Acta Neurologica Belgica
https://doi.org/10.1007/s13760-020-01299-1

REVIEW ARTICLE

# Role of endoscopic surgical biopsy in diagnoses of intraventricular/periventricular tumors: review of literature including a monocentric case series

Luca D'Angelo[1] · Daniele Armocida[1,2] · Luigi Sampirisi[1] · Francesco Paglia[1] · Luigi Valentino Berra[1] · Antonio Santoro[1]

Received: 11 September 2019 / Accepted: 9 February 2020


## Abstract

The intra- and periventricular location tumor (IPVT) of a brain remains a hard challenge for the neurosurgeon because of the deep location and eloquent anatomic associations. Due to this high risk of iatrogenic injury, many surgeons elect to perform biopsies of such lesions to establish a diagnosis. On the one hand, stereotaxic needle biopsy (SNB) is a minimally invasive procedure but with a significant risk of complications and a high risk of lack of tissue for molecular analyses for this region [Fukushima in Neurosurgery 2:110–113 (1978)]; on the other hand, the use of endoscopic intraventricular biopsy (EIB) allows for diagnosis with minimal surgical intervention [Iwamoto et al. in Ann Neurol 64(suppl. 6):628–634 (2008)]. IPVTs and related CSF pathway obstructions can be safely and effectively treated with endoscopic techniques. It is not possible to compare EIB with diagnoses made by any other method or with the established treatment. We aim to analyze the accuracy of EIB results by comparing them with results of biopsies performed later, in other methods and thereby evaluating the treatment evolution considering our personal experience. The difficulties and complications encountered are presented and compared with those reported in the literature to obtain the best review possible for this topic. A systematic review of literature was done using MEDLINE, the NIH Library, PubMed, and Google Scholar yielded 1.951 cases for EIB and 1912 for SNB, according to standard systemic review techniques. Review was conducted on 50 studies describing surgical procedures for lesions intra- and para-ventricular. The primary outcome measure was a diagnostic success. We also consider 20 patients with IPVT treated in our department. Clinical characteristics and surgical outcome were evaluated and a systematic review of the literature was performed. Overall, all our biopsies were diagnostic, with a positive histologic sample in 100% of our patients. 8 patients underwent a concurrent endoscopic third ventriculostomy. 4 patients underwent a concurrent ventriculostomy combined with septostomy. For 1 patient was necessary the only septostomy combined with biopsy. Every case has obtained a histological diagnosis. The percentage of complications was very low with only 1 case of post-operative infection and 1 case of hemorrhage. It was impossible to create a specific comparison from literature data of IPVTs between a stereotactic and endoscopic procedure, it presents only the collection of pineal gland tumor [Kelly in Neurosurgery 25(02):185–194 (1989); Quick-Weller in World Neurosurgery 96:124–128 (2016)] or unknown location of the lesion in major review [Marenco-Hillembrand et al. in Front Oncol 8:558 (2018)]. The present study aims to report our experience with the surgical management of IPVTs. The EIB sample yields an accurate histologic diagnosis tumor, with a positive histologic sample in 87, 95% of patients. The choice of the appropriate procedure should consider not only the preference and the experience of the neurosurgeon but also the several other variables as the location. While some periventricular lesions are better approached by endoscopic techniques, others are more suited for stereotactic-guided approaches. The ability to perform an EIB and relieve tumor-associated hydrocephalus by neuroendoscopy is considered to be a benefit of this procedure since this is less invasive than other treatments.

**Keywords** Neuroendoscopy · Biopsy · Intraventricular brain tumor · Preventricular · Ventricular · Oncologic surgery · Hydrocephalus

Extended author information available on the last page of the article

## Abbreviations

IPVTs Intraventricular, periventricular tumors
GTR Gross total resection

| | |
|---|---|
| STR | Subtotal resection |
| EIB | Endoscopic intraventricular biopsy |
| ETV | Endoscopic third ventriculostomy |
| GBM | Glioblastoma multiforme |
| SNB | Stereotaxic needle biopsy |
| CT | Computed tomography |
| MRI | Magnetic resonance imaging |

## Introduction

The intra- and periventricular location of a brain tumor remains a hard challenge for the neurosurgeon because of the deep location and eloquent anatomic associations [1–3], leading to potential functional and cognitive complications [1]. Due to this high risk of iatrogenic injury, many surgeons elect to perform biopsies of such lesions to establish a diagnosis. The biopsy of a brain tumor, particularly of deep-seated small lesions, must differentiate the lesion from the surrounding brain tissue to obtain optimal tissue samples [4].

On the one hand, stereotaxic needle biopsy (SNB) is a minimally invasive procedure but with a significant risk of complications and a high risk of lack of tissue for molecular analyses [5]; on the other hand, the use of a neuroendoscopy allows for diagnosis with minimal surgical intervention [6].

Intraventricular or periventricular tumors (IPVTs) and related CSF pathway obstructions can be safely and effectively treated with endoscopic techniques.

The aims of endoscopy intraventricular biopsy (EIB) in IPVTs are usually the restoration of CSF pathway obstruction and clarification of the histology. IPVTs are ideal indications for neuroendoscopic surgery because these lesions can easily be approached with the endoscope through the ventricular system.

We present our case series of patients who underwent EIB of the intra- and para-ventricular tumor; the data are from patients presenting at a single neurosurgical unit and compared with a literature's data collection.

Our objective was to analyze the accuracy of EIB results by comparing them with results of biopsies performed by SNB, in other methods and thereby evaluating the treatment evolution considering our personal experience. The difficulties and complications encountered are presented and compared with those reported in the literature to obtain the best review possible for this topic.

## Materials and methods

The study was conducted in accordance with preferred reporting items for systematic reviews.

The English literature was systematically investigated using MEDLINE, the NIH Library, PubMed, and Google Scholar. The last search date was February 25, 2019.

Search terms included: "biopsy" or "biopsies" in combination with "neuro-endoscopic" or "ventricular lesion". In parallel, we performed an investigation with terms included "biopsy" or "biopsies" in combination with "stereotactic" and "ventricular lesion".

Searches were limited to human studies and there were no limits regarding language; and we excluded a period of publication before 1978. Backward citation tracking was applied to identify articles not retrieved by electronic searches.

### Selection criteria

The selection of abstracts for full review was conducted by two independent authors based on predefined inclusion and exclusion criteria. Studies were eligible if they reported original data on the biopsy of any lesions in intra- and para-ventricular location. Studies were excluded if they: (a) reported procedures conducted for any other approach than such as open biopsies; (b) presented a reanalysis of subpopulations already included in other studies; (c) were commentaries or review articles summarizing the results of the previous series; (d) year of publishing was also included to understand a possible year of experience/improvement of the technologic setup, and (e) number of patients enrolled in each of the included cohorts.

Conversely, we excluded the following. First, we excluded short reports concerning the clinical courses of a limited number of patients, including case reports. Second, we excluded incomplete reports according to at least 3 of the 4 aforementioned endpoints. Third, we excluded reports before the collection of Fukushima in 1978 [7]. Each author reviewed the abstracts independently and generated a list of studies to retrieve for full-text review.

### Data extraction

The main search returned a total of 44 papers, including a total of 2221 patients. To this initial cohort, the aforementioned exclusion criteria were applied, accordingly eliminating a total of 290 patients. To this cohort of patients, the personal experience of the senior author (A. S.) of the present paper was added. Clinical data of these 20 patients were retrieved according to the aforementioned inclusion and exclusion criteria, resulting in a total final cohort composed of 1951 patients regarding the analysis; the second search resulting in a total final cohort composed of 1912 patients including 147 IPVTs patients, where we reported the number of all general complications.

A data extraction sheet was prospectively designed to extract all the necessary information visible in Table 1. The

**Table 1** Studies reporting endoscopic procedures for periventricular and intraventricular tumors

| Authors | Study design | Period | Average age | VP-L Cases | Diagnostic | Hydrocephalus | Hemorrhage | Infection | Fistulas | Others (seizure memory impairment) | Death | Endoscope type |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Fukushima [7] | Retrospective | ?–1978 | \ | 21 | 11 | \ | 1 | \ | \ | \ | \ | Rigide |
| Ellenbongen et al. [72] | Case report | 1995 | 19 | 1 | 1 | 1 | \ | \ | \ | \ | \ | Rigide |
| Ferrer et al. [73] | Case series | 1994 | 25 | 4 | 4 | 1 | 1 | \ | \ | \ | \ | Flexible |
| Robinson et al. [74] | Case series | 1997 | \ | 3 | 3 | 3 | \ | \ | \ | \ | \ | Rigide |
| Gaab e Schroeder [75] | Prospective | 1993–1996 | 56 | 28 | 27 | 19 | 2 | 1 | \ | 5 | \ | Rigide |
| Decq et al. [76] | Retrospective | 1994–1999 | 41 | 20 | 4 | 20 | \ | \ | \ | \ | \ | Rigide |
| Oi et al. [77] | Prospective | 1993–1998 | \ | 6 | 6 | 4 | \ | \ | \ | \ | \ | Both |
| Gangemi et al. [78] | Case series | 2001 | 36 | 5 | 5 | 3 | 1 | \ | \ | 1 | \ | Flexible |
| Pople et al. [19] | Retrospective | 1983–2000 | 41 | 34 | 30 | 18 | 1 | 1 | \ | 1 | \ | Rigide |
| Macarthur et al. [79] | Prospective | 1993–2000 | \ | 26 | 17 | 6 | \ | \ | \ | 4 | \ | Rigide |
| Yurtseven [80] | Retrospective | 2000–2003 | 65 | 18 | 18 | 10 | \ | \ | 3 | | \ | Rigide |
| Yamini et al.[ 81] | Case series | 1997–2001 | 9 | 6 | 6 | 6 | \ | \ | \ | \ | 1 | Flexible |
| Kim et al. [82] | Case series | 2004 | 27 | 5 | 5 | \ | \ | \ | \ | \ | \ | Rigide |
| Souweidane [83] | Retrospective | 1995–2004 | 40 | 63 | 63 | 41 | 3 | \ | \ | \ | \ | Rigide |
| O'Brien et al. [31] | Prospective | 1998–2006 | 37 | 41 | 33 | 28 | 2 | \ | \ | 2 | \ | Rigide |
| Chernov et al. [20] | Retrospective | 2001–2004 | 36 | 23 | 23 | 6 | \ | \ | \ | 1 | \ | Flexible |
| Luther et al. [84] | Retrospective | 1995–2004 | 13 | 12 | 11 | 12 | \ | \ | \ | \ | \ | Rigide |
| Depreitere et al. [22] | Retrospective | 1990–2005 | 9 | 31 | 22 | 29 | 1 | \ | \ | 2 | 1 | Rigide |
| Kumar et al. [85] | Retrospective | 2000–2003 | \ | 23 | 23 | 23 | 1 | \ | \ | \ | 1 | Rigide |
| Tirakotai et al. [23] | Retrospective | 1994–2004 | 4 | 46 | 46 | 19 | 1 | 2 | 1 | \ | \ | Rigide |
| Fiorindi e Longatti [29] | Retrospective | \ | 68 | 23 | 16 | 14 | \ | \ | \ | \ | \ | Flexible |
| Al-tamimi et al. [25] | Case series | 2008 | 10 | 8 | 8 | \ | \ | \ | \ | \ | \ | Rigide |
| Prat et al. [86] | Retrospective | | 48.5 | 22 | 22 | 22 | 1 | 1 | \ | 1 | \ | Rigide |
| Ahn e Goumnerova [87] | Retrospective | 1995–2007 | 11 | 31 | 23 | 24 | \ | \ | \ | 2 | \ | Rigide (21), flexible (12) |
| Song et al. [24] | Retrospective | 2001–2008 | 12 | 49 | | 31 | 7 | 1 | \ | 4 | \ | Rigide |
| Hayashi et al. [30] | Retrospective | 2005–2009 | \ | 677 | 604 | 317 | 26 | 97 | 13 | 33 | \ | \ |
| Kinfe et al. [32] | Retrospective | 2000–2011 | 37 | 17 | 37 | 17 | 1 | \ | \ | \ | \ | Rigide |
| Morgenstern et al. [17] | Retrospective | 2002–2010 | 37 | 15 | 13 | 11 | \ | \ | \ | \ | \ | |
| Dominguez-Papez et al. [18] | Prospective | 2003–2010 | \ | 28 | 25 | 23 | 4 | \ | 1 | 5 | 2 | \ |

**Table 1** (continued)

| Authors | Study design | Period | Average age | VP-L Cases | Diagnostic | Hydrocephalus | Hemorrhage | Infection | Fistulas | Others (seizure memory impairment) | Death | Endoscope type |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Oppido et al. [50] | Retrospective | 1997–2007 | | 60 | 49 | 32 | 8 | / | 1 | 2 | / | Rigide (40), flexible (15), both (5) |
| Mohanty et al. [33] | Retrospective | 2000–2009 | / | 87 | 72 | 52 | / | / | / | 1 | 3 | Rigide |
| Wong et al. [26] | Retrospective | 2007–2008 | / | 25 | 24 | 25 | 2 | / | / | / | 1 | / |
| Chibbaro et al. [88] | Prospective | 2005–2009 | / | 8 | 8 | 6 | 1 | / | / | / | / | Rigide |
| Constatntini et al. [27] | Retrospective | 1998–2009 | 28 | 293 | 293 | | 54 | 8 | 4 | 6 | 1 | Rigide |
| Giannetti et al. [15] | Retrospective | 2002–2013 | 68 | 48 | 37 | 48 | 3 | 2 | / | 1 | 1 | Rigide |
| Ros-Sanjuán et al. [89] | Retrospective | 2004–2016 | 27 | 80 | 71 | 61 | 2 | 1 | / | 3 | 4 | |
| Oertel et al. [90] | Retrospective | 2013–2018 | | 12 | 12 | 7 | / | / | / | 2 | / | Rigide |
| Stachura [91] | Retrospective | 2003–2018 | 51 | 32 | 32 | 9 | 3 | / | / | 4 | / | Flexible |
| D'Angelo et al. (our series) | Retrospective | 2015–2018 | 59 | 20 | 12 | 12 | 1 | 1 | / | / | / | Rigide |
| Total | | | | 1951 | 1716 (87.95%) | 960 (49.2%) | 127 (6.5%) | 115 (5.9%) | 23 (1.2%) | 80 (4.1%) | 15 (0.77%) | |

data were subsequently verified between the two authors. The following details were extracted: authors and year of publication, study design, number of patients, age (mean age of the study population), number of patients with a valid radiological diagnosis of IPVTs, number of diagnostic cases, number of patients with verified symptoms of hydrocephalus, procedure-related (overall and permanent) morbidity and mortality data including hemorrhage, infection, fistula, focal neurological deficit or sensory/memory disturbance, and type of endoscope used for procedures (Table 1).

## Variables and dataset

The final cohort was composed of 1951 patients: in 1931 cases, the clinical records were investigated in 38 previously published series, and the remaining 20 patients were derived from our institutional experience.

The range of the beginning and end of the accrual ranged, respectively, between 1978 and 2018, which is considered the golden age of the scientific interest toward intracranial biopsies.

We performed a retrospective observational study of a single-center case series. Data were collected by an independent researcher, who reviewed radiological and clinical records. We report a retrospective analysis of the diagnostic outcome and complications appearing after surgical treatments of patients affected by symptomatic intra and paraventricular lesions who needed a biopsy for histological analysis and treated in the period between 2014 and 2017 in the Neurosurgical Departments of the "Policlinico Umberto I" University Hospital of Rome.

We included all patients with symptomatic paraventricular localization of tumor diagnosed with a brain computed tomography (CT) and magnetic resonance imaging (MRI) scan admitted in our Neurosurgical center.

Patients' data (age, sex, presence, and localization of paraventricular lesion, neurological status pre- and post-surgery, pre- and post-operative incidence of complications), were recorded. We excluded patients with major comorbidity and performance status scale under 40.

All the patients included underwent a preoperative brain MRI scan including a high-field 3.0-Tesla volumetric study with the following sequences: T2w, isotropic volumetric T1-weighted magnetization-prepared rapid acquisition gradient echo (MPRAGE), FLAIR, before and after intravenous administration of paramagnetic contrast agent [8].

Six patients revealed a thalamic lesion, six patients had a lesion located adjacent to lateral ventricle, two patients had involvement of septum pellucidum, four patients had the lesion which involved the third ventricle and two patients had a lesion located on suprasellar floor (Table 2). A table reports the procedure that occurred for each patient, selected by a presence of hydrocephalus (evaluated by MRI scan), or inability to conduct a stereotaxic biopsy (for impossibility to draw an adequate trajectory or comorbidity).

For all procedures, a rigid endoscope Model Storz DECQ with optic system model HOPKINS was used. For each patient, it was made a small linear incision and burr hole is with bipolar cauterization of the dura followed by cruciate incision with a No. 11 blade. The edges of the dura are coagulated back with the bipolar cautery. We generally did not use a sheath. Rather, the endoscope was placed along the desired trajectory without the inner stylet. Biopsies are generally performed with cupped biopsy forceps that, on seizing the tissue sample, are rotated to free the biopsy sample [9]. The warm lactated Ringer's solution was connected to the irrigation port to dilate the ventricles gently. The surgeon navigated the endoscope through the foramen of Monroe into the third ventricle. The choice between an ipsilateral or contralateral trajectory depends on the modifications of ventricular anatomy modified for the lesions (Figs. 1, 2). For most endoscopic third ventriculostomies (ETVs), we find that a 0-degree endoscope allows adequate visualization of the contents of the third ventricle. When navigating the endoscope for septostomy before the foramen of Monroe, care should be taken to avoid injury to the fornix. When the endoscope is well positioned within the third ventricle, the anatomic landmarks along the floor of the third ventricle should be defined. In particular, the infundibular recess, the tuber cinereum, and the mammillary bodies should be identified. The desired trajectory for ETV allows for passage through the foramen of Monroe and visualization of the midline floor of the third ventricle.

All the patients included underwent a postoperative brain MRI scan including a high-field 3.0-Tesla volumetric study and CT scan to exclude major early post-operative complications [10].

## Results

Our series consisted of 7 males and 13 females, and the average age was 59 years. The incidence of episodes of complications was 2/20 patients in a selected group (10%). It was not possible to retrieve a statistically significant analysis; data are resumed in Table 2.

In the follow-up data reported, any one patient needed a ventriculoperitoneal shunt placement, with a significative improvement of hydrocephalus-correlated symptoms. For every patient, it was possible to determine the histological diagnoses, without problems of "insufficient pathologic material". Histological diagnosis was obtained in 90% of cases, a success rate more high than that reported by literature. The major diagnosis of our series is glioblastoma multiforme grade IV WHO (GBM); in literature, there is currently no commonly accepted standard of care for the treatment of GBM in the elderly population [2, 11–14].

The medical literature includes several articles addressing the usefulness of endoscopic biopsy for the management of IPVTs. The type of articles selected was cohort studies, surgeon general's report, retrospective studies, and follow-up patient databases. References in relevant articles were examined to identify additional eligible studies and discuss them below.

For our knowledge, the most complete review of literature about this topic is the work of Giannetti et al. [15] that describes a wide variation of results that may be explained by several methodological differences. Some articles consider only tumors; others assess only a single, specific site (such as the pineal region [16–20]) or limit patients to a selected age range (e.g., children [1, 21–26]), variation in the type of endoscope 45 (rigid or flexible) and in the experience of the surgeon.

We complete this collection, modify some incorrect data and specify the type of comorbidity in the post-operative period. Analysis of the final series retrieved a total of 1951 endoscopic brain biopsies in which the procedure led to diagnostic information in 1716 cases, a collective diagnostic yield of 87.95%. From previously large studies, the diagnostic yield of this type of procedure was attempted between 69.6% and 100% [27–30], so we found a positive trend of success.

An interesting data regard the percentage of diagnosed hydrocephalus (with radiological and clinical findings) that is attempted in 49.2% of all cases, therefore making the ETVs procedure almost always necessary.

Neuroendoscopic biopsy is not entirely without risk. Mortality of 0.77% and morbidity of 17.68% have been reported according to each series (mortality attempted of 0.8% and morbidity between 6 and 18% [29–32]). However, because the number of patients in most series (including that reported herein) was low, any single complication might have considerably affected these rates. To overcome this effect, we collected data from all of the articles (including the series reported herein) and summed their absolute number of infections ($n=115$), hemorrhage ($n=127$), fistulas ($n=23$), focal neurological complications (which include cranial nerve impairment, focal sensory-motor deficit, confusion and dizziness, $n=80$) and deaths ($n=15$). We divided this sum by the number of surgeries (1951 cases) and arrived at percentage rates of 5.9%, 6.5%, 1.2%, and 4.1%, respectively, with a mortality rate under 1% (0.77%, Table 1).

The most common complication is intraventricular bleeding due to the inherent difficulty in its control. The risk of hemorrhage (with clinical repercussions) normally reported in the literature is 2.33–3.6% [22, 31–33]. These bleeding complications may be related to the histological findings; in our series, the percentage is higher as we considered

**Table 2** Patients details

| No | Age, sex | Year of surgery | Clinical presentation | Origin/involvement | Procedure | Diagnosis | Compliance | Follow-up month |
|---|---|---|---|---|---|---|---|---|
| 1 | 77, M | 2015 | Hydrocephalus | Thalamus | Biopsia + TVE | Glioblastoma | None | 6 |
| 2 | 55, M | 2015 | Motor deficit | Thalamus | Biopsia + TVE | Linfoma | None | 12 |
| 3 | 34, F | 2015 | Seizures | Lateral ventricle | Biopsia + TVE | Astrocitoma basso grado | None | 36 |
| 4 | 43, F | 2015 | Seizures | Septum pellucidum | Biopsia + TVE + Settotomia | Glioblastoma | None | 6 |
| 5 | 64, F | 2015 | Hydrocephalus | Lateral ventricle | Biopsia + Settotomia | Glioblastoma | None | 36 |
| 6 | 72, F | 2016 | Hydrocephalus | Third ventricle | Biopsia + TVE | Glioblastoma | None | 12 |
| 7 | 33, F | 2016 | Hydrocephalus | Thalamus | Biopsia | Astrocitoma basso grado | None | 24 |
| 8 | 60, M | 2016 | Motor deficit | Third ventricle | Biopsia | Metastasi | None | 18 |
| 9 | 79, M | 2017 | Seizures | Lateral ventricle | Biopsia + TVE + Settotomia | Glioblastoma | Infection | 12 |
| 10 | 67, M | 2017 | Hydrocephalus | Septum pellucidum | Biopsia + TVE | Ependimoma | None | 12 |
| 11 | 49, F | 2018 | Hydrocephalus | Thalamus | Biopsia + TVE | Glioblastoma | None | 12 |
| 12 | 64, M | 2018 | Hydrocephalus | Third ventricle | Biopsia | Linfoma | None | 6 |
| 13 | 78, F | 2018 | Motor deficit | Lateral ventricle | Biopsia | Metastasi | Hemorrhage | 6 |
| 14 | 56, F | 2018 | Hydrocephalus | Sovrasellar | Biopsia + TVE + Settotomia | Linfoma | None | 6 |
| 15 | 55, F | 2018 | Hydrocephalus | Lateral ventricle | Biopsia + TVE | Glioblastoma | None | 6 |
| 16 | 67, F | 2018 | Motor deficit | Sovrasellar | Biopsia + TVE + Settotomia | Ependimoma | None | 3 |
| 17 | 57, F | 2018 | Motor deficit, seizures | Thalamus | Biopsia | Linfoma | None | 6 |
| 18 | 58, F | 2018 | Hydrocephalus | Third ventricle | Biopsia + TVE | Linfoma | None | 6 |
| 19 | 58, F | 2015 | Hydrocephalus | Lateral ventricle | Biopsia | Linfoma | None | 24 |
| 20 | 63, M | 2017 | Hydrocephalus | Thalamus | Biopsia | Metastasi | None | 12 |

every bleeding peri-procedural, which means that it remains unclear in what proportion of patients such procedures had to be abandoned because of peri-procedural bleeding in the ventricles or by failed attempts to identify the lesion.

The second search resulting in a total final cohort composed of 1912 patients including 147 IPVT patients, where we are not able to define a morbidity and mortality analysis.

It was impossible to create a specific comparison from literature data of IPVTs between stereotactic and endoscopic procedure; it presented only the collection of pineal gland tumor [34, 35] or unknown location of lesion in major review [36]. We found just an interesting study of Kinfe et al. [32] that compared a single-center collection of patients who were undergoing a biopsy procedure. The choice of the appropriate procedure should consider not only the preference and the experience of the neurosurgeon but also several other variables such as the location. While some periventricular lesions are better approached by endoscopic techniques, others are more suited for stereotactic-guided approaches (e.g., small lesions in the ventricular wall or the periventricular thalamus in patients with small ventricles). There are a large group of patients, however, in whom both approaches are useful and feasible, but these data are not clarified.

The advantages of stereotactic surgery are that it can be performed under local anesthesia, it produces only minimal tissue trauma and it can virtually be performed at any site of lesion location within the brain. Generally, SB is characterized by a favorable risk profile (1.6% in our analysis) and high diagnostic yield, allowing tissue-based therapeutic consequences even in patients with high comorbidity and anticoagulant medication [37].The literature is currently replete with reports of endoscopic brain biopsies in a high success rate range.

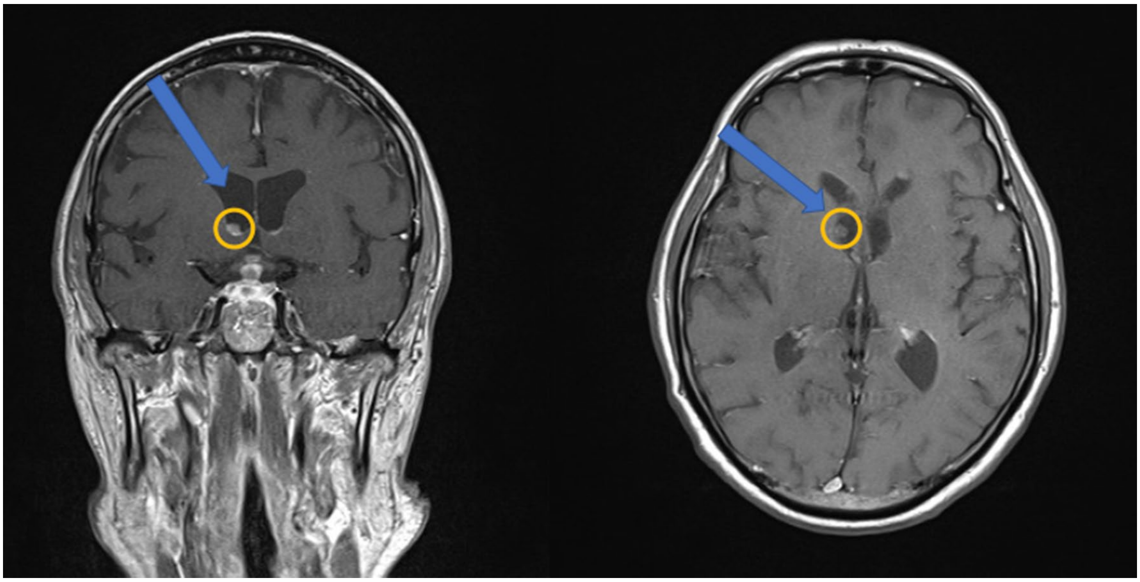

**Fig. 1** Thalamic lesion with involvement of large part of ventricular space needs a contralateral approach through the foramen of Monroe

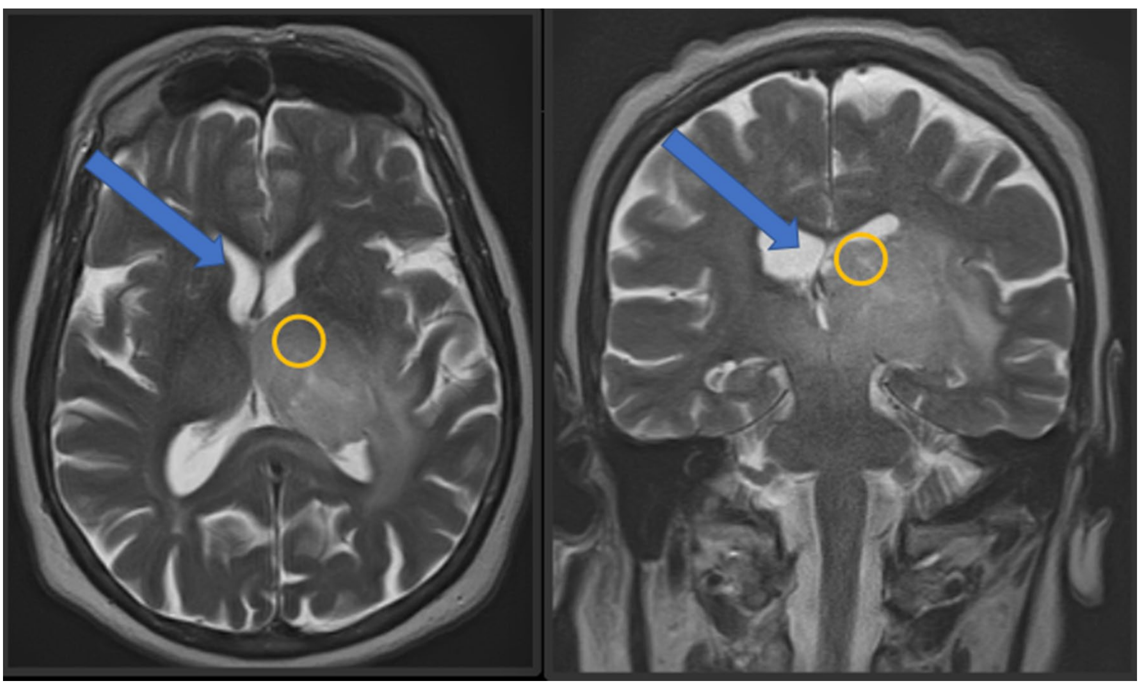

**Fig. 2** For lesions involving the sovrasellar floor or only the frontal horn the operator navigated the endoscope through the omolateral foramen of Monroe into the third ventricle

## Discussion

IPVTs include a variety of benign and malignant lesions located within the ventricular cavity or arising from neural structures forming the ventricular system [9]. These tumors are uncommon (accounting for less than 1% of all intracranial lesions), and their treatment involves significant morbidity and mortality [5, 38]. IPVTs are classified into primary tumors, such as colloid cysts, choroid plexus papillomas, and ependymomas; or secondary tumors, such as craniopharyngiomas, gliomas, pineal tumors, and meningiomas [5].

The low incidence, deep location, and narrowness of the surgical field make this kind of tumor a constant challenge to neurosurgeons [38].

The risks associated with operative resection may also influence the surgeon's decision to favor the biopsy. Microneurosurgical approaches almost always require the dissection and retraction of eloquent and delicate brain structures [39], and can potentially lead to neurological deficits and significant morbidity [5, 40, 41]. As a result, palliative treatment options are typically offered for these lesions including biopsies. Also, older patients often do not tolerate major surgeries due to existing medical comorbidities, multiple medication use, and reduced physiological reserve [5, 40, 42]. Age should not be the sole determinant for precluding aggressive surgical resection and even elderly patients undergoing gross total resection (GTR) and subtotal resection (STR) may experience superior survival compared to partial resection [43] or biopsy with an acceptable risk of postoperative complications [44–48]. Because of this high risk of iatrogenic injury, many surgeons elect to perform biopsies of such lesions to establish a diagnosis, relying on adjuvant chemoradiation [49] for tumor-killing effects [50, 51].

The choice of the type of biopsy intervention may depend on the experience of the neurosurgeon, but with the development of new surgical tools and techniques, minimally invasive approaches have allowed for the treatment of these lesions previously associated with significant morbidity [52, 53]. The microsurgical approaches enable complete resection of paraventricular tumors [52]. There are many options for an open craniotomy microsurgical approach to the third ventricle and anterior lateral ventricle tumors [2, 38]. Although these approaches have been reported to be relatively safe, they can still be associated with serious complications [52]. Tubular retractor systems and exoscopes [50] have garnered much interest in the neurosurgical community for the resection or biopsy of IPVTs [54].

The needle biopsy is the least invasive; however, only a limited resection can occur with this method. Therefore, there is a significant residual tumor and mass effect, lack of tissue for molecular analyses and banking, and it still carries significant risks [54, 55].

Another alternative in the management of the IPVTs is the SNB procedure [56]. But, nowadays, its utility in deep-seated lesions is debated for the risk of sampling error because of the migration of the tumor from the target after puncture of the ventricle and cerebrospinal fluid CSF drainage and because it never contributes to treating the obstructive hydrocephalus. Symptoms and signs are related to the non-communicating hydrocephalus in the majority of patients with these tumors. In contrast to traditional SNB, neuroendoscopy allows for direct visualization of the lesion, permitting selection of a suitable region for biopsy and improving diagnostic efficacy.

Largest collections that studies safety and efficacy of SNB 57,89 suggest individual reasons for failure in this group of patients included the inability to penetrate a ''hard'' pineal region tumor, lesion location adjacent to the ventricles, and inaccurate tissue sampling despite multiple specimens at several different depths [57], all the major studies reported in Table 3 identifies the patients treated and the analysis of comorbidity and mortality referred at biopsies of lesions located anywhere within the brain; for this reason is not possible to perform an accurately statistical analysis of risk and results for IPVTs treatment.

There are several reasons why a histopathological diagnosis could not be made, for example, the size of the biopsy samples was too small, there was poor visualization of the

**Table 3** Most large studies reporting stereotactic procedures for periventricular and intraventricular tumors

| Authors | Study design | Period | Total cases | VP-L cases | Complications general |
|---|---|---|---|---|---|
| Kinfe et al. [32] | Retrospective | 2000–2011 | 70 | 55 | 2 |
| Apuzzo et al. [34] | Retrospective | ?–1983 | 80 | 7 | 4 |
| Apuzzo et al. [35] | Retrospective | ?–1984 | 42 | 19 | 0 |
| Hall et al. [36] | Retrospective | 1991–1996 | 122 | 2 | 1 |
| Yu et al. [92] | Retrospective | 1995–2000 | 550 | 35 | 4 |
| Kreth et al. [93] | Retrospective | 1996–2001 | 326 | 6 | 3 |
| Yamada et al. [94] | Retrospective | 1998–2004 | 87 | 4 | 1 |
| Smith [95] | Retrospective | 2000–2005 | 207 | 3 | 5 |
| Dammers et al. [57] | Retrospective | 1998–2007 | 355 | 7 | 4 |
| Qin et al. [96] | Prospective | 2012–2018 | 29 | 3 | 4 |
| Iijima [97] | Case series | 1998–2013 | 44 | 6 | 3 |
| Total | | | 1912 | 147 | 31 (1.6%) |

tumor, lack of neuronavigation; presence of glial, white, or gray matter; poor tumor visualization; increased distance between tumor and ventricular wall, bleeding, excessive tumor hardness or a crush artifact of the samples may have been present. The major causes of poor visualization in the present study were that the tumor was located in the subependymal region and that there was intraventricular hemorrhage caused by biopsy [7, 15, 58].

The application of neuroendoscopy used for biopsy of IPVTs is still a matter of technical debate and variants, but yet ETV and frame-based stereotactic biopsy, used in the same operative sittings, would appear to be the gold standards in hydrocephalus management and accurate tissue diagnosis, respectively, especially in cases involving obstructive hydrocephalus due to the anatomic location of these lesions and their mass effect [6, 31].

Endoscopy has clear advantages over the stereotaxic procedure guided with navigation: sampling under direct vision, which implies better control of the hemorrhage and the site where the samples are taken and resolve hydrocephalus during the same procedure using a single trajectory to achieve the surgical goals but it requires an adequate neuroendoscopic training to optimize neuroanatomic knowledge, three-dimensional depth perception, and manual dexterity skills [59].

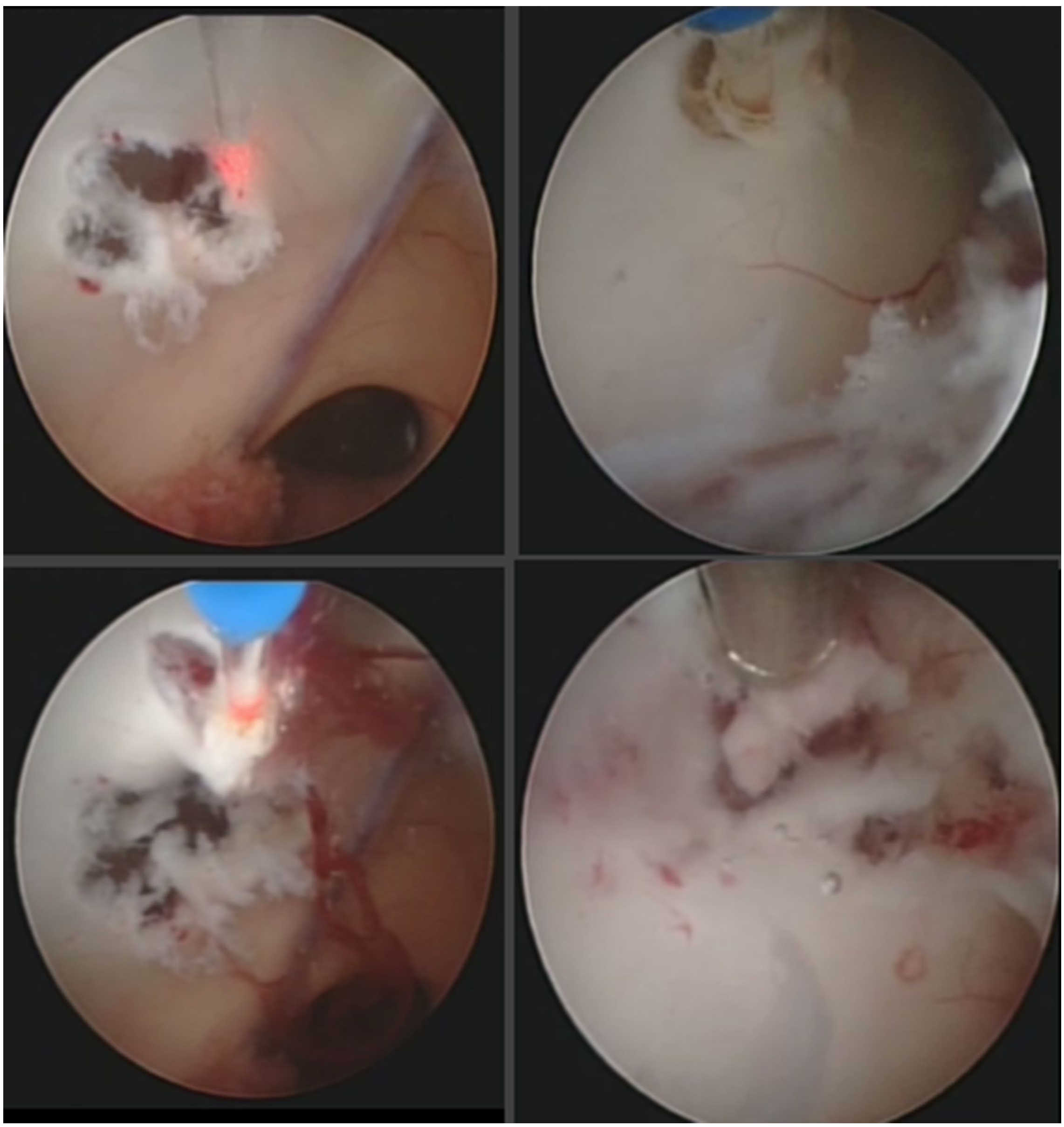

**Fig. 3** **a** Visualization of foramen of Monroe and the execution of septostomy with the Tullium Laser; (**b**–**d**) after a minimal coagulation of ependymal plane it could visualize the tumor in a paraventricular lesions (**c**) A quickly control of venous hemorrhage after lesion's removal

Despite established as one of the best options for IPVTs resection or biopsy in selected cases, the method is not exempt from complications and limitations [38]. Severe complications resulting in mortality and permanent morbidity are fortunately very rare [60, 61]. Intra-operative hemorrhage is the most frequently reported complication. Other complications include memory deficits, subdural hematomas, CSF leaks, and meningitis [3]. Our case series reports a very small percentage of these events. Some authors consider hypervascularization to be a contraindication for the endoscopic approach of ventricular lesions [62]. However, superficially vascularized tumors are usually softer and, therefore, good candidates for neuroendoscopic aspiration especially for tumors with an exophytic intraventricular component. In our experience, bleeding can usually be controlled by continuous irrigation with Ringer's solution, and the use of Thulium laser (Fig. 3). The complications were linked with the histopathological origin of the tumor rather than the experience of the surgeon [40] (for example, choroid plexus papillomas are the most likely IPVTs to demonstrate hemorrhage [63]), or the introduction of new technologies like the neuronavigation system [64, 65]. We routinely use neuronavigation with intraventricular endoscopic procedures because it allows for more accurate selection of an entry site and visualization of surgical corridors to the ventricular system [9, 16].

We demonstrated that IPVTs should be approached using a rigid or flexible endoscope with or without a transparent plastic retractor without any differences in diagnostic yield and surgical outcome. Some authors have advocated the use of multiple endoscopes or entry sites for additional instrumentation [66, 67]; however, this is technically troublesome and not so minimally invasive.

Since, in 1978, Fukushima [7] reported the first case series on the use of cerebral endoscopy in the diagnosis of ventricular tumors; in the last three decades the role of endoscopy in neurosurgery has substantially increased, and has facilitated access to regions of the central nervous system with enhanced visualization and decreased morbidity [68]. Although the diagnostic rate of biopsies in Fukushima's series was suboptimal, he suggested that once advanced technology and experience were obtained, cerebral endoscopy would have a fundamental role in the diagnosis of ventricular tumors [69].

Patients with hydrocephalus and IPVTs serve as ideal candidates for endoscopic surgery, whether for resection or biopsy [70]. The establishment of a histologic diagnosis can be coupled with the relief of the obstructive hydrocephalus using endoscopic techniques. This use of an endoscope allows for the relief of symptoms and diagnosis with minimal surgical intervention [6]. IPVTs and related CSF pathway obstructions can be safely and effectively treated with endoscopic techniques. Furthermore, small tumors may be partially or fully removed when aspiration is achievable [3, 62, 71] with improved visualization and illumination in the depth of the ventricles as well as less brain tissue dissection and retraction. Craniotomies can be avoided because endoscopes are inserted through simple burr holes [3].

EIB might be probably less accurate than frame-based stereotactic biopsy in establishing a histological diagnosis of tumors in this area, but it is associated with fewer complications and probably a lower mortality rate. Furthermore in our experience, EIB had the same degree of accuracy as the stereotactic technique, but without the mortality and limited permanent morbidity of this procedure [98].

## Conclusions

An EIB is a minimally invasive and useful procedure for the diagnosis and initial management of tumor-associated hydrocephalus.

We analyzed the data obtained from 20 consecutively performed EIBs for different diseases and found that the diagnostics provided by the biopsy results were accurate. We also compared our complication rates with those reported in the literature and concluded that this procedure is very safe. The neurosurgical community has found the intraventricular neuroendoscopic approach as a useful tool for biopsy of obstructive lesions because it allows for concomitant treatment of associated hydrocephalus with a ETV.

At present, the endoscopic technique is broadly used for the treatment of tumor-related hydrocephalus, ventricle tumor biopsy, and/or resection in a minimally invasive way, with minimal manipulation of normal brain tissue. It is possible to predict that in the future, the pure endoscopic removal of brain tumors located in the paraventricular region will be allowed with novel techniques. Considering the small diameter of endoscopes and the high number of available instruments for endoscopic surgery, it is possible to use this technique for almost complete resection of tumors [64]. This study aimed to determine the accuracy of the initial diagnosis. Is not possible to compare the endoscopic diagnosis with diagnoses made by any other method or with the established treatment. The complication rate is variable because of differences in techniques and the small number of cases assessed in most published studies.

The ability to both perform a biopsy and relieve tumor-associated hydrocephalus by neuroendoscopy is considered to be a benefit of this procedure since this is less invasive than other treatments. In our experience, EIB had the same degree of accuracy as the stereotactic technique, but without the mortality and limited permanent morbidity of this procedure.

The authors certify that they have NO affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation

in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements), or non-financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript. The authors confirm their adherence to ethical standards and have NO financial disclosures that would be a potential conflict of interest with this publication.

**Funding** This study was not funded by any association.

## Compliance with ethical standards

**Conflict of interest** We wish to confirm that there are no known conflicts of interest associated with this publication and there has been no significant financial support for this work that could have influenced its outcome. We wish to draw the attention of the Editor to the following facts which may be considered as potential conflicts of interest and to significant financial contributions to this work.

**Ethical approval** All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. This article does not contain any studies with animals performed by any of the authors.

**Informed consent** Informed consent was obtained from all individual participants included in the study. The patient has consented to the submission of this review article to the journal. We confirm that the manuscript has been read and approved by all named authors and that there are no other persons who satisfied the criteria for authorship but are not listed. We further confirm that the order of authors listed in the manuscript has been approved by all of us. We confirm that we have given due consideration to the protection of intellectual property associated with this work and that there are no impediments to publication, including the timing of publication, with respect to intellectual property. In doing so, we confirm that we have followed the regulations of our institutions concerning intellectual property. We further confirm that any aspect of the work covered in this manuscript that has involved either experimental animals or human patients has been conducted with the ethical approval of all relevant bodies and that such approvals are acknowledged within the manuscript. We understand that the Corresponding Author is the sole contact for the Editorial process (including Editorial Manager and direct communications with the office). He/she is responsible for communicating with the other authors about progress, submissions of revisions and final approval of proofs. We confirm that we have provided a current, correct email address which is accessible by the Corresponding Author and which has been configured to accept email from.

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## Affiliations

**Luca D'Angelo**[1] · **Daniele Armocida**[1,2] · **Luigi Sampirisi**[1] · **Francesco Paglia**[1] · **Luigi Valentino Berra**[1] · **Antonio Santoro**[1]

✉ Daniele Armocida
danielearmocida@yahoo.it

1 Human Neurosciences Department, Neurosurgery Division, "Sapienza" University, AOU Policlinico Umberto I, Rome, Italy

2 Azienda Ospedaliera Policlinico Umberto I, Viale del policlinico, 155–1039, 00189 Rome, Italy