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Early CT Findings After Interstitial Radiation Therapy for Primary Malignant Brain Tumors

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The CT findings after interstitial radiation therapy for brain tumors have not been extensively described. We evaluated retrospectively the CT scans of 13 patients who were treated with brachytherapy for malignant glioma. We found no typical CT appearance that differentiates recurrent tumor from radiation effect. After undergoing brachytherapy, eight of the 13 patients scanned demonstrated enhancement of brain tissue beyond the margins of the original enhancing tumor mass. In most cases, the pattern of enhancement diminished and extended more peripherally from the central necrotic area with time. We also report a new CT finding of focal calcification developing at the site of the radioactive implant.

Interstitial radiation therapy of brain tumors has been used in Europe for more than 30 years, but experience in the United States is limited [1]. Leibel and coworkers have reported a palliative benefit in patients with recurrent malignant gliomas and an early improvement in survival when brachytherapy is part of the primary treatment [2–3].

Although the appearance of the brain on CT after conventional external radiation therapy has been widely described [4–7], few studies address the CT findings after interstitial radiation therapy [8–11]. Whether postimplant CT can be used to identify tumor persistence, tumor recurrence, or radiation reaction has not been established.

Serial CT scans were evaluated retrospectively in 13 patients who were treated by brachytherapy for malignant gliomas. The objective was to identify any typical CT findings associated with this treatment.

Materials and Methods

The pre- and posttherapy CT scans of 13 patients with supratentorial grade III–IV gliomas were studied retrospectively. The patients included five men and eight women ages 40–77 years old (median, 55 years). Five of the patients were treated for recurrent tumors; all had been treated previously with external-beam irradiation. The time from initial radiation therapy to recurrence ranged from 5–33 months. One of these patients with recurrent tumor received BCNU chemotherapy as part of her initial treatment. All five patients received subtotal resection of their tumors prior to the initial external-beam radiation therapy. To diagnose tumor recurrence, repeat subtotal resection was performed on two patients and stereotaxic biopsy prior to brachytherapy was performed on three patients. The remaining eight patients who received interstitial irradiation as part of their primary treatment also received prior external-beam radiation therapy. Six underwent subtotal resection and two were biopsied prior to brachytherapy. All patients studied received external-beam radiation in doses ranging from 5040–6880 cGy. The 13 patients received iridium-192 interstitial radiation therapy in doses of 3000–6480 cGy according to a protocol developed at our institution.

CT scans were obtained immediately after stereotaxic catheter placement in most cases. Thereafter, patients were reevaluated with CT at approximately 2-month intervals and more frequently when clinically indicated. Whenever possible, both unenhanced and enhanced CT

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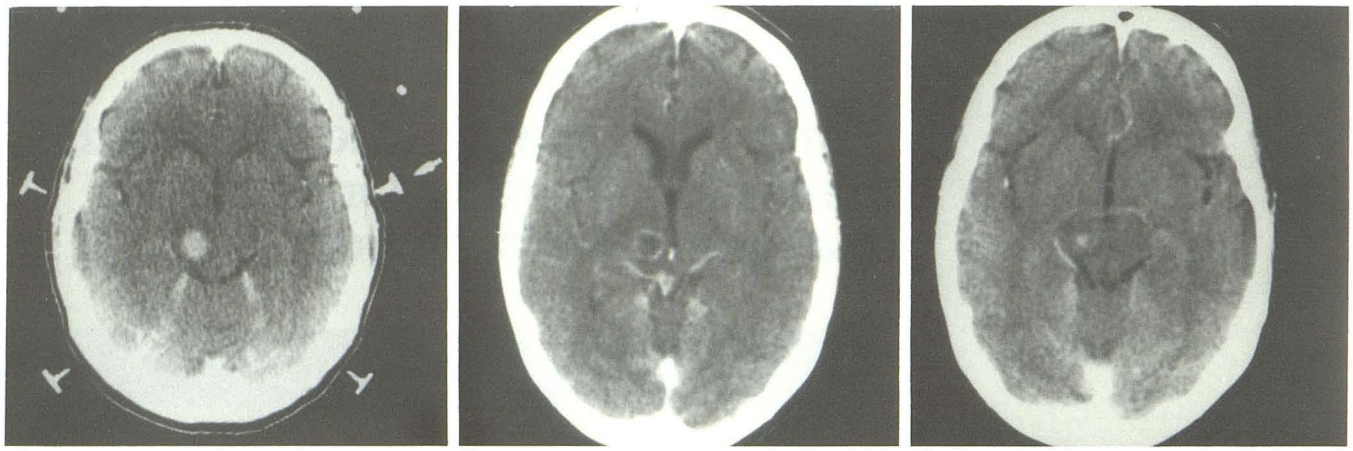

Fig. 1.—40-year-old man with right thalamic glioblastoma multiforme.
***A*, Enhanced CT brain scan shows lesion before biopsy or therapy. Note stereotaxic frame in position.**
***B*, Enhanced CT scan obtained 2 months after brachytherapy. Ring enhancement peripheral to original lesion and central low-attenuation area are identified.**
***C*, Enhanced CT scan obtained 4 months after therapy reveals an enhancing lesion much smaller in size than original tumor. The region of central low attenuation has disappeared. Enhanced CT scan was normal at 7½ months after irradiation.**

scans were obtained. Contrast administration consisted of an IV infusion of 150 ml of Reno-M-DIP* during CT examination. Parameters used to evaluate the CT scans included presence, size, and configuration of any enhancing lesion; degree of contrast enhancement; presence and size of any central low-attenuation region within an enhancing mass; and extent of any edema or mass effect.

An attempt was made to differentiate local and hemispheric mass effect. Whenever possible, measurements of edema, enhancing lesions, and low-attenuation regions were made on corresponding CT cuts between serial CT studies.

The CT studies were interpreted by an experienced radiologist retrospectively in a blind fashion, without the knowledge of tumor grade, type of therapy used, or patient's clinical condition.

Results

Three of the 13 patients had progressive neurologic deterioration and died at 3 months, 5 months, and 7 months, respectively, after brachytherapy treatment. A fourth patient was neurologically stable through the implant procedure and for 6 weeks after treatment; however, after 3 months on steroid therapy he died of septicemia, thought to be from an infected cardiac pacemaker. One patient developed tension pneumocephalus immediately after catheter removal; however, intervention was successful. The longest period of survival in this series is 12 months.

Prior to brachytherapy, the CT scans of all 13 patients revealed an area of low attenuation associated with the brain tumor mass. After brachytherapy, the central low-attenuation region showed a gradual decrease in size in seven of the patients and in two of these the region eventually disappeared (Fig. 1). Three patients demonstrated increasing size of this low-density region after therapy.

The following patterns of tissue enhancement after brachytherapy were identified:

1. The diameter of an enhancing ring or the greatest dimension of an enhancing mass increased in eight patients after interstitial irradiation. Two patients showed a decrease in this dimension over time.

2. The degree of contrast enhancement became more faint in seven patients, while three cases demonstrated more intense enhancement of the involved tissues.

3. In seven cases, the enhancing ring or mass became fragmented, often showing serpentine margins (Fig. 2). Thickening of the ring lesion was seen in three patients.

4. The extent of edema and/or mass effect in any one patient often varied on consecutive studies. This is attributed to fluctuating steroid requirements.

5. In one patient, who died 7 months after brachytherapy, autopsy revealed residual grade IV glioma and extensive radiation reaction in the left temporal and occipital lobes. Moreover, in two patients who had repeat surgery at 2 months and 6 months, respectively, for clinical deterioration, pathology revealed grade IV glioma.

In four (31%) of the original 13 patients, focal high attenuation within the brain parenchyma was identified at the site of the radioactive implant (Fig. 3.). These high-attenuation foci likely represent calcification. This focal calcification was identified in 10 days, 2 weeks, and 2 months (two patients) after brachytherapy.

Discussion

Radiation therapy is an accepted and proved treatment for brain tumors, but it is associated with recognized adverse effects [12]. The human brain tolerance for limited-field external irradiation is in the range of 6000 cGy fractionated over 6 weeks [13]. Both acute and delayed effects of radiation to the CNS have been described [4, 5, 13].

Acute effects are seen clinically as an exacerbation of the patient's neurologic symptoms and somnolence. These changes commonly occur within the early weeks or months

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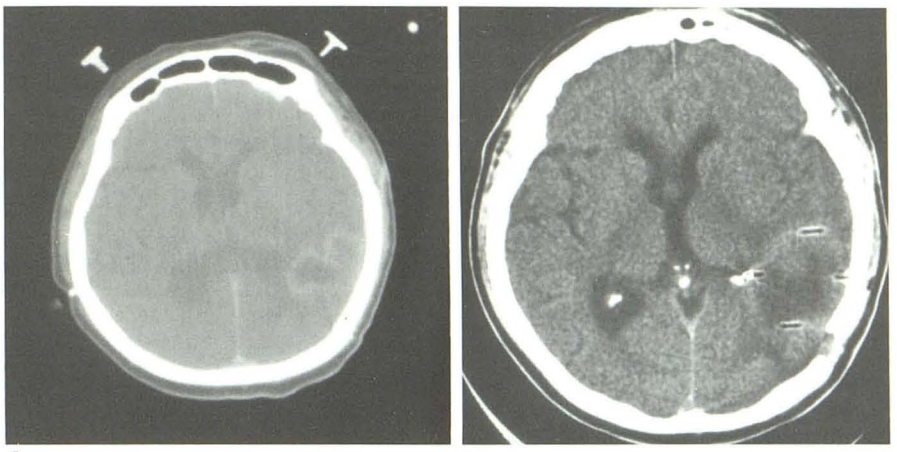

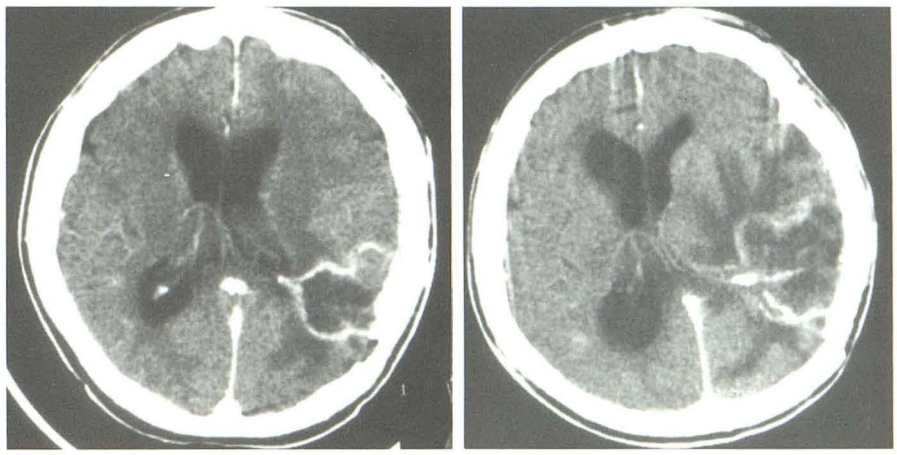

Fig. 2.—67-year-old woman with left temporoparietal glioblastoma multiforme.

***A*, Enhanced CT brain scan obtained immediately before stereotaxic surgery reveals irregular ring-enhancing lesion with central region of low attenuation.**

***B*, Immediate postoperative CT scan shows catheter position (radioactive seeds not yet in place).**

***C*, Enhanced CT scan obtained 1 month after brachytherapy shows intense, thin, ring enhancement similar in size to original tumor. Central low attenuation persists.**

***D*, Enhanced CT scan 6 months after therapy shows more diffuse and fragmented ring enhancement peripheral to original tumor. There is increased edema and mass effect. An autopsy performed 1 month later revealed radiation necrosis and residual malignant astrocytoma in left temporoparietal region and adjacent occipital lobe tissues.**

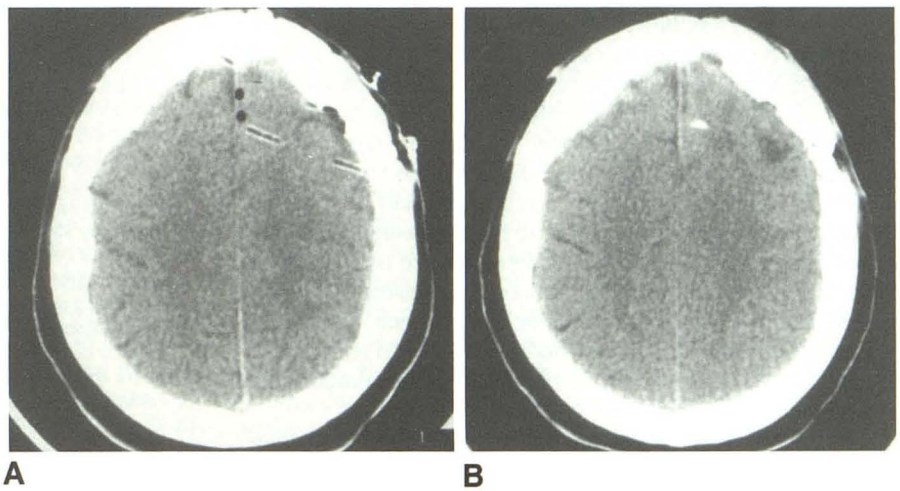

Fig. 3.—40-year-old woman with left frontal glioblastoma multiforme.

***A*, CT brain scan obtained immediately after stereotaxic surgery documents catheter position.**

***B*, Unenhanced CT scan obtained 20 days after brachytherapy reveals focal calcification at the site of implanted radioactive source.**

following therapy. The proposed underlying cause is transient demyelination [14]. CT changes corresponding to these acute radiation effects are not well documented, but decreased attenuation in the white matter has been described [15, 16].

The late delayed effects, radiation necrosis, can appear from 6 months to 14 years after therapy and may mimic tumor recurrence clinically with progression of symptoms. This process is often aggressive and irreversible, and has well-described CT findings [4–6, 16]. An enhancing mass with new areas of low attenuation and associated edema are commonly identified on CT scans of radiation necrosis. These findings cannot be reliably differentiated from recurrent tumor.

Since stereotaxic brain surgery and implantation of radioactive sources to treat gliomas are relatively new procedures,

little has been reported on the CT changes within the brain after such therapy. Fike et al. [9] demonstrated that, in canine models, an enhancing ring can be seen surrounding the implant site at 2–4 weeks. This enhancing ring tends to move away from the point source and decreases in degree of enhancement over time. Contrast enhancement is thought to be due to inflammation and increased vascular permeability. More peripheral to this enhancing ring, white matter is seen to be decreased in attenuation, likely representing edema, and often is accompanied by some mass effect. Within the enhancing ring is a low-density region uniformly corresponding to coagulation necrosis [8, 9]. There is evidence that the development of radiation necrosis is accelerated with brachytherapy and that, as with external-beam irradiation, it cannot be differentiated from recurrent tumor by CT criteria [10, 16–19].

Our study demonstrated CT findings that often corroborated work previously described. Within 2 months of therapy an enhancing ring or mass was identified on all subjects scanned, as was a central necrotic region. The state of white-matter edema peripheral to the ring was variable but this is strongly influenced by steroid therapy. Progression of tissue enhancement away from the radiation source was also supported by our study. A decrease in degree of contrast enhancement was noted after therapy.

CT evaluation of the patients in this study is complicated by the fact that in all cases the tumor and adjacent brain had received irradiation by both external-beam and interstitial implants. Many of the patients had also undergone recent craniotomy, so it is likely that many separate processes of damage and repair were occurring simultaneously.

The finding of focal calcification developing at the radioactive implant site, to our knowledge, has not been described previously. Calcification developing in the brain after external-beam radiation has been described rarely and developed 21 months to 8 years after therapy [4, 5, 20, 21]. It is of interest that the four patients in our series developed focal calcification within 10 days to 2 months after implant irradiation. We speculate that this is dystrophic calcification deposited in response to the focal intense radiation near the implant seed. Of the four patients with this finding, three had their serum calcium levels measured just prior to brachytherapy; two were normal and one was minimally decreased from normal.

In the face of clinical deterioration, increasing enhancing mass, and central necrosis, tumor recurrence cannot be assumed. These findings may represent radiation effects, and patients have been shown to benefit from reoperation and resection of necrotic debris [3, 18].

This article reports only early CT findings after brachytherapy for high-grade gliomas. Although we present no survival data at this time, we believe that interstitial irradiation therapy may improve the prognosis of this aggressive and lethal lesion. Perhaps future investigations with MR imaging and positron emission tomography will help differentiate post-radiation effects from recurrent neoplasms [7].

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