Diagnostic yield in CT-guided stereotactic biopsy of gliomas

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Twenty-seven patients underwent 29 computerized tomography (CT)-guided stereotactic biopsy procedures for untreated or recurrent malignant astrocytomas. Biopsies were obtained from the hypodense center, enhancing margin, and hypodense periphery as seen on contrast-enhanced CT scans, with diagnostic yields of (number of biopsies yielding tumor/number of biopsies obtained): 34/61 (56%), 68/101 (67%), and 8/22 (36%) from these three zones, respectively. Although tumor was identified in all three zones, diagnostic yield was significantly higher in the hypodense center and enhancing margin. Comparison of patients with untreated tumors to those with recurrent tumors demonstrated no statistical difference in tumor distribution, although there was a trend toward a higher yield from the hypodense periphery in the recurrent tumor group. Tumor was found up to 15 mm beyond the CT-enhancing margin, in addition to extending beyond the area of abnormality on T2-weighted magnetic resonance images. These findings suggest that serial stereotactic biopsies should be targeted to the hypodense center and enhancing margin for improved diagnostic yield. Biopsy material obtained from the hypodense periphery that demonstrates tumor also indicates that a tumor volume beyond the confines of the CT-enhancing margin should be considered when calculating dosimetry for interstitial radiation.

KEY WORDS - brain neoplasm - glioma - computerized tomography - magnetic resonance imaging - stereotaxis

COMPUTERIZED tomography (CT) has been used to guide serial stereotactic biopsies for histological diagnosis of gliomas. Additional biopsies can be obtained at the time of implantation of radioactive seeds for interstitial radiation when treating recurrent gliomas. Previous studies have suggested a correlation between the histological features of the biopsy and the CT-defined zone from which it was obtained. More recent reports have emphasized the extent of the lesion in comparison to its appearance on enhanced CT and magnetic resonance (MR) imaging. Differences in diagnostic yield based on zones of attenuation defined by contrast-enhanced CT and selection of the optimal site for biopsy remain in question. Comparisons of histological features and extent of tumor infiltration based on serial stereotactic biopsies in patients with untreated or recurrent gliomas are also unclear.

This publication presents a retrospective review of 27 patients with untreated or recurrent malignant astrocytoma (Kernohan system grade 3 or 4, excluding grade 2) who underwent serial stereotactic biopsies. The diagnostic yield of these biopsies is reported, based on the CT-defined zone of attenuation, and differences in histological features of the biopsies between the patients with untreated and with recurrent gliomas are discussed.

Clinical Material and Methods

Patient Selection

Twenty-seven patients with untreated or recurrent malignant astrocytomas underwent 29 serial stereotactic biopsy procedures using the Brown-Roberts-Wells (BRW) stereotactic system* between January, 1982, and September, 1987. There were 16 men and 11 women whose ages ranged between 20 and 77 years (mean 51.2 years). Viewing each of the 29 procedures as a separate patient, 18 patients (10 men and eight

* Brown-Roberts-Wells stereotactic system manufactured by Radionics, Inc., Burlington, Massachusetts.
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women whose ages ranged between 20 and 77 years (mean 54.9 years) were previously untreated and 11 patients (six men and five women whose ages ranged between 23 and 64 years (mean 45.1 years) presented with recurrent tumors. The characteristics of both groups of patients were similar.

Serial Stereotactic Biopsy Technique

The BRW localizing ring was placed on all patients under local anesthesia. Contrast-enhanced CT scans were obtained and the lesions with three CT-defined zones were identified, including the hypodense center, enhancing margin, and hypodense periphery. A target point within the lesion was selected. When possible, the trajectory used for serial stereotactic biopsies was along the long axis of the tumor; otherwise, a coronal entry point was selected. The patients were taken to the operating room and a burr hole was placed at the entry point under local anesthesia. Serial biopsies using a 2-mm biopsy forceps were obtained superficial to, at, and deeper than the target point. Postoperatively, the biopsy locations were correlated with the CT-defined zone of attenuation. Sixteen patients also underwent MR imaging and the biopsy site was later localized on the T2-weighted (TR 2000 to 2450 msec, TE 80 to 100 msec) MR image.

Histological Classification

Biopsy specimens were stained with hematoxylin and eosin (H & E) and the histological features of specimens were individually characterized. Specimens with features adequate to make a diagnosis of malignant astrocytoma were labeled “tumor.” The predominant histological feature of the nondiagnostic specimens was assigned to a single category: necrosis, atypical cells, reactive cells/radiation changes, or other (inadequate tissue, normal brain, blood). Retrospectively, the histological findings from the biopsy material were correlated with their location on the CT and MR images. Biopsy results were statistically analyzed using the chi-square test unless otherwise noted. P values less than 0.05 were considered to be statistically significant.

Results

Twenty-nine serial stereotactic biopsy procedures were performed, 18 in the untreated group and 11 in the recurrent tumor group. In total, 184 biopsy specimens were obtained. Considering the number of biopsies yielding tumor/number of biopsies obtained, in the total patient group the tumor yield of biopsies was 34/61 (56%) from the hypodense center, 68/101 (67%) from the enhancing margin, and 8/22 (36%) from the hypodense periphery (Table 1). The difference in diagnostic yield between the hypodense center and enhancing margin compared to the hypodense periphery was statistically significant (p = 0.02). Similar results were obtained when comparing the diagnostic yield within the untreated group alone (p = 0.04). In the recurrent tumor group, however, the difference in diagnostic yield between the three zones did not differ significantly. There was a trend toward a higher yield in the hypodense periphery from the recurrent group compared to the untreated group, although this difference was not statistically significant (p = 0.31, Fisher’s exact test).

The diagnostic yield was also analyzed in terms of the number of patients with tumor in each of the three CT-defined zones after multiple biopsies were obtained from these zones. This analysis demonstrates the importance of repeat sampling within a zone to obtain adequate tissue for diagnosis. Of the 29 biopsy procedures, the tumor yield of biopsies was 16/19 (84%) in the hypodense center, 24/27 (89%) in the enhancing margin, and 6/9 (67%) in the hypodense periphery (Table 2). Biopsies were not obtained in all zones in each patient. Again, a trend was noted toward a higher yield in the hypodense center and enhancing margin compared to the hypodense periphery, but this was not statistically significant (p = 0.14). Similar results were obtained when comparing the patients within each of the untreated and recurrent tumor groups, although there was a trend toward a lower yield from the hypodense center in the recurrent tumor group compared to the untreated patients (p = 0.23, Fisher’s exact test).

The predominant histological features of the biopsy specimens were compared for each of the three CT-defined zones (Table 3). In the hypodense center, tumor was encountered most often followed by necrotic tissue.

### Table 1

<table>
<thead>
<tr>
<th>Biopsy Site</th>
<th>All Biopsies</th>
<th>Untreated Group</th>
<th>Recurrent Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>hypodense center</td>
<td>34/61 (56%)</td>
<td>24/42 (57%)</td>
<td>10/19 (53%)</td>
</tr>
<tr>
<td>enhancing margin</td>
<td>68/101 (67%)</td>
<td>39/61 (64%)</td>
<td>29/40 (73%)</td>
</tr>
<tr>
<td>hypodense periphery</td>
<td>8/22 (36%)</td>
<td>5/17 (29%)</td>
<td>3/5 (60%)</td>
</tr>
</tbody>
</table>

* Data are given as number of biopsy procedures yielding tumor/number of biopsy procedures.

### Table 2

<table>
<thead>
<tr>
<th>Biopsy Site</th>
<th>All Procedures</th>
<th>Untreated Group</th>
<th>Recurrent Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>hypodense center</td>
<td>16/19 (84%)</td>
<td>10/11 (91%)</td>
<td>6/8 (75%)</td>
</tr>
<tr>
<td>enhancing margin</td>
<td>24/27 (89%)</td>
<td>14/16 (88%)</td>
<td>10/11 (91%)</td>
</tr>
<tr>
<td>hypodense periphery</td>
<td>6/9 (67%)</td>
<td>4/6 (67%)</td>
<td>2/3 (67%)</td>
</tr>
</tbody>
</table>

* Data are given as number of biopsy procedures yielding tumor/number of biopsy procedures.

† Either a 0.5-tesla (manufactured by Picker International, Highland Park, Ohio) or a 1.5-tesla (manufactured by General Electric, Milwaukee, Wisconsin) superconductive unit was used.
TABLE 3

Predominant histological characteristics of 184 biopsy specimens

<table>
<thead>
<tr>
<th>Histological Features</th>
<th>Hypodense Center</th>
<th>Enhancing Margin</th>
<th>Hypodense Periphery</th>
<th>Totals</th>
</tr>
</thead>
<tbody>
<tr>
<td>tumor</td>
<td>34</td>
<td>68</td>
<td>8</td>
<td>110</td>
</tr>
<tr>
<td>necrosis</td>
<td>13</td>
<td>4</td>
<td>0</td>
<td>17</td>
</tr>
<tr>
<td>atypical cells</td>
<td>6</td>
<td>11</td>
<td>1</td>
<td>18</td>
</tr>
<tr>
<td>reactive cells/radiation changes</td>
<td>4</td>
<td>7</td>
<td>7</td>
<td>18</td>
</tr>
<tr>
<td>other (inadequate tissue, normal brain, blood)</td>
<td>4</td>
<td>11</td>
<td>6</td>
<td>21</td>
</tr>
<tr>
<td>totals</td>
<td>61</td>
<td>101</td>
<td>22</td>
<td>184</td>
</tr>
</tbody>
</table>

All of the specimens of hypodense center with reactive features or radiation changes were obtained from the recurrent tumor group, contributing to the lower tumor yield from the hypodense center in the patients with recurrent tumor as noted above. Specimens from the enhancing margins yielded tumor in the large majority of cases. Biopsies from the hypodense periphery most often yielded tumor, although reactive features and radiation changes were encountered with nearly equal frequency.

Biopsies from the hypodense periphery which yielded tumor were evaluated to determine their distance from the enhancing margin. As the distance from this margin increased, the number of biopsies with tumor decreased (Fig. 1). However, tumor was identified up to 10 mm beyond the enhancing margin in patients with untreated gliomas, and up to 15 mm beyond the enhancing margin in the recurrent tumor group. No biopsies were obtained more than 15 mm beyond the enhancing margin in either group.

Magnetic resonance imaging was performed in 16 of the 27 patients undergoing biopsy procedures. Overall, on the T2-weighted MR images, the radius of abnormalities along the biopsy trajectory (28 ± 4 mm, mean ± standard error of the mean) was greater than the radius spanned by the enhancing CT margins (21 ± 2 mm) (p < 0.05); the radius on the T2-weighted MR images equaled or exceeded the CT radius in 10 of the 16 patients undergoing both procedures. Six of the nine patients who had biopsies obtained from the hypodense periphery also underwent MR examination. Of the 11 biopsy specimens submitted for these six patients, one specimen was obtained beyond the margin of the abnormality demonstrated by T2-weighted MR imaging and yielded tumor.

Discussion

Contrast-enhanced CT-guided serial stereotactic biopsy of malignant astrocytomas yielded tumor in all three zones of attenuation. Tumor yield was statistically highest in the enhancing margin and hypodense center compared to the hypodense periphery. The biopsy yield from patients with untreated gliomas was similar to that in patients with recurrent gliomas (Table 1), although there was a trend toward a higher yield from the hypodense periphery in the patients with recurrent tumor, suggestive of more widespread disease at the time of recurrence. As multiple biopsies and more tissue were obtained from each zone, the overall diagnostic yield by zone for individual patients increased (Table 2), emphasizing the importance of multiple biopsies.

Autopsy studies comparing the topographic location of glioblastoma multiforme to contrast-enhanced CT scans have confirmed tumor distribution in all three zones of attenuation. In addition, they have demonstrated that the hypodense center represents predominantly necrosis, the enhancing margin is a cellular zone of viable neoplasm, and the hypodense periphery represents a surrounding zone of tumor infiltration. These findings correlate well with the predominant histological features of the present biopsy specimens (Table 3), in which necrosis was prominent in the hypodense center, tumor was most common in the enhancing margin, and features of reactive or radiation changes were nearly as common as tumor in the hypodense periphery. Demonstration of tumor infiltrating beyond the CT-enhancing margin at the time of stereotactic biopsy corroborates previous authors' experience with widespread progression of malignant astrocytoma at autopsy, often involving the contralateral hemisphere or posterior fossa structures. In addition, the present finding of tumor extending farther from the enhancing rim in recurrent tumors than in untreated ones is reminiscent of the correlation studies of Burger and coworkers. In their CT-autopsy correlations, tumor was far more widespread in recurrent tumors than in untreated glioblastomas.

Boethius and associates reported eight patients with glioblastomas who underwent stereotactic biopsy procedures. Biopsy material was obtained from areas of...
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**TABLE 4**

<table>
<thead>
<tr>
<th>Authors &amp; Year</th>
<th>Hypodense Center</th>
<th>Enhancing Margin</th>
<th>Hypodense Periphery</th>
</tr>
</thead>
<tbody>
<tr>
<td>Boëthius, et al., 1978</td>
<td>4/8 (50%)</td>
<td>5/7 (71%)</td>
<td>1/5 (20%)</td>
</tr>
<tr>
<td>Kelly, et al., 1987</td>
<td>4/9 (44%)</td>
<td>33/34 (97%)</td>
<td>15/16 (94%)</td>
</tr>
<tr>
<td>Greene, et al., 1989</td>
<td>24/42 (57%)</td>
<td>39/61 (64%)</td>
<td>5/17 (29%)</td>
</tr>
</tbody>
</table>

* Data are given as number of biopsies yielding tumor/number of biopsies obtained.

low- and high-contrast uptake and from the low-attenuation areas surrounding the tumor and corresponding to the hypodense center, enhancing margin, and hypodense periphery in the present study. Diagnostic yield in these three zones of attenuation was (biopsies yielding tumor/biopsy procedures): 4/8 (50%), 5/7 (71%), and 1/5 (20%), respectively, and is comparable to the present diagnostic yield (Table 4).

Kelly, et al., recently reported 40 patients with untreated glioblastoma who underwent serial stereotactic biopsy procedures. Fifteen of these patients were diagnosed with malignant astrocytomas (grade 3 or 4) and are comparable to the 18 patients in this series with untreated neoplasms. Fifty-nine biopsy specimens were obtained from the three CT-defined zones in their series and diagnostic yield for tumor may be compared to the present series (Table 4). Yield in the hypodense center was similar between the two studies, although yield in the enhancing margin and hypodense periphery was lower in the present series. As these authors did not specifically address diagnostic yield in their biopsies, this difference may reflect inclusion of specimens with both “infiltrating tumor cells” and “tumor tissue” in the numerator; whereas in the present study only those specimens adequate for a diagnosis of malignant astrocytoma were included in the numerator. Kelly, et al., also emphasized the larger volume of abnormality on T2-weighted MR imaging compared to the contrast-enhanced CT scan abnormality, a finding substantiated in the present study. They also confirmed the finding of tumor cells extending beyond the margins of T2-weighted MR abnormalities. Johnson and colleagues recently reported a comparison of postmortem MR imaging to autopsy evaluations of whole-brain sections in cases of glioblastoma multiforme. In their patients, tumor cells without edema were seen infiltrating 3 to 5 cm beyond the abnormality demonstrated on the T2-weighted MR images.

References


Manuscript received October 21, 1988.
Accepted in final form March 14, 1989.
This study was supported in part by a Merit Review Grant from the Veterans Administration.
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