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Original Investigation

# Computerized Tomography-Guided Stereotactic Biopsy of Intracranial Lesions: Report of 500 Consecutive Cases

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## ABSTRACT

**AIM:** Computed tomography (CT)-guided stereotactic brain biopsy has been performed in our clinic since March 1998. In this prospective study, we examined the patient data undergoing stereotactic biopsy and the results of biopsies in 500 consecutive patients.

**MATERIAL and METHODS:** Between the dates of March 1998 and January 2015, CT-guided stereotactic biopsies were performed by using the Leksell stereotactic frame system (Elekta Instruments EU, Sweden) in 500 patients. A total of 512 procedures were performed in patients consisting of 184 females (36.8%) and 316 males (63.2%), ages ranging from 3 to 81 years (mean 50.40±16.67).

**RESULTS:** Conclusive histopathological diagnosis was not achieved in 17(3.3%) of 512 procedures. Of the others, 173 (33.8%) were high-grade gliomas, 103 (20.1%) were low-grade gliomas, 36 (7%) were malignant lymphomas, 34 (6.6%) were other types of brain tumors, 82 (16%) were metastasis and 67 (13.1%) were non-tumoral lesions. Complications were occurred in ten cases: 3 tumoral bleedings, 2 hypertensive cerebral hematomas, 2 peroperative convulsions, 1 epidural hematoma, 1 myocardial infarction and 1 brain edema. The patients who developed myocardial infarction and hypertensive thalamic hematoma died. The mortality was 0.4% and morbidity was 1.6% in 512 procedures.

**CONCLUSION:** CT-guided stereotactic biopsy is a reliable and a safe procedure in cases with intracranial lesions when histopathological diagnosis is required for the appropriate treatment.

**KEYWORDS:** Brain tumors, Computerized tomography, Stereotactic biopsy

## INTRODUCTION

Despite the tremendous improvement in neuroradiology and nuclear medicine, especially in magnetic resonance imaging (MRI) and positron emission tomography (PET), definitive diagnosis in most brain lesions require histopathological examination. When a bulk excision of the

mass should not be taken in consideration, especially in the diagnosis of deeply located, diffused infiltrative or multiple space-occupying lesions, computerized tomography (CT) or MRI-guided stereotactic biopsies have been proven to be safe and reliable by various studies (2,4,7-9,11-13,15,16,18,19, 21-23,25-29,31-38). Frameless stereotactic techniques have



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been improved with the use of neuronavigation devices; however, they are not yet as safe as framed systems, especially in terms of target acuity of small lesion biopsies, despite the presence of studies claiming the opposite (1,6,11,12,15,16,26,31-33,37,38).

In this prospective study, we provide the results of CT-guided stereotactic biopsies of consecutive 500 cases that carried out in a single center.

## ■ MATERIAL and METHODS

Between the dates of March 1998 and January 2015, CT-guided stereotactic biopsies were performed by using the Leksell stereotactic frame system (Elekta Instruments EU, Sweden) in 500 patients. A total of 512 procedures, with 2 times in ten cases and 3 times in one case, were made. Surgery was repeated due to the request of the neuropathologist in six cases and the detection of growth of the lesion and/or change in contrast material enhancement in MRI examinations in five cases. The series comprised of 184 female (36.8%) and 316 male (63.2%) patients, ages ranging from 3 to 81 years (mean  $50.40 \pm 16.67$ ). Lesions were found to be diffuse in 256 patients (51.2%), deeply located in 175 patients (35%), multiple in 69 patients (13.8%) (Table I). The stereotactic frame was placed under general anesthesia in seventeen children and one adult cases and local anesthesia in other cases. Contrast enhanced cranial CT scans in 3-5 mm thickness were taken and the coordinates of the target were determined in CT device console. Sedative and/or analgesic drugs were administered in addition to local anesthesia for patients aged, anxious or with a low pain threshold. After the monitoring of the patient, a burr-hole 8 mm in diameter on the mid-pupillary line at the level of ipsilateral coronary suture was performed for the deeply located lesions and for the superficially located lesions the burr hole was made immediately above the lesion. Biopsies were carried out when the patient was normotensive. Backlund's spiral needle and side cutting needle with a 3 mm hole were used to perform biopsies in solid lesions while Backlund's aspiration set was used in cystic lesions. Side cutting needle was only preferred when biopsy could not be performed with a spiral needle. A sample was taken from 1-4 (mean  $1.86 \pm 0.74$ ) targets in total 512 attempts. Due to the conditions of our hospital, intraoperative cytologic examination was carried out only in 11 procedures. The material, which was taken for cytological examination, was spread over the glass lamina and fixed by alcohol by the surgeon. After that, it was taken to the pathology laboratory where it was examined by staining with Hematoxylin-Eosin (HE). Other biopsy materials were sent to the pathology laboratory after fixation in 10% buffered formaldehyde solution. Patients without any complication were discharged from the hospital on the following day. Paraffin sections were taken in the pathology laboratory and firstly, they were stained by HE and after the preliminary examination, immunostaining was performed. The result of histopathological examination was reported within 6-10 days.

## ■ RESULTS

The histopathological examinations revealed no conclusive

diagnosis in 17 (3.3%) of total 512 procedures; tumors in 428 (83.6%) procedures and non-tumoral lesions in 67 (13.1%) operations were detected (Table II). Necrosis, fibrinoid material, cyst fluid containing degenerate cells etc. were found in samples in which no diagnosis could be made. Complications occurred in 10 patients (1.9%) (Table III). One of the symptomatic tumor bleeding was removed by craniotomy and one patient underwent externally ventricular drainage upon the development of hydrocephalus. The epidural hematoma was removed by craniotomy. The patient who developed hypertensive thalamic hematoma six hours after the surgery passed away on the following day and the case who had a myocardial infarction died 6 days later. The other patients were received medical treatment. Consequently, a conclusive diagnosis was identified in 96.7% of procedures with a 0.4% surgical mortality and 1.6 % morbidity.

## ■ DISCUSSION

Stereotactic biopsy (SB) has been one of the techniques to make a diagnosis, which ensures the implementation of appropriate treatment modality in brain lesions especially after the use of CT (2,4,7-9,11-13,15,16,18,19,21,22,25,26,28,29,31-38). It is a reliable and safe diagnostic method which is preferred especially in deeply placed, widespread and multiple lesions. Whether diagnosis rates are high and mortality and morbidity rates are low depend on especially the experience of the surgical team and the neuropathologist (2,7,9,14,16-24,26-29,31-38).

Adaptation of PET, MR perfusion and MR spectroscopy (MRS) examinations to the planning of stereotactic biopsy procedures is significant in the determination of access to the target and the selection of appropriate target and plays a crucial role in increasing the diagnostic success and decreasing the sampling errors (10,12,26,30,36). The success rate is reported to be 100% in the latest studies in which patient numbers are relatively low (12). Furthermore, the use of metabolite scanning findings obtained in MRS examinations and specifically the rates of N-acetyl aspartate (NAA) and choline (Ch) increase the diagnostic success of the surgery by playing a role in the selection of a target location (10-12).

In order not to damage the motor area, we prefer to use a burr-hole on the mid-pupillary line at the level of ipsilateral coronary suture for the deeply located lesions such as pineal and thalamic region, although the trajectory seems to be longer. For the lesions of pineal area, the relation of the internal cerebral veins with the lesion should especially be taken in consideration while planning the trajectory to the target. We do not have any experience with stereotactic biopsy for brain stem lesions.

**Table I:** Location of the Lesions (n=500)

<b>Diffuse</b>	256 (51.2%)
<b>Deep</b>	175 (35%)
<b>Multiple</b>	69 (13.8%)

**Table II: Histopathological Diagnosis**

<b>Diagnosis</b>	<b>n= 512</b>
<b>Tumoral lesions</b>	<b>428 (83.6%)</b>
Diffuse fibrillary astrocytoma	77 (15%)
Anaplastic astrocytoma	47 (9.2%)
Glioblastoma	121 (23.6%)
Pilocytic astrocytoma	8 (1.6%)
Pleomorphic xantoastrocytoma	1 (0.2%)
Oligodendroglioma	12 (2.4%)
Anaplastic oligodendroglioma	1 (0.2%)
Oligoastrocytoma	5 (1%)
Anaplastic oligoastrocytoma	1 (0.2%)
Anaplastic ependymoma	3 (0.6%)
Gliomatosis cerebri	5 (0.8%)
Ganglioglioma	1 (0.2%)
Dysembryoblastic neuroepithelial tumor	1 (0.2%)
Central neurocytoma	4 (0.8%)
Pineocytoma	2 (0.4%)
Pineoblastoma	8 (1.6%)
Pineal parenchymal tumor medium differentiated	1 (0.2%)
Medulloblastoma	2 (0.4%)
Meningioma	3 (0.6%)
Malignant lymphoma	36 (7%)
Germ cell tumor	6 (1.2%)
Craniopharyngioma	1 (0.2%)
Metastasis	82 (16%)
<b>Non-tumoral lesions</b>	<b>67 (13.1%)</b>
Reactive gliosis	35 (6.8%)
Abscess	10 (1.9%)
Granulomatous inflammation	9 (1.8%)
Areas of former hemorrhage	4 (0.8%)
Infarction	2 (0.4%)
Vasculitis	2 (0.4%)
Leukodystrophy	1 (0.2%)
Demyelinating disease	1 (0.2%)
Calcium deposition disease	1 (0.2%)
Acute disseminating encephalomyelitis	1 (0.2%)
Encephalitis	1 (0.2%)
<b>No conclusive diagnosis</b>	<b>17 (%3.3)</b>

**Table III: Complications of CT-Guided Biopsies**

Tumoral bleeding	3 (0.6%)
Hypertensive intracerebral hematoma (Thalamic/Putaminal)	2 (0.4%)
Peroperative seizure	2 (0.4%)
Epidural hematoma	1 (0.2%)
Cerebral edema	1 (0.2%)
Myocardial infarction	1 (0.2%)

SB is a multidisciplinary technique in which neurosurgeon, neuropathologist and neuroradiologist work in cooperation. Small size of the samples is the factor that brings adversity and difficulty to the neuropathologist. Increasing the number of access trace to increase amount of samples to be taken increases the risks of mortality and morbidity. In order to ensure the reliability of the ranking of glial tumors, it is requested to examine as much amount as possible. In order to make the definite diagnosis in stereotactic biopsies performed in heterogeneous lesion, sampling must be conducted in the areas both with enhancement of contrast material and with no enhancement. Sampling must be conducted in multiple areas by carrying out serial longitudinal biopsies (1,2,4,6,9, 16,18-20,28,29,31-38). In CT guided SB in lesions with no enhancement with contrast media; software programmes fusing the MRS and CT scans and the selection of area which is high in terms of Ch/NAA in MRS would enable carrying out a biopsy from the tumoral tissue instead of reactive gliosis. In this study, despite the fact that we managed to perform intraoperative cytologic examination only in 11 (2.1%) out of 512 procedures, our conclusive diagnosis rate was 96.7%.

Intraoperative cytologic examination increases the diagnostic rate by enabling to take adequate sample from accurate target. The most significant advantages of intraoperative cytologic examination are its fastness, simplicity and having high levels of diagnosis rate (5,19,32,34). Although there are studies which argue that there is no need for a routine intraoperative neuropathological examination in SB (11,12, 33), we do believe that intraoperative cytologic/histological examination is essential in order to increase the diagnostic yield and to decrease the number of biopsy specimens taken in stereotactic biopsies carried out in cases where there are no MRS/CT fusion images.

Small tissue samples taken during the SB may not always be sufficient in conclusive diagnosis of non-tumoral lesions. In our series definitive diagnosis were established in only 47.8% of non-tumoral lesions while in the others, it was reported only as "reactive gliosis". Reactive gliosis could be seen in specific neurological diseases as well as areas close to the tumoral tissue. Tissue samples should be taken in different areas of the lesion. In our series, the rate of reactive gliosis is 6.8%. Most of the procedures were carried out when it was not possible to get advanced MRG examinations in our hospital; in other words, when we could not have detailed information regarding the distinction between tumoral and non-tumoral

lesions by neuroradiological examinations before the year of 2005. In our series, patients that were diagnosed with reactive gliosis are closely followed up, and there has been no tumoral progress determined so far. When patients were consulted to our clinic for the purposes of SB, MRS and MR perfusion scans are obtained first in lesions with no enhancement of contrast media, if there is any suspicion of tumoral lesion in these examinations, we plan to do SB. We think that SB must be carried out in multiple space occupying lesions when the primary lesion site is not clear in PET examinations or sufficient biopsy material cannot be taken from the primary lesion. We do not approve to perform the biopsy procedure, which is an invasive method having a mortality and morbidity risk although lower, before these examinations are performed.

Complication and definitive diagnostic rates vary in studies conducted so far. It is shown that the good results of SB, meaning low levels of complication rate together with high levels of conclusive diagnostic rates, is in direct correlation with surgical technique, experience of the neuropathologist and the surgeon (2,7,9,1,17-19,21-24,27-29,32,34,37). Comparison of our series with the results of other large series was shown in Table IV. In our series, one of our cases went through myocardial infarction in the early postoperative period and passed away on the 6<sup>th</sup> day. In our two cases, hypertensive hematoma was observed out of the target and the access trace within the postoperative 6-12 hours. Applying sedative analgesia in addition to local anesthesia may prevent possible complications such as high blood pressure in patients with anxiety and a low pain threshold as well as in cases having a coronary ischemia or a cardiac arrhythmia.

The biopsy sample taken by Backlund spiral needle has 1 mm width and 1cm length (3). Encountering resistance when a needle being withdrawn by 1-2 mm gives rise to a sense that a vessel twined the spiral needle. When confronted such a situation, instrument is withdrawn together with a cannula after the spiral being turned down. Although it is possible to take a larger tissue sample with a side-cutting cannula, the bleeding risk is higher due to the fact that there is no possibility to understand if a vessel is inside the cannula by the tactile warning. In our series, we used the side-cutting needle in very soft or very hard lesions where we could not take a sample by the spiral needle; unfortunately symptomatic tumoral bleeding developed in 2 out of the total 12 sampling procedures.

Performing SB first in cases where microsurgical resection is needed is controversial. It is carried out to make a histopathological diagnosis for the purposes of planning of oncological treatment in cases when patients themselves or patient's family does not accept the craniotomy as gospel. SB should not be performed if an additional adjuvant treatment cannot be done in patients who are advanced aged or has a score of <30 on the scale of Karnofsky performance.

Various clinical studies have been conducted regarding frameless stereotactic systems since the beginning of the century (1,6,10-12,15,16,26,31,33,37,38). Especially with the advancement of the MR/PET practices, right target and suitable sampling rates have been increasing. Comparing with the framed systems, its cost is significantly higher. Although recent studies showed there are no significant differences in diagnostic yield among the frame-based and frameless

**Table IV:** Diagnostic Yield, Morbidity and Mortality in Stereotactic Biopsy Series (%)

Author	n	Diagnostic yield	Morbidity	Mortality
Ostertag et al. 1980 (29)	302	100	3.3	2.3
Mundinger 1985 (28)	815	83.0	3.0	0.6
Voges et a. 1993 (35)	338	88.0	1.2	0.6
Apuzzo et al. 1987 (2)	500	95.6	1.0	0.2
Bernstein et al. 1994 (7)	300	95.3	1.7	4.7
Field et al. 2001 (14)	500	94.4	9.6	0.2
Kreth et al. 2001 (24)	345	98.0	3.1	0
Kim et al. 2003 (22)	308	91.7	3.9	0.6
Grossman et al. 2005 (17)	355	93.8	3.6	0.6
Tilgner et al. 2005 (34)	5000	90.3	2.7	0.7
Dammers et al. 2008 (11)	465	89.5	11.7	3.9
Kongkham et al. 2008 (23)	622	98.4	6.9	1.3
Kickingereder et al. 2013 (21)	1480	96.2	7.8	0.9
<i>Total</i>	<i>11330</i>	<i>93.2</i>	<i>4.6</i>	<i>1.3</i>
Present series	512	96.7	1.6	0.4

\*Only series greater than 300 cases were included.

stereotactic procedures, they seem not to be as safe as framed-based systems especially in deeply located small lesions in terms of their target acuity.

## ■ CONCLUSION

In this clinical study, our mortality rate is 0.4% and morbidity rate is 1.6% while the conclusive diagnostic rate is 96.7%. The results showed that CT guided stereotactic biopsy is safe and reliable procedure with acceptable mortality and morbidity rates, especially in deeply located, diffused infiltrative or multiple space-occupying intracranial lesions where surgical resection is not suitable and when there is a need of histopathological examination for the planning of an appropriate treatment.

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