Outpatient Stereotactic Brain Biopsies

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Research Article

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Abstract

Background

Outpatient neurosurgery is rising popularity leading to patients' satisfaction and cost-savings. Although several North-American teams have shown the safety of outpatient stereotactic brain biopsies, few data from other countries with different health care systems are available.

Objective

We therefore conducted a feasibility and safety study on the outpatient stereotactic brain biopsies.

Methods

We prospectively examined all the consecutive stereotactic brain biopsies performed in an outpatient setting at our tertiary medical center, between June 2018 and September 2020.

Results

Among the 437 patients who underwent stereotactic brain biopsy during the study period, 40 (9.2%) patients were enrolled for an outpatient management. The sex ratio was 1 and the median age on biopsy day was 55 [41-66] years. The median distance from patients' home to hospital was 17 kms [3-47]. 95% of patients had prebiopsy ASA score of 1 or 2 and mRs equal to 2 or less. The rate of same-day discharge was 100%. No patient experienced post-biopsy symptomatic complication necessitating readmission within the month following the biopsy. One patient (2.5%) resorted to an unplanned consultation. Histological findings obtained from brain biopsy led to a diagnosis in all patients; the most frequently found were neoplastic lesions (77.5%)

Conclusion

Stereotactic brain biopsies can therefore be safely achieved on an outpatient setting in carefully selected patients. This process could be more widely adopted in other neurosurgical centers, without affecting the quality of patient's health care and safety. In this article, we propose management guidelines and pre-biopsy checklist for performing ambulatory stereotactic brain biopsies.

Introduction

Given improved perioperative care and reduced intervention invasiveness as well as increasing budget constraints on health care systems, there is a trend towards shorter hospital stays in all surgical subspecialities. In this context, outpatient surgery is rising popularity as safe surgical modality that leads to patients' satisfaction and cost-savings.

As a minimally invasive and time-efficient procedures, stereotactic brain biopsies were some of the first cranial neurosurgical operations to be achieved on an ambulatory basis. They are commonly performed

interventions, displaying a favorable safety profile, and the frequency and timing of their complications are well-known [11, 13, 14, 19, 29]. Several studies have demonstrated that symptomatic post-biopsy complications occur usually either within 6 hours, or more than 24 hours after the biopsy [4, 15, 29, 30, 32]. These findings have thereby enabled to propose an early hospitalization discharge.

In the late 1990's, the Mark Bernstein's team (Toronto Western Hospital, Toronto, Ontario, Canada) pioneered neurosurgical interventions in an outpatient setting [3]. Some North-American teams have since shown the safety of outpatient stereotactic brain biopsies, with no patients developing complications related to anticipated discharge [2, 5, 12]. Because of substantial socio-economic differences and health care system discrepancies between continents and countries, ambulatory cranial neurosurgery has grown nearly exclusively on the North American continent. Very rare publications about outpatient brain biopsies emerged from European countries [10] or elsewhere [24]. From a French tertiary center organization model, we therefore conducted a feasibility and safety study on the outpatient stereotactic brain biopsies.

Methods

Ethics Statement

The database is registered with the Commission Nationale de l'Informatique et des Libertés. In accordance with the ethical standards of our hospital's institutional review board and French law, written informed consent was not needed for demographic and hospital-outcome data analyses because this observational study did not modify existing diagnostic or therapeutic strategies; however, patients were informed of their inclusion in the study. This work adheres to the World Medical Association Declaration of Helsinki. The manuscript was prepared in accordance with the STrengthening the Reporting of Observational studies in Epidemiology (STROBE) statement.

Patients selection and study variables

We enrolled all adult patients who underwent outpatient stereotactic brain biopsy at our institution between June 2018 and September 2020. The exclusion criteria for ambulatory stereotactic brain biopsy were i) whether the patient has refused an outpatient management, ii) whether the patient was over 80 years, iii) whether the patient had medical comorbidity necessitating more than 4 hours of postoperative observation (e.g. thrombopenia requiring iterative platelet transfusions), iv) whether the patient was living no more than 1 hour away from the hospital (approximately 100 kms – 62 mi) and v) whether the patient was already an inpatient because of a poor neurological status (modified Rankin score ≥ 4).

The following variables were registered and analyzed: demographic, clinical, radiological and biopsy characteristics, duration of the biopsy procedure, duration of the postbiopsy observation in postanesthetic care unit, duration between completion of biopsy and discharge, discharge to home or hospital, unplanned hospital admission or consultation within 30 days after biopsy and biopsy-related complication within 30 days after biopsy.

Preoperative period, surgical methodology and postoperative management

All information and instructions regarding the biopsy day were given to the patient and his caregiver during preoperative consultations conducted by the neurosurgeon and the anesthesiologist. We also delivered to the patients an information form including the relevant information.

All patients had more than 100,000/L platelets, 0.8-1.1 INR and < 1.20 activated partial thromboplastin time the day of biopsy. In addition, oral anticoagulant therapy and anti-platelet agent were suspended at least 5-7 days before the day of biopsy according to the type of medication.

All biopsies were scheduled for the morning allowing for sufficient postoperative observation and discharge before 7.00 PM on the day of biopsy. A povidone iodine shower was performed in the morning of the biopsy at home, and patient was admitted in the early morning in the day surgery unit. The patient had an intravenous line placed by the nurse and was positioned in a Leksell-G stereotactic frame. Tridimensional gadolinium-enhanced and fluid-attenuated inversion recovery sequences were performed on a 1.5 Tesla MR scanner (Signa, General Electric, Boston, MA). Once these images were acquired, the trajectory and depth coordinates were calculated with Framelink (Medtronic, Minneapolis, MN) software. The biopsy path was carefully chosen so as to avoid damaging critical superficial and deep veins and arteries. This route was simultaneously controlled millimeter-by-millimeter in the 3 spatial planes (3D view), and in the perpendicular and parallel oblique views of the needle trajectory. After the MRI, the patient was transported to the operating room. Oxygen goggles, electrodes for electrocardiographic monitoring, pulse oximeter and an automatic blood pressure cuff were placed on the patient. The biopsies were taken under local anesthesia ± intravenous conscious sedation and were obtained under standard aseptic surgical conditions without antibiotic prophylaxis. The stereotactic arc was used to determine the incision site. After making a stab incision, a 3-mm twist-drill hole was made at the previously calculated coordinates. An intracerebral biopsy needle was then introduced through the drill hole and advanced towards the target. The tissues samples, ~1 x 10 mm, were submitted to a senior neuropathologist for smear for immediate confirmation of abnormal tissue and for definitive analysis [21, 22]. At the end of the procedure, the biopsy needle was removed, and the wound closure was made using a single 3/0 absorbable stitch.

The patient was then observed for at least 4 hours in the postanesthetic care unit. Postoperative CT scan was performed 4 hours after the end of biopsy to rule out complications, before transfer to the day surgery unit. A snack and beverages were provided to the patient upon return to the day surgery unit. Patient was discharged if the following clinical discharge criteria (CDC [7]) were satisfactory: 1) stable vital signs, 2) patient is alert and oriented, 3) patient is free of nausea and vomiting, 4) ability to eat and drink and 5) patient has no significant bleeding. Precautionary instructions and warning signs as well as emergency call numbers and hospitalization report were given to the patient and his caregiver on discharge. One of the board-certified neurosurgeons can be contacted by mobile phone 24 hours a day, 7 days a week.

The day after biopsy, the patient was contacted by a specialty trained nurse. If the patient had problems or complaints, he received further supervision. The patient was instructed to shampoo with povidone iodine every other day for one week. Upon the biopsy results were available, the patient consulted the neurosurgeon or neurologist to learn about his diagnosis and plan the adjuvant management.

Classification of complications

Brain biopsy-related complications were defined as related medical event during the month following the intervention. In this study, we divided complications in asymptomatic hemorrhages visible only on postoperative computed-tomography (CT) scan (described as grade 1A complication in a previously published grading severity scale tailored for stereotactic brain biopsy [22, 30]) and symptomatic complications.

Judgement criteria

The study endpoints were: 1) an unplanned hospitalization following brain biopsy, 2) brain biopsy–related complications and 3) an unplanned hospital admission or consultation related to brain biopsy within one month following the biopsy.

Statistics

Continuous variables are expressed as median [25–75th percentile interquartile range] (minimum–maximum); categorical variables are expressed as n (%).

Data Availability Statement

Anonymized data will be shared on request from any qualified investigator.

Results

Patients and biopsy characteristics

During the study period, 437 patients underwent stereotactic brain biopsy at our institution. Among them, 40 (9.2%) patients were enrolled for an outpatient management. The general characteristics of the 40 included patients and their brain biopsies are presented in **Table 1**. Notably, 95% of patients had prebiopsy American society of anesthesiologists (ASA) score of 1 (completely healthy) or 2 (mild systemic disease) and modified Rankin score (mRs) equal to 2 or less (no symptoms, no significant disability or slight disability). This was the first brain biopsy procedure for all patients.

Patients' outcomes

The median duration of postbiopsy observation in the postanesthetic care unit was 260 minutes [240 - 280] (range, 240 – 320 min). The systematic post-biopsy CT-scan performed 4 hours after then end of the procedure revealed an asymptomatic hemorrhage (grade 1A complication) in 11 (27.5%) of patients.

Among these patients, the largest diameter of the hemorrhage measured on CT-scan was 10 mm [7.2 - 12] (range, 3 – 20 mm). There has been no symptomatic complication. Then, the median duration of stay in day surgery unit was 95 minutes [61 - 120] (range, 45 – 180 min). During the post-biopsy observation, the clinical discharge criteria have been reached for all patients enabling discharge to home the day of biopsy. The discharge success rate was thus 100%. Taking into account the patients clinical and radiological characteristics, the intraoperative constatations and the post-biopsy CT-scan findings, corticosteroids have been newly prescribed in 10 (25%) patients, reinforced in 3 (7.5%), maintained in 8 (20%) and withdrawn in 1 (2.5%) while antiepileptic drugs have been introduced in 2 (5%) patients and maintained in 24 (60%).

No patient needed further supervision by a neurosurgeon following the phone discussion with the nurse from the outpatient surgery unit the day after the biopsy procedure. One patient (2.5%) resorted to an unplanned consultation in a peripheral emergency department for headaches six days after the biopsy. A brain CT-scan was carried out and showed no abnormality. The patient was then able to go back home with a prescription of usual pain relievers. No patient was hospitalized within the month following the biopsy for a post-biopsy complication. In addition, there was no biopsy-related symptomatic complication during patients' follow-up.

Histological findings obtained from brain biopsy led to a diagnosis in all patients; the most frequently found were neoplastic lesions (77.5%) (**Table 1**).

Discussion

Our study demonstrates the feasibility and safety of outpatient stereotactic brain biopsies in a French tertiary center, with a 100% discharge rate on the biopsy day and no post-biopsy symptomatic complication necessitating patient readmission.

Timing of post-biopsy complications

The timing of occurrence of post-biopsy complications is the major point in the patient's management since it defines the appropriate moment for his discharge. Literature suggests that most symptomatic complications occur promptly after the biopsy. Several retrospective studies showed that all the neurological complications were observed within 6 hours after the biopsy [12, 16, 36], while for some other authors, symptomatic complication may appear with a delay when related to brain edema or seizure [9, 15]. In a prospective study, Bhardwaj and Bernstein concluded that 4 hours were sufficient observation time to detect a complication or not in the patient [5].

For years, we observed in PACU for 6 hours the patients who had just underwent a stereotactic brain biopsy. In 2018, when we put in place ambulatory biopsies, we reduced post-biopsy observation in PACU to 4 hours both for inpatient and outpatient biopsies. More recently, in a large study including 1,500 consecutive stereotactic brain biopsies, we reported that half of symptomatic complications occur within the first hour following the biopsy and almost three-quarters within the two first hours [30]. Given these

findings, we now recommend a systematic observation for 2 hours in the PACU and CT scanning 2 hours after the end of the biopsy procedure. In this series, 82% of late complications (> 6 hours after the end of the biopsy) occurred after 48 hours when the patients had already returned to their home. Moreover, we found that asymptomatic hemorrhages visible on systematic post-biopsy CT-scan were associated with the occurrence of late symptomatic complications such as brain edema and/or seizure. Thus, for the patients who have an asymptomatic hemorrhage on the 2-hour CT scan, we recommend prescribing corticosteroids and antiepileptic medications in order to preclude these types of delayed complications.

Patient selection and institutional prerequisites for an outpatient management

Patient selection is a crucial step when looking at the feasibility of performing an ambulatory brain biopsy. We summarized in **Table 2** the recommended general inclusion and exclusion criteria required for outpatient surgery as well as those specifically adapted for stereotactic brain biopsies. The biopsy-targeted location is notably not included in these criteria, because, as we discussed above, the timing of post-biopsy complications is not depending on the biopsied lesion location. However, as a structure associated with critical functions, biopsies targeting the brainstem are associated with more neurological complications [27, 29, 30] and could be less easily performed in an outpatient setting. In our study, we performed only one brainstem lesion biopsy in a meticulously selected patient with immediate and long-term favorable outcomes. In definitive, in addition to consider the above-mentioned prespecified criteria, patient's clinical and radiological characteristics as well as his home environment components should be pooled together to decide whether the patient is eligible for an outpatient procedure.

Concerning the institutional prerequisites, the existence of an appropriate structure including a day surgery unit with a dedicated team and clearly established protocols is obviously needed to avoid misunderstanding and errors on the biopsy day. Before performing cranial neurosurgery in an ambulatory setting, it is advised to smooth out the process with less-risky interventions such as peripheral nerve surgeries and spine surgeries.

During the post-biopsy observation period, careful clinical evaluation and judgment is required to determine when a patient can be discharged. The conversion to a hospitalization is done by a simple demand from the patient or recommendation by the neurosurgeon at any point in time, and concerns about 5–10% of patients in previously published studies (**Table 3**, [33]). An effective readmission process must also exist to enhance patients' fast return to the hospital in case of unexpected symptoms.

What proportion of patients may be managed in an outpatient setting?

In our study, almost 10% of patients undergoing stereotactic brain biopsy, were allocated to ambulatory management. In previously published series, this rate ranged from 26 to 62% (**Table 3**) [5, 6, 10, 12, 26]. Several factors can explain these differences in practice between our center and others. First, although our neurosurgical department had extensive experience in ambulatory management for peripheral nerve surgery patients and functional procedures, brain biopsies were the first cranial interventions to be performed in an ambulatory setting. Thus, we applied a drastic selection before enrolling patients in this

pilot study in order to ensure an optimal success rate. Second, as a referral tertiary center, 40% of patients who are operated in our department are living in another region of France making outpatient management impossible. In the same way, many complex cases and/or patients with significant comorbidities that preclude early discharge are referred to our center. Third, some patients did not accept the concept to leave the hospital within the same day [31]. This may be attributed to the anxiety of undergoing neurosurgical intervention, the various reading on the web about their own disease and management [8] and different second medical opinion from an attending physician with a lack of knowledge of recent surgical advances or from another practitioner who does not practice outpatient neurosurgery [18]. So, the patients remain obsessed with the risk of post-biopsy adverse events and often do not accept this process as easily as expected. The fundamental role played by the referring neurosurgeon should therefore be to instill sufficient trust in the patient and their loved ones prior to the biopsy-day. Last, we have had to deal with the reluctance of some of our own surgeons towards the concept of outpatient surgery for cranial neurosurgery.

We are aware that a higher proportion of patients are potentially eligible for day-case biopsy than those who underwent the process during the study period. There are ways to potentially increase this proportion. For example, our DSU closes by 7:00 PM, therefore, to enable 4 hours of post-biopsy observation in PACU plus 2 hours of observation in DSU, the biopsy had to be completed by 1:00 PM. By reducing the duration of observation in PACU by 2 hours as we suggested above, some biopsies could be performed in the early afternoon. The organization of the surgery schedule may also be facilitated by dedicating an operating room to the outpatient interventions performed under local anesthesia. In addition, in order to reassure the most worried patients, the latter could be visited at home by a home care nurse in the evening after the biopsy, as described in the Canadian protocol [5].

It is apparent that more acceptance might be gained in the society as well as in the medical and surgical communities for the day surgery, by educating medical professionals including general practitioners about safety and advances in these fields of surgery and perioperative medicine [10]. Finally, we hypothesize that this ambulatory process could be possible for 40-50% of stereotactic biopsy cases in our institution.

Advantages of the outpatient management

In addition to its well-known psychological advantages for the patient and his family [23, 33], shorter hospital stay limits the risk of hospital-based complications such as thromboembolic events and nosocomial infections [35], especially at the time of the COVID-19 pandemic exposing patients to hospital clusters and therefore to nosocomial contamination [17, 28].

Moreover, outpatient neurosurgery optimizes hospital bed flow and healthcare costs. In a multicentric US study, institutional charges for outpatient brain biopsies were four times lower than for inpatient procedures [2]. A Canadian study showed savings on the order of 800€ ($950) per patient in favor of the ambulatory management [20]. In a public French hospital, there are 35% financial benefits between the cost of outpatient stereotactic biopsy and the cost of spending one night as an inpatient after the biopsy.

The role of patient's education in outpatient neurosurgical procedure

It has been shown that preoperative patient's education increases early discharge rate, which underscores the importance of detailed explanations of potential post-biopsy symptoms of complications and worsening [1]. At discharge, patients often have concerns related to their medications, the warning signs to recognize complications, the measures that need to be taken to prevent them and activities to avoid within days following the biopsy. Besides the surgeon and the anesthesiologist, dedicated nurses play a fundamental role by providing information and education to the patient and their loved ones [25]. Meticulously preparing the patient for its operation and guiding him manage its care postoperatively are of great importance in reducing adverse events and readmission. This role necessitates continuous and iterative explanations and reinforcement for the process to succeed [33]. The ultimate goal of patient's education is to obtain his full adherence to the ambulatory care project.

Medicolegal issues

The outpatient management of stereotactic brain biopsy may increase the risk of litigation, discouraging neurosurgeons from using this approach. The increasing patients' trend to resort to litigation could be prevented by creating awareness concerning the above-mentioned advantages of the outpatient process. However, although the education of the patient and his caregiver is mandatory and valuable, it does not prevent litigation by a patient who experiences a post-biopsy complication that is not managed in time.

During the pre-biopsy consultation, all surgical options should be offered to the patient, allowing him or her to make an informed decision. Patients reluctant to undergo outpatient biopsy should be managed as inpatients, and neurosurgeons awkward with this process should refer patients to a colleague who perform this if the patient wishes to be operated in an outpatient setting.

Limitations

This study, intended to communicate our early experience with outpatient stereotactic brain biopsies, presents some limitations. No attempts were made to assess patient's satisfaction nor to evaluate cost savings related to outpatient management. However, these points have already been covered in previous papers [2, 33]. No limitations exist concerning the evaluation of safety, as all patients were prospectively followed for at least one month following the biopsy.

Applicability of outpatient stereotactic brain biopsy may differ between centers within a country and even more between various health care systems. It seems more appropriate for hospitals that have a high influx of patients and dedicated day surgery unit. Concerns about litigation can also limit the broad adoption of this process. As pointed out by our colleagues from India [34], this issue needs to be addressed by each neurosurgical center on a case-by-case basis.

Conclusion

In this study, we reported same-day discharge for all patients and no readmission. There have been no complications related to early discharge in these 40 patients. Stereotactic brain biopsies can therefore be safely achieved on an outpatient setting in carefully selected patients. Our results altogether with reports from abroad teams suggest many benefits over systematic post-biopsy hospitalization, not only in terms of efficiency and resource saving, but also patient's satisfaction and medical outcome.

We thereby strongly believe that this process could be more widely adopted in France, without affecting the quality of patient's health care and safety. However, our neurosurgical community should keep in mind that early discharge must be a result of good care and satisfactory patient health status, and not a primary endpoint. We do not suggest that performing brain biopsy as an outpatient procedure should represent the standard of care. It is up to the neurosurgeon to define on a case-by-case basis the feasibility of outpatient brain biopsy based on the patient's socio economic and medical environments.

On the basis of our experience and the available literature findings, we propose management guidelines in order to disseminate the outpatient practice to neurosurgical centers performing stereotactic brain biopsies (**Fig. 1** and **Table 2**).

Declarations

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Tables

Table 1. Patient and biopsy characteristics.

Characteristics	Value
General Characteristics	
Age, y	55 [41-66] (21-77)
Males	20 (50%)
Distance from home to hospital, km	17 [3-47] (0.5-103)
Occupational category:	
Worker	23 (57.5%)
Unemployed	3 (7.5%)
Retired	14 (35%)
Treatments before biopsy	
Antiplatelet therapy	2 (5%)
Anticoagulant	0 (0%)
Corticosteroids	13 (32.5%)
Antiepileptics	24 (60%)
Clinical findings before biopsy	
Neurological defect	16 (40%)
Intracranial hypertension	6 (15%)
Seizure	21 (52.5%)
ASA score:	
1	19 (47.5%)
2	19 (47.5%)
3	2 (5%)
Modified Rankin score:	
0	13 (32.5%)
1	15 (37.5%)
2	10 (25%)
3	2 (5%)
MRI findings before biopsy	
Multifocal lesions	21 (52.5%)
Peritumoral edema	19 (47.5%)

Mass effect	9 (22.5%)
Radiological brain herniation	2 (5%)
Hydrocephalus	0 (0%)
Biopsy-targeted lesion characteristics	
Gadolinium enhancement	31 (77.5%)
Left hemisphere	21 (52.5%)
Largest lesion diameter, mm	26 [13-35] (7-75)
Location:	
Temporal lobe	11 (27.5%)
Deep-brain	6 (15%)
Insular lobe	5 (12.5%)
Frontal lobe	4 (10%)
Rolandic region	4 (10%)
Parietal lobe	3 (7.5%)
Corpus callosum	3 (7.5%)
Occipital lobe	2 (5%)
Cerebellum	1 (2.5%)
Brainstem	1 (2.5%)
Depth:	
Cortical	5 (12.5%)
Subcortical	17 (42.5%)
Deep-seated	18 (45%)
Biopsy procedure characteristics	
MRI-guided	40 (100%)
Biopsy procedure duration, min	12 [10-15] (7-20)
Anesthesia type:	
Local anesthesia	16 (40%)
Local anesthesia + intravenous conscious sedation	24 (60%)
General anesthesia	0 (100%)

Biopsy-related histology	
Grade IV glioma	16 (40%)
Grade III glioma	4 (10%)
Grade II glioma	6 (15%)
Grade I glioma	1 (2.5%)
Metastasis	2 (5%)
Lymphoma	2 (5%)
Cerebral vasculitis	4 (10%)
Other autoimmune or inflammatory diseases	3 (7.5%)
Histiocytosis	1 (2.5%)
Tuberculosis	1 (2.5%)

Continuous variables are expressed as median [25–75th percentile interquartile range] (minimum–maximum); categorical variables are expressed as n (%).

ASA, American society of anesthesiologists.

Table 2. Preoperative checklist for patients who may be candidates for ambulatory stereotactic brain biopsy.

Prerequisites related to the institution	Inclusion criteria	Exclusion criteria	Information given to the patient prior to the biopsy
1. Existence of a day surgery unit. 2. Ability to schedule brain biopsies in the morning. 3. Close cooperation between neurosurgeons, anesthesiologists and the day surgery unit nurses. 4. A standardized protocol for stereotactic brain biopsy as day-surgery (see **Fig.1**). 5. Phone call by the ambulatory surgery unit nurse the day after the biopsy.	1. Patient relative proximity to the hospital (one hour of transport or approximately 100 kms – 62 mi). 2. Available adult caregiver for overnight observation.	1. Patient's reluctance for ambulatory management. 2. Medical comorbidity necessitating more than 4 hours of postoperative observation (e.g. hemostasis disorders). 3. Already an inpatient. 4. Poor neurological status (mRs > 3). 5. Uncontrolled seizures. 6. ASA score > 3 7. Age > 80 years.	1. Detailed explanations about stereotactic brain biopsy procedure. 2. Information about the outpatient biopsy process. 3. A thorough description of possible post-biopsy complications (seizure, delayed neurological defect, loss of consciousness) and their early warning signs. 4. Telephone numbers that could be needed after the discharge: day surgery unit, surgeon's secretary, neurosurgery resident on call (available 24/7).

ASA, American society of anesthesiologists; mRs, modified Rankin score.

Table 3. Summary of the articles assessing outpatient stereotactic brain biopsies.

Reference	Institution	Number of patients	Outpatient procedure rate	Successful discharge rate	Symptomatic complications
Kaakaji et al., 2001	Cleveland Clinic, Ohio, USA	71	62%	82%	6%
Bhardwaj and Bernstein, 2002	Toronto Western Hospital, ON, Canada	76	26%	97%	3%
Grundy et al., 2008	Wessex Neurological Centre, Southampton, UK	30	45%	90%	3%
Boulton and Bernstein, 2008	Toronto Western Hospital, ON, Canada	117	49%	93%	5%
Purzner et al., 2011	Toronto Western Hospital, ON, Canada	152	62%	94%	6%
Current study	La Pitié-Salpêtrière Hospital, Paris, France	40	9%	100%	0%