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Diagnostic yield and morbidity by neuronavigation-guided frameless stereotactic biopsy using magnetic resonance imaging and by frame-based computed tomography-guided stereotactic biopsy

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Abstract

Background: We compared the diagnostic yield and morbidity by frame-based computed tomography-guided stereotactic biopsy (CTSTB) with Brown-Roberts-Wells (BRW) unit and by neuronavigation-guided frameless stereotactic biopsy (NSTB) using magnetic resonance imaging (MRI).

Methods: The subjects' age range was 15-83 years. CTSTB with BRW unit was performed for 59 tumors (58 cases, 1988-2007). NSTB was performed for 38 tumors (35 cases, 2007-2013) with the needle sheath attached to the head holder. By NSTB, target locations of sampling points and trajectories were confirmed by using MRI. Diffusion tensor imaging-based fiber tractography was used to achieve safe trajectories. STB by using BRW did not visualize the trajectory virtually; however, the planning images for NSTB were able to show the trajectory virtually before the procedure.

Results: Histological diagnoses were established for 93 tumors at the first biopsy. The diagnostic yield was 94.9% by CTSTB and 97.4% by NSTB ($P = 0.944$). The morbidity rate was 5.1% by CTSTB and 0% by NSTB ($P = 0.417$). The absolute risk reduction was 23.1% by NSTB when the targets were basal ganglia (putamen, globus pallidus) or thalamus. In the cases of glioma for which the targets were basal ganglia (putamen, globus pallidus) or thalamus, the absolute risk reduction by NSTB was 30%.

Conclusions: There was no significant difference between CTSTB and NSTB concerning the diagnostic yield and morbidity. However, when the target is the basal ganglia (putamen, globus pallidus) or thalamus and glioma is suspected, NSTB by using MRI with virtual trajectory is preferable to CTSTB concerning morbidity.

Key Words: Brain tumor, neuronavigation, stereotactic biopsy

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INTRODUCTION

Frame-based computed tomography-guided stereotactic biopsy (CTSTB) with Brown-Roberts-Wells (BRW) units achieved point accurate intracranial access with an accuracy of less than 1 mm. In addition, procedural objectives can be achieved satisfactorily without mortality.[1,2] It is a less-invasive method to obtain the samples of brain tumors for diagnosis, compared with the open craniotomy surgery. However, postoperative neurological deterioration after biopsy was sometimes seen. Several authors reported that glioma of the basal ganglia (putamen or globus pallidus) and thalamus constituted a risk factor of morbidity by the frame-based stereotactic biopsy.[7,9,10,13,15] Recently, the technology of the neuronavigation system has been developed. Neuronavigation-guided frameless stereotactic biopsy (NSTB) by using magnetic resonance imaging (MRI) is also an accurate and less-invasive method.[3-5,9,11,16] Unfortunately we did not have the clinical data of stereotactic biopsy by using MRI with stereotactic frame for consecutive cases. Therefore, we were not able to compare frame-based MRI guided stereotactic biopsy with CTSTB. However, we were able to compare NSTB [VectorVision 7, iPlan (BrainLAB AG, Heimstetten, Germany) and Cranial software (Mach) Planning 4.6 (Medtronic, Minneapolis, MN, USA)] that visualized trajectory virtually with CT-guided stereotactic biopsy without showing trajectory virtually. In this article, we compared frame-based CTSTB with NSTB by using MRI, concerning the diagnostic yield and morbidity.

MATERIALS AND METHODS

This is retrospective study of the prospective databases of three hospitals. The patients gave permission to publish these features, and the identities of the patients have been protected. We obtained additional consent from the parents of subjects aged 15-19 years. The age distribution of the patients ranged from 15 to 83 years. There was no experimental surgery for the patients in this study. Cases with severe neurological deformities whose radiological findings showed increased intracranial pressure were excluded for stereotactic biopsy. Patients with bleeding tendency that could not be controlled were also excluded. The procedures of biopsy were performed by the neurosurgeons certified by the Japan Neurosurgical Society and whose experiences of neurosurgery were over 6 years. The locations of the targets for stereotactic biopsy are shown in Table 1. CTSTB with BRW unit was performed for consecutive 59 tumors (58 cases) at Hyogo Cancer Center from 1988 to 2007. NSTB was not available at Hyogo Cancer Center during that period. The target location was confirmed on CT. We used a side-cutting biopsy needle kit to obtain the samples. All biopsies were performed under local anesthesia with a single burr hole. It took less than 2 h to reach the target and obtain the sample. NSTB was performed for 38 tumors (35 cases). We used VectorVision 7 and iPlan (BrainLAB AG) for 12 consecutive tumors (11 cases) at Kobe University Hospital and StealthStation TRIA and Cranial software (Mach) Planning 4.6 with Passive Biopsy Kit (Medtronic) for 26 consecutive tumors (24 cases) at Nishi-Kobe Medical Center from 2007 to 2013. NSTB was selected during that period if the patient was a candidate for the stereotactic biopsy for intracranial lesions. By NSTB, target locations of the sampling points and trajectories were confirmed by MRI before biopsy. Diffusion tensor imaging-based fiber tractography was also used to obtain safe trajectories and not to pass the pyramidal tracts [Figure 1]. The entry point was chosen within a noneloquent area such as the Kocher point or superior parietal lobule. We made trajectories in such a way that they would not pass the vessels, sulcus, and ventricle [Figures 2 and 3]. By using the frameless biopsy arm that attached to the head holder and pre-calibrated biopsy needle and sheath, we performed the neuronavigation-guided biopsy procedure. It took between 1 and 2 h to make the tractography and

Table 1: Locations of the target

Total	CTSTB	NSTB	*P*=0.9167 (6×2 Yates Chi-square test)
	59 tumors (%)	38 tumors (%)	
Lobe	43 (72.9)	25 (65.8)	
Pineal gland	2 (3.4)	0	
Thalamus	8 (13.6)	6 (15.8)	
Basal ganglia	5 (8.5)	5 (13.2)	
Brainstem	1 (1.7)	0	
Cerebellum	0 (0)	2 (5.3)	

CTSTB: Computed tomography-guided stereotactic biopsy,
NSTB: Neuronavigation-guided frameless stereotactic biopsy

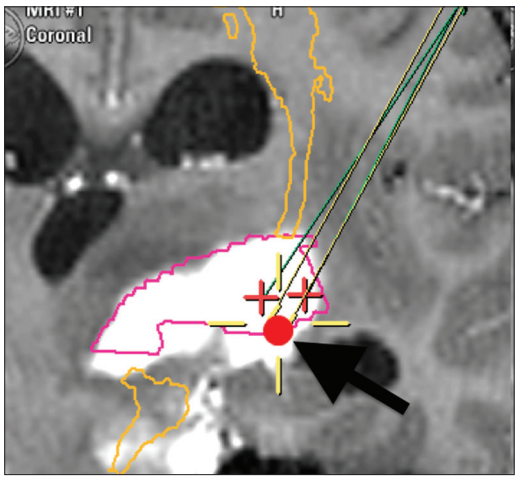

Figure 1: Tractography and the target of the tumor for biopsy. This image was made by using iPlan on the basis of the T1-weighted image of the patient. The tumor was enhanced by gadolinium diethylenetriamine pentaacetic acid. The ocher lines show presumed pyramidal tract. Arrow indicates the target of the tumor for biopsy

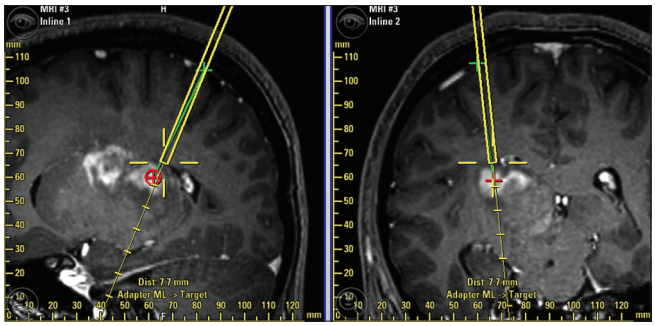

Figure 2: Trajectory, the entry point, and the target. The yellow lines show the trajectories. The entry point was made in the left superior parietal lobule (green circle). The target point is indicated by a red circle. Trajectories were made in such a way that they would not pass the vessels, sulcus, and ventricle

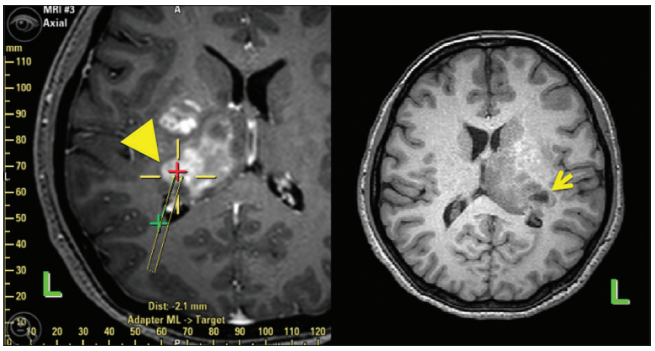

Figure 3: The target of the tumor and biopsy site on postoperative MRI. Arrowhead shows the target of the tumor (left). Postoperative MRI T1-weighted image shows the biopsy site (arrow, right)

achieve safe trajectories. We performed biopsy under local anesthesia (general anesthesia as patients desired) with burr holes. A side-cutting biopsy needle kit was used to obtain the samples. It took less than 2 h to obtain the samples. The diagnostic yield and morbidity were studied in each case and Yate's *P* values were calculated.

RESULTS

Histological diagnoses were established for 93 tumors (89 cases) at the first biopsy. We examined equivalence of the population of patients statistically between CTSTB and NSTB. The locations of the targets for stereotactic biopsy are shown in Table 1. There were no significant differences between CTSTB and NSTB concerning target locations for biopsy ($P = 0.9167$, 6×2 Yates Chi-square test). CTSTB with BRW unit revealed that 17 tumors were astrocytomas, 6 were anaplastic astrocytomas, 12 were glioblastomas, 8 were metastatic brain tumors, 9 were malignant lymphomas and leukemias, 2 were germ cell tumors, and 2 were abscesses. In 3 of 59 tumors (5.1%) examined by CTSTB with BRW unit, the diagnoses were not apparent at the first biopsy. Two patients underwent a second biopsy, which confirmed the diagnosis of glioblastoma. Diagnostic yield was 94.9% by CTSTB. NSTB revealed that 3 tumors were anaplastic astrocytomas, 9 were glioblastomas, 1 was fibrillary astrocytoma, 12 were malignant lymphomas, 1 was anaplastic oligodendroglioma, 3 were metastatic brain tumors, 4 cases had demyelinating disease, 2 cases had infarction, and 2 cases had abscess. In 1 of 38 tumors (2.6%) examined by NSTB, the diagnoses were not apparent at the first biopsy. The patients underwent a second biopsy, which confirmed the diagnosis of glioblastoma. Diagnostic yield was 97.4% by NSTB. There was no significant difference between NSTB and CTSTB regarding the diagnostic yield ($P = 0.944$, Yates Chi-square test). Complications are shown on Table 2. Severe hemorrhage was noted just after CTSTB with BRW unit in three cases, requiring emergency surgery to remove the hematoma and tumor. One case had astrocytoma (putamen, globus pallidus), one had anaplastic astrocytoma (thalamus), and another one had glioblastoma (putamen, globus pallidus). Hematoma was caused by artery injury. According to the medical records of the emergent surgery, several abnormal arteries were recognized within the hematoma, glioma, and sulcus near the lesions. Neurological deficits of hemiparesis remained in all cases. Acute myocardial infarction occurred in one case after NSTB within 24 h. Percutaneous coronary intervention was performed successfully. Regarding neurological deficits, the morbidity rate of NSTB was 0% and that of CTSTB with BRW unit was 5.1%. There was no significant difference between NSTB and CTSTB regarding morbidity ($P = 0.417$, Yates Chi-square test). The absolute risk reduction by NSTB compared with CTSTB is shown on Table 3. When the target was basal ganglia (putamen, globus pallidus) or thalamus, the absolute risk reduction was 23.1%. In the cases of glioma for which the targets were basal ganglia (putamen, globus pallidus) or thalamus, the absolute risk reduction by NSTB was 30%. Also, the number needed to treat is shown in Table 3.

Table 2: Complications after biopsy surgery within 24 h and death within 30 days

	CTSTB (cases)	NSTB (cases)	*P* value, Yates Chi-square test
Hematoma >50 mm	3	0	0.446
Infection, meningitis	0	0	1
Acute myocardial infarction	0	1	0.797
Convulsion	2	0	0.709
Neurological deficits	3	0	0.446
Death within 30 days	0	0	1

CTSTB: Computed tomography-guided stereotactic biopsy, NSTB: Neuronavigation-guided frameless stereotactic biopsy

Representative case

An 18-year-old woman was admitted to our hospital because of sensory disturbance of the right upper and lower limbs for a month. She had no history of disease.

Table 3: Absolute risk reduction by the neuronavigation-guided frameless stereotactic biopsy compared with the frame-based computed tomography-guided stereotactic biopsy

Factor	Absolute risk reduction by NSTB (%)	Number needed to treat
Location of target		
Basal ganglia (putamen, globus pallidus) or thalamus	23.1	5
Other regions	<5	
Pathology		
Glioma	8.8	12
Other pathology	<5	
Glioma and basal ganglia (putamen, globus pallidus), glioma and thalamus	30	4

NSTB: Neuronavigation-guided frameless stereotactic biopsy

The Karnofsky Performance Status (KPS) score was 80%. A CT scan revealed a high-density area in the left globus pallidus and putamen, which showed calcification. The T1-weighted image revealed an area of iso and low signal intensity in the left thalamus and an area of iso and high signal intensity in the left globus pallidus and putamen. The T2-weighted image revealed areas of high signal intensity in the left thalamus, globus pallidus, and putamen. The tumor of the left thalamus was enhanced by gadolinium diethylenetriamine pentaacetic acid. Cerebral angiography showed weak vascular staining. We selected NSTB to obtain a sample of the tumor. Tractography and trajectories were made by using iPlan [Figure 1]. The entry point was chosen within the region in the left superior parietal lobule. The target point was made in the left thalamus [Figure 2]. Complications and postoperative neurological deterioration were not seen after biopsy. Postoperative MRI revealed that the neuronavigation-guided system worked correctly [Figure 3]. The histological diagnosis was anaplastic astrocytoma. MIB-1 positivity was 18%. Fluorescence *in situ* hybridization examination showed no 1p and 19q loss of heterozygosity. Subsequent treatment consisted of radiation therapy (60 Gy) and administration of temozolomide.

DISCUSSION

Frame-based stereotactic biopsy is still regarded as an important diagnostic tool.[8] It requires less anesthesia resources, less operating room time, and shorter hospital stays than the frame-less stereotactic navigation. NSTB by using MRI is more labor-intensive compared with CTSTB. In some cases, it takes several hours to obtain safe trajectories. Registration just before biopsy also takes time in some cases.[14] Concerning the diagnostic yield and morbidity, our results did not show significant difference between NSTB by using MRI and CTSTB. Lunsford *et al*. reported that 6 of 1664 patients (0.36% of the total diagnostic biopsy series with stereotactic frame) required a craniotomy and evacuation of clot. Unfortunately, we could not compare our results of NSTB with those results concerning target locations and pathological diagnoses because the article did not show the results related to the target and pathological diagnosis.[8] Our results showed the rate of hemorrhage in the frame-based group was high. However, when we excluded the glioma of the basal ganglia and thalamus cases, the rate of major hemorrhage was 0%. Our experiences of major hemorrhages after biopsy were due to injury of arteries. According to the medical records of the emergent surgery, several abnormal arteries were recognized within the hematoma, glioma, and sulcus near the lesions. So, we assumed for avoiding hemorrhage it is also important that the trajectory selected should not pass the sulcus and vessels near the target. When the target for biopsy was basal ganglia (putamen, globus pallidus) and thalamus, the absolute risk reduction and the number needed to treat showed benefits of NSTB. Furthermore, the absolute risk reduction by NSTB showed preferable outcome in the case of glioma. A limitation of this study is that this study was not based on randomized controlled trials. However, we used prospective databases of three hospitals in order to compare the two different modalities. Hyogo Cancer Center, Kobe University Hospital, and Nishi-Kobe Medical Center treated patients of brain tumors at different areas. Hyogo Cancer Center is situated in the western part of Hyogo Prefecture. Kobe University Hospital is situated in the central part of Kobe City. Nishi-Kobe Medical Center is situated in the western part of Kobe City. From 1988 to 2007, the frame-based CTSTB was performed for the stereotactic biopsy and NSTB was not available at Hyogo Cancer Center. The neuronavigation system is available for the stereotactic biopsy at Kobe University Hospital and Nishi-Kobe Medical Center. NSTB was performed for consecutive cases and CTSTB was not selected at the both hospitals from 2007 to 2013. We examined equivalence of the population of patients statistically between CTSTB and NSTB. There were no significant differences between CTSTB and NSTB concerning target locations ($P = 0.9167$, 6×2 Yates Chi-square test). We were not able to analyze the influence of our learning curve. All recent cases showing fewer complications had undergone NSTB; however, most physicians were inexperienced in neuronavigation-guided biopsy as NSTB was a new modality. On the other hand, the medical staffs at Hyogo Cancer Center were completely proficient in stereotactic biopsy with BRW. Some authors reported that several factors are considered to be associated with lower morbidity associated with stereotactic biopsy. Basal ganglia lesions, thalamic lesions, deep-seated lesions, brain stem lesions, poor control of blood pressure during

the biopsy itself, hyperglycemia, performing a second trajectory, poor immune status, failed biopsy group, and preoperative use of antiplatelet agents or chronic corticosteroids are the risk factors for biopsy-associated complications, morbidity, and mortality.[6-10,13,15] Highly vascular tumors such as malignant glioma are a strong risk factor of morbidity associated with stereotactic biopsy. It is useful to assess the tumor by cerebral angiography before biopsy. For tumors that show hy pervascularity, it might be better to perform resection of the tumor with widely opened craniotomy enough to stanch the bleeding using hemostasis tools if the general condition of the patient is acceptable for surgery. The basal ganglia (putamen or globus pallidus) and the thalamus are highly vascularized regions with several perforating vessels. Our results showed that the absolute risk reduction by NSTB was 30% in the cases of glioma of basal ganglia and glioma of thalamus, compared with the results of CTSTB. The number needed to treat was 4. Making a trajectory by using MRI and proceeding with NSTB yielded favorable outcomes. We considered the following as the reasons as follows. STB by using BRW does not visualize the trajectory virtually; however, NSTB [VectorVision 7, iPlan and Cranial software (Mach) Planning 4.6] shows the trajectory virtually. Furthermore, we can alter the trajectory intraoperatively. Many vessels are shown as flow void signals or enhanced lines on MRI. In order to perform safe biopsies, it is important that physicians avoid injury to vessels and the pyramidal tract. The MRI-guided biopsy provides solutions for safe trajectories and high diagnostic accuracy.[12] Representative figures [Figures 1-3] show preplanning the trajectory avoiding vessels, sulcus, ventricle, and presumed pyramidal tract. We considered that the stability of neuronavigation-guided stereotactic biopsy with the holder and sheath was almost equal to that of frame-based biopsy. Preplanning the trajectory and consideration of safe tract are the benefits of NSTB with the special software and workstation. We conclude that if the location of the tumor is not deep and, for example, if malignant glioma is not suspected, CTSTB with BRW can be easily performed with a low morbidity rate. However, if malignant glioma is suspected and the location of the tumor is deep, for example, in basal ganglia or thalamus, it would be better to select NSTB by using MRI. Indeed, this study was not based on the meta-analysis of randomized control trials. We need further examinations to show that NSTB with visualization of the virtual trajectory for deep-seated glioma is superior to frame-based biopsy without software to preplot probe trajectories.

CONCLUSIONS

There was no significant difference between CTSTB and NSTB by using MRI concerning the diagnostic yield and morbidity. However, when the target is basal ganglia (putamen, globus pallidus) or thalamus and glioma is suspected, NSTB that enables to visualize virtual trajectory during surgery is preferable to CTSTB to reduce morbidity.

Protection of patients' rights to privacy

The patients have provided permission to publish these features in written form, and the identities of the patients have been protected in this article without showing patients' names. We obtained additional consent in written form from the parents of subjects aged 15-19 years.

Human rights

There is no experimentation on human beings in this study. We compared the outcome of the navigation-guided biopsy and CT-guided biopsy. Both techniques are standard surgical techniques to obtain the tissues.

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