Value of sequential postoperative brain scans in patients with anaplastic gliomas

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The authors analyze the postoperative course of 30 patients with anaplastic supratentorial gliomas to evaluate the usefulness of sequential brain scanning as an adjunct to clinical neurological examinations in the early detection of tumor recurrence. The correlation between sequential scanning and clinical evaluation was excellent; no examples of divergent results were seen. With the exception of scans made very early in the postoperative period or when postoperative scalp flap infections were present, initial postoperative scans were easily interpreted in terms of both the superficial (postcraniotomy) and parenchymal changes. The specific type of postoperative therapy (radiation therapy, chemotherapy, or both) could not be correlated with whether scan or examination ultimately changed first. However, analysis of original tumor location revealed that while sequential postoperative scanning offered no advantage over repetitive neurological examinations in the detection of recurrent tumor in the neurologically dominant left hemisphere, scan changes preceded examination changes in eight of 17 cases involving tumors of the neurologically nondominant right hemisphere.

KEY WORDS • brain tumor • brain scan • tumor recurrence

In this study, sequential brain scanning and clinical evaluations are compared for their sensitivity as indicators of tumor behavior in postoperative follow-up of patients with anaplastic intracerebral gliomas.

Clinical Material and Methods

Selection of Patients

To control many of the variables occurring in the postoperative evaluations, cases in our study were selected from patients treated under the Phase III therapy protocol of the Brain Tumor Study Group of the National Cancer Institute. Patients had first undergone osteoplastic craniotomy with subtotal resection of supratentorial anaplastic gliomas and were then entered into the protocol within 3 weeks after surgery. The protocol consisted of a random selection of these patients for postoperative treatment with cobalt therapy and/or chemotherapy.* Thirty patients (22 males and eight females) were admitted to this study: eight received cobalt therapy alone, eight chemotherapy alone, and 14

*For further details, see the Phase III therapy protocol of the Brain Tumor Study Group, National Cancer Institute.
received combined treatment. Corticosteroids were utilized only during the first 5 days after surgery and were not administered later as a primary therapeutic agent or as a terminal palliative measure.

Sequential postoperative neurological examinations and brain scans were begun 2 months following randomization and were repeated bimonthly thereafter. The first postoperative neurological evaluations and scans were used as baseline data for each patient in the interpretation of subsequent scan or examination changes.

**Scanning Technique**

A total of 129 postoperative brain scans were performed on the 30 patients. Four-view rectilinear brain scans were obtained 30 minutes following the intravenous administration of 30 mCi 99m Tc pertechnetate. Sodium perchlorate was administered to minimize parotid gland and choroid plexus activity. All studies were performed on an Ohio-Nuclear dual detector scanner (Model 54)* using standardized technique.

Model H collimators were cut from their original 5 in. length to 4 in. which extended the focal length from 3 to 4 in. The radius of resolution of this modified collimator is 0.41 in. The overall system length of 8 in. results in a less tomographic representation of the target, the depth of the focal plane being about 2 in. Resolution of this collimator compares favorably with the 53524-L (Ohio-Nuclear) with about half the sensitivity of the latter. The Ohio-Nuclear 54 couch was fitted with a raised head rest to facilitate scanning in a flexed head position. Technique setup was based on the maximal counting rate observed over the sagittal sinus. Scanning speed was adjusted to yield a count density of 600 counts/cm². A 30% enhancement was employed. Anterior and posterior scans were obtained with each detector 1 in. away from the patient's head. Lateral scans were positioned with each detector equidistant from the patient's head a measured 8 in. apart. This placed the central focal plane at the midline of the brain for both detectors. Technique is standard and reliably reproducible, allowing comparison of lesion appearance on serial studies.

*Ohio-Nuclear dual detector scanner (Model 54) made by Ohio-Nuclear, Inc., 6000 Cochran Road, Solon, Ohio 44139.

Scans were interpreted at the time of the patient's study by the Division of Nuclear Medicine and were then subsequently reviewed by the authors as the study was being compiled. The scans were analyzed in terms of superficial (postcraniotomy) activity and deep (parenchymal) activity. Increase in the size of the area of abnormal parenchymal activity was assumed to represent tumor recurrence or progression, while decrease in the size of abnormal uptake was interpreted as tumor regression. Analyses were based on changes obvious on direct examination of a particular scan or confirmed on comparison of that scan with previous scans, but without knowledge of the patient's clinical status.

**Results**

All of the baseline postoperative scans showed increased superficial activity in the area of the scalp flap. In nine of the 30 patients, this change prevented interpretation in the area of tumor resection. An analysis of factors influencing the interpretability of the scans is given in Table 1. Ultimately, eight of these nine scans became completely interpretable for presence or absence of tumor, as superficial activity decreased with time.

The subsequent bimonthly scans and associated neurological examinations were evaluated to determine which parameters first showed significant change as compared with the baseline postoperative scan and neurological examination. Table 2 lists the possible outcomes anticipated in the postoperative period and shows the distribution of patients according to the results seen. There were no instances of disagreement or divergence between scan findings and neurological status, that is, scans improving in neurologically deteriorating patients or worsening in improving individuals. In 26 of the 30 patients, there was a stable phase of variable length in which neither scan nor neurological status changed. This period was eventually terminated by worsening of the scan, examination, or both. In the remaining four patients, either improvement or no further change in one or both of the parameters was seen throughout the period of follow-up. Table 3 analyzes the relationship of these results to the intracranial location of the tumors. A typical scan sequence from a patient with a right occipital glioblastoma multiforme is shown in Fig. 1.
Sequential postoperative brain scans

**TABLE 1**

Factors affecting interpretability of initial postoperative scans

<table>
<thead>
<tr>
<th>Scans</th>
<th>Scalp Infection</th>
<th>Time of Scan</th>
<th>Lesion Location</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Yes</td>
<td>Early</td>
<td>Anterior</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>On Time</td>
<td>Posterior</td>
</tr>
<tr>
<td>uninterpretable*</td>
<td>3</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>(9 cases)</td>
<td>6</td>
<td>7</td>
<td>7</td>
</tr>
<tr>
<td>interpretable</td>
<td>0</td>
<td>2</td>
<td>15</td>
</tr>
<tr>
<td>(21 cases)</td>
<td>21</td>
<td>19</td>
<td>6</td>
</tr>
</tbody>
</table>

* Tracer concentration in area of scalp flap obscured area preoperatively identified as tumor.
† Yates corrected \(x^2\) for difference in early interpretability following anterior craniotomy (2/17 uninterpretable) compared to posterior craniotomy (7/13 uninterpretable) = 4.37, \(p = 0.037\).

In 21 of the 30 initial postoperative scans, superficial tracer uptake could be easily differentiated from the abnormal uptake in the area of tumor resection. Examination of the remaining nine scans was difficult because of increased peripheral uptake due in part to early postoperative scanning or scalp infection. When scans made very early in the postoperative period were repeated at or after the average time for the entire group (8 to 9 weeks) they were interpretable. Individuals with infected scalp flaps required eradication of the infection before scans became interpretable. The high incidence of posterior lesions in this group (seven of nine) was not anticipated, but understandable. Posterior lesions had been approached with parieto-occipital craniotomy, which resulted in increased superficial uptake on both the lateral and posterior views of the initial postoperative scans and tended to mask any underlying parenchymal uptake. Any increase in this masking effect, either through earlier scanning or because of scalp flap infection, made diagnostic interpretation in the area of the lesion much more difficult (see scans B and C, Fig. 1). The masking of temporal lobe lesions by superficial uptake, as noted previously by Wilkins, et al., was not a problem in our series. Examination of all scan sequences showed a steady decrease in the superficial tracer accumulation for 6 to 8 months and then stabilization of the amount of uptake. In only one patient did increased peripheral activity prevent interpretation of tumor status throughout the entire clinical course.

**Discussion**

Early detection of tumor recurrence is important in the treatment of patients with anaplastic intracerebral gliomas because of the development of more effective chemotherapy for these lesions. The usefulness and limitations of radioisotope brain scanning in the primary detection of intracranial neoplasms are reasonably well established. However, the value of postoperative brain scanning in the early detection of tumor recurrence, especially recurrence of malignant supratentorial gliomas, has been uncertain.

**TABLE 2**

Relationship between postoperative scans and examinations

<table>
<thead>
<tr>
<th>Response</th>
<th>Improved</th>
<th>Worse</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>scan changed first</td>
<td>1</td>
<td>8</td>
<td>9</td>
</tr>
<tr>
<td>exam changed first</td>
<td>1</td>
<td>6</td>
<td>7</td>
</tr>
<tr>
<td>scan and exam findings</td>
<td>1</td>
<td>12</td>
<td>13</td>
</tr>
<tr>
<td>similar</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>scan and exam findings</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>divergent</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>neither scan nor exam</td>
<td>—</td>
<td>—</td>
<td>1</td>
</tr>
<tr>
<td>changing</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**TABLE 3**

Types of response according to region of tumor

<table>
<thead>
<tr>
<th>Response</th>
<th>Right Hemisphere (n=17)</th>
<th>Left Hemisphere (n=13)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Anterior</td>
<td>Total</td>
</tr>
<tr>
<td>scan changed first</td>
<td>5</td>
<td>3</td>
</tr>
<tr>
<td>exam changed first</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>both changed</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>neither changed</td>
<td>0</td>
<td>1</td>
</tr>
</tbody>
</table>

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In 1967 Wilkins, et al., described the findings in postoperative brain scanning. The study emphasized the differentiation of superficial tracer activity secondary to postsurgical scalp and skull changes from any abnormal intracranial, parenchymal activity. Postoperative scans were used only in a supportive role to confirm the clinical impression of recurrent disease. Flipse, et al., investigated sequential brain scanning in the postoperative follow-up of patients with metastatic and primary brain tumors. The high degree of correlation between scan sequences and clinical findings was emphasized;
Sequential postoperative brain scans

however, as with the earlier work of Wilkins, et al., the study did not examine scanning as a method for early detection of recurrent disease.

The results reported by Flipse, et al., based on 21 patients undergoing radiation therapy for malignant intracranial tumors, coincide with our own in that a high degree of correlation was found between scan results and clinical evaluation, but while Flipse, et al., noted several cases in which scan change preceded clinical change, no attempt was made to elucidate responsible factors. Handel, et al., demonstrated a correspondence between 99m Tc pertechnetate brain scintiphotography and clinical improvement or worsening in patients with anaplastic intracerebral gliomas receiving chemotherapy. Because the Handel study examined the capacity of brain scintiphotography to detect changes in recurrent tumor tracer uptake in response to systemic chemotherapy, all patients were scanned following clinical evidence of tumor recurrence and usually in the face of a deteriorating clinical course. Consequently, the question of whether scans could detect tumor recurrence earlier than the clinical examination was not considered. Because our study focused on this question, we began the evaluations early in the postoperative period at a time when most of our patients exhibited only mild to moderate neurological impairment, and most were free of symptoms of tumor recurrence. The majority enjoyed reasonably lengthy postoperative survivals, which allowed an average of five bimonthly evaluations per patient.

In contrast to the report by Handel, et al., we found no instances of disagreement or divergence between scan findings and neurological status. In addition, when each of our scans was evaluated individually, we did not see large fluctuations in lesion size from scan to scan as reported by Handel's study. The reasons for these differences remain unclear. Although the chemotherapy programs of Handel's patients and ours were similar, our more restricted use of corticosteroids may be a factor since recent studies indicate that corticosteroids may significantly affect scan lesion size, presumably through a direct effect on tumoral and peritumoral edema.

To evaluate the ability of scanning to detect changes in tumor activity, we examined closely the scan sequences and clinical courses of the nine patients in whom the scan changed first and compared them to those of the seven patients in whom the neurological examination changed first. Analysis showed these two groups to be comparable, both in terms of scan technical quality and level of neurological function at the beginning of the study.

Examination of these two groups, as well as the remaining groups, for possible effects of the various postoperative treatment programs on scan or examination change indicated that the different treatment programs did not appear to influence whether the scan or clinical examination had changed first.

The initial tumor location was then investigated for a possible relationship between tumor location and whether the significant postoperative change ultimately occurred first in the scan, the examination, or in both concurrently. As shown in Table 3, in 13 left hemisphere lesions the scan changed first in only one case, and both the scan and examination changed together in the majority of the cases (nine of 13). This result suggested that scanning was not superior to repetitive neurological examinations in the early detection of recurrent left hemisphere lesions. However, in eight of 17 right hemisphere lesions, scan changes clearly preceded examination changes. Moreover, patients with right hemisphere lesions constituted eight of the nine total instances in which the scan changed first.* The observed difference between left and right hemisphere lesions is understandable in part since the right hemisphere was the neurologically nondominant hemisphere in 29 of the 30 patients. Consequently, right hemisphere lesions, especially the anterior lesions, might be expected to occupy neurologically silent areas where recurrent tumor could grow sufficiently to be detected by scanning prior to production of clinical neurological change. However, the results were not confined to anteriorly located right hemisphere tumors. Almost half (three of eight) of the posteriorly located right hemisphere lesions showed a scan change first, while none of the five posterior left hemisphere lesions showed scan change prior to clinical change.

The results of this study seem to suggest that repetitive brain scanning is valuable in

*Yates corrected $\chi^2$ for right and left hemisphere differences = 3.72; $p = 0.053$. 

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the postoperative follow-up of patients with anaplastic intracerebral gliomas. The degree of correlation between scan findings and clinical findings has been very good, both in our series and that of Flipse, et al. The problems encountered in the first postoperative scans were either self-limiting or readily remediable, as in the cases of the scalp flap infections, and in only one of 30 cases was the scan useless in postoperative evaluation. The differences observed between nondominant and dominant hemisphere lesions are interesting. In the dominant hemisphere, repetitive scanning is at least as good as repetitive clinical examination in detection of recurrent tumor, but does not appear to offer an advantage. However, we feel the usefulness of repetitive scanning is underscored by the results seen in almost half of the patients with nondominant hemisphere lesions in whom scan change clearly preceded clinical change. Given the advantage of earlier detection of tumor recurrence, many of these patients may become candidates for additional aggressive therapy, including newer antitumor agents, immunotherapy, or perhaps further surgery in an effort to increase not only the length but also the quality of their survival.

References

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