OBJECTIVE: Although hemorrhage is a well-known complication of microelectrode-guided deep brain stimulation (DBS) surgery, risk factors for the development of hemorrhage have not been well defined. We analyzed the risk factors for symptomatic and asymptomatic hemorrhage in a large series of DBS implantations into the subthalamic nucleus, ventrolateral thalamus, and internal globus pallidus.

METHODS: All DBS procedures performed by a single surgeon at our institution between June 1998 and May 2004 were included in this study. All patients had postoperative imaging (magnetic resonance imaging or computed tomography) 4 to 24 hours after surgery. Hematomas were noted and scored as symptomatic or asymptomatic. Statistical correlation of factors affecting risk of hematoma formation was performed by use of logistic regression analysis.

RESULTS: The total number of lead implantations was 481. There were 6 symptomatic hematomas and 10 asymptomatic hematomas. Three of the symptomatic hematomas resulted in permanent new neurological deficit. The risk of hematoma (of any type) per lead implantation was 3.3%, whereas the risk of permanent deficit from hematoma was 0.6%. Patients who developed hematomas had a slightly greater number of microelectrode recording penetrations than patients who did not have hematomas, but this difference did not reach statistical significance. There was not a statistically significant relationship between risk of hematoma and patient age or diagnosis. There was a significant effect of brain target ($P = 0.001$), with only 1 hemorrhage detected after thalamic DBS.

CONCLUSION: DBS is generally safe, with only 0.6% of implantations associated with permanent neurological deficit. The incremental risk of successive serial microelectrode penetrations is small.

KEY WORDS: Deep brain stimulation, Globus pallidus, Hemorrhage, Microelectrode recording, Subthalamic nucleus, Thalamus

Deep brain stimulation (DBS) is an increasingly well-established therapeutic option for alleviation of symptoms of a variety of movement disorders, including Parkinson’s disease (8a, 20, 26), essential tremor (17, 23, 36), and generalized dystonia (8, 22, 24, 37). Recently, a number of articles have discussed the risks of this procedure (8a, 20, 33, 35). Although intracranial hemorrhage is the most severe complication of DBS surgery, most studies have not assessed the incidence of asymptomatic hematoma, nor do they clearly distinguish between symptomatic hematomas associated with full recovery versus those associated with permanent neurological deficit. In addition, few studies of DBS complications have systematically analyzed the risk factors for hematoma occurrence. Results of a multicenter trial of DBS for Parkinson’s disease suggested that microelectrode recording (MER) may increase risk of hemorrhage (8a), but this remains to be confirmed.

In this study, we report the incidence of symptomatic and asymptomatic intraoperative and early postoperative hemorrhage in a large series of patients with DBS implanta-
tions into the subthalamic nucleus (STN), ventrolateral (VL) thalamus, and internal globus pallidus (GPI). Symptomatic hematomas are further divided into those that produced permanent neurological deficit and those that did not. We examine the relationship between hematoma formation and number of MER penetrations, patient age, brain target, and diagnosis and compare our results with those of previously published series.

PATIENTS AND METHODS

Patient Characteristics

All DBS procedures performed for movement disorders by a single surgeon (PAS) at our institution between June 1998 and May 2004 were included in this study. In these procedures, 280 patients (203 men and 77 women) underwent implantation of DBS electrodes into the STN, GPI, or VL thalamus. Procedures were performed either as simultaneous bilateral implantation (n = 92), staged bilateral implantation (n = 99), or unilateral implantation (n = 99). Bilateral procedures were counted as two separate lead implantations for the purpose of hemorrhage risk calculations. Patient age ranged from 11 to 85 years (mean ± SD, 58 ± 14 yr).

Surgical Procedure

The Leksell Series G stereotactic frame was applied under local anesthesia and aligned with the midsagittal plane of the brain and the anterior commissure-posterior commissure line (31). Stereotactic magnetic resonance imaging (MRI) was performed to define the anatomic target (STN, GPI, or VL thalamus). Trajectory planning was accomplished with the Stealth FrameLink system (Medtronic Sofamor Danek, Memphis, TN). In the operating room, under monitored anesthesia care/local anesthesia, a 15-mm burr hole was drilled and the dura opened widely for direct cortical visualization.

Microelectrode mapping was then performed in most cases as previously described (31, 32). Multiple microelectrode penetrations were performed serially, not simultaneously. A small number of cases (typically insertion of a new lead near a previously placed, suboptimally positioned lead) were performed without MER. Multiple types of microelectrodes and microelectrode positioning devices were used over the course of this study. Microelectrodes were obtained from three sources: 1) custom-made at Toronto Western Hospital (18); 2) MicroProbe, Inc. (Gaithersburg, MD); and 3) Frederick Haer Co. (FHC) (Brunswick, ME). The micropositioner systems used to advance microelectrodes and DBS electrodes into the brain were: 1) a custom-made system using a Kopf hydraulic microdrive (David Kopf Instruments, Tujunga, CA); 2) an Axon Clinical Micropositioner (Axon Instruments, Foster City, CA); and 3) an FHC Micropositioner. Microelectrode mapping was performed sequentially along multiple parallel trajectories to define the motor territory of the appropriate target nucleus.

After microelectrode mapping, the quadripolar DBS lead (Model 3387; Medtronic, Inc., Minneapolis, MN; intercontact distance, 3 mm center to center) was inserted. Guide tubes for microelectrodes terminated 35 or 40 mm superior to the stereotactic target (depending on the positioning system), and guide tubes for DBS leads terminated 15 mm superior to the target. Test stimulation was performed to document voltage thresholds for adverse effects. The burr hole was sealed with Gelfoam (Upjohn Co., Kalamazoo, MI) and Tisseal fibrin sealant (Baxter Healthcare Corp., Deerfield, IL), and the lead was anchored in place either with methylmethacrylate and a tantalium miniplate (4, 10) or with the Navigus cranial base and cap (Image Guided Neurologics, Melbourne, FL). After lead placement, the stereotactic frame was removed, general anesthesia was induced, and placement of the pulse generator was performed.

Measures taken in the attempt to avoid hemorrhagic complications in all patients included preoperative verification of absence of coagulopathy and maintenance of intraoperative systolic blood pressure <140 mm Hg. Most but not all patients were managed with an arterial line.

Postoperative Imaging and Scoring of Hematomas

All patients underwent postoperative imaging (MRI or computed tomographic [CT] imaging) 4 to 24 hours after surgery. MRI was performed in this postoperative window in all but four patients in our series. CT scanning instead of MRI was performed in three patients who had procedures aborted because of intraoperative neurological deficit and one patient with previous implantation of an MRI-incompatible cardiac pacemaker. A CT scan was obtained in addition to an MRI scan in any patient with a postoperative neurological deficit. All hematomas greater than 0.2 cm³ in volume were noted and logged into a database. Because of lead artifact, we would not have detected a small amount of blood layering along the DBS lead. Hematomas were scored as symptomatic (associated with any new neurological deficit lasting >24 h) or asymptomatic. Follow-up on the symptomatic hematomas was performed for at least 1 year, or until time of death, to assess ultimate neurological outcome. Symptomatic hematomas were scored as those resulting in permanent new neurological deficit if the patient had not recovered by 6 months or had died before 6 months without neurological recovery.

Statistical Analysis

Multinomial logistical regression analysis was used to assess the risk of hemorrhage occurrence by patient age, brain target, number of MER penetrations, and diagnosis. The median number of MER penetrations was compared between patients with and without hemorrhage by Mann-Whitney U test. The median number of MER penetrations by the three targets (STN, GPI, and ventralis intermedius) was compared by Kruskal-Wallis test (nonparametric analysis of variance). The incremental risk of successive MER penetrations was estimated by logistic regression of the number of MER penetrations by hematoma incidence (including 95% confidence
intervals of the estimate). An odds ratio for the odds of having a hematoma with or without MER could not be calculated, because the number of implants performed without MER was very small.

RESULTS

The total number of lead implantations in this series was 481 (269 STN, 129 GPi, and 83 VL thalamus). The numbers of leads for each of the following diagnoses were Parkinson’s disease (n = 344 leads), essential tremor (n = 62), generalized dystonia (n = 50), atypical parkinsonism (n = 16), multiple sclerosis tremor (n = 3), and other cerebellar outflow tremors (n = 6). Ninety-five percent (457 of 481) of the lead implantations were with MER. In the remaining 5% (24 of 481) of implantations, MER was not performed. The total number of MER penetrations was 1153. The number of MER penetrations per lead implantation ranged from 0 to 8 (median, 2; mode, 3). In only nine patients was the DBS lead removed and replaced in the same operation (usually because of low thresholds for stimulation-induced adverse effects). No hematomas occurred in these patients. In 12 patients, a DBS lead was inserted into the same target region as a poorly positioned lead that had been placed in a previous surgery. An asymptomatic subdural hemorrhage (thalamic target) occurred in one of these patients.

Incidence of Hematoma

Sixteen intraoperative or early postoperative hemorrhages were observed. Of these, 6 were symptomatic and 10 were asymptomatic. All hematomas were intraparenchymal except for 1 asymptomatic hematoma that was subdural. Table 1 details the characteristics of the six lead implantations associated with symptomatic hemorrhage. Examples of symptomatic hematomas are shown in Figure 1, together with potential contributory factors in each patient. Symptomatic hemorrhages were accompanied by hemiparesis with diminished level of consciousness (n = 4), arm monoparesis and facial droop (n = 1), or facial droop alone (n = 1). Of the 6 symptomatic hematomas, 3 resulted in permanent neurological deficit.

Location of Hematoma

Of the 10 asymptomatic hematomas, 5 occurred adjacent to the ventricle in or near the caudate nucleus approximately 3 cm from the base of the target. This corresponds to the location of the termination of the MER guide tube. Three were in the globus pallidus externus. One each was in the genu of the internal capsule and in the subdural space.

For symptomatic hematomas, four of six occurred in or near the target nucleus. The other two symptomatic hematomas were hemorrhagic venous infarcts related to interruption of cortical veins. For the symptomatic hemorrhages, we attempted to infer the specific surgical maneuver responsible for the hematoma. In three patients, this was possible. In two of these three patients, neurological deficit occurred during or immediately after microelectrode mapping (Table 1, Patients 3 and 6); in the third, deficit occurred shortly after opening of the dura with interruption of a cortical vein (Table 1, Patient 4). In the other three patients, symptoms were not noted until the immediate postoperative period (Table 1, Patients 1, 2, and 5), preventing a determination of which step during surgery was responsible for the hematoma.

Risk Factor Analysis

Table 2 shows the incidence of hematoma of each type, subdivided by target. The risk of any hematoma (symptomatic or asymptomatic) per lead implantation was 3.3%. The only statistically significant predictor of the risk of hemorrhage (any type) was brain target (P = 0.001), with only one hemorrhage detected after thalamic DBS (1.2%) compared with six hemorrhages in the STN group (2.2%) and nine hemorrhages

<table>
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<th>TABLE 1. Characteristics of six symptomatic hematomas associated with deep brain stimulator lead implantation surgerya</th>
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a MER, microelectrode recording; PD, Parkinson’s disease; STN, subthalamic nucleus; GPi, globus pallidus internus.
in the GPi group (7.0%) (Table 2). There was no statistically significant relationship between risk of hematoma and patient age, number of MER penetrations, or diagnosis.

Of note, the median number of MER penetrations was different by target, with most in the GPi group (median, 3; 25–75% quartiles, 3–3), fewer in the STN group (median, 2; 25–75% quartiles, 1–3), and least in the VL thalamus group (median, 1; 25–75% quartiles, 1–2) (Kruskal-Wallis test, P < 0.001). However, the multivariate analysis showed that surgical target was a significant predictor of hematoma risk independent of the fact that the number of MER penetrations differed by target.

Finally, we analyzed whether the numbers of MER penetrations were different in the patients who developed hemorrhage (Table 3). There was a trend toward a higher number of MER penetrations in patients with hemorrhage (median, 3; 25–75% quartiles, 2–4) compared with those without hemorrhage (median, 2; 25–75% quartiles, 1–3). This trend was not statistically significant (Table 3; P = 0.21, Mann-Whitney U test). We assumed that the lack of significance was related to the size of the data set, rather than a true absence of risk associated with MER, and used regression analysis to estimate mean and 95% confidence limits on the incremental risk of hemorrhage for each additional MER penetration. The estimated increased risk per MER penetration was 1.3 (95% confidence interval, 0.9–1.8).

**Nonhemorrhagic Stroke**

Ischemic stroke was never observed during the surgery or during the postoperative hospitalization. One patient did develop an ischemic capsular infarction 1 week after STN DBS.

**DISCUSSION**

**Risk of MER-guided DBS**

This study evaluated the risk of hematoma formation in DBS surgery in a large series of lead implantations. We found that the risk of any radiographically detectable hematoma, over all targets, was 3.3% per lead implantation. The risk of symptomatic hemorrhage, over all targets, was 1.2%, and the risk of symptomatic hemorrhage resulting in permanent neurological deficit was 0.6%. Patient age, diagnosis, and number of MER penetrations did not show a significant correlation with occurrence of hematoma. Considering all hematomas (asymptomatic as well as symptomatic), brain target had a significant effect on hemorrhage risk: GPi was associated with the highest risk (7.0%), STN was associated with an intermediate risk (2.2%), and VL thalamus had the lowest risk (1.2%). However, when only symptomatic hemorrhages were considered, there was not a statistically significant difference in hemorrhage risk by target.

It is possible that differences in hemorrhage rates between targets reflect differences in their vascular supply. Although both the thalamus and globus pallidus may be irrigated by the anterior choroidal artery, there are differences with respect to the origins of perforating vessels that supply each target. Perforators that supply the thalamus and STN typically arise from the posterior circulation, whereas the globus pallidus is supplied by lenticulostriate vessels arising from the anterior circulation. The perforators in these two territories may differ in their sensitivity to surgical trauma, perhaps related to the greater sensitivity of lenticulostriate vessels to hypertension-induced changes.

The overall low risk of MER-guided DBS found in our study agrees with previous reports. The largest previous series documenting hemorrhagic complications of DBS surgery was published by the DBS Study Group in 2001 (8a). In this 18-center study of 143 patients with advanced Parkinson’s disease with electrodes implanted in either the STN or GPi, intracranial hemorrhage was observed in 7 patients (3 of the 102 patients in the STN group [2.9%] and 4 of the 41 patients in the GPi group [9.8%]). Six of 7 patients had symptomatic hemorrhage associated with neurological deficits, and 4 had persistent dysfunction (8a). Our study concurred in demonstrating a higher frequency of hemorrhage associated with GPi compared with STN DBS. Other DBS series report a similar
low risk of symptomatic hemorrhage (0–4.3% per lead implantation) (5, 6, 9, 19, 20, 27, 30, 33–35).

### Risk of MER-guided DBS Compared with MER-guided Lesioning Surgery

Many previous reports document rates of hemorrhagic complications of lesonal stereotactic surgery (primarily pallidotomy and thalamotomy) between 1 and 8% (2, 9, 13, 15, 16, 35, 38). Recently, three large series have been reported. Higuchi and Iacono (15) reported surgical complications in a retrospective study of 884 pallidotomies in 796 patients over a 7-year period. Routine postoperative MRI was performed. The overall (asymptomatic plus symptomatic) incidence of hemorrhage was 2.1% per procedure, and the incidence of symptomatic hemorrhage was 0.6%. In that study, occurrence of intracranial hemorrhage correlated with MER (occurring in 8.2% [6 of 73] of cases performed by use of MER) and history of chronic hypertension (15). Favre et al. (9) reported a 0.7% incidence of symptomatic hematomata in MER-guided stereotactic lesioning procedures (1 of 137 procedures). In the largest pallidotomy series reported to date, Hua et al. (16) studied 1116 patients undergoing MER-guided radiofrequency pallidotomies at one center and found a 1.5% incidence of symptomatic hemorrhage.

From these studies, the incidence of hemorrhage complicating surgery for movement disorders does not seem to differ greatly for lesioning surgery versus DBS. However, lesioning procedures may carry a higher risk of nonhemorrhagic complications, such as ischemic subcortical infarction (3, 25), and obviously carry a higher risk of inadvertent thermoleisioning of an eloquent structure.

### Risk of MER-guided DBS Compared with Stereotactic Biopsy

Reports from large series of stereotactic biopsies have demonstrated a higher hemorrhage rate, especially with respect to asymptomatic hemorrhage. Bernstein and Parrent (7) in 1994 reported a 4.7% hemorrhage rate in a series of 300 consecutive stereotactic biopsies for intraxial brain lesions. More recently, Sawin et al. (29) reported a 4% hemorrhage rate in 225 consecutive brain biopsies analyzed retrospectively. However, these studies would have missed asymptomatic hemorrhages, because no routine postoperative imaging was performed. To specifically examine the question of silent hemorrhage incidence, Kulkarni et al. (21) obtained postoperative CT scans in 102 patients undergoing stereotactic biopsies and found that 61 (59.8%) of the 102 patients had detectable hemorrhage on the immediate postoperative scan; 6 patients had observable neurological deficit, and in the other 55, it was clinically silent. A study of 500 consecutive patients undergoing stereotactic brain biopsy with immediate postbiopsy intraoperative CT scanning (11) found an 8% hemorrhage risk and a 1.2% risk of neurological deficit.

Thus, available data indicate that stereotactic biopsy carries a higher risk of hemorrhage than DBS procedures and may be associated with a high incidence of asymptomatic hemorrhage. This higher risk could be because a biopsy requires removal of tissue and/or because the tissue may have increased vascularity because of the presence of tumor.

### Does Increasing the Number of MER Penetrations Confer Additional Hemorrhage Risk?

Detailed analyses (1, 14), including one meta-analysis (28), of many series of stereotactic procedures have indicated some
increased risk of MER. In the largest previous DBS-only series, the DBS Study Group reported that the number of MER penetrations differed significantly in those patients with hemorrhage: patients without hemorrhage had a mean of 2.9 ± 1.8 penetrations, compared with 4.1 ± 2.0 among those who had hemorrhage (P < 0.05) (8a). In the present series of 481 lead implantations, there was a nonsignificant trend toward increased number of MER penetrations in those patients who developed hemorrhage compared with those who did not (P = 0.21) (Table 3).

Because almost all of our procedures were performed with MER, we were not able to determine the odds ratio for the chance of hematoma occurrence with or without MER. However, because the number of MER penetrations was highly variable in this series, we used logistical regression to estimate the incremental risk for each additional MER penetration. This incremental risk was 1.3, with a 95% confidence interval of 0.9 to 1.8. The incremental risk for each additional MER penetration was 1.3, with a 95% confidence interval of 0.9 to 1.8. This incremental risk was not statistically significant. Logic dictates that, given a large enough clinical series with a large variability in the number of MER penetrations per patient, increasing instrumention of the brain could be shown to be statistically associated with an increased risk of hematoma. Although we do not believe that increasing numbers of MER penetrations can be performed with impunity, the incremental increase in risk of each additional MER penetration seems to be low.

Recommendations for Avoiding Hemorrhage

For any elective intracranial procedure, it is standard practice to screen patients preoperatively for coagulopathy, uncontrolled hypertension, or recent use of antithrombotic agents and to pay close attention to intraoperative control of blood pressure and meticulous hemostasis. Our experience has suggested some additional steps to further reduce the risk of hemorrhage during MER-guided DBS surgery. 1) Use computer-assisted preoperative trajectory planning with gadolinium-enhanced stereotactic MRI. We recently adopted the use of contrast enhancement for the preoperative MRI, and we believe this might have avoided the two hemorrhagic venous infarctions in this series. 2) Advance or withdraw microelectrodes or other instruments at a rate no greater than 0.5 mm/s. 3) Avoid advancing microelectrodes more than 2 mm below the base of the globus pallidus so as to decrease the risk of damaging blood vessels in the choroidal fissure. 4) Avoid operating on patients with any reversible cause of coughing or sneezing, such as a mild upper respiratory infection or allergy exacerbation.

CONCLUSION

In this series of 481 DBS lead implantations for movement disorders, the incidence of intraoperative and early postoperative hemorrhage after DBS surgery was 3.3% per lead. The incidence of symptomatic hemorrhage was 1.2% per lead, and that of symptomatic hemorrhage with permanent neurological deficit was 0.6% per lead. Our study confirms the general safety of this technique. The incremental risk of each additional microelectrode penetration was too small to reach statistical significance.

REFERENCES


Acknowledgments

This work was supported in part by the Parkinson’s Disease Research, Education, and Care Center at the San Francisco Veterans Affairs Medical Center and in part by a grant from Medtronic, Inc., to the senior author (PAS).

COMMENTS

The use of the physiological localization technique of micro-electrode recording (MER) in deep brain stimulation (DBS) surgery is becoming increasingly common as equipment for this technology evolves and the users are becoming more experienced. The majority of centers performing DBS surgery for Parkinson’s disease, tremor, and dystonia use MER to verify anatomic targeting, because the current imaging has limitations for precise and reproducible visualization of the lateral thalamus, the globus pallidus internus (GPI), and the subthalamic nucleus (STN) and their motor subcomponents.

This is a report from an experienced DBS surgical team. The authors attempt to uncover the relative risk of performing DBS with MER guidance. The risk is defined with relation to DBS implant insertion, providing a logical framework to assess the data. In addition, the hemorrhages are stratified into asymptomatic and symptomatic categories, with a further definition of hemorrhages that led to permanent deficit. This careful organization of the hemorrhage complications is important for determining the clinical risks that a patient faces when undergoing DBS with MER. They report on 237 patients undergoing 406 implants in the STN, ventrolateral (VL) thalamus, and GPI. They report a 3.7% risk of hemorrhage per lead implantation, with six symptomatic and nine asymptomatic hemorrhages. Three symptomatic hematomas resulted in permanent neurologic deficits. The incidence of symptomatic hemorrhage was 1.5% per lead, with a 0.7% risk of permanent neurologic deficit. The authors report additional MER penetrations leading to a 20% relative risk of MER versus non-MER in their series, but this was not statistically significant, and the cohort is small. The authors report that the GPI had the highest risk of hemorrhage, compared with the STN and the VL thalamus, the risk being independent of the number of penetrations and most likely as a result of the vascular structures on the ventral border. However, the low number of patients in each group warrants caution about this conclusion. The authors provide useful recommendations, such as contrast-enhanced imaging, avoiding a path close to the wall of the ventricles, and maintaining strict blood pressure control to decrease bleeding complications.

There has been a great deal of controversy regarding the necessity for MER in DBS surgery for movement disorders, because both MER and non-MER groups are reporting good outcomes, with similar morbidities. The non-MER advocates emphasize factors such as the increasing requirements of time, risks, expense, and expertise for MER. Conversely, the MER supporters highlight the importance of more precise localization and lack of increased morbidity in their experience. This debate will undoubtedly continue until a prospective trial is performed comparing MER and non-MER approaches. Until then, we are left with descriptive reports of outcomes and complications from individual groups and meta-analysis attempts. Future studies need to definitively address the risk of MER with regard to bleeding and infection (presumably a result of increased numbers of penetrations and operating.
room time, respectively), as well as the potential added benefit of MER by improving the accuracy of targeting as assessed with standardized outcome measures. Overall, this study provides further useful information. It seems that additional MER penetrations may have a small increased, but ill-defined, level of risk with regard to hemorrhagic complications, but this needs to be demonstrated more definitively with additional studies.

Brian H. Kopell
Ali R. Rezai
Cleveland, Ohio

The article by Binder et al. deals with the currently debated problem of risk of microelectrode-induced hemorrhage, which is at the basis of the controversy between the pros and cons of microrecording during surgery, on the basis of the increased morbidity, as well as, on the other side, the impact on the improvement of the determination of the best target for MER. From this point of view, this article participates in the establishment of data that could be taken into account in the definition of guidelines.

A large number of patients and procedures, leading to a total number of 406 lead implantations, have been considered in this study over a 5-year period, all surgery having been performed by the same neurosurgeon with a previous large experience of this surgery, which almost takes the learning curve phenomenon out of consideration. This study is therefore homogeneous, except that the different targets (STN, GPi, thalamus) used for the various forms of treatment of Parkinson’s disease were included in the study. The numbers are different for each target, which weakens the conclusion that can be proposed, particularly when the authors consider the lower risk of the thalamic target. This is something generally admitted, although there is no control study or sufficiently statistically sound study to confirm this subjective opinion from the neurosurgeon. This present study does not solve this problem of the difference in morbidity for targets, but it does provide data that participate in the trend.

Another source of heterogeneity is provided by the use of several types of microelectrode, although this might not be the most significant factor to determine the bleeding risk. Another factor of heterogeneity, which is not independent of the target location, was the various diagnoses presented by the patients (parkinsonism, essential tremor, dystonia, etc.), which, in addition to the different targets, may also be accounted for by possible differences in brain tissue fragility or susceptibility to bleeding. In particular, it is currently known that the pallidal area is different on magnetic resonance imaging (MRI) scans from that in other diseases.

Although a calculation between the number of patients and number of cases can be made by the readers, it would have been better to state how many bilateral procedures were performed among the population. It is clear that multiple passes of instruments along the same trajectory were made, because guide tubes for microelectrodes were used, then replaced by guide tubes for DBS leads, terminating at different distances from the target. This introduction, withdrawal, and reintroduction of guide tubes might potentially be responsible for hemorrhage, in addition to the specific risk of using electrodes, and particularly microelectrodes. How could this be taken into account to specifically separate the risk resulting from these gross manipulations and the microrecording itself?

In this article, as in many studies, the opening of the dura in coagulation of the cortex is supposed to diminish the risk of bleeding. This is probably true at the level of the visible surface of the brain, but it does not preclude the risk of hitting vessels that are in a deeper situation, particularly along the frontal sulci. How did the number of passes not increase the risk of hemorrhage? And what do the authors think of the possibility of having subsequent tracks not being separated by the expected distance because of the movement of the micropositioner, because the brain may be moving from one track to another?

This article has a good discussion, and there is an extensive statistical analysis, which is performed with expertise and tries to correlate the observations of bleeding with all available parameters. It seems through this study that there is a need for quantification of hemorrhages for further studies, such as the presence of blood along the track visible on the control MRI scan, which is different from a blood collection itself, which defines a hematoma; and then the estimation of the volume, in which some mistakes have been made in this article, also has to be precisely evaluated in further studies. Although these data do not solve the problem and provide a definite answer and therefore a definite argument with regard to the controversy about MER, the data presented are sound and honestly examined and do participate in the establishment of a data-based discussion on the usefulness of this technical approach.

Alim-Louis Benabid
Grenoble, France

It is difficult to comment on this article. I agree with everything the authors say. This article summarizes a large series of patients and shows that the risk of neurological deficit resulting from hematoma after subcortical placement of DBS systems is low (0.6%). Furthermore, the risk was not significantly increased by the use of microelectrode corroboration of the ideal target site before lead placement.

It is understandable that DBS implantation procedures would have a lower risk of postoperative hemorrhage than would stereotactic biopsy procedures. In the latter, the surgeon is taking a bite (or several bites) out of a tumor that may have its own blood supply. And there is no way to stop tumor bleeding in a closed stereotactic biopsy procedure.

Nonetheless, as the authors point out, there are important principles that must be observed to reduce the risk of postoperative hematoma after stereotactic biopsy or stereotactic functional procedures (lesioning and DBS placement). These include careful management of perioperative and postoperative hypertension, monitoring of coagulation status, and preoper-
ative administration of a suspension of antiplatelet agents for 10 days to 2 weeks before surgery. In addition, it is not a good idea to sacrifice large bridging surface veins under a burr hole without knowing the collateral circulation. As the authors suggest, preoperative enhanced MRI or magnetic resonance venography may be useful as part of the preoperative workup and reduce the risk of postoperative venous infarction.

Patrick J. Kelly  
New York, New York

Binder et al. at the University of California, San Francisco, have provided an excellent review of their hemorrhagic complications during DBS surgery for the treatment of movement disorders. The study includes 280 patients with 481 lead implants and 10,010 MER tracts. The risk of any type of hemorrhage was 3%, the risk of symptomatic hemorrhage was 1.5%, and the risk of permanent deficit from symptomatic hemorrhage was 0.6%. In this retrospective analysis, the only correlation they found with the hemorrhage rate was the target location, and not age, diagnosis, or number of MER penetrations.

The breakdown of symptomatic and asymptomatic hemorrhage is very important, but just as important is the hemorrhage location. All patients underwent imaging immediately after surgery. The two venous infarctions are very interesting and unusual. This complication tends to occur when draining veins are occluded. It can occur with any kind of intracranial procedure and is not specific to stereotactic or functional procedures. That there should be two such rare complications in this study simply reflects the arbitrary nature of complication rates. Most of the time, the vein or a significant branch will be in the dura, and coagulation of the dura results in the occlusion of the draining vein. If the vessel complex is on the surface, it is mandatory to move the entry point and, if necessary, create a new burr hole. The authors’ recommendations of neuronavigation using computer-assisted preoperative trajectory planning with enhanced MRI scans is an excellent suggestion. We do this on all functional stereotactic procedures to avoid putting burr holes over draining veins and plan trajectories that avoid sulci and deep vascular structures (it also will help prevent the penetration of blood vessels while searching for the optic tract). I have had no experience with venous infarction during DBS or lesioning operations for movement disorders.

There were no symptomatic subdural hematomas in this series. Again, this complication is possible with any intracranial procedure. It is most likely the result of a torn bridging vein as the result of CSF loss or penetration of a probe pushing the brain away from the dura. In this regard, special care must be taken when patients have considerable atrophy. We always take the time to open the pia-arachnoid before penetration so as to minimize any depression of the brain and to seal the CSF space with fibrin glue to minimize any leakage. Gentle handling of all probes is essential. Obviously, every effort should be made to avoid coughing, sneezing, or other types of Val-salva maneuvers. I have had two experiences with subdural hematomas, and both occurred away from the operative field.

The other four symptomatic hematomas occurred near the target nucleus. In this regard, I would clearly agree with the authors that careful screening of the patient is necessary to identify and avoid operating in the presence of a coagulopathy. Obviously, consumption of any antiplatelet medication is to be avoided preoperatively. There are an extraordinarily large number of over-the-counter medications that contain aspirin and other compounds that can affect coagulation. In my opinion, uncontrolled hypertension is an absolute contraindication. Hypertension is not common among movement disorder patients, but when present, it needs to be treated aggressively before surgery. I always look carefully at the blood pressure recordings of patients in the office, and if they are high, I repeat them at the conclusion of the office visit. Ideally, the patient is more relaxed by then, and an accurate pressure can be obtained. If the latter measurement is still high, I insist on treatment by the family physician and clearance only after the blood pressure has been controlled for at least several months before surgery. Intraoperative blood pressure control is essential. The authors use a systolic blood pressure of less than 140 mm Hg as their upper limit, whereas I prefer using a mean blood pressure of less than 90 mm Hg as my upper limit. These may only be empirical suggestions, but the dogma is widely believed because of the problems that have occurred when they are ignored.

Because of the small number of symptomatic hemorrhages, the target location is not statistically significant. However, when all hematomas are included, the authors are able to statistically identify the highest hemorrhage rates in the GPi and the least in the VL thalamus. A more logical review would look only at the intracerebral hematomas to determine the relative risk of hemorrhage from each site, because venous infarctions and subdural hemorrhages will occur independently of target location. Nevertheless, it should be pointed out that in their previous report (3), they had no hematomas in the VL thalamus (0%), whereas they have one now (1.2%). Complication rates change continuously. The simple addition of a single hematoma in their next VL thalamus surgery could shatter the apparent differences between the VL thalamus and STN hemorrhage rates, and both would be essentially identical. Although not a randomized or a systematic study, the results from the DBS Study Group (5), in which 18 centers and 143 patients were evaluated regarding placement of DBS leads in either the STN or the GPi, also suggests increased hemorrhages in the GPi (9.8%) compared with the STN (2.9%). There just is not enough power to be certain with Class III data.

The question of whether or not the number of microelectrode passes adds additional risks was raised, and no statistically significant differences were identified between incremental increases in MER penetrations. The incremental risk was 1.3, which is for all types of hemorrhages, and symptomatic hemorrhages should occur at less than half that rate. This is at variance with the findings of the DBS Study Group (5),
but Benabid’s five simultaneous electrode penetrations rarely result in hemorrhages (7). Again, an analysis of only intracerebral hemorrhage would be more logical. It is possible that hemorrhage percentage in the lower number of penetrations is overestimated, because the procedure would be stopped should a hemorrhage be identified intraoperatively. But I disagree with the statement, “Logic dictates that, given a large enough clinical series with a large variability in the number of MER penetrations per patient, increasing instrumentation of the brain could be shown to be statistically associated with an increased risk of hematoma.” Logic is not necessarily on their side. Trends are not assurances that, given larger numbers, statistical significance will occur. Although it is conceivable that increased penetration should result in an increased hemorrhage rate, it is also conceivable that there is a certain propensity to hemorrhage and that it would occur with the first several passes of the MER. Therefore, if it has not occurred by the first several passes, then it might not occur in a few more passes. Although I believe that the former is more probable than the latter, there are no reliable data. Nevertheless, I strongly would agree with the authors that everything should be done to decrease the number MER penetrations. A serious question of whether or not the information gained is really necessary should be asked before each penetration. It would be nice to have a risk/benefit ratio on which to base this decision, but nothing reliable exists at this time.

Unfortunately, as frequently occurs whenever MERs are performed, the question of their value emerges. As the authors indicate, the rates of intracerebral hemorrhage are similar in groups that do and do not use MER for DBS. A difference of 1 to 3% would take huge numbers of randomized patients studied in a standardized manner to define a significant difference. We seem to be able to accept that fact when it comes to studies of antibiotics, but not for microelectrodes. Most of the controversy between MER-guided functional surgical procedures and those that are guided by macrostimulation go back to the pallidotomy literature. There are case reviews that suggest that MER carries an increased rate of hemorrhage (1, 4). These reviews unfortunately compare apples and oranges. Despite the cautionary note that the nature of the data available does not lead to conclusions about the voltage of benefit or adverse effects related to microelectrode or macroelectrode methods, these have been used inappropriately to argue against the use of MER. The worst offender is a “meta-analysis” (8) that is indefensible from a statistical standpoint (2). The problem with these types of analysis is that the same old bad data keep being recycled and the same inappropriate conclusions reached, i.e., “garbage in, garbage out.” It is unfortunate that these neurosurgeons did not involve statisticians to seriously evaluate the data and to point out the obvious flaws in any attempt at an analysis. Both neurologists and clinical trial experts have discussed the lack of reliable clinical data (4, 6, 9). It is pitiful that there are very few properly designed and carefully conducted studies in the surgical treatment of movement disorders. Reviewing the published literature, Stowe et al. (9) found 503 studies of functional stereotactic surgery for Parkinson’s disease that included 10,896 patients, among which there are only seven randomized clinical trials (1.7% of the total number of cases). They concluded that a proper meta-analysis could not be conducted. The relative efficacy and safety of procedures with and without MER cannot be evaluated. No stereotactic approach is 100% on target, and I prefer to establish the target electrophysiologically by moving a 0.125-mm probe rather than a 1.24-mm probe. Regardless of the technique used, we can all agree that mastery of that technique is essential to maximize benefit and minimize complications.

Again, this is a very interesting report. Obviously, far more patients need to be studied and more rigorous analysis needs to be performed before the true relative risk of hemorrhage based on surgical technique, site, etc., can be determined. Although nothing has really been proved conclusively, there is at least the foundation upon which to initiate further pursuit of these important questions and to contemplate how to modify our surgical technique to what appears to be the best and the safest technique available at this time.

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This study evaluated the risk factors of hemorrhage during microelectrode-guided implantation of DBS electrodes for movement disorders. The study included a high number of patients who were treated by a very experienced group. They adopted a series of measures to avoid and to promptly diagnose hemorrhagic complications.

The general risk for the development of hematomas (asymptomatic and symptomatic) across targets was 3.3% per lead implanted. Approximately one-third of hemorrhages were symptomatic, and the risk of permanent neurological
deficits was 0.6% per lead implanted. Using a multivariate analysis, the authors did not observe a significant correlation between the incidence of hemorrhagic complications and the age of the patients, clinical diagnosis, or number of microelectrode penetrations. They found that hematomas were more frequent in the GPi, followed by the STN and then the thalamus.

Hemorrhagic complications are relatively uncommon after stereotactic procedures (1, 2). In fact, the low incidence of these events limits the analysis and interpretation of correlated factors. In our view, one of the most striking findings presented here is that, in experienced hands, there is no clear relation between the number of microelectrode passes and the incidence of hemorrhagic complications. This provides a rebuttal to the critics of MER and provides supporting evidence for using this technique to help in target identification and improve outcomes in functional neurosurgery.

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