Visual-Controlled Endoscopic Biopsy of Paraventricular Intraparenchymal Tumors

Joachim Oertel and Dörthe Keiner

OBJECTIVE: **Frame-based stereotaxy represents the gold standard for biopsy of deep-seated lesions. Visual control of possible bleeding in these lesions is not possible. Neuroendoscopic biopsy represents an alternative procedure for tissue sampling in deep-seated intraventricular lesions. The authors present a technique for transventricular-navigated endoscopic biopsy of lesions that are located in the paraventricular region.**

METHODS: **Biopsy of paraventricular pathologies was performed in 6 male and 6 female patients between March 2013 and September 2018. The patient age ranged from 18 to 82 years. All patients underwent a pure endoscopic procedure over a burr hole trepanation supported by frameless navigation of the sedan probe.**

RESULTS: **Histologic diagnoses were established in all biopsies. In all patients, a direct control of the biopsy area was feasible, and hemostasis could be obtained. In 5 patients, endoscopic third ventriculostomy was performed first due to obstructive hydrocephalus. In 1 patient suffering from obstructive hydrocephalus, a pellucidotomy was performed. In 9 cases, the initial postoperative course was uneventful. Three patients suffered from persistent hydrocephalus and had to be treated with ventriculoperitoneal shunt insertion.**

CONCLUSIONS: **Endoscopically conducted biopsies with the aid of navigated tracking of the probe represent a possible additional technique in selected paraventricular intraparenchymal pathologies. The endoscopic approach enables the direct visualization of the intraventricular surface and its vessels. In contrast to standard stereotactic biopsy, direct visual control of hemostasis can be obtained even in paraventricular tumors.**

INTRODUCTION

In the past 25 years, distinguished neuroendoscopic techniques for the treatment of intracranial pathologies have evolved with a constantly enlarged spectrum of indications.[1-4] With refined neuroendoscopic instruments, high-resolution camera systems, and additional neurosurgical armamentarium such as neuronavigation, it is possible to treat even complex cases.[2,3] Combined neuroendoscopic procedures such as tumor biopsy plus endoscopic third ventriculostomy (ETV) are performed frequently.[1,5,6]

So far, biopsy of pathologies is performed in a frame-based or frameless stereotactic technique in the majority of deep-seated intra- and paraventricular tumors. Alternatively, an endoscopic approach can be performed with tissue sampling under direct visual control; and if the tumor mass leads to disturbance of the cerebrospinal circulation resulting in obstructive hydrocephalus, the increased intracranial pressure can be treated with ETV in the same procedure.[6-9]

In general, neuroendoscopic intracranial procedures with frameless neuronavigation enable a free-hand movement of the endoscope—if necessary, with real-time control of the endoscope position and of the trajectory of the approach into the ventricular system.[10] However, whereas the freehand approach and minor position correction of the endoscope within the ventricles is adequate in hydrocephalic ventricles, additional image guidance is important in case of small ventricles, a narrow Foramen of Monro, or in case of a small intra- or paraventricular tumor. In

Key words
- Intraparenchymal tumors
- Neuroendoscopy
- Neuronavigation
- Tumor biopsy

Abbreviations and Acronyms
CNS: Central nervous system
CT: Computed tomography
ETV: Endoscopic third ventriculostomy
FM: Foramen of Monro
MRI: Magnetic resonance imaging
WHO: World Health Organization

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Table 1. Patient Collective and Symptoms

Patient	Age, Years	Sex	Symptoms	Localization of Pathology	Obstructive Hydrocephalus	Combined Procedure	Complications
A.B.	50	F	Double vision	Right thalamus	Yes	ETV, pellucidotomy	No
H.B.	61	F	Transient confusion, decrease of consciousness	Left thalamus	Yes	ETV	No
K.H.	82	M	Confusion, disorientation	Left thalamus	Yes	ETV	No
W.D.	72	M	Confusion, disorientation	Left thalamus, fornix	Yes	Foraminotomy	Fatal pulmonal deterioration
W.S.	81	M	Left hemiparesis	Right thalamus	No	No	No
N.S.	27	M	Headache, vertigo, vomitus, gait disturbance	Left thalamus	Yes	ETV	Persistent hydrocephalus
T.S.	18	M	Headache, vertigo, general seizure	Right thalamus	Yes	ETV	No
A.Z.	64	M	Confusion, disorientation	Bithalamic right > left	No	No	Epileptic seizure
A.L.	74	F	Confusion, disorientation	Dorsal splenium	No	No	No
E.N.	80	F	Confusion, disorientation	Right thalamus, temporal	No	No	No
O.M.	51	F	Confusion, disorientation	Left mesencephalon and thalamus	No	No	No
H.M.	45	M	Gait disturbance Lumbar back pain	Left thalamus	Yes	No	No

F, female; ETV, endoscopic third ventriculostomy; M, male.

a small tumor or if the differentiation between brain tissue and tumor tissue is difficult to distinguish, an endoscopic free-hand biopsy might be less precise than a frame-based technique regarding the histologic yield.

However, in the past years, an increasing number of neurosurgeons have compared the accuracy of frame-based versus frameless approaches to deep structures of the brain with emphasis on deep brain electrode positioning.[11] Although frameless techniques may be more appropriate and cost-effective for the treatment of larger deep-seated structures or pathologies, a variety of studies have shown that the frame-based technique is still associated with superior accuracy.[11-14] However, in frame-based systems, the mobility is restricted due to the quite-bulky stereotactic frame and arc. Another major disadvantage of frame-based stereotactic biopsies is that bleeding at the biopsy site cannot be noticed and treated appropriately. The risk of asymptomatic hemorrhages reaches from 3% up to 10%.[15-17] The incidence of symptomatic intracranial hemorrhages is reported to be from less than 1%, more than 2%, and up to 4.9%.[18-22]

In contrast to the "blind" needle-biopsy with a frame-based (or frameless) stereotactic system, the endoscopic controlled biopsy of intra- and paraventricular tumors allows a good intraoperative hemostasis. However, the grasping forceps used for biopsy harbor a risk of significant bleeding during the biopsy, and at least minimal bleeding is reported frequently by neurosurgeons who perform endoscopic biopsies on a daily basis. Also, intraoperative hemorrhages might occur in various intraventricular endoscopic procedures such as ventriculostomy, ventriculocystostomy, or septostomy.[23,24] In most procedures, these bleedings are minor, short in bleeding time, and do not result in a visual impairment. However, although multiple series of advantages/disadvantages, special indications and special risks in intraventricular endoscopic procedures have been published in the past years, detailed reports about intraoperative hemorrhages in general, their incidence and recommendations for the best surgical management in case of a hemorrhage have been only rarely reported so far.[24]

In the present series, the authors report the surgical findings and management of a pure endoscopic transventricular biopsy in paraventricular tumors passing the intact ependyma using a navigated sedan probe. This stereotactic instrument enables the sampling of tissue that is located in deeper areas of the pathology.

The goal of the present study is to evaluate whether the advantages of a stereotactic needle biopsy used in a frameless stereotactic procedure with its very high diagnostic yield can be combined with the advantage of an immediate bleeding control as it is experienced in an endoscopic approach.

METHODS

Ethical Approval

This article does not contain any studies with human participants performed by any of the authors.

Patient Data

Between March 2013 and September 2018, a pure neuroendoscopic-navigated sedan probe biopsy was performed in 6 male and 6 female patients. The patients' age ranged from 18 to 82 years. Six patients presented with behavioral changes such as disorientation and

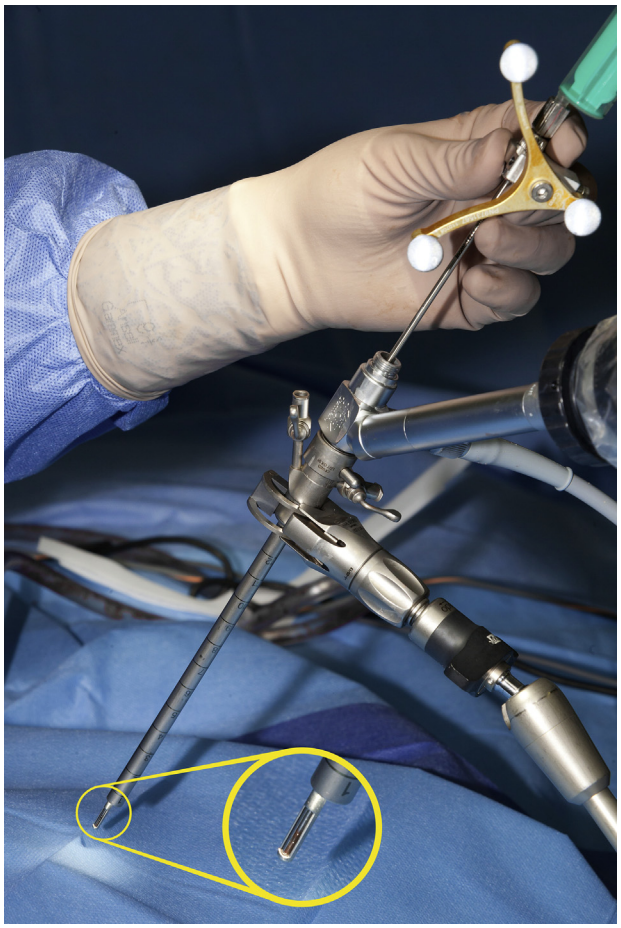

Figure 1. Surgical approach. The trocar of the endoscope is fixed at the endoscope holder in direction of the pathology. After visualization of the biopsy site, the sedan probe can be inserted. For biopsy of the pathologies, a stereotactic sedan probe was used (*yellow marking*).

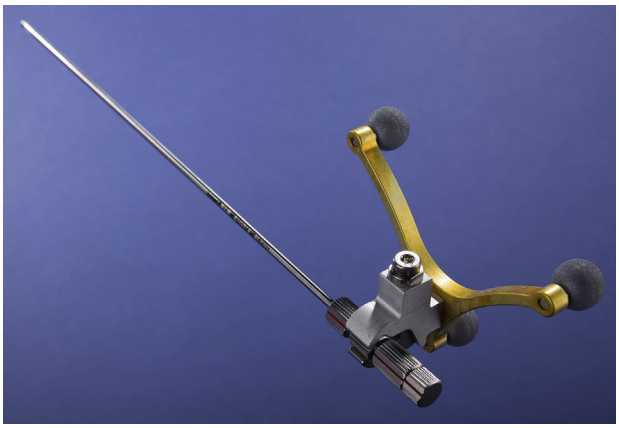

Figure 2. Surgical armamentarium. Shown is the sedan probe connected to the passive tracking system. The system is available in different sizes. For tracking of a fine instrument such as the sedan probe, a small tracker was fixed at the proximal end of the probe. By adjusting the tool to the neuronavigation system, the length of the probe is calculated. Thus, the distal end can be monitored constantly in "real-time" imaging during the procedure.

mental confusion as a major symptom. Other symptoms that lead to a magnetic resonance imaging (MRI) and/or computed tomography (CT) scan of the head were double vision, gait disturbance, dizziness, headache, and hemiparesis (Table 1). Preoperatively, a cranial MRI scan was obtained including a T1-weighted magnetization prepared rapid acquisition gradient echo sequence (repetition time = 1900 milliseconds, echo time = 3.52 milliseconds; field of view = 256 × 256 mm²; slice thickness 1 mm, axial) in all patients. MRI scans were performed with 3.0-T system (MAGNETOM Skyra; Siemens, Erlangen, Germany).

The data of pre- and perioperative clinical courses including postoperative follow-up examination were evaluated retrospectively. In all cases, full video documentation of the endoscopic procedure was obtained. The procedure was performed by four neurosurgeons with experience in neuroendoscopy and in neuronavigation.

Surgical Armamentarium and General Surgical Technique

For endoscopy, the GAAB universal neuroendoscopic system (Karl Storz GmbH & Co., Tuttlingen, Germany) was used. For the needle biopsy, bipolar forceps and a sedan probe synchronized to the passive tracking system were used. In one patient, the SHUNTSCOPE (Karl Storz GmbH & Co.), a miniature 0°-optic with a diameter of 1 mm for positioning intraventricular catheters under direct view, was used additionally. In all patients, the tumor was localized with the help of neuronavigation with the Stealth Station S7 planning station (Medtronic, Minneapolis, Minnesota, USA). For passive navigated tracking of the probe, the Medtronic SureTrak system was fixed at the sedan probe for supplemental representation of the biopsy site (Figures 1 and 2). In addition to a safe approach to the lesion, another goal to use neuronavigation was to get additional visual information for identification of the best biopsy site (i.e., best contrast-agent enhancement, prevention of biopsy in an area of necrosis). Although pathologic alterations can often already be seen at the ependyma wall, the intention was to harvest pathologic tissue located beyond the wall evading direct visualization. In case of obstructive hydrocephalus and intention to perform an ETV, the ETV was done before the biopsy to prevent decreased visibility of the surgical field. All procedures were performed with the patients under general anesthesia. Patients were placed in supine position with Mayfield fixation in 30° anteflexion.

Biopsy Technique

Durotomy, corticotomy, and puncture of the lateral ventricle were performed. Anatomic landmarks of the lateral ventricle were identified, i.e., the foramen of Monro (FM), the fornix, the choroid plexus, the septum, and its veins. The wall of the lateral ventricle was examined for possible alterations of the surface due to the tumor. After inspection including a 0°-diagnostic optic and various angled optics, the working optic was inserted, and the endoscope was fixed with the endoscope holder in direction of the planned biopsy. Under endoscopic view, the biopsy was performed using the

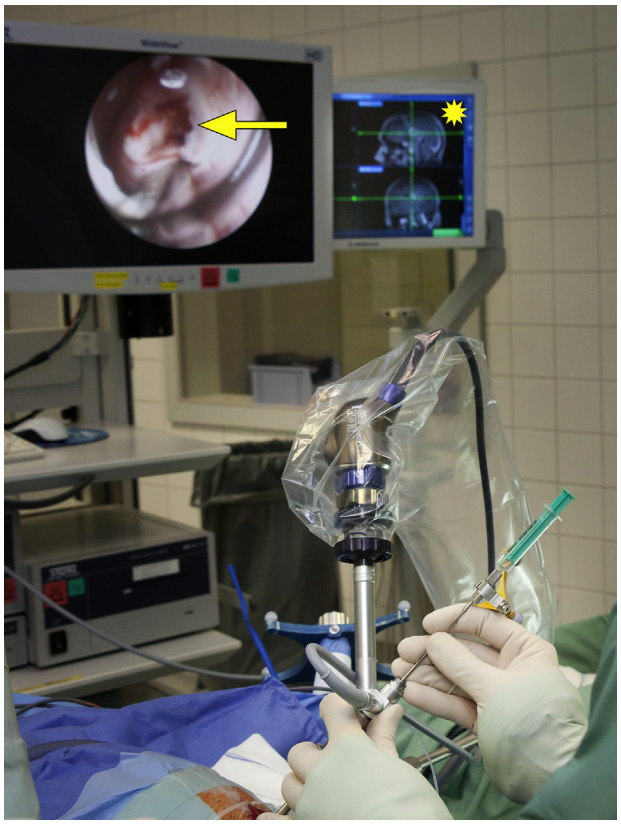

Figure 3. Intraoperative setting of a biopsy. Biopsy in a patient suffering from a high-grade glioma. On the left-sided monitor, the endoscopic camera shows the tumor site (*arrow*). Using the passive navigated tracker, "real-time" display of the probe's position during neuronavigation is possible (*asterisk*).

navigated sedan-probe (Figure 3). Special attention was given to the surface of the ventricle wall and possible bleeding following the biopsy. A final inspection of the ventricle was performed before removing the endoscope.

RESULTS

General Results

In all, no intraoperative complications occurred, nor they were monitored in the video data that were reviewed. The duration of the surgical time was 26–99 minutes with a median time of 62 minutes. A histologic diagnosis was established in every patient. In all procedures, a direct control of the biopsy area was feasible, and hemostasis could be obtained. In 5 surgical procedures, ETV was performed due to obstructive hydrocephalus. One female patient suffered from an isolated left ventricle that was treated with pellucidotomy. In another male patient, an isolated left ventricle was treated with foraminotomy. In 9 patients, the postoperative course was uneventful. Two male patients and 1 female patient with a large tumor mass and tumor growth into the third ventricle suffered from hydrocephalus and were treated with external ventricular drainage. In these patients, a safe ETV and/or pellucidotomy via the same surgical approach was technically not possible due to the large tumor mass. The final histologic results revealed an anaplastic oligoastrocytoma and 2 midline gliomas (World Health Organization [WHO] IV°) respectively. The anaplastic oligoastrocytoma was eventually treated with microsurgical gross total tumor resection. After tumor resection, the hydrocephalus remained and had to be treated with ventriculoperitoneal shunt insertion. Both patients diagnosed with a midline glioma (WHO IV°) had to be treated with a ventriculoperitoneal shunt system due to development of a hydrocephalus before starting radiochemotherapy.

Histologically, high-grade gliomas (5× glioblastoma multiforme including the 2 midline gliomas, 1× anaplastic oligoastrocytoma) were diagnosed in 6 patients. In 1 patient, the histology revealed an astrocytoma WHO II°. In another patient, a primary central nervous system (CNS) lymphoma was diagnosed; and in 2 patients a CNS inflammatory disease was diagnosed. A 61-year old female patient was admitted to the authors' Department of Neurosurgery for surgical treatment of a lumbar stenosis. Due to a transient decrease of consciousness during hospitalization, a cranial MRI scan was performed. The scan revealed an obstructive hydrocephalus caused by a large cystic formation located at the left thalamus. Thus, ETV was performed. Biopsy of the cyst tissue did not reveal malignant tissue. The follow-up course was regular so far without any signs of progress of the cystic formation (Table 1).

Surgical Results

In 4 of 6 gliomas and in the CNS lymphoma, the tumor site could be identified for its prominence into the ventricular system intraoperatively (Table 2; Figure 4). ETV could be performed without problems in every procedure using bipolar forceps, Decq forceps, and a double-balloon catheter. No patient had a Liliequist membrane. The tumor biopsy was performed using bipolar forceps before insertion of the navigated sedan probe in 7 procedures (Figures 5A–F and 6). The sedan probe was inserted into the periventricular area up to 1 cm depth. In 3 patients, endoscopic visualization revealed conspicuously rich vascular configuration of the ventricular wall. No technical problems regarding the handling of the instruments occurred. The sedan probe could be used without problems in every procedure.

A direct view of the biopsy area after obtaining the tissue samples was possible in all patients using the 0°- and 30°-optics. Regarding bleeding within the biopsy area, there was only minor bleeding in all patients after tissue sampling and in most procedures, hemostasis could be controlled with irrigation using body warm Ringer's solution (used in all patients, $n = 12$). In 6 procedures, bipolar forceps were used after the biopsy (Figure 7A–F). The average time of irrigation after tissue sampling and before completing the surgery was 3:20 minutes ranging from 20 seconds to 10 minutes. In every procedure, bleeding could be controlled soon and without technical difficulties (Videos 1 and 2).

Postoperative CT scans were performed on the day of surgery, if the patient was transferred from the intermediate care unit to the normal ward of the department a few hours after surgery (4 patients), or

Video

Video available at www.sciencedirect.com

Table 2. Histologic Diagnoses and Anatomical Specificities

Patient	Diagnosis	Localization of Pathology	Imaging Characteristics (MRI)	Contrast Agent Enhancement	Histologic Morphology	Histologic Features
A.B.	Diffuse astrocytoma	Inhomogenic tumor of right thalamus with expansion to mesencephalon	Hyperintense in FLAIR and T2W	++	Diffuse glioma cell infiltration, no hyperplasia, no necrosis	No special features
H.B.	No malignant tissue, no tumor	Cystic formation within left thalamus, crus cerebri and pons with compression of third and fourth ventricle	Cystic formation, regular signals	–	Regular tissue, no pathology	No special features
K.H.	Glioblastoma	Inhomogenic tumor right thalamus, occlusion of aqueduct	hyperintense in FLAIR and T2W	++	Pleomorphic tumor cells with nuclei of variable shape, single giant cells, necrosis	GFAP +, MAP2 +, NF –, Ki67 20%, PHH3 -, p53–, IDH1–
W.D.	Glioblastoma	Inhomogenic tumor of left thalamus with contact to left lateral ventricle, infiltration of third ventricle/FM, expansion to chiasma opticum	Paraventricular signal enhancement in FLAIR and T2W	++	Glioma manifestation of various cell density, pleomorphic tumor cells, hyperplasia of endothelium, necrosis	GFAP +, NF +, MAP2 +, Ki67 5%, PHH3 –, p53 +, IDH 1 +
W.S.	Glioblastoma	Tumor of right thalamus with expansion to right putamen, cystic lesions dorsal/ medial thalamus, prominence into ventricles	Paraventricular signal enhancement in FLAIR and T2W	++	Glioma manifestation of various cell density, pleomorphic tumor cells, hyperplasia of endothelium, necrosis	GFAP (+), NF +, MAP2 +, Ki67 40%, PHH3 –, p53 +, IDH 1 –
N.S.	Anaplastic astrocytoma	Inhomogenic (nodular/cystic) tumor, bilateral thalamus/left > right, compression of mesencephalon and lateral ventricles, third and fourth ventricle, occlusion of aqueduct	Hypo- and hyperintense in T2 and FLAIR	++	Glial tumor of high density, slightly distorted nuclei within myxoid matrix, dense capillary network, no necrosis	GFAP –, MAP2 +, synaptophysin (+), NF (+), EMA –, S-100 +, Ki67 20%, PHH3 (+), IDH1 –, p53 –
T.S.	Glioblastoma	Inhomogenic cystic tumor formation of right thalamus with mesencephalic and tectal compression, occlusion of aqueduct, prominence into ventricles	Hyperintense signal in FLAIR	+	Glioma manifestation of various cell density, pleomorphic tumor cells, hyperplasia of endothelium, nuclear division	GFAP +, MAP2 +, NF ++, Ki67 30%, PHH3 ++, p53 –, IDH1 –
A.Z.	Encephalitis	Bithalamic neoplastic formation right > left side, contact to third ventricle on left side. Second neoplastic formation located in brainstem	Hyperintense signal in FLAIR	+++	Brain parenchyma with edema, loosened tissue, single neurons, single cell with lipofuscinosis	GFAP +, MAP2 +, synaptophysin +, NF ++, Ki67 –, PHH3 –, p53 –, IDH1 –
A.L.	Encephalitis	Corpus callosum edema left > right side, cellular proliferation (DWI) paraventricular posterior horn	Diffuse signal enhancement in FLAIR, corpus callosum edema left > right	+	Strongly altered dysplastic neurons with completely distorted nuclei; low proliferation rate, single mitoses in Neun + giant cells, reactive gliosis	GFAP +(reactive gliosis), synaptophysin +, CD34 +, IDH1 –, ATRX +, Ki67 3%, p53 2%–3%, NeuN: single giant cells, p62 –, CD 3 (–), CD 8: sporadic

E.N.	CNS lymphoma	Paraventricular tumor with involvement of right thalamus and crus posterior of internal capsula. Intraventricular growth into posterior horn of right lateral ventricle	Homogenic tumor formation T1 MPRAGE	+++	Soft glial tissue with infiltration of small and blue pleomorphic tumor cells, chromatin inhomogenic, and dense	CD3 (+), CD8 ++, CD20 +++, PAX5 +++, CD138 −, Ki67 80%, EBV −
O.M.	Glioblastoma	Ventral mesencephalic tumor from mammillary body to interthalamic adhesion without infiltration, involvement of pons, thalamus bilaterally, beginning involvement of left basal ganglia, occlusion of aqueduct	Slightly inhomogenic T1 MPRAGE, hyperintensitiy in SPACE	−	Dense and uniform tumor cells, perivascular radiating structure, no noticeably mitotic activity	GFAP +, vimentin +, ATRX +, IDH1 −, p53 < 1%, H3K27M +, Ki67 5%−10%, Synapto −
H.M.	Glioblastoma	Left thalamus with caudal expansion to diencephalon and opposite side, occlusion of left FM and aqueduct	Hyperintensity in FLAIR	−	Dense and pleomorphic glial cells, necrosis, capillary proliferation	GFAP +, vimentin +, IDH1 −, H3K27M +, ATRX +, p53 −, NF: axons, Olig2 (+), Ki67 5% −7%, PHH3 −

MRI, magnetic resonance imaging; FLAIR, fluid-attenuated inversion recovery; T2W, T2-weighed; FM, foramen of Monro; DWI, diffusion-weighted imaging; NeuN, neural nuclei antibody; CNS, central nervous system; MPRAGE, magnetization prepared rapid acquisition gradient echo; EBV, Epstein–Barr virus; SPACE, Sampling Perfection with Application optimized Contrasts using different flip angle Evolution.

on the first postoperative day (8 patients). No radiologic signs of postoperative bleeding at the biopsy site were seen. In 3 patients, minimal hemorrhage within the trajectory of the neuroendoscopic approach without space occupying effect was observed.

Peculiarities

In a 73-year-old male patient, who was diagnosed with a large left-sided paraventricular tumor leading to an isolated ventricle, ventriculoscopy revealed a complete blocking of the left FM. Furthermore, after pellucidotomy and right-sided ventriculoscopy, a stenosis of the right FM was seen. Thus, a catheter was placed through the foraminotomy into the right foramen with the aid of the SHUNTSCOPE (Karl Storz SE & Co.).[25] The catheter was connected to a burr hole-reservoir for possible connection to a shunt system in case of obstructive hydrocephalus due to bilateral occlusion of the FM. The patient, who suffered from mitral valve insufficiency and aortic insufficiency as well, died in the latter clinical course due to worsening of the pulmonary function.

A 27-year-old male patient was admitted to the authors' department with acute signs of increased intracranial pressure, including headache, vomitus, vertigo, and gait disturbance. MRI scan showed a large intraparenchymal tumor located in the left thalamus with prominence into the third ventricle. After ETV and tumor biopsy, remaining signs of hydrocephalus required an extraventricular drainage. Histologically, an anaplastic astrocytoma was diagnosed, and the patient underwent gross total tumor resection followed by concomitant radiation and chemotherapy. In the follow-up, the patient had to be treated with ventriculoperitoneal shunting due to persistent symptoms of increased intracranial pressure.

DISCUSSION

In the past, increasing experience of combined intracranial neuroendoscopic procedures was achieved by an increasing number of neurosurgeons. The availability of refined neuroendoscopic instruments, refined camera systems, as well as additional neurosurgical armamentarium leads to the possibility of treating even complex cases with combined neuroendoscopic procedures.[26,27] Using neuronavigation, a complex intraventricular anatomy is not an exclusion criterion anymore per se, but a distinct preoperative planning with high-quality MRI as well as an experienced surgeon is required in these cases.

Several authors have reported their experience of neuroendoscopic biopsy in case of deep-seated tumors.[28-31] However, larger series of endoscopic biopsies in intraparenchymal tumors or even prospective-randomized controlled trials have not been conducted so far. Knaus et al.[29] published a series of 15 intraventricular endoscopic-navigated tumor biopsies. In this series, tumor biopsy was performed using microforceps for tissue sampling at the tumor surface. They stated that the optimal entry point, computer-assisted planning and a navigated endoscopic procedure are feasible for paraventricular tumor biopsy with similar results regarding histologic yield and risks/complications.

In the present series, the navigated sedan probe allowed a transventricular approach for intraparenchymal tissue sampling. In contrast to the series of Knaus et al., the technique is not limited for tissue sampling at the surface of the pathology,

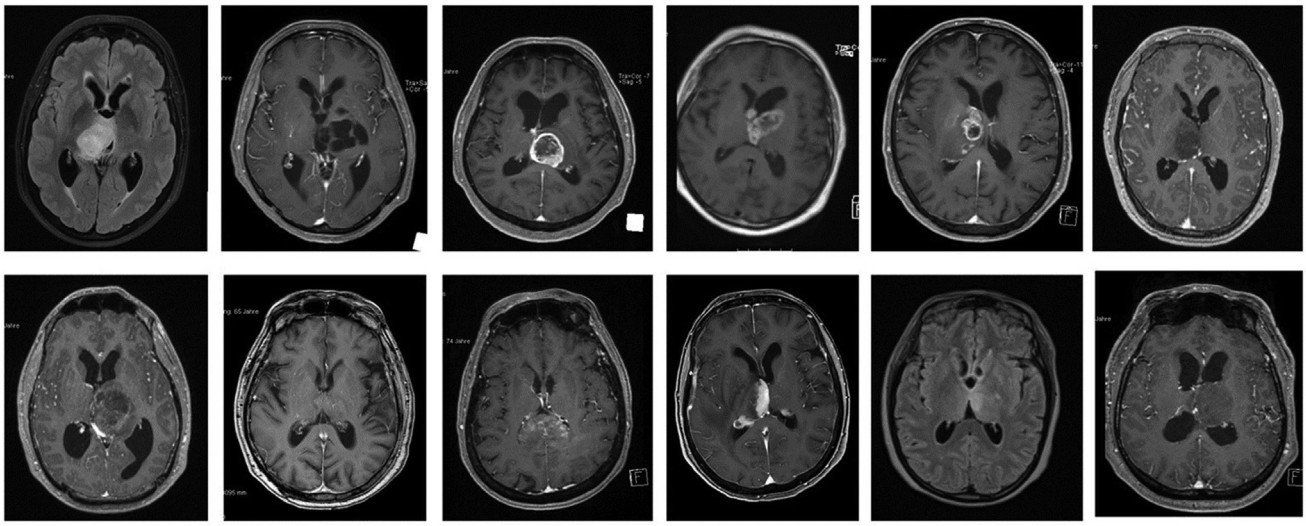

Figure 4. Overview of patients' preoperative T1-weighted axial magnetic resonance images with contrast medium. In 4 of 6 gliomas and in the central nervous system lymphoma, the tumor was protruding into the ventricle.

because the probe can be inserted into deeper regions of the pathology similar to a stereotactic procedure, but under direct visual control.

In 2013, Nagahisa et al.[30] published a series of 21 patients who were treated endoscopically for intraparenchymal tumors. They approached the lesion by using a pure intraparenchymal trajectory without relation to the intraventricular system. In this series, a transparent rigid scope was used in combination with a navigation system. They concluded that using the transparent scope has advantages in terms of direct observation of the lesion site and confirmation of hemostasis. However, in contrast to commonly performed intraventricular procedures, with this technique a combined procedure, as may be required in the treatment of obstructive hydrocephalus, is not possible.

However, regarding hemorrhage control and hemostasis, a main advantage of neuroendoscopic biopsies is the possibility of a direct visualization and bleeding control. In the majority of cases, only minor bleeding without vision impairment and short bleeding time after irrigation occurs.[24] Irrigation does not only stop bleeding but enables an optimal visualization of the biopsy site's vessels. This enables meticulous hemostasis with bipolar forceps or balloons, if necessary. In the present study, minor bleeding occurred in 8 of 10 procedures. In 3 patients, irrigation was performed for more than 3 minutes. Bipolar forceps were used in one half of the patients—even, if only minor bleeding occurred. No special hemorrhage-related complications were observed and no signs of hemorrhage at the biopsy site were observed on the postoperative CT scans.

Nevertheless, due to the possibility of highly vascularized ependymal walls at the planned intraventricular "entry point" for access of paraventricular lesions, there might be an increased risk of severe hemorrhage caused by iatrogenic injury of ependymal vessels. Whereas several publications have addressed the general problem of perioperative bleeding caused by endoscopic, stereotactic, or open biopsy of deep-seated lesions, the proportion of hemorrhage caused by iatrogenic injury of highly vascularized ependymal walls is not known. Regarding stereotactic (frameless or frame-based) biopsies, surprisingly only few publications have addressed the risk of perioperative hemorrhage, with special emphasis on lesion located next to the ventricles/basal ganglia. In most publications, the incidence of perioperative hemorrhage was evaluated for all included cases (i.e., lobar, deep-seated, cerebellar) of the presented series.

In general, over the past years symptomatic hemorrhage was found to occur in 3.6%—4.8% of stereotactic procedures.[32-34] In a retrospective analysis by Sato et al.[33] published in 2018, a total of 125 consecutive stereotactic biopsies including 55 deep-seated pathologic lesions was analyzed. Twenty-four of these lesions were in the basal ganglia. In this cohort, the incidence of postoperative hemorrhage and postoperative symptomatic hemorrhage was significantly greater ($P = 0.006$) in biopsies that were performed in the basal ganglia compared with other locations such as lobar lesions or "deep-seated lesions other than basal ganglia." The authors concluded that—due to the perforating arteries—deep-seated lesions including basal ganglia tumors have statistically high risks of biopsy-related mortality/morbidity and suggested using a target-planning method with 3-dimensional 3-T time of flight MRI.

In another series, 12 patients with small deep-seated brain tumors having image-guided stereotactic biopsy with the aid of depth microrecording for analyzation of the electrical activities along the trajectory were evaluated retrospectively. However, for concentrating on the exact location of deep-seated and small lesions with support on microrecording, no detailed information was given regarding complication rate.[35] In all, intraparenchymal hemorrhage is still the most frequent complication associated

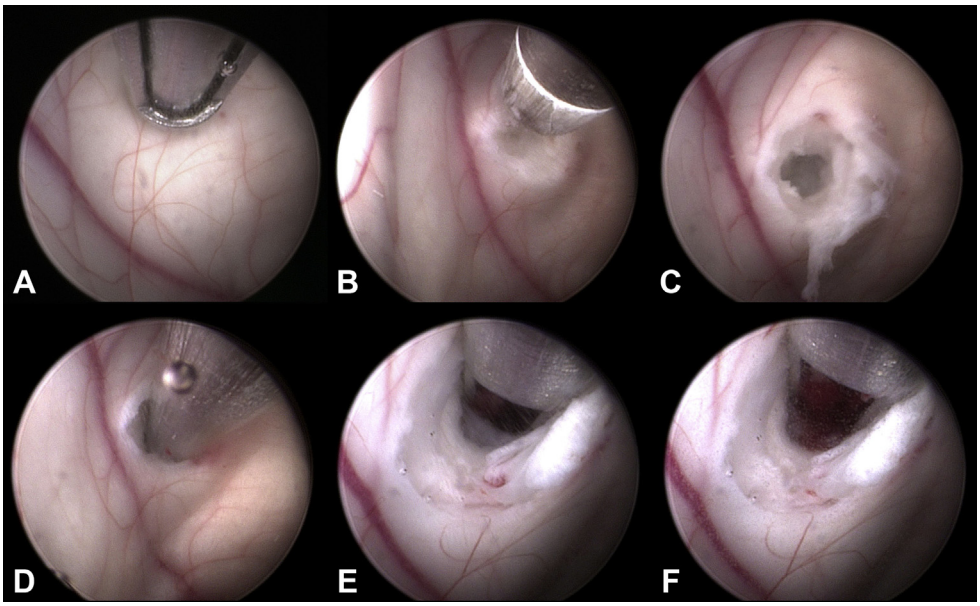

Figure 5. Neuroendoscopic view example 1. Tumor biopsy in a patient suffering from a glioblastoma located at the left thalamus. After identification of the ideal area for insertion of the probe (**A**), thermocoagulation with bipolar forceps is performed (**B**, **C**). After that, the sedan probe is inserted again (**D**) and several tissue samples are obtained (**E**, **F**).

with stereotactic needle biopsy. In comparison with that, in recent studies of different centers intraoperative hemorrhage as a complication of neuroendoscopic procedures was reported to occur in about 3% of procedures.[24]

Besides the benefit of direct visualization of the biopsy site, neuroendoscopic approaches might have additional advantages compared with stereotactic transcortical biopsies. Frameless and frame-based stereotactic procedures are based on the pre- and intraoperative CT and/or MRI. The entry point and target point usually are planned before surgery based on these images. With the aid of modern software systems, meticulous planning of the stereotactic trajectory to reach even smallest pathologies is

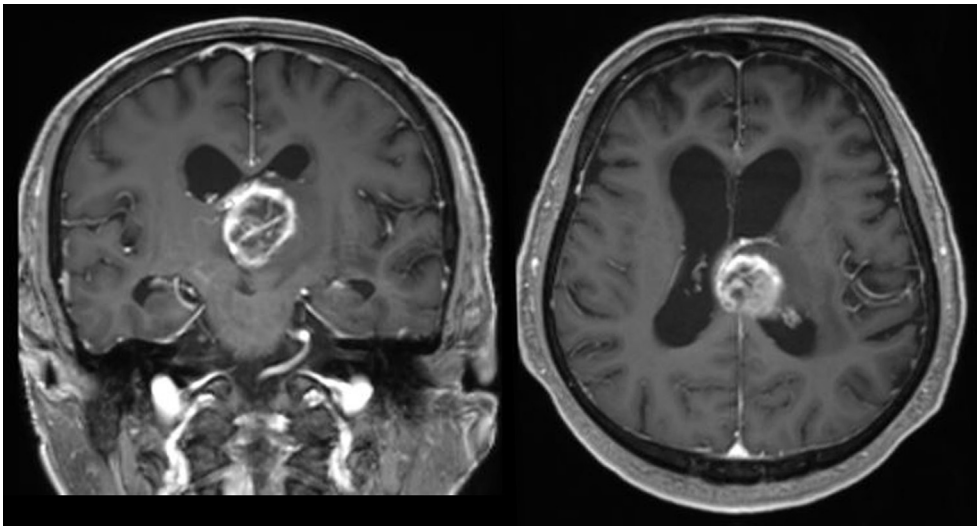

Figure 6. Preoperative T1-weighted coronal (*left side*) and axial (*right side*) magnetic resonance images showing a large tumor located in the left thalamic region with positive contrast enhancement. The histologic investigation confirmed a glioblastoma.

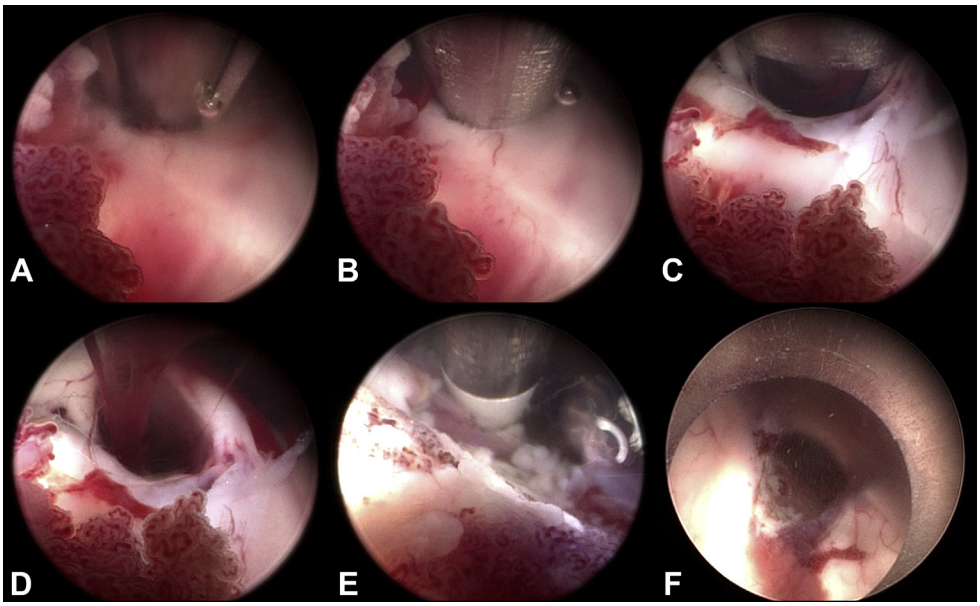

Figure 7. Neuroendoscopic view example 2. Biopsy of a pathology located in the right thalamus. Again, histologic results revealed a glioblastoma. After identification of the ideal biopsy area, the sedan probe is inserted (**A**) and several tissue samples are obtained (**B**, **C**). (**D**) Minimal hemorrhage is shown. Bleeding could be easily controlled with bipolar thermocoagulation (**E**). After 20 seconds of irrigation, the procedure is finished and the trocar is removed without further signs of hemorrhage (**F**).

possible. However, by approaching the target via coordinates that have been calculated and transmitted to the stereotactic frame, as it is done in frame-based stereotactic biopsies or under "real-time" MRI-guided control as it is done in frameless systems, the surgeon relays on somehow "indirect" information. Brain shift due to loss of cerebrospinal fluid after durotomy or even slight deflection of the needle probe (i.e., by crossing a sulcus) can impede the correct diagnosis.

In addition, if the biopsy fails to reveal at least a preliminary diagnosis, several biopsies within the lesion or at the peripheral zone of the lesion must be obtained. In some cases, a second trajectory must be used, which is associated with a greater risk of hemorrhage[36-38] In neuroendoscopic procedures, biopsy under MRI guidance as well as inspection of the biopsy site for peculiarities is possible. As mentioned previously, basically deflection of the needle probe in stereotactic biopsies meant to have a straight trajectory is not desired. However, a neuroendoscopic approach allows a minimal movement of the scope and thus the trajectory. This minimal movement might be enough to obtain the optimal trajectory for tumor biopsy without the necessity of performing a second transcortical approach. And finally, in case of the rare complication of intraoperative bleeding resulting in a secondary open approach, the head ring used in frame-based stereotactic procedures can prohibit an adequate craniotomy, resulting in a time delay caused by changing the stereotactic ring to Mayfield fixation.

Regarding the diagnostic yield, Somji et al.[39] published a systematic review of diagnostic yield, morbidity, and mortality in 30 studies and 2069 total intraventricular neuroendoscopic biopsies. In 82.7% of the cases, a combined procedure was performed with a diagnostic yield of 87.9% in total.[39] Somji et al. recommended neuroendoscopic biopsies due to the good diagnostic yield and an overall low complication rate. They also recommended intraventricular endoscopic biopsy, especially in respect to the possible additional therapeutic benefit in case of obstructive hydrocephalus.

In comparison, a meta-analysis including 63 studies (of 5800 studies of potential interest) revealed a diagnostic yield between 89.4% and 100% after stereotactic frame-based and frameless biopsies.[40] A subanalysis comparing frame-based and frameless techniques in 4 studies that were included, diagnostic yield, morbidity, and mortality rates did not differ significantly. Thus, the stereotactic procedures still seem to be more accurate at present. However, excellent results with a diagnostic yield of more than 90% and up to 100% in neuroendoscopic series—including the presented analysis—can be achieved even in deep-seated intracranial pathologies.[41-43]

In summary, in the present study it was shown that a pure neuroendoscopic biopsy of deep-seated pathologies that were located in the brain parenchyma and were not passing the ependyma was safe and precise with all advantages of a direct inspection of the surgical site. Certain characteristics such as a special vessel formation or the amount of hemorrhage at the biopsy site were closely observed. Further, the use of a tracking-system adds to an optimal diagnostic yield. The use of a stereotactic sedan probe enables tissue sampling in central areas of the pathology. The tracking supports the "real-time" location of the ideal intraparenchymal biopsy site and verification of the probe

position during the procedure is possible. Thus, this technique may enable a faster procedure with—in respect to the risk of intraoperative bleeding—less biopsy samples.

CONCLUSIONS

An endoscopically conducted biopsy with the aid of a navigated probe fixed at a passive tracking-tool represents an additional technique in certain intraparenchymal pathologies. The endoscopic intraventricular approach enables the direct visualization of the surface. Special characteristics in terms of tissue formation and vessels can be identified, and hemostasis can be obtained safely and quickly under direct view. "Real-time" imaging of the probe position—even if it is positioned in the paraventricular tissue—is possible. A transparenchymal surgical approach passing highly sensitive, eloquent areas can be avoided. In the authors' view, this technique is a very useful addition in selected pathologies. Nevertheless, the surgeon should be aware of the risk and management in case of extended intraoperative hemorrhage in neuroendoscopic surgery. Thus, this procedure should be performed by neuroendoscopically experienced hands.

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