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Increasing the diagnostic yield of stereotactic brain biopsy using intraoperative histological smear

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ABSTRACT

Objective: The negative biopsy rate approaches 5% in the literature. In our institution, this rate was 2.6% (42/1638) over a ten-year period (2007–2016). We aimed to assess the diagnostic yield of intraoperative smear during stereotactic biopsies to reduce this negative biopsy rate.
Patients and methods: We retrospectively analyzed all consecutive MRI-guided frame-based stereotactic biopsies for which an intraoperative histological smear was carried out, performed over 29 months from January 2017 to May 2019 at the Pitié-Salpêtrière University Hospital (Paris, France).
Results: 145 stereotactic biopsies for which an intraoperative histological smear was carried out were performed in 145 adult patients. Mean age at biopsy was 52.4 ± 12.2 years. Histological diagnoses encountered in this series were: primary or secondary cerebral neoplasm (90.3%), inflammatory diseases (4.8%) and infectious diseases (4.8%). All biopsies were contributory to diagnosis. The negative biopsy rate was therefore significantly lower in the patient group for which an intraoperative histological smear was carried out than in our historical control group (0% versus 2.6%, p = 0.04).
Conclusion: Considering the diagnostic yield benefit contributed by the intraoperative histological smear, we advocate for its routine use during brain stereotactic biopsies.

1. Introduction

Brain biopsy is an established method to obtain histopathological diagnosis and guide management for cerebral lesions. Stereotactic biopsy is the most common form of brain biopsies and the least invasive. Although stereotactic biopsy uses 3-D imaging technology, as well as data from MRI scans, the negative biopsy rate approaches 5% in the literature in patients with suspected neoplastic lesions [1,2]. In our institution, this rate was 2.6% (42/1638) over a ten-year period (from January 2007 to December 2016). The aim of this study was to assess if intraoperative smear during stereotactic biopsies would help reduce this negative biopsy rate.

2. Patients and methods

2.1. Patients

We retrospectively analyzed all consecutive MRI-guided frame-based stereotactic biopsies for which an intraoperative histological smear was carried out, performed over 29 months from January 2017 to May 2019 at the Pitié-Salpêtrière University Hospital (Paris, France) by the same surgeon (B.M.).

2.2. Surgical and histological methodologies

The biopsies were taken under local anesthesia with all the patients placed in a Leksell-G stereotactic frame; 3-dimensional, spoiled, gradient-recalled, gadolinium-enhanced MRI and FLAIR sequences were obtained on a 1.5 T MR scanner (Signa, General Electric, Boston, MA) after intravenous injection of gadolinium contrast material. An

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enhanced CT scan was rarely obtained instead of the MRI for technical reasons. Once these images were acquired, the trajectory and depth were planned according to the lesion to be targeted. Stereotactic 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. The entry site was shaved, and biopsy was obtained under standard aseptic surgical conditions without antibiotic prophylaxis. Patients were place in a semi-recumbent position and 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.

We then sent biopsy samples (~1 × 10 mm) to the neuropathology laboratory for an urgent intraoperative smear. A two-millimeter-long piece of a stereotactic fragment is cut and gently put on a slide with forceps. A second slide allows to smear the fragment by pressure. The smear is processed by fixation in ethanol 100° (1 × 1'), washing in water, staining by hemalum (1 × 1'), washing in water, staining by phloxine (1 × 2"), dehydration by alcohol 100° (3 × 30") and xylene (3 × 30") and mounting.

If the histology showed no abnormality, further samples were obtained at different depths along the same trajectory and sent for further smear (Fig. 1A). A second trajectory was rarely performed after obtaining a negative smear especially in cases with multiple brain lesions (Fig. 1B). At the end of the procedure, the biopsy needle was removed, and the wound closure was made using a single 3/0 absorbable stitch.

2.3. Statistical analysis

We statistically compared the negative biopsy rate between our historical patient cohort (2007–2016) and the patient group for which an intraoperative histological smear was carried out (2017–2019), to evaluate the potential benefit of this technique. After applying a correction coefficient, comparison between the groups was assessed using Fisher exact test. $P < 0.05$ defined statistical significance. Analyses were computed with IBM SPSS Statistics v22.0 software (IBM Corp, Armonk, NY).

2.4. Ethical considerations

The database is registered with the "*Commission Nationale de l'Informatique et des Libertés*" (n°. 2214386). In accordance with the ethical standards of our hospital's institutional review board, the Committee for the Protection of Human Subjects, and French law, written informed consent was not needed for demographic, physiological 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.

3. Results

3.1. Patient demographics

One hundred and forty-five MRI-guided frame-based stereotactic biopsies for which an intraoperative histological smear was carried out were performed in 145 adult patients. Mean age at biopsy was 52.4 ± 12.2 years (range, 18.1–89.2). The sex ratio male/female was 1.16. Final histological diagnoses encountered in this study are listed in Table 1.

3.2. Negative biopsy rate

The negative biopsy rate was 0%. In five patients (3.4%), the first intraoperative smear was initially considered as non-diagnostic, thus further biopsies were then performed deeper along the trajectory (Fig. 1A). The second smear resulted in a diagnosis in four out of five patients. The latter experienced a second trajectory targeting another lesion in a context of several intracranial lesions (Fig. 1B). The smear from this further trajectory was ultimately conclusive.

The negative biopsy rate was significantly lower in the patient group for which an intraoperative histological smear was carried out than in our historical control group (0% versus 2.6%, $p = 0.04$).

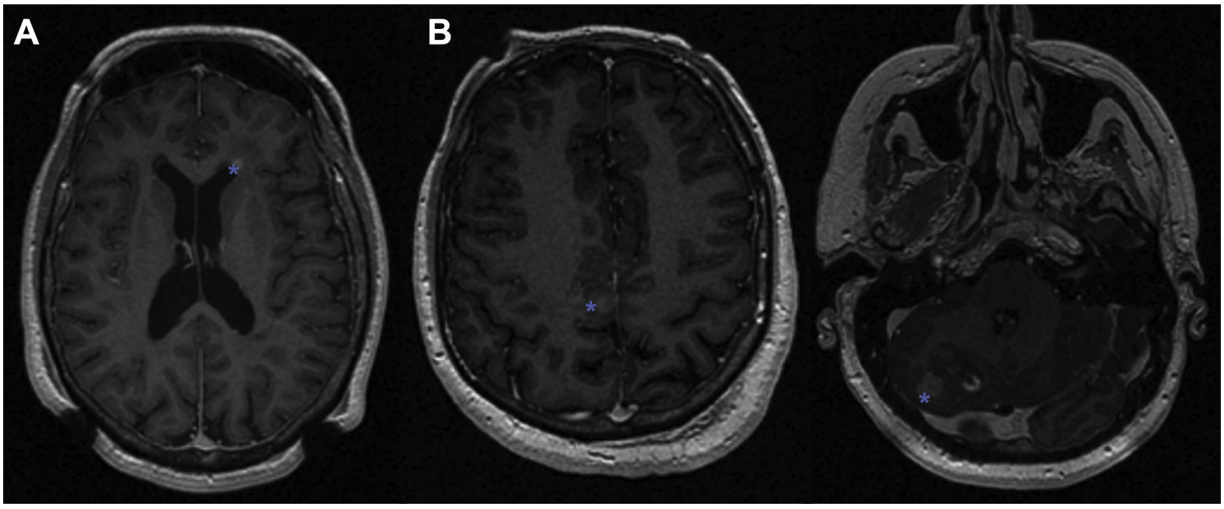

Fig. 1. Examples of two patient cases (stereotactic 3D T1-weighted MRI with gadolinium, axial views) for which was performed an intraoperative histological smear during the stereotactic brain biopsy. A. Stereotactic biopsy targeting a deep left frontal 5mm-lesion in a 60-year old woman. The intraoperative smear was initially considered as negative and then further biopsies were made 2 mm and 4 mm more deeply along the same trajectory and sent for further smear. The latter showed histological abnormalities reflecting the pathological nature of the biopsy. The definitive histological diagnosis showed a granuloma consistent with a neurosarcoidosis. B. Stereotactic biopsy targeting first a right medial parietal 8 mm-lesion (left panel) in a 47-year old man with several intracranial lesions. The intraoperative smears assessing samples from different depths were non-diagnostic. We then performed a second trajectory targeting a right 10 mm cerebellar lesion (right panel). The smear from this further trajectory was ultimately conclusive and definitive histological examination led to diagnose a histiocytosis.
Blue star: targeted lesion.

Table 1
Numbers and final histological diagnoses of stereotactic brain biopsies included in the study (January 2017 to May 2019).

Histological diagnosis	2017	2018	2019	Total
Grade IV glioma	25	29	13	67
Grade III glioma	4	5	2	11
Grade II glioma	3	5	1	9
Grade I glioma	–	1	–	1
Lymphoma	9	16	6	31
Metastasis	2	3	2	7
Anaplastic ganglioglioma	–	–	1	1
Ganglioglioma	1	–	–	1
Dysembryoplastic neuroepithelial tumor	1	–	–	1
Leptomeningeal glioneuronal tumor	–	1	–	1
Cerebral vasculitis	1	2	1	4
Progressive multifocal leukoencephalopathy	1	1	–	2
Sarcoidosis	2	1	–	3
Histiocytosis	–	1	–	1
Tuberculosis	2	2	–	4
Toxoplasmosis	1	–	–	1
Total	52	67	26	145

3.3. Intraoperative data

Excluding frame application, image acquisition and processing, the mean duration of the biopsy was 14 +/− 3 min (11–29 min): 4 min to reach the first target and take the sample for the intraoperative analysis, 9 min to take the definitive samples and for the simultaneous histological consultation, 1 min for wound closure.

4. Discussion

These results and our experience demonstrate the considerable value of intraoperative histological smears on increasing the yield of stereotactic brain biopsy. A previous retrospective study reported that an intraoperative smear reduces the risk of negative biopsy from 11.1% to 3.7% [2]. Therefore, this technique has shown to be very helpful especially for small and/or deep location lesions [3]. This would avoid performing a second biopsy operation at a later, involving patient safety and supplementary costs [4,5]. Moreover, the intraoperative smear takes only a few minutes and does not unduly prolong the procedure. However, the neuropathology laboratory should be located close to the operative room in order to receive the intraoperative sample without delay. To obtain a high level of reliability, skilled and experienced neuropathologists should examine the intraoperative smears.

We performed a smear of stereotactic biopsy without additional frozen section. The method of smear is faster than the frozen section. It uses a smaller amount of tissue than frozen section. So, it allows to spare the amount of tissue for the final histopathological examination and for the molecular analysis. Moreover, the smear allows to examine the thin glial or neuronal cytoplasmic processes and so allows to identify the glial or neuronal phenotype of tumor cells, or the presence of reactive astrocytes or of a fibrillary background. The visualization of thin cytoplasmic processes is enhanced by the intense pink color of the phloxine staining that we use. Smear also shows sharp nuclear details. By contrast, the frozen section does not allow to study the thin glial cytoplasmic processes, and nuclear details are less well observable [6].

5. Conclusion

Considering the diagnostic yield benefit contributed by the intraoperative histological smear, we advocate for its routine use during brain stereotactic biopsies.

Ethical publication statement

We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

Author contributions

B.M. analyzed data, searched the literature and wrote the manuscript. F.B. and K.M. analyzed histological data and revised the manuscript. A.A. supervised the analysis and revised the manuscript. All authors have approved the final version.

Declaration of Competing Interest

On behalf of all authors, the corresponding author states that there is no conflict of interest.

References

[1] W.A. Hall, The safety and efficacy of stereotactic biopsy for intracranial lesions, Cancer 82 (1998) 1749–1755.
[2] L.J. Livermore, R. Ma, S. Bojanic, E.A.C. Pereira, Yield and complications of frame-based and frameless stereotactic brain biopsy—the value of intra-operative histological analysis, Br. J. Neurosurg. 28 (2014) 637–644, https://doi.org/10.3109/02688697.2014.887657.
[3] A. Frati, A. Pichierri, S. Bastianello, A. Raco, A. Santoro, V. Esposito, F. Giangaspero, M. Salvati, Frameless stereotactic cerebral biopsy: our experience in 296 cases, Stereotact. Funct. Neurosurg. 89 (2011) 234–245, https://doi.org/10.1159/000325704.
[4] K. Bekelis, S. Missios, D.W. Roberts, Institutional charges and disparities in outpatient brain biopsies in four US States: the State Ambulatory Database (SASD), J. Neurooncol. 115 (2013) 277–283, https://doi.org/10.1007/s11060-013-1227-y.
[5] A.V. Kulkarni, A. Guha, A. Lozano, M. Bernstein, Incidence of silent hemorrhage and delayed deterioration after stereotactic brain biopsy, J. Neurosurg. 89 (1998) 31–35, https://doi.org/10.3171/jns.1998.89.1.0031.
[6] M.B.S. Lopes, Diagnostic histochemistry in neuropathology, Semin. Diagn. Pathol. 36 (2019) 71–82, https://doi.org/10.1053/j.semdp.2018.10.004.