Image-guided Procedures in Brain Biopsy

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Abstract

Image-guided procedures, such as computed tomography (CT)-guided stereotactic and ultrasound-guided methods, can assist neurosurgeons in localizing the relevant pathology. The characteristics of image-guided procedures are important for their appropriate use, especially in brain biopsy. This study reviewed the results of various image-guided brain biopsies to ascertain the advantages and disadvantages. Brain biopsies assisted by CT-guided stereotactic, ultrasound-guided, Neuronavigator-guided, and the combination of ultrasound and Neuronavigator-guided procedures were carried out in seven, eight, one, and three patients, respectively. Four patients underwent open biopsy without a guiding system. Twenty of 23 patients had a satisfactory diagnosis after the initial biopsy. Three patients failed to have a definitive diagnosis after the initial procedure, one due to insufficient volume sampling after CT-guided procedure, and two due to localization failure by ultrasound because the lesions were nonechogenic. All patients who underwent biopsy using the combination of ultrasound and Neuronavigator-guided methods had a satisfactory result. The CT-guided procedure provided an efficient method of approaching any intracranial target and was appropriate for the diagnosis of hypodense lesions, but tissue sampling was sometimes not sufficient to achieve a satisfactory diagnosis. The ultrasound-guided procedure was suitable for the investigation of hyperdense lesions, but was difficult to localize nonechogenic lesions. The combination of ultrasound and Neuronavigator methods improved the diagnostic accuracy even in nonechogenic lesions such as malignant lymphoma. Therefore, it is essential to choose the most appropriate guiding method for brain biopsy according to the radiological nature of the lesions.

Key words: biopsy, brain, Neuronavigator, stereotactic surgery, ultrasound

Introduction

Computed tomography (CT) and magnetic resonance (MR) imaging provide precise three-dimensional information on the location and configuration of intracranial lesions. Even before the advent of CT guidance, stereotactic surgery was used to localize, biopsy, and treat certain deep-seated lesions. Certain modern technological modifications have facilitated this kind of surgery. Although stereotactic procedures with the aid of CT have been widely used in brain biopsy, there are several limitations. First, the rigid coordinate frame that is attached to the patient's skull is bulky and restrictive and only provides a temporary frame of reference. Second, the aiming arc assembly that guides surgical instruments is often cumbersome and complex, and can only select one target point and trajectory at a time. Third, real time intraoperative display of the surgeon's position is not currently possible. Because of these restrictions, some investigators have pursued novel technologies for surgical intervention such as the use of ultrasound and the use of the passive localization arm in “Neuronavigator.”

The greatest clinical impact of image-guided surgery, such as CT-guided, ultrasound-guided, and Neuronavigator-guided methods, has been in brain biopsy. It is very important for neurosurgeons to select the most appropriate method in brain biopsy because a definite diagnosis should be made with minimal invasiveness. This study analyzed the results of brain biopsies to investigate the charac-
teristics of each procedure and to determine their appropriate use.

Materials and Methods

The guiding instruments used in this series were Komai's CT-stereotactic apparatus (Mizuho Ika Co., Tokyo), ultrasound scanner with 5 MHz transducer (Aloka Co., Tokyo), and the Neuronavigator (Mizuho Ika Co.).

The components of Komai's frame system are used as follows. The head ring is fixed to the skull to provide a constant reference plane. The localizing system is attached to the base ring, and the patient is scanned by CT. The anteroposterior and lateral coordinates of the localizing rods and any number of target points are read from the CT display monitor. In the operating room, the approximate anteroposterior, lateral, and vertical coordinates are set up on the guidance arc, and the operative procedure is started. The Neuronavigator is a passive articulated localization arm with computer video display of the intraoperative end-point position marked on preoperative CT images. The arm end-point position is determined by digitizing the angles at each of the arm joints. Registration of the image space, the patient's intracranial space, and the localizing arm depend on three skin-mounted radiopaque markers. Surgery can proceed in a standard fashion with the localization arm employed when necessary.

In principle, we intended to perform CT-guided stereotactic biopsy for lesions appearing as low-density homogeneous and hypodense lesions on CT, and ultrasound-guided biopsy through a small craniotomy to avoid an intraoperative hemorrhage for lesions appearing as inhomogeneous or hyperdense on CT. Twenty-six brain biopsies were performed on 23 patients aged 16 to 75 years over a 13-year period (1985-1997). Seven of the 23 initial biopsies were performed with a CT-guided stereotactic procedure using the Komai frame, and the remaining 16 biopsies were performed by craniotomy. Among 16 craniotomy procedures, eight were performed with ultrasound guidance, one with Neuronavigator guidance, and three with combined ultrasound and Neuronavigator guidance (ultrasound-assisted Neuronavigator guidance). The

Table 1  Summary of the cases

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Biopsy methods</th>
<th>Lesions</th>
<th>CT findings</th>
<th>Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>CT stereotactic</td>
<td>lt FL</td>
<td>superficial</td>
<td>low</td>
</tr>
<tr>
<td>2</td>
<td>CT stereotactic US + Navi</td>
<td>lt TL</td>
<td>superficial</td>
<td>low (+ high)</td>
</tr>
<tr>
<td>3</td>
<td>CT stereotactic</td>
<td>rt BG</td>
<td>deep</td>
<td>low</td>
</tr>
<tr>
<td>4</td>
<td>CT stereotactic</td>
<td>rt BG</td>
<td>deep</td>
<td>low</td>
</tr>
<tr>
<td>5</td>
<td>CT stereotactic</td>
<td>rt FL</td>
<td>deep</td>
<td>low</td>
</tr>
<tr>
<td>6</td>
<td>CT stereotactic</td>
<td>rt BG</td>
<td>deep</td>
<td>low</td>
</tr>
<tr>
<td>7</td>
<td>CT stereotactic</td>
<td>lt BG</td>
<td>deep</td>
<td>iso</td>
</tr>
<tr>
<td>8</td>
<td>US</td>
<td>rt FL</td>
<td>superficial</td>
<td>high</td>
</tr>
<tr>
<td>9</td>
<td>US</td>
<td>rt FL</td>
<td>superficial</td>
<td>high</td>
</tr>
<tr>
<td>10</td>
<td>US</td>
<td>rt FL</td>
<td>superficial</td>
<td>high</td>
</tr>
<tr>
<td>11</td>
<td>US</td>
<td>rt FL</td>
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<td>low</td>
</tr>
<tr>
<td>12</td>
<td>US</td>
<td>lt FL</td>
<td>deep</td>
<td>low</td>
</tr>
<tr>
<td>13</td>
<td>US</td>
<td>cerebellum</td>
<td>deep</td>
<td>low</td>
</tr>
<tr>
<td>14</td>
<td>US</td>
<td>CT stereotactic</td>
<td>lt BG, rt OL</td>
<td>deep</td>
</tr>
<tr>
<td>15</td>
<td>US open biopsy</td>
<td>bil BG, pons</td>
<td>superficial</td>
<td>low</td>
</tr>
<tr>
<td>16</td>
<td>Navi</td>
<td>lt FL</td>
<td>superficial</td>
<td>low</td>
</tr>
<tr>
<td>17</td>
<td>US + Navi</td>
<td>lt FL</td>
<td>superficial</td>
<td>high</td>
</tr>
<tr>
<td>18</td>
<td>US + Navi</td>
<td>lt FL</td>
<td>superficial</td>
<td>low</td>
</tr>
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<td>19</td>
<td>US + Navi</td>
<td>lt TL</td>
<td>superficial</td>
<td>low</td>
</tr>
<tr>
<td>20</td>
<td>open biopsy</td>
<td>bil FL</td>
<td>superficial</td>
<td>high</td>
</tr>
<tr>
<td>21</td>
<td>open biopsy</td>
<td>lt PL</td>
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<td>low</td>
</tr>
<tr>
<td>22</td>
<td>open biopsy</td>
<td>bil FL, rt PL</td>
<td>superficial</td>
<td>low</td>
</tr>
<tr>
<td>23</td>
<td>open biopsy</td>
<td>cerebellum</td>
<td>superficial</td>
<td>low</td>
</tr>
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remaining four were performed by craniotomy without a guiding system because the lesions were superficially located.

There was no facility for frozen section diagnosis in our hospital, so no intraoperative examination of brain tissues was performed.

**Results**

Twenty of 23 patients had a satisfactory diagnosis after the initial biopsy but three patients required an additional operation. The histological diagnoses were 15 neoplastic (astrocytoma 7, malignant lymphoma 4, others 4) and eight nonneoplastic tumors (Table 1).

Seven patients with hypodense or isodense lesions initially underwent CT-guided stereotactic biopsy. Most lesions were deep-seated, and there were no hemorrhagic complications. Insufficient sample volume for a definitive diagnosis was obtained in Case 2. Ultrasound-assisted Neuronavigator-guided biopsy was then performed and the definitive diagnosis was malignant lymphoma.

Ultrasound-guided biopsy was used to investigate both superficially located hyperdense lesions and deep-seated hypodense lesions in eight patients. This procedure was effective for the diagnosis of hyperdense lesions, but was less effective for the diagnosis of deep-seated hypodense lesions. Two deep-seated hypodense lesions were misdiagnosed because ultrasound did not help localize the lesions (Cases 14 and 15) as inflammation and edematous white matter. Case 15 underwent an open biopsy later because the lesion became larger and the definitive diagnosis was malignant lymphoma. Case 14 underwent a CT-guided stereotactic procedure as a second biopsy and the definitive diagnosis was also malignant lymphoma.

Three patients who underwent biopsy with combined ultrasound and Neuronavigator-guided method and one with the Neuronavigator-guided method had satisfactory diagnoses after the initial procedure. Therefore, seven of eight CT-guided procedures (7 as the initial procedure and 1 as the second procedure), six of eight ultrasound-guided procedures, one of one Neuronavigator-guided procedure, four of four ultrasound-assisted Neuronavigator-guided procedures (3 initial procedure and 1 second procedure), and five of five open biopsy without guiding system (4 initial procedure and 1 second procedure) showed successful results. In this series, no operative complications, such as postoperative bleeding, were observed.

**Representative Cases**

**Case 2**: A 68-year-old female presented with recent memory disturbance. CT revealed a mixed density lesion in the left temporal lobe. MR imaging showed a lesion with low signal intensity on the T1-weighted image and high signal intensity on the T2-weighted image in the left temporal lobe, with homogeneous enhancement after gadolinium injection (Fig. 1). The patient underwent a CT-guided stereotactic biopsy.

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![Image](image_url)

**Fig. 1** Case 2 with malignant lymphoma. T1-weighted magnetic resonance image (left) showing a hypointense lesion, and T2-weighted image (center) showing a hyperintense lesion in the left temporal lobe. T1-weighted image after gadolinium injection showing lesion enhancement with an unclear border (right).
but no histological diagnosis was possible due to insufficient sample volume. Subsequently, an ultrasound-assisted Neuronavigator-guided biopsy was performed. Ultrasound failed to localize the lesion because the lesion was nonechogenic, but accurate localization was confirmed by concomitant Neuronavigator. The definitive diagnosis was malignant lymphoma. This case demonstrates the disadvantages of both the CT-guided and ultrasound-guided procedures, and the advantage of the combined use of ultrasound and the Neuronavigator.

Case 14: A 75-year-old male presented with consciousness disturbance. CT revealed homogeneous hypodense lesions in the left basal ganglia and the right occipital lobe. MR imaging revealed two lesions, one in the left basal ganglia and the other in the right occipital lobe, both appearing low signal intensity on the \( T_1 \)-weighted image and high signal intensity on the \( T_2 \)-weighted image, with homogeneous enhancement after gadolinium injection (Fig. 2). The patient underwent ultrasound-guided brain biopsy of the lesion in the left basal ganglia, but ultrasound failed to localize the lesion because it was nonechogenic. The sample was diagnosed as edematous white matter. CT-guided stereotactic biopsy was then performed, and the final diagnosis was malignant lymphoma. This case demonstrates the disadvantage of the ultrasound-guided procedure.

**Discussion**

CT-guided stereotactic biopsy can be performed under local anesthesia, and various areas within the cranium can be reached easily. However, inadequate sampling in 1.5% to 31% of procedures has been reported. Measurement errors and brain distortion due to outflow of cerebrospinal fluid can cause these failures. Moreover, as we experienced in Case 2, it is not easy to obtain a sufficient sample volume, because the hemorrhagic complication rate of the CT-guided stereotactic procedure is from 0.4% to 3.1%. In the current study, the CT-guided procedure was employed to investigate hypo- or isodense lesions, most of which were deep-seated. Different enhancement patterns were observed, but there were no hemorrhagic complications. Irrespective of enhancement, the CT-guided stereotactic procedure was effective for the diagnosis of hypodense lesions. Therefore, the CT-guided procedure should be considered when investigating deep-seated hypodense lesions.

The main advantage of ultrasound imaging is real-time intracranial information, which is useful for detecting the lesion irrespective of brain shift, and for detecting bleeding. Intracranial lesions are easily localized with intraoperative ultrasound in most cases, but localization failures have been reported. Most localization failures occurred in the case of superficial lesions in the near field of the ultrasound transducer. In the current study, the ultrasound-guided procedure was employed to investigate both superficially located hyperdense le-
Ultrasound was effective in the diagnosis of the superficially located hyperdense lesions, but failed to localize two hypodense lesions in the current study, both of which were nonechogenic. The diagnostic ultrasound method is based on the principle that ultrasound is reflected at the interface between media of different acoustic impedances. If the difference between the two media (normal brain and lesion) is small, ultrasound will not demonstrate the extent of the lesion clearly.\textsuperscript{10} For example, ultrasound failed to localize lesions of malignant lymphoma, gliosis, and encephalopathy.\textsuperscript{3,4,19} Thus, ultrasound is effective only for localizing echogenic lesions, and cannot easily detect certain kinds of lesions such as malignant lymphoma as an obvious mass. Although the ultrasound-guided procedure was effective in the diagnosis of the hyperdense lesions, two of four deep-seated hypodense lesions (Cases 12–15) required additional procedures to reach a satisfactory result. Therefore, careful consideration is required when choosing CT-guided or ultrasound-guided procedures for the diagnosis of deep-seated hypodense lesions.

Another disadvantage of ultrasound is that it cannot be applied over the skull, so does not assist in designing the appropriate craniotomy. In contrast, Neuronavigator is useful for designing the appropriate craniotomy, in approaching deep-seated lesions accurately, and in tracing the edge of lesions.\textsuperscript{25,26} A systematic spatial accuracy of less than 5 mm and errors during operations have been reported.\textsuperscript{22,23,25–27} The coordinate conversion error is caused by skin traction from the skull’s fixation or cranial slippage at the time of craniotomy, and by brain shift which takes place mainly following craniotomy and outflow of cerebrospinal fluid.\textsuperscript{21,23,25} Obtaining real-time information during the procedure can compensate for the shortcomings of the Neuronavigator.\textsuperscript{16,17,25,26}

We performed four ultrasound-assisted Neuronavigator-guided biopsies (Cases 2 and 17–19), all of which had a satisfactory result. We think that the combined use of ultrasound and Neuronavigator works well in most situations by compensating for the disadvantages of each method. In open biopsies, Neuronavigator was very useful in approaching various lesions accurately, even if they were not echogenic. In our Case 2, the lesion could not be detected as an obvious mass on ultrasound, but it was confirmed by the Neuronavigator. Therefore, an ultrasound-assisted Neuronavigator-guided system should be employed to improve the diagnostic accuracy and to achieve minimally invasive surgery, particularly when the lesion is deep-seated and expected to be nonechogenic such as malignant lymphoma.

There was no facility for frozen section or smear examination in our hospital, so we could not perform intraoperative diagnosis of brain tissues. In general, the smear preparation technique is employed intraoperatively for stereotactic brain biopsies, whereas the frozen section technique is used in conventional operations, as larger tissue specimens can be obtained. It is sometimes difficult to obtain sufficient sample volumes in stereotactic brain biopsies, but the intraoperative frozen section technique is recommended for stereotactic brain tumor biopsies.\textsuperscript{21} The greatest difficulties in the diagnosis arise in cases of suspected lymphoma.\textsuperscript{21} Interestingly, all our three cases without a satisfactory diagnosis after the initial biopsy were malignant lymphoma. However, intraoperative histological examination using frozen section or smear preparation techniques may provide a more accurate pathological assessment of the brain tissue.

The characteristics of each image-guided procedure are as follows:

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
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<tbody>
<tr>
<td>CT-guided stereotactic</td>
<td>craniotomy is not required, done under local anesthesia, accurate trajectory</td>
<td>blinded procedure, hemorrhagic complication, insufficient sample volume, aiming assembly is often cumbersome, poor detectability in nonechogenic lesion, useless in designing craniotomy, requires craniotomy and general anesthesia, coordinate conversion error, influence by brain shift</td>
</tr>
<tr>
<td>Ultrasound-guided</td>
<td>obtaining real-time information</td>
<td></td>
</tr>
<tr>
<td>Neuronavigator-guided</td>
<td>useful in designing craniotomy, useful for nonechogenic lesions, accurate trajectory</td>
<td>requires craniotomy and general anesthesia</td>
</tr>
<tr>
<td>Ultrasound-assisted Neuronavigator-guided</td>
<td>useful in designing craniotomy, useful for nonechogenic lesions, accurate trajectory, obtaining real-time information</td>
<td>requires craniotomy and general anesthesia</td>
</tr>
</tbody>
</table>
dure are summarized in Table 2. The greatest clinical impact of image-guided surgery has been in brain biopsies. The most efficient biopsy for deep-seated hypodense homogeneous lesions will be achieved by a CT-guided stereotactic procedure. Biopsy through a small craniotomy with the aid of ultrasound should be considered for hyperdense lesions. In the case of suspected lymphoma, the ultrasound-assisted Neuronavigator-guided system should be considered. Neurosurgeons should select the most appropriate method for brain biopsy according to the radiological nature of the lesions.

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Commentary

The authors described various methods of biopsy such as CT-guided stereotactic, ultrasound-guided, neuronavigator-guided and the combination of ultrasound and neuronavigator-guided procedures, and compared the characteristics of each. In twenty of 23 patients, the pathological diagnosis was confirmed by the initial procedure. But in three patients, they failed to have appropriate tissue samples. The reason for diagnostic failure was insufficient sampling volume in one and inability of localizing lesions in two. However, these failures could be avoided if they performed intraoperative pathological examination of the frozen section in every case to see whether they could obtain adequate fragments of the tissue.

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Osaka, Japan

This paper reviews a variety of image guided procedures that are used for biopsy of the brain. The information provided is valuable, and addresses the various complications and precautions that should be taken in order to perform effective biopsy. Clearly, each individual decision on the part of a neurosurgeon to perform a biopsy must be based on the needs of the patient. In some patients it will be prudent to do a procedure under general anesthesia with a craniotomy. In some it will be desirable to do a frame-based stereotactic needle biopsy under local anesthesia. Image guided techniques of all kinds are continuing to evolve as technology improves, and as neurosurgeons, we should be grateful for the versatility that these techniques offer us in the care of our patients.

One cautionary note is appropriate with regard to patients suspected of having lymphoma of the brain. In these patients it is wise not to give any corticosteroid medications prior to the imaging study that will be used for the biopsy. The reason for this is that many patients with this lesion respond dramatically and essentially disappear, making localization all the more problematical. Another important issue of course is the amount of tissue one obtains for biopsy. The problem with tumors that may be heterogenous with regard to degree of anaplasia is that the opportunity for a "sampling error" exists if the pathologists are not given enough tissue for study.

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This report focuses on a differential study of image-guided procedures for brain biopsy, using CT-guided, ultrasound-guided and neuronavigation. Their main conclusion is that the combined use of ultrasound with the Neuronavigator is an important one, since it compensates for the disadvantages of each method in particular, improving diagnostic accuracy and thus achieving minimally invasive procedures.

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After making a precise histological diagnosis, an appropriate treatment for brain tumor should be started. I like usually to get the surgical specimen with microsurgical technique, even if the tumor is seated in the deep area. The surgical specimen obtained with microsurgery is always large enough for precise histological diagnosis, and above all, surgical resection have soon a significant decreasing mass effect to the brain. None the less, we have no choice but to do needle biopsy for histological diagnosis of the lesions around the basal ganglia or brain stem. Although very precise access to the small deep seated lesion is possible with the CT-guided stereotactic method, the specimen obtained is sometimes too small to make the diagnosis. It is considered that neuronavigation technology will develop and occupy an important area in the neurosurgical field, but at present, unfortunately it is unreliable in the shifted brain after craniotomy. Ultrasound can demonstrate cystic or solid lesions in real time, but it is less effective for the diagnosis of hypodense lesions. Authors showed good biopsy results by the combination of these image guided techniques. I would like to place a high value on this...
author's effort. However, in the brain tumor cases illustrated by authors, I would choose microsurgical resection as a first stage procedure of the treatment without any hesitation.