 56 (4) (2005) 722–732 (discussion 722-732).

[17] S. Ben-Haim, W.F. Asaad, J.T. Gale, E.N. Eskandar, Risk factors for hemorrhage during microelectrode-guided deep brain stimulation and the introduction of an improved microelectrode design, Neurosurgery. 64 (4) (2009) 754–762 discussion 762–753 https://doi.org/10.1227/01.NEU.0000339173.77240.34.

[18] A. Gorgulho, A.A. De Salles, L. Frighetto, E. Behnke, Incidence of hemorrhage associated with electrophysiological studies performed using macroelectrodes and microelectrodes in functional neurosurgery, J. Neurosurg. 102 (5) (2005) 888–896.

[19] A. Umemura, J.L. Jaggi, H.I. Hurtig, A.D. Siderowf, A. Colcher, M.B. Stern, G.H. Baltuch, Deep brain stimulation for movement disorders: morbidity and mortality in 109 patients, J. Neurosurg. 98 (4) (2003) 779–784.

[20] H. Xiaowu, J. Xiufeng, Z. Xiaoping, H. Bin, W. Laixing, C. Yiqun, et al., Risks of intracranial hemorrhage in patients with Parkinson's disease receiving deep brain stimulation and ablation, Parkinsonism Relat. Disord. 16 (2) (2010) 96–100, https://doi.org/10.1016/j.parkreldis.2009.07.013.

[21] T. Morishita, M.S. Okun, A. Burdick, C.E. Jacobson 4th, K.D. Foote, Cerebral venous infarction: a potentially avoidable complication of deep brain stimulation surgery, Neuromodulation. 16 (5) (2016) 407–413, https://doi.org/10.1111/ner.12052.