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The Safety and Diagnostic Value of Frame-Based and CT-Guided Stereotactic Brain Biopsy Technique

Bilgisayarlı Tomografi Rehberliğinde Stereotaktik Beyin Biyopsisi Tekniğinin Güvenilirliği ve Tanısal Değeri

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ABSTRACT

AIM: Histopathological diagnosis is always necessary to make an effective treatment plan for intracranial mass lesions. This study aimed to evaluate the diagnostic efficacy, and associated mortality and morbidity of CT-guided stereotactic biopsy procedures in a large number of patients with intracranial lesions.

MATERIAL and METHODS: A total of 290 cases undergoing CT-guided stereotactic biopsy for intracranial lesions were included in this retrospective study. Clinical, radiological and histological data in patient records were examined.

RESULTS: The mean age of the patients was 46.6 years (range: 2-82 y). Pediatric patients comprised 6.3% (n=13) of the total population. Examination of paraffin embedded histological preparations revealed a tumoral mass in 240 (82.8%), a non-tumoral mass in 37 (12.8%), and non-definable lesions in 13 (4.5%). Therefore, the diagnostic value in this series was 95.5%. Postoperative mortality rate was 0.8% (n=2). When histopathological diagnoses made after biopsy and surgical resection were compared in 42 patients with available data, a complete or partial agreement was present in 90.5%.

CONCLUSION: Our findings support that frame based-stereotactic biopsy is a safe and valuable technique that allows the neurosurgeon to obtain tissue samples for histopathological diagnosis of intracranial mass lesions in almost any region.

KEYWORDS: Stereotactic brain biopsy, CT-guide, Histopathological diagnosis, Diagnostic value

ÖZ

AMAÇ: İntrakraniyal kitle lezyonlarında etkili bir tedavi planı yapabilmek için histopatolojik tanı her zaman gereklidir. Bu çalışmada, intrakraniyal lezyonu olan büyük bir hasta grubunda BT rehberliğinde yapılan stereotaktik biyopsi işleminin tanısal değeri ve bu işlemle ilişkili morbidite ve mortalite değerlendirilmiştir.

YÖNTEM ve GEREÇLER: İntrakraniyal lezyon nedeniyle BT rehberliğinde stereotaktik biyopsi yapılan toplam 290 olgu bu retrospektif çalışmaya alınmıştır. Hasta kayıtlarındaki klinik, radyolojik ve histolojik veriler incelenmiştir.

BULGULAR: Hastaların ortalama yaşı 46.6'dır (aralık: 2-82). Toplam hasta popülasyonunun %6.3'ü (n=13) çocuk hastalardır. Histopatolojik inceleme sonucunda hastaların 240'ında (%82.8) tümoral kitle, 37'sinde (%12.8) tümöral olmayan kitle, 13'ünde ise (%4.5) tanımlanamayan lezyon bulunmuştur. Dolayısıyla, bu seride tanısal değer %95.5'dir. Postoperatif mortalite oranı %0.8 (n=2) olarak gerçekleşmiştir. Biyopsi sonucu ve cerrahi rezeksiyon sonucu histopatolojik tanılar verisi bulunan 42 hastada karşılaştırıldığında, %90.5 oranında kısmi ya da tam uyum saptanmıştır.

SONUÇ: Bulgularımız bilgisayarlı tomografi rehberliğinde frame tabanlı stereotaktik biyopsinin güvenli ve değerli bir teknik olduğunu desteklemektedir. Bu teknik, cerrahın intrakraniyal kitle lezyonlarından histopatolojik tanı için doku örnekleri almasına olanak tanımaktadır.

ANAHTAR SÖZCÜKLER: Stereotaktik beyin biyopsisi, BT rehberliği, Histopatolojik tanı, Tanısal değer

INTRODUCTION

Stereotactic technique was first used by Dittmar during his experimental work on mice in 1873 (26), and shortly thereafter, Zernov tested its role in intracranial localization studies in 1889 (75). At the beginning of 20th century, stereotactic frames based on cartesian coordinate principles were developed by Robert Henry Clarke and Victor Horsley for experimental purposes (14). Initial reports of clinical stereotactic studies under direct X-ray guidance were first published in 1947 (66). The Horsley-Clarke apparatus was fundamentally based on

cartesian system, and Leksell incorporated other systems to yield a device with an apparatus fixed to the cranium and a mobile arc-quadrant (44). This and other frame-based techniques have been further refined through the development and implementation of diagnostic tools such as ventriculography, computed tomography, positron emission tomography, and magnetic resonance imaging (46, 48, 50, 66).

Along with the introduction of computed tomography in 1970s (48) and magnetic resonance imaging in 1980s (46), a new field referred to as "stereotactic surgery" has come forth together with stereotactic biopsy techniques under imaging guidance, and since that time considerable advance has been made in this field. Despite the improvement in neuroradiological imaging modalities, histopathological diagnosis is indispensable for any effective treatment plan for intracranial mass lesions (5, 6, 10, 21). Traditionally, frame-based techniques have been the standard method used to achieve a reliable and accurate sampling of intracranial lesions with proven superiority over freehand biopsy procedures in terms of morbidity, mortality, and diagnostic yield (45, 46, 48).

This retrospective study aimed to evaluate the safety and diagnostic efficacy of CT-guided stereotactic biopsy procedures performed for histological diagnosis of intracranial lesions.

MATERIAL and METHODS

Patient Population

A total of 290 cases undergoing CT-guided stereotactic biopsy for intracranial lesions between March 1995 and September 2010 at the Department of Neurosurgery, Haydarpasa Numune Training and Research Hospital were included in this study. Clinical, radiological and histological data in patient records were retrospectively examined. The following were the indications for CT-guided stereotactic biopsy for an intracranial mass lesion requiring histological or microbiological diagnosis: deep-seated lesion or a lesion localized at an eloquent area, high-risk for open surgical biopsy, a cystic lesion suggestive of abscess or granulamatous infection, multifocal lesions, lesions possibly better treated using noninvasive methods after histological diagnosis such as lymphoma or germ cell tumor, and co-morbidities posing a high-risk for general anesthesia such as advanced age. Patients undergoing stereotactic craniotomy, brachytherapy, and stereotactic Ommaya reservoir application were not included.

Preoperative Clinical Assessment

Clinical, radiological and neurological assessments were done in all patients before the biopsy procedure. Although procedures were routinely performed under local anesthesia, a possibility of transition to general anesthesia was taken into consideration in each case. If present, history of bleeding diathesis was assessed by an internal medicine specialist and high-risk patients were excluded. Patients on antithrombotic medications were instructed to discontinue their treatment at least seven days prior to biopsy. A Karnofsky Performance Scale (KPS) was administered before and after the procedure.

Stereotactic Procedure

A Leksell Stereotactic System (Elekta Instruments AB, Sweden) was used for biopsy procedures in all subjects where a total of four screws were used for the fixation of the basal frame onto the cranium. Prior to the procedure, subperiostal and subcutaneous lidocaine HCl (Aritmal, Biosel, Turkey) injections, 2 ml and 4 ml in frontal and occipital areas, respectively, were administered to the fixation points. Then, patients were secured to the tomography table together with the frame using special adaptors. After the outer frame carrying the indicator plaques was also secured, a test CT image was obtained to verify the parallelism between tomographic cross-sections and the basal frame. The midpoint of the frame was ascertained (X, Y = 100). One-millimeter thick axial cross-section images encompassing the whole margins of the target lesion were obtained following the administration of intravenous contrast medium. Standard CT-guided stereotactic biopsy procedure was performed under local anesthesia as previously described elsewhere (5, 19). Under some special circumstances including young age, simultaneous shunting with the biopsy procedure or major intracranial surgical interventions such as mass resection, general anesthesia was preferred.

A burr-hole was prepared at the nearest point to the lesion for superficial lesions, while an ipsilateral coronal or precoronal burr-hole was used for deeply located lesions. The tissue samples were obtained using a Backlund spiral needle with a diameter of 1.05 mm and/or a Sedan canulla with a side window and a diameter of 2.5 mm (Elekta Instruments AB, Sweden). An aspiration cannula 1.05 mm in diameter (Elekta Instrument AB, Sweden) was used for the aspiration of cystic lesions and abscesses.

Histopathological Assessments

Initial diagnostic assessments were performed by a neuropathologist examining the imprinted and/or squash smears. The tissue samples were fixed with 95% alcohol, spread on the microscope slide, and stained with hematoxylin-eosin (H&E) before examination with light microscope. The biopsy procedure was continued until verification of adequate tissue sampling for diagnosis. The remaining tissue samples were fixed in 10% buffered formaldehyde and sent to the pathology laboratory for histopathological examination. Paraffin tissue sections were stained with H&E, and if required, with other staining techniques such as immunohistochemical staining as well. The histopathological diagnoses were based on 2007 Central Nervous System Tumor Classification system proposed by the World Health Organization (WHO) (69).

RESULTS

Of the patients, 178 were male and 112 were female, with a mean age of 46.6 years (range: 2-82 y). Pediatric patients

comprised 6.3% (n=13) of the total population. Most frequent presenting complaint was weakness in lower and/or upper extremities (30.3%) followed by seizures (22.4%), headache (19.3%), impaired conscious (12.8%), nausea and vomiting 10.7%), vertigo (8.6%), speech disorder (7.9%), facial asymmetry (5.2%), diplopia/visual loss (4.1%), urinary incontinence (2.4%), fever (1.4%), and hearing loss (1.0%). Frequency of neurological findings at admission was as follows: objective loss of strength in extremities (51.7%), normal neurological examination (26.9%), impaired conscious (20.3%), facial paresis (7.6%), cerebellar findings (5.2%), clonus (5.2%), dysphasia/aphasia (4.5%), dysarthria (3.1%), paresis of extraocular muscles (2.4%), hearing loss (1.0%), and neck stiffness (0.7%). All patients underwent a cranial CT scan, while a cranial MRI was performed in 240. Localizations of the lesions are shown in Table I.

Examination of paraffin embedded histological preparations revealed a tumoral mass in 240 (82.8%), a non-tumoral mass in 37 (12.8%), and non-definable lesions in 13 (4.5%). Of the tumoral lesions, 206 (71.0%) were primary central nervous system tumors, 32 (11.0%) were metastatic, and 4 (1.4%) were unclassified. Histopathological diagnoses of the lesions are depicted in Table II. No diagnosis could be made in 13 subjects (4.5%). Therefore, the diagnostic value in this series was 95.5%.

Biopsy procedures were performed under local or general anesthesia in 280 and 10 patients, respectively. In the latter group, seven patients underwent a ventriculoperitoneal (VP) shunting during the same session. Main indications for general anesthesia were young age and need for lesion resection in the remaining patients.

Twelve patients (4.1%) had a neurological deficit due to bleeding (Table III), which was major in three and minor in nine cases. Two of the major episodes were intraventricular bleedings that were managed with external ventricular drainage (EVD) or conservative treatment, one each. The other major intracerebral bleeding was evacuated through craniotomy. Subjects with minor bleeding were closely followed under conservative treatment.

The focal motor failure developing after biopsy in two patients was considered as Todd's paralysis not secondary to the biopsy procedure since they were readily reversible and no radiological explanation could be made. Motor failure resolved within 24 hours in these patients. In three patients

Table I: Localizations of the Lesions

Localization	n (%)
Hemispheric lesions	***139 (47.9%)***
Frontal	21 (7.2%)
Frontotemporal	7 (2.4%)
Frontoparietal	11 (3.8%)
Temporal	29 (10.0%)
Temporoparietal	15 (5.2%)
Parietal	41 (14.1%)
Parieto-occipital	7 (2.4%)
Occipital	8 (2.8%)
Deep-seated lesions	***78 (26.9%)***
Thalamus	20 (6.9%)
Corpus callosum	18 (6.6%)
Basal ganglion	12 (4.1%)
Sellar/suprasellar	8 (2.8%)
Periventricular	8 (2.8%)
Intraventricular	7 (2.4%)
Brain stem	5 (1.7%)
Multiple lesions	***73 (2.5%)***

Table II: Histopathological Diagnoses of the Lesions

Histological diagnosis	n (%)
Tumoral lesions	***240 (82.8%)***
Glioblastome multiforme	80 (27.6%)
Metastatic	32 (11.0%)
Anaplastic astrocytoma (Grade III)	31 (10.7%)
Lymphoma	31 (10.7%)
Diffuse astrocytoma (Grade II)	27 (9.3%)
Oligodendroglioma (Grade II)	12 (4.1%)
Pilocytic astrocytoma	5 (1.7%)
Anaplastic oligoastrocytoma	4 (1.4%)
Unclassified malign tumors	4 (1.4%)
Pineoblastoma	3 (1.0%)
Craniopharyngioma	3 (1.0%)
Central neurocytoma	2 (0.7%)
Oligoastrocytoma	2 (0.7%)
Papilloma of choroid plexus	1 (0.3%)
Primary neuroectodermal tumor	1 (0.3%)
Plasmacytoma	1 (0.3%)
Malign germ cell tumor	1 (0.3%)
Non-tumoral lesions	***37 (12.8%)***
Abscess	22 (7.6%)
Necrotising granulomatous caseification	10 (3.5%)
Echinococcus multilocularis (hydatid cyst)	1 (0.3%)
Toxoplasmosis	1 (0.3%)
Demyelinating disease	1 (0.3%)
Arachnoid cyst	1 (0.3%)
Rathke cleft cyst	1 (0.3%)
Unclassified	***13 (4.5%)***

Table III: Patients that Developed Neurological Deficit Secondary to Hemorrhage

Age/Gender	Localization	Stereotactic diagnosis	Type of bleeding	Treatment	Outcome
8/F	Pineal	Pinealoma	Right temporal	Conservative	Recovery
20/M	Multiple	Abscess	Subcortical	Conservative	Recovery
22/F	Brain stem	Unclassified	Intraventricular	EVD	Exitus
24/M	Thalamus	Metastatic tumor	Thalamic	Conservative	Recovery
28/M	Temporal	Oligodendroglioma	Intracerebral	Surgery	Recovery
30/M	Occipital	GBM	Intracerebral	Conservative	Recovery
37/F	Temporal	Gliosis	Intracerebral	Conservative	Recovery
38/M	Parietal	Gliosis	Intracerebral	Conservative	Recovery
50/F	Parietal	Metastatic tumor	Intracerebral	Conservative	Recovery
50/F	Multiple	Metastatic tumor	Intracerebral	Conservative	Recovery
59/F	Deep thalamus	GBM	Intracerebral	Conservative	Recovery
67/M	Thalamus	GBM	Thalamic, intraventricular	Conservative	Exitus*

*****due to severe cerebral edema. **M,** male; **F,** female; **EVD,** external ventricular drainage; **GBM,** glioblastoma multiforme.

experiencing a convulsion during the preparation phase for biopsy, anticonvulsive treatment was given and the procedure was completed at a subsequent occasion. None of our patients had infection.

Postoperative mortality rate was 0.8% (n=2), with intraventricular bleeding and severe cerebral edema being the causes of death. The first patient underwent an EVD after a diagnosis of bleeding established by cranial CT and died after seven days. Other patient had impaired consciousness and focal neurologic signs after biopsy associated with cerebral edema and minimal ventricular bleeding as established by a CT scan. The patient did not respond to intensive anti-edema treatment and died after 5 days.

Average follow up duration was 18.4 months (7 days-130 months), and 40 patients were lost to follow-up at different time points. Postoperatively, there was no change in KPS score in 230 patients (79.3%). In patients with a tumoral cystic lesion or intracranial abscess formation, a rapid improvement in clinical and neurological findings was observed after aspiration with a corresponding increase in KPS scores (n=47, 16.2%). Totally 14 patients had a worsening in KPS scores, and of these, 12 were those who had a neurological deficit following the biopsy, while in the remaining two patients the worsening was due to disease progression during hospital stay.

A mass resection was performed in 42 subjects following stereotactic biopsy. Histopathological diagnoses made after biopsy and resection were compared. A complete (n=33, 78.6%) or partial (n=5, 11.9%) agreement of diagnoses was present in most patients, while there was a disagreement in four patients (9.5%).

DISCUSSION

Despite recent advances in diagnostic modalities, management of intracranial lesions and particularly gliomas largely depends on obtaining a reliable histopathological diagnosis (3, 10, 21, 32, 38). When open microsurgical resection is deemed inappropriate (e.g. due to increased risk etc.), stereotactic brain biopsy is a safe, accurate, and effective means of obtaining tissue samples for histological examination (5, 6, 29, 32). Its indications include obscure radiological diagnosis or unfeasible surgical resection (6, 21, 32, 38, 40). The procedure is also a viable option in patients who have lesions in functionally critical or deep regions of the brain, in critically ill subjects in whom general anesthesia poses a high-risk, and in the elderly.

Advances in stereotactic systems alongside their integration with computed tomography (48), magnetic resonance imaging (46) and positron emission tomography (50) and development of new software have resulted in a substantial reduction in the morbidity and mortality associated with stereotactic biopsy (55), which not only gives valuable information regarding the histological type, level of anaplasia, and progression of the tumor but also allows simultaneous introduction of cystic lesion aspiration or interstitial radiotherapy with treatment (32, 43, 59). Additionally, resection margins in operable tumors, the decision to commence radiotherapy or chemotherapy in inoperable tumors, and the prognosis are estimated in a more accurate and timely manner with this technique. Multiple sampling from different sites of the tumor provides valuable information on tissue characteristics as well as the internal structure of the lesion (21, 25, 32).

However, a limitation of stereotactic brain biopsy (SBB) that should be underlined is its diagnostic accuracy, which is defined as the "correct pathological diagnosis" along with correct tumor type and grading. The extent and the number of biopsies are limited in a SBB procedure and the obtained material may not be representative of the whole lesion. The reported diagnostic accuracy of SBB ranges from 80% to 96.7% (10, 11, 22, 38, 43) with higher figures for homogenous

lesions as compared to heterogeneously enhanced ones. Avoiding the central hypo-dense areas and obtaining biopsy samples only from well-enhanced regions result in under-grading (11, 41, 43). Even lower rates have been reported on the diagnostic accuracy of the method. For instance, in a study by Jackson et al., a total of 81 cases whose imaging studies suggested glioma and who were referred to a center for open resection following stereotactic biopsy has been reviewed and diagnoses based on biopsy or resection in the same patient differed in 49% of the biopsy pairs (35). However, it should be born in mind that the report by Jackson et al. includes only the referred patients for the purpose of diagnosis and/or due to the "inoperability" of the tumor, without any reference to the total number of stereotactic biopsies performed. In our patient group, 42 subjects underwent a craniotomy after SBB, confirming that postoperative diagnosis was in complete or partial agreement with SBB diagnosis in 90.5% of the patients, which is consistent with the reported diagnostic accuracy figures that range between 80% and 96.7%. However, only a limited fraction of patients underwent craniotomy after stereotactic biopsy (i.e. 42 out of 290 patients, 14.5%), limiting the value of diagnostic accuracy estimates in this study.

The reported figures for the diagnostic value of stereotactic biopsy, defined as the ability to reach a diagnosis, vary between 89% and 100% (1, 5, 10, 16, 32, 64, 74). In our series with the use of CT guided stereotactic biopsy the diagnostic value was 95.5%, and totally there were 13 patients for whom a diagnosis could not be established with biopsy. Of these, a subsequent diagnosis of tuberculoma was made in one patient based on clinical and CSF examination. Anti-TBC treatment resulted in resolution of the lesions. Previous studies have also emphasized the difficulty of sampling in tuberculomas (21, 56, 65). Sampling was immediately discontinued in accordance with previous recommendations (8, 41) in two patients due to a bleeding episode that developed during the procedure. One of these patients died, while the other underwent mass excision and hematoma evacuation. In two other patients, follow up revealed growth of mass lesions, which were treated with open surgery. In another patient, a second biopsy was done upon the increase in the dimensions of the lesion that subsequently proved to be a lymphoma. In this patient, a possible explanation for the initial failure to establish a histopathological diagnosis was the use of steroids. Previous evidence is supportive of such an effect on diagnostic accuracy associated with steroid use (31). In three patients, long-term follow up showed no neoplastic growth. The initial radiological evaluation was probably inadequate in these patients since spectroscopic MRI was not applied. It is well established that MR spectroscopy provides valuable information regarding the indications for biopsy and the localization of the lesion (13, 33, 62). In two patients, the samples mainly consisted of necrotic tissue precluding proper histopathological assessment and they underwent microsurgical mass excision, which subsequently revealed high-grade glial tumors. Again, an unfavorable effect of cystic necrotic tissue samples on the diagnostic accuracy of histopathological examination has been reported previously (10, 32, 57). In two patients, sampling was inadequate due to the occurrence of generalized convulsions during biopsy, and the biopsy was terminated in accordance with recent recommendations (2, 41).

Sedan side cutting needle and Backlund spiral needle were used as the biopsy instruments to provide more voluminous tissue samples as compared to forceps. For example, in the study by Hirschfeld et al. study (34), the percentage of non-diagnostic tissue samples were 45% and 0% for biopsies performed using forceps or cannula with a side window, respectively. Inadequate tissue material is considered to be one of the primary reasons for negative biopsy results. In our study, the cannula with a side window was used for biopsies, while Backlund spiral needle was preferred for granulomatous lesions posing difficulty in removing tissue pieces as indicated previously (21, 56).

Tissue samples from the central part of the lesion have been reported to provide highest rates of diagnostic accuracy compared to other sampling sites (63). In primary tumors, sampling from highly enhanced areas and hypodense central parts increase diagnostic accuracy and value, while additional sampling from peripheral hypodense areas is also recommended in recurrent tumors (27). MR spectroscopy is a valuable tool in determining the biopsy sites (13); however, this facility was not available in 80 out of 240 patients that underwent MRI in this study since these were the earlier cases, representing a potential limitation.

Overall, the mortality and morbidity rates in our study population were 0.8% and 2.9%, respectively with corresponding figures of 0.0 % - 3.7% (3, 8, 9, 12, 15, 17, 19, 23, 24, 28, 30, 32, 37, 38, 41, 42, 47, 49, 51-54, 58, 60, 61, 67, 68, 71, 74) and 0.4 % - 17.2 % (3, 8, 9, 12, 15, 17, 19, 20, 23, 24, 28, 30, 37, 38, 41, 42, 49, 51, 52, 54, 58, 60, 61, 68, 70, 72, 74) in previous reports. Table IV shows a summary of previous studies reporting mortality and morbidity rates for stereotactic brain biopsy procedures.

Kelly does not recommend routine use of CT imaging following stereotactic biopsy; however, a cranial CT may be required when a bleeding is suspected during the procedure or to verify the target direction (38). For example, Yu et al. (74) have reported the use of post-biopsy CT to rule out intracranial hemorrhage when required, while Kim et al., (38) Kondziolka et al. (39), and Lunsford et al. (47) have routinely used CT scans for the determination of asymptomatic bleeding after biopsy. Similarly, a cranial CT examination was routinely performed 4 to 6 hours after the stereotactic procedure in our patient group, while it was performed promptly after the biopsy in suspected cases of bleeding during the procedure.

Most infections in stereotactic biopsies are limited to scalp and/or subgaleal region. Apuzzo et al. (3) reported only one case with infection (0.2%) among 500 patients undergoing biopsy, while this figure was 2.0% (2/102) in the study by Lunsford et al. (47). There were no cases of infection in our

Table IV: Summary of Previous Studies Reporting Mortality and Morbidity Rates Associated with Stereotactic Brain Biopsy Procedure*

Author	Year of publication	N. of cases	Morbidity rate (%)	Mortality rate (%)
Osertag et al. (54)	1980	302	3.3	2.3
Edner (19)	1981	345	2.9	0.9
Sedan et al. (61)	1984	318	4.7	0.6
Mundinger (51)	1985	815	3.0	0.6
Apuzzo et al. (3)	1987	500	1.0	0.2
Davis et al. (17)	1987	439	0.4	0.2
Blaauw et al. (9)	1988	243	4.1	0.4
Kelly (37)	1989	226	9.3	0.4
Thomas et al. (68)	1989	300	4.7	0.3
Wild et al. (72)	1990	200	6.0	1.0
O'Neill et al. (53)	1992	259	6.5	3.3
Voges et al. (71)	1993	338	1.2	0.6
Bernstein et al. (8)	1994	300	4.7	1.7
Grunert et al. (30)	1994	200	3.0	1.0
Regis et al. (58)	1996	370	7.3	1.3
Nicolato et al. (52)	1997	200	17.2	2.4
Sawin et al. (60)	1998	225	4.9	0.4
Yu et al. (74)	2000	550	7.8	0.0
Field et al. (24)	2001	500	9.6	0.2
Kreth et al. (42)	2001	345	3.1	0.0
Ulm et al. (70)	2001	200	2.5	0.0
Kim et al. (38)	2003	300	3.9	0.6
Grossman et al. (28)	2005	355	-	0.6
McGirt et al. (49)	2005	270	13.0	1.0
Ferreira et al. (23)	2006	170	2.9	1.2
Kongkham et al. (41)	2008	622	6.9	1.3
Dammers et al. (15)	2008	391	3.8	1.5
Teixeira et al. (67)	2009	176	6.4	0.6
Chen et al. (12)	2009	299	4.35	1.34
Dammers et al. (16)	2010	465	2.7	3.7
Ersahin et al. (Present)	2011	290	2.9	0.8

*****Only series with greater than 150 cases were included.*

patient group, probably associated with the fact that the procedure was carried out in the surgical theatre, a pre-evaluation with regard to infection risk was performed, the procedure was of short duration, antibiotics were given after the procedure, and careful wound care was done.

Despite many publications reporting complication rates associated with stereotactic brain biopsy, relatively few have systematically examined clinical or radiological variables associated with increased risk (28, 32, 42, 49, 55, 60, 68, 73). Variables that have been assessed for a possible association with increased risk of operative complications include patient factors such as age, sex, Karnofsky score, pre-biopsy radiation therapy and co-morbid conditions such as hypertension, diabetes mellitus (16, 24, 28, 41, 49, 68). In our patients with uncontrolled hypertension or diabetes, these conditions were first addressed to achieve adequate control, then the biopsy was performed. Pre-operative anti-platelet and/or anti-aggregating agent use and thrombocytopenia have also been examined for their possible association with adverse outcomes (16, 24, 28, 41, 43) and the biopsy was performed 1 week after discontinuation of these agents. Patients with thrombocytopenia were excluded.

In subjects older than 2 years of age, stereotactic biopsy has been reported to be a safe procedure provided that the frame screws are fixed carefully (7, 36). Previously, stereotactic biopsy has been safely accomplished in a 9-month old

patient (18). The youngest three patients in our sample (2, 4 and 6 year old) underwent biopsy with general anesthesia without any complications. Most of the surgeons carry out stereotactic biopsy with local anesthesia (10, 16, 32) with general anesthesia usually reserved for young children and uncooperative or agitated adults (3, 4, 47). Except for 10 patients, all of our study subjects were given local anesthesia during the procedure for effective use of time and avoidance from complications associated with general anesthesia.

Our findings lend substantial support to the notion that frame based- stereotactic biopsy is an effective surgical technique that allows the neurosurgeon to assess accurately almost any region in the intracranial space, and to obtain tissue samples for histopathological diagnosis of intracranial mass lesions. Furthermore, it is a safe procedure with minimal associated morbidity and mortality compared to other cranial surgical procedures.

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