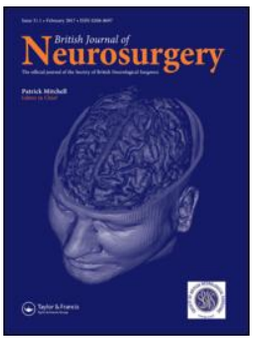

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ORIGINAL ARTICLE

A single-centre study of frame-based stereotactic brain biopsies

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ABSTRACT

Objective: We aimed to evaluate the concordance between the image-based and the tissue-based diagnosis using frame-based stereotactic biopsy.

Materials and methods: Medical records of biopsy procedures from 2000 to 2017 were reviewed. The radiologists' preoperative reports, biopsy procedures and postoperative histopathological diagnoses were retrieved. We compared the preoperative image-based diagnosis with the final histopathological diagnosis.

Results: We identified 125 biopsy procedures performed in 123 patients. The concordance between image-based and histopathological diagnoses varied between 53.3% and 87.5%. The concordance of diagnosis concerning both tumor entity (i.e. cell type) and WHO grade was 54.6%. The diagnostic yield was 95.2%. There was overall morbidity of 10.4%, and a mortality rate of 0.8%. Minor complications occurred in 4.0% of the cases, while clinically significant complications occurred in 6.4% of the cases.

Conclusions: There was suboptimal concordance between radiological and histopathological diagnosis. Also, there was a tendency of histopathological undergrading. We confirm that frame-based stereotactic biopsies have a high diagnostic yield and a low rate of clinically significant complications and mortality.

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KEYWORDS
Frame-based; stereotactic brain biopsy; diagnostic yield; histopathological diagnosis

Introduction

The principal indication for brain biopsy in neuro-oncology is the need for tissue diagnosis in a presumed tumour where resection has been considered inappropriate. A large proportion of these biopsies are performed by stereotactic procedures, either frame-based or the frameless neuro-navigation guided procedures. Earlier reports have shown similar results for both methods regarding diagnostic yield and complication rates.[1–4]

Preceding every biopsy is an examination with magnetic resonance imaging (MRI) or computed tomography (CT). Few studies have examined the matching rate between the image-based and the histopathological diagnosis. One study from 2006 that compared the proposed radiological diagnoses with the histopathological diagnoses in patients with brain tumour, found that concordance varied depending on how the groups were sorted.[5] Since a brain biopsy is an invasive procedure with the potential for serious complications,[6] it is important to know the correlation between the imaging and the histopathological diagnosis.

Materials and methods

Patients, data collection and biopsy procedure

Sahlgrenska University Hospital is a tertiary hospital and the sole provider of neurosurgical services for about 1.8 million people in the western region of Sweden. All patients who had undergone a stereotactic frame-based brain biopsy at Sahlgrenska University Hospital between 2000 and 2017 were eligible for inclusion. Patients were identified through the electronic operating room logs. For cases evaluated in a neuro-oncology Multidisciplinary Team Meeting (MDTM), the MRI and CT scans were reviewed by a specialist in neuroradiology. For these cases, the decision to perform a biopsy was made following the MDTM.

The collected baseline variables were: patient age, gender and comorbidities. From the surgical procedure the date and operating surgeon was noted, the anatomic region and the number of samples taken from it, as well as any in-hospital complications, were recorded. The radiology report was used to register the localisation of the lesion and the suggested radiological diagnosis. From the pathology report, the histopathological diagnosis was retrieved. No re-evaluation of the radiological or histopathological diagnoses was done, so as to reflect information at the time of the clinical decisions.

All stereotactic surgeries were performed by one of two neurosurgeons, and three different stereotactic systems were used (*Laitinen stereotactic frame, Norrlands University Hospital, Umeå, Sweden; CRW stereotactic frame, Integra Life- Sciences, Cincinnati, USA; Leksell's stereotactic system, Elekta Instruments, Stockholm, Sweden*). Contrast-enhanced CT or MRI scans were used for the identification of targets and for the calculations of the stereotactic coordinates. Routine postoperative care was provided but postoperative CT scans were not routinely performed, that is, only performed upon clinical indication (e.g. neurological deterioration).

Analysis procedure

The original radiology reports were reviewed, and the suggested diagnoses from free-text fields were collected. The diagnoses

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Table 1. Specification of the study population.

Specifications	
Age (years ± SD)	50 ± 15.7
Average number of samples taken per biopsy procedure	2
Number of biopsy procedures	125 (in 123 patients)
Male gender	76 (61.8%)

were noted in the given order or according to the given probability of lesion classification, if such was provided. The diagnosis first mentioned in a sequence, or referred to as the most likely diagnosis, was classified as *'first-hand diagnosis'*. Cases were then divided into three categories. Group one contained all the biopsy procedures and the *'first-hand diagnosis'* from the radiologists' statements. Groups two and three consisted of the cases where the radiologists had only stated one diagnosis, those being *'astrocytoma grade 4'* and *'lymphoma'*.

Results

Study population

During the study period, 125 stereotactic frame-based brain biopsies were performed in 123 patients with a mean age of 50 ± 15.7 years (range 6–75 years). Sixty-two percent of the patients were male (see Table 1). From the group of 125 cases, a total of 120 cases were discussed at a team meeting for treatment; 105 at a MDTM devoted to brain tumours and 15 cases at a neurosurgical team meeting. The five remaining cases were lymphomas and did not have a recorded official team meeting discussion in the neurosurgical clinic. The majority of patients spent one or two days in the neurosurgical ward for post-operative care before discharge.

Results from the biopsy procedures

A histopathological diagnosis was achieved in 119 of the 125 biopsy procedures for a diagnostic yield of 95.2%. The diagnoses are presented in Table 2. An average of two biopsy samples was taken during each procedure (range 1–5 biopsies). The most common biopsy indication was *'primary brain tumour'*. From 2013, there was an increase in the percentage of biopsies performed on the primary indication of *'lymphoma'*. A decline in the number of procedures performed with the frame-based technique was seen from 2002 but re-emerged with more frequent use from 2010. The frequency of histopathological diagnoses was, in decreasing order: *'astrocytoma grade 3'*, *'B-cell lymphoma'* and *'astrocytoma grade 4'*.

The overall morbidity rate was 10.4% (13 of 125 cases) and the mortality rate was 0.8% (1 of 125). The single fatality was due to an intracranial haemorrhage that occurred in the operating theatre. The complications are presented in Table 3 and consisted of a transient neurologic deficit in 5.6% of the cases (where two cases were CT-verified swelling of the brain with symptoms of clinically significant dignity); a permanent neurologic deficit in 1.6% of the cases; complications not related to the biopsy in 2.4% of the cases (one case of damage to the teeth from intubation, one case of aspiration pneumonia after intubation and one case of pulmonary embolism).

Table 2. Histopathological diagnoses acquired from the biopsies.

Histopathological diagnosis	*n* (%)
Neoplasms	
Astrocytoma grade 3	30 (24.0)
B-cell lymphoma	22 (17.6)
Astrocytoma grade 4	21 (16.8)
Astrocytoma grade 2	20 (16.0)
Primitive neuroectodermal tumour	4 (3.2)
Anaplastic oligodendroglioma grade 3	3 (2.4)
Dysgerminoma	2 (1.6)
Ganglioglioma grade 1	2 (1.6)
Chronic lymphocytic leukemia	1 (0.8)
Diffuse intrinsic pontine glioma	1 (0.8)
Glioma grade 1	1 (0.8)
Metastasis	1 (0.8)
Oligoastrocytoma	1 (0.8)
Non-neoplasms	
Inflammation	3 (2.4)
Reactive gliosis	2 (1.6)
Infection	1 (0.8)
Progressive multifocal leukoencephalopathy	1 (0.8)
Reactive changes, steroid treated lymphoma	1 (0.8)
Scar tissue	1 (0.8)
Vasculitis	1 (0.8)
Inconclusive	6 (4.8)
Total	125

Table 3. Outcome of biopsy procedures.

Type of complication	*n* (%)
No complication	112 (89.6)
Transient neurologic deficit	7 (5.6)
Other complications[a]	3 (2.4)
Permanent neurologic deficit	2 (1.6)
Death (intracranial haemorrhage)	1 (0.8)
Total	125

[a]Aspiration pneumonia, damage to teeth from the intubation procedure, pulmonary embolism.

Result of the comparison of diagnoses

In the group *'first-hand diagnosis'* the statement from the radiologists matched the histopathological diagnosis, concerning both cell type and grading, in 54.6% (65 of 119) of the cases. In the group where cell or lesion type differed, the correct match was present in the differential diagnoses of the radiologist in 14 of 24 (58.3%) cases. In the group where the radiologists had only provided one single diagnosis in the final statement: *'astrocytoma grade 4'*, a matching diagnosis was found in 53.3% (8 of 15) cases. The radiologists suggested *'lymphoma'* in 8 patients, where 7 of these cases were given the same histopathological diagnosis, thus 87.5% matched (see Table 4).

The group of 119 cases was also analysed for diagnostic mismatches, with particular regard to cases where the discrepancy could have affected the treatment (see Table 5). This cut-off was set to cases where: the cell type differed (44.4%); where lesion type differed (e.g. *abscess* vs. *astrocytoma*) (22.2%); where the lesion was unspecified in the radiologists' statement (16.7%); and also, where the grade of malignancy of the tumour was two or more levels over/under the histopathological diagnosis (16.6%). This resulted in a total of 30.3% (36 of 119) of cases, where the discrepancy might have affected the treatment regimen. As seen in Table 6, the overall mismatch with regard to WHO grade, decreased towards the end of the study period.

Discussion

Due to the design of this study and the nature of the diseases, it was not possible to validate the histopathological diagnosis with

Table 4. Radiologists' diagnosis compared to histopathological diagnosis.

Group	No. of matching cases (%)
First hand diagnosis	65 of 119 (54.6)
Astrocytoma grade 4	8 of 15 (53.3)
Lymphoma	7 of 8 (87.5)

Table 5. Mismatch factor between radiologists' and the pathologists' diagnosis.

Mismatch factor	No. of cases (%)
Different malignant cell type	16 (44.4)
Different type of lesion	8 (22.2)
Unspecified lesion	6 (16.7)
≥2 lower grades of tumour stage[a]	3 (8.3)
≥2 higher grades of tumour stage[a]	3 (8.3)
Total	36

[a]With matching cell-type.

Table 6. Number of cases with grade mismatch between radiologists' and pathologists' diagnosis.

Years	No. of procedures	No. of cases with grade mismatch (%)
2000–2005	59	16 (27.1)
2006–2011	27	5 (18.5)
2012–2017	39	3 (7.7)

tissue from complete resection material. As mentioned in the study by Jackson et al.,[7] the difference between diagnostic yield and diagnostic accuracy needs to be noted. In their study, comparing the biopsy-acquired histopathological diagnosis with that from resection of the entire tumour, a discrepancy was seen in 30 of 80 cases (37.5%). The discrepancy consisted mainly of a grading difference, where resection-based material showed a higher level of malignancy compared to the biopsy material. In the present study, only 1–5 biopsy samples were taken from the lesion in each procedure. Therefore, it is possible that the samples were not representative of the entire lesion. The report by Quick-Weller et al.[8] underlines the importance of taking multiple biopsy samples to allow for the pathologists to perform an examination that results in grading that is representative of the entire lesion.

A similar result was found in this investigation, where several cases were identified in which the histopathological diagnosis was graded one WHO grade below the radiological diagnosis. However, the gap between the matching grade decreased towards the end of the study period, in a gradual manner.

If one grade of tumour stage were added to each of the mismatched cases in the group *'first-hand diagnosis'* the matching rate would increase to 69.7% (83 of 119 cases), and in the *'astrocytoma grade 4'* group, 80% (12 of 15) of the cases would match. The three remaining cases where the diagnosis did not match, had a histological diagnosis of: *'metastasis of adenocarcinoma'*, *'PNET grade 4'* and *'astrocytoma grade 2'*. Thus, the percentage of matching of cases seems to depend on how the groups were divided (i.e. tumour grading and cell type). This pattern was also seen in the article by Julià-Sapé et al.,[5] where sensitivity in some groups decreased with increasing attributes to match: for example, in the group *'astrocytoma high-grade'*, the sensitivity was 42.5% (95% CI 34.0–51.4), but in the group *'glial tumour'* (no grading considered), the sensitivity was 86.7% (95% CI 81.3–90.8). The patients undergoing a brain biopsy is a highly selected population; therefore, this also reflects the relative difficulty in giving a correct radiological diagnosis. Even if the first-mentioned diagnosis in the statements was not a match, the differential diagnoses that followed often included the matching one. There are several noteworthy difficulties in comparing the two modalities. It was not possible to know how certain the radiologists' were of the presented diagnoses, and the two disciplines were not entirely synchronized in the nomenclature of how they classify lesions.

Concerning diagnostic yield, morbidity and mortality, our results are comparable to those presented in earlier biopsy studies with frame-based methods.[1–4,9–12] However, a morbidity rate of 10.4% is in the upper spectrum, as seen in the report by Dammers et al.[13] On the other hand, when accounting only for the clinically significant complications (6.4%) it is indeed comparable to earlier studies.[1,2,9–11] Even though the minor complications that were detected did not affect the patients long-term, or required image-based examinations, it is relevant to know the rate of transient neurologic deficits that occur from the procedure. Such transient deficits are not surprising due to the selection of biopsies in highly eloquent areas or in deep-seated lesions.

The observation that there was an increase in the percentage of biopsies performed on the indication *'lymphoma'* during the study period might be caused by several factors. First, in several places of the world,[14–16] an increase in the incidence of *'primary CNS lymphomas'* has been observed in the past decade. Second, at Sahlgrenska University Hospital, after the publication of articles by Jakola et al. on increased survival of early resection of *'low-grade gliomas'*,[17–19] there has been a shift towards more aggressive treatment with primary surgery of these lesions. Thus, this approach has reduced the need for biopsies in *'low-grade gliomas'* making *'lymphomas'* relatively more common in stereotactic biopsies.

Furthermore, molecular information of brain tumours receives increasing attention and is used in clinical practice, as mentioned in Tsankova et al.[20] The detection of specific mutations of tumours can also aid in the prediction of clinical outcome, and since 2016, it is used for classification purposes.[21] Thus, the importance of acquiring a biopsy sample remains, even though advances in radiology reduce the risk of mismatched diagnoses.

Conclusions and implication

This study shows that preoperative image-based diagnosis differed from the histopathological diagnosis in a clinically relevant number of cases, with matching between 53.3% and 87.5%, depending on the classification and the subgroup analysed. Frame-based stereotactic brain biopsy has a high diagnostic yield and a low rate of clinically significant complications and mortality.

Ethical approval

This study has been approved by the Swedish Ethical Review Authority (Etikprövningsmyndigheten) (2019-04258). Formal consent from the study population was not required.

Disclosure statement

No potential conflict of interest was reported by the author(s).

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