

Detection of Brain Metastases: Comparison of Contrast-Enhanced MR with Unenhanced MR and Enhanced CT

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Contrast-enhanced MR studies were compared with noncontrast MR and contrast-enhanced CT scans in the evaluation of intraparenchymal brain metastases. Fifty consecutive inpatients were studied with short and long repetition time (TR) sequences before and after the administration of gadopentetate dimeglumine. In addition, a delayed short TR sequence was performed. The contrast CT, noncontrast MR, immediate postcontrast short TR sequence, postcontrast long TR sequence, and delayed postcontrast short TR sequence were each read blindly and independently by two neuroradiologists. These results were then compared with a final interpretation, reached by all the neuroradiologists in the study, using all the clinical information and imaging findings. Postcontrast short TR scans proved to be superior to other sequences. They were particularly useful in the detection of metastases in the posterior fossa and cortex. The delayed postcontrast short TR scan held no definite advantage over the immediate postcontrast short TR scan, although metastases were sometimes seen slightly better after the delay. While long TR sequences were not always sensitive or specific, they often did provide ancillary information and were particularly useful in cases of hemorrhagic metastases.

Because of these findings, we recommend that the evaluation of intraparenchymal metastases consist of a single postcontrast long TR scan followed by a single postcontrast short TR scan. While these sequences should be very accurate in the detection of metastases, we also generally perform a single precontrast short TR scan as well, since the question of hemorrhage or bone lesion may be clinically relevant.

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MR imaging has been highly praised for its sensitivity to intracranial abnormalities [1, 2]; yet, in a recent large clinical series, neither noncontrast MR imaging nor contrast-enhanced CT was consistently superior when compared for the evaluation of intraparenchymal metastases [3]. While CT failed to detect some punctate metastases, especially when hemorrhagic, and some posterior fossa lesions, MR missed some metastases hidden in edema from adjacent lesions and some metastases that, surprisingly, were nearly isointense with normal brain parenchyma.

Two other recent papers have demonstrated the utility of gadopentetate dimeglumine, formerly known as gadolinium-DTPA, as a contrast agent in the evaluation of intraparenchymal brain metastases in a smaller number of patients [4, 5]. Healy et al. [4] noted the superior sensitivity of contrast-enhanced MR compared with unenhanced MR in the detection of small gray matter lesions. Russell et al. [5] found that contrast enhancement was able to help identify small lesions that otherwise might not be visualized because of edema of adjacent larger lesions. The purpose of this study was to examine the comparative utility of noncontrast MR, contrast-enhanced CT, and contrast-enhanced MR in a large series of patients who were accrued consecutively, without regard for age or previous treatment. In addition, particular attention was paid to the development of optimal screening sequences and technique.

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Subjects and Methods

Fifty consecutive inpatients were studied in our institution for the evaluation of possible intraparenchymal brain metastases. Patients ranged from 6 months to 79 years old, with 80% over 40 years old. There were no restrictions with respect to previous treatment. All patients had known systemic malignancies. Even patients with malignancies unlikely to cause intraparenchymal metastases, such as prostatic carcinoma or leukemia, were included. All patients were referred either in the course of routine evaluation for assessment of the extent of disease or because of specific neurologic symptoms and signs, such as headache, seizure, mental status changes, sensory or motor abnormalities, nausea and vomiting, dizziness, or ataxia.

For logistic reasons, only inpatients were included in this study. Of these patients, those who were uncooperative, clinically unstable, or allergic to CT contrast material were excluded. With these few exceptions, all patients were accrued consecutively. None of the patients were excluded because of clinical demands on the MR unit. None of the eligible patients had a history of aneurysm surgery or pacemaker implantation, although such patients would also have been excluded. None of the patients proved to be too claustrophobic for this study, although several were given diazepam to make them feel more comfortable.

In all patients CT was performed on a high-resolution scanner and contrast material was administered intravenously. Approximately two thirds of the patients also had CT without contrast enhancement. All patients received a single bolus of 42 g of iodine or 150 ml of 60% contrast material (Reno-M-60; Squibb, New Brunswick, NJ). Scanning began immediately upon completion of the injection.

All MR imaging was performed on a superconductive magnet operating at 1.5 T. Long repetition time (TR) sequences (2000/35,70/1) (TR/TE/excitations) were obtained. In addition, short TR sequences were also obtained. Five-millimeter axial images with an intersection gap of 2.5 mm were obtained in all cases for both short and long TR scans. The matrix was always 256 × 256. One excitation was used for the long TR scans; two excitations were used in the short TR scans. MR and CT were always performed within 1 week of each

other. In 54% of patients, scans were done within 3 days of each other.

Each patient had preliminary short and long TR scans before contrast administration. Scanning was initiated immediately after the administration of gadopentetate dimeglumine in a concentration of 0.1 mmol/kg. Three postcontrast sequences were obtained—a short TR acquisition, followed by a long TR acquisition, followed by a final short TR acquisition. Taking the midpoint of each sequence as the time elapsed since injection, the sequences were obtained 4 min, 12 min, and 20–30 min after the administration of contrast. The timing of the third postcontrast sequence varied more than that of the first two sequences because a pause of up to 10 min was introduced after the second scan was completed in order to provide more of a true delayed scan. During this time, the patient remained motionless

TABLE 1: Analysis of Patients by Diagnosis*

Diagnosis	No. of Patients
Lung carcinoma	13
Breast carcinoma	7
Lymphoma	6
Melanoma	6
Colon carcinoma	3
Prostate carcinoma	2
Leukemia	2
Ovarian carcinoma	2
Bladder carcinoma	2
Adenocarcinoma of unknown primary	2
Esophageal carcinoma	2
Renal cell carcinoma	1
Testicular carcinoma	1
Pancreatic carcinoma	1
Neuroblastoma	1
Wilms tumor	1
Squamous cell carcinoma of head and neck	1

* The total number of diagnoses is greater than the total number of patients because three patients had two primary tumors each.

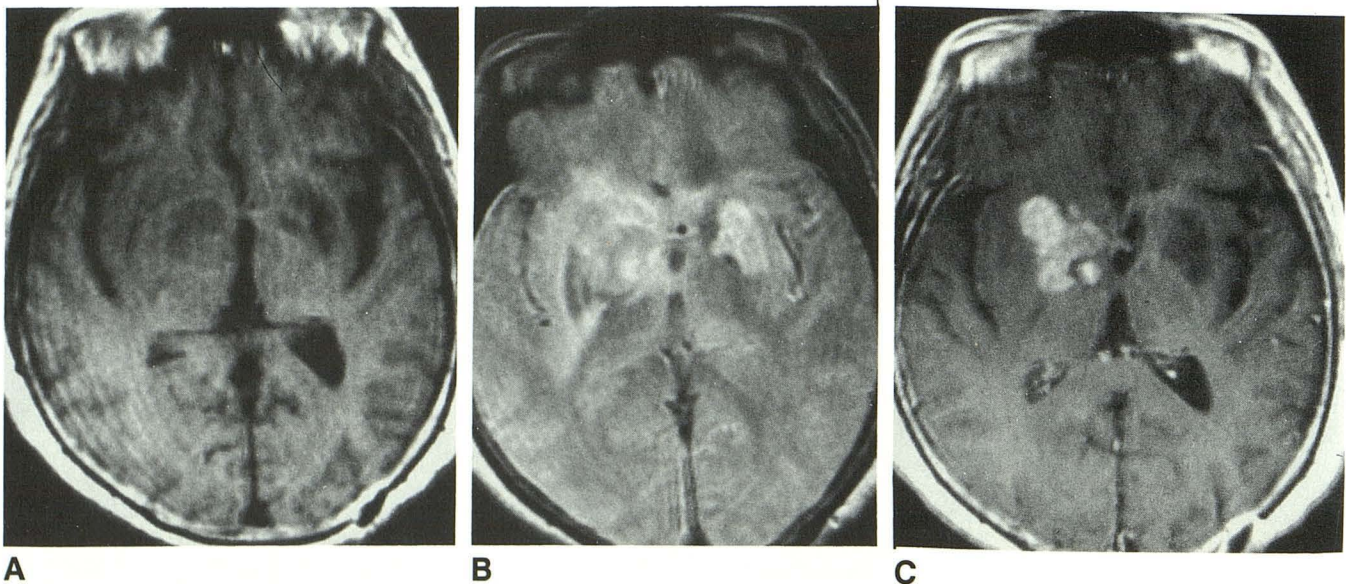


Fig. 1.—56-year-old woman with lymphoma.

A and B, Unenhanced short TR (400/20) (A) and long TR (2000/35) (B) scans show abnormal basal ganglia bilaterally. Differentiating between tumor and infarct is difficult.

C, Postcontrast short TR (400/20) scan shows enhancement of right lesion (proved by stereotactic-guided biopsy to be a metastasis) and lack of enhancement of the left lesion, which behaved like an infarct. CT disclosed similar findings.

in the scanner so that sections on the delayed scan could be compared accurately with sections from previous acquisitions.

Two neuroradiologists independently evaluated the images. The two readers came from an affiliated institution and had no prior exposure to the cases in this study. No information regarding the patients' histories, symptoms, or physical findings was provided although the readers were aware that the patients all had systemic tumors. The scans were set up on view alternators prior to the readings and the neuroradiologists were handed score sheets that were ordered by number and not by the patients' names. The neuroradiologists were informed that they should record all the intracranial lesions noted in these cases. If more than seven lesions were seen, then the patient was considered to have lesions too numerous to count. The likely diagnosis for a particular lesion was also recorded.

The noncontrast MR studies were analyzed first by themselves. After 1 week, readings of the postcontrast sequences were initiated. The postcontrast images were divided into three groups—immediate postcontrast short TR scans, postcontrast long TR scans, and delayed postcontrast short TR scans. The two neuroradiologists were first asked to read one of these three sets of scans, chosen at

random. Separated by intervals of at least 1 week, the remaining two sets of postcontrast scans were read. Finally, the contrast-enhanced CT scans were interpreted. In this way, each patient had five different sets of scans analyzed independently. Because of the large number of patients and scans, it was considered unlikely that the readers would remember the results from one session to the next.

After the blinded readings were completed, the noncontrast MR, contrast MR, and contrast CT scans were reviewed together by all the neuroradiologists in the study as a group. A final interpretation utilizing all the relevant clinical information and imaging studies was made. If questions persisted, further validation was sought. This validation consisted of: (1) surgical removal of the lesion, (2) follow-up CT or MR scans, (3) autopsy results, or (4) clinical neurological examination after 4 months or longer without treatment. If follow-up CT or MR scans were used to verify results, then these scans were considered positive for metastases if lesions decreased in size with radiation treatment or if lesions increased in size without treatment after a 3-month interval. The scans were considered negative for metastases if lesions disappeared or ceased to enhance spontaneously. If clinical examination was made, the diagnosis of metastasis

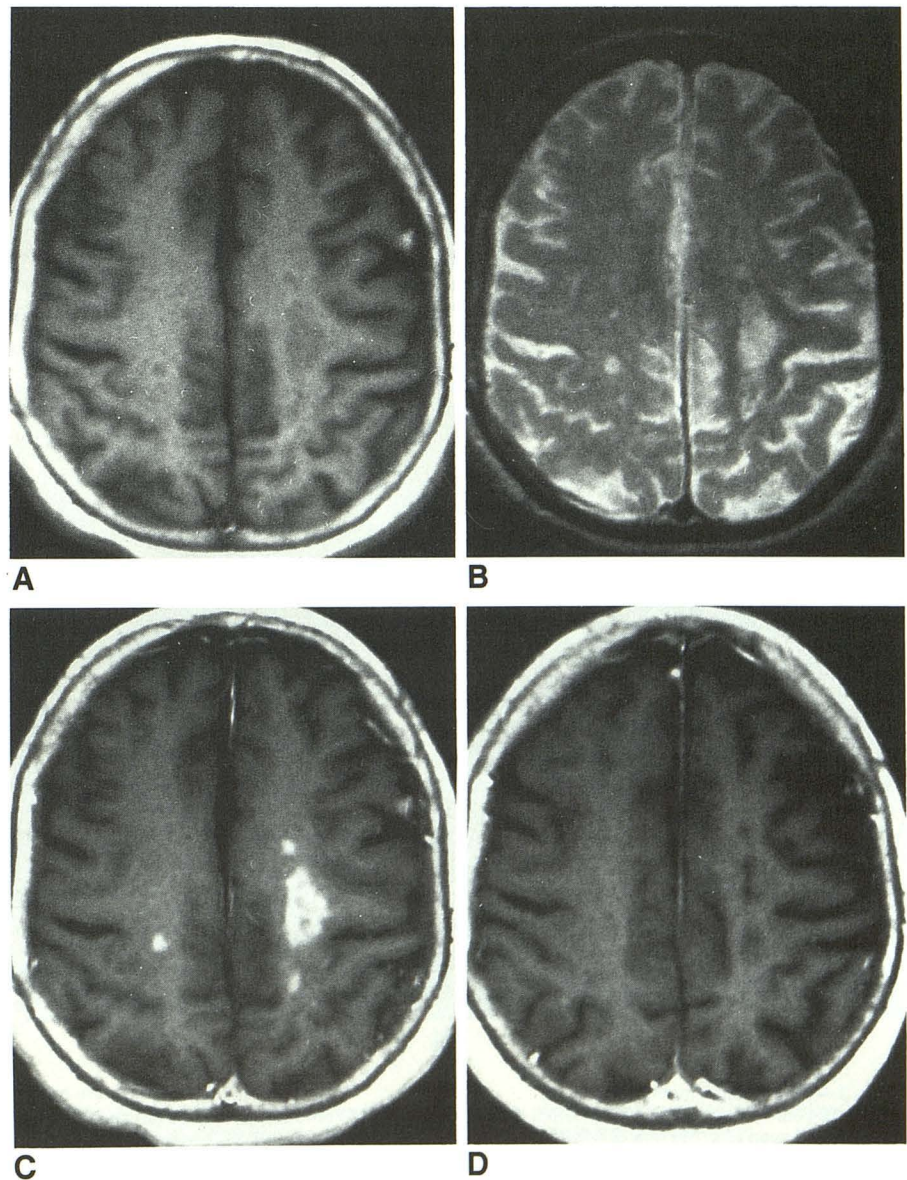


Fig. 2.—75-year-old woman with breast carcinoma and colon carcinoma, who presented with right hemiplegia.

A and B, Unenhanced short TR (400/20) (**A**) and long TR (2000/70) (**B**) axial scans show bilateral centrum semiovale lesions, left greater than right. On other sections, the left lesion was most consistent with a subacute infarct.

C, Postcontrast short TR (400/20) axial scan shows enhancement of all lesions, including the punctate right white matter focus. Clinically, the patient improved without treatment and the lesions were thought to be most consistent with infarcts.

D, Follow-up postcontrast short TR (400/20) axial scan 3 months later shows lack of enhancement of all lesions, as would be expected with infarcts.

was considered unlikely if the patient was neurologically unchanged or improved after 4 months without treatment.

Results

Relevant clinical data are listed in Table 1. Fourteen patients had received previous whole brain radiation. In the final interpretation, 27 of the 50 patients were found to have metastases.

Of the 50 scans, 12 were considered unambiguously negative on all scans by all readers and in the final interpretation. In an additional 14 cases, the results of all the blinded readings for each scan and the final interpretation were unanimous. In the remaining 24 cases, there were differences among the blinded readings and the final interpretation. In seven of the 24 cases, white matter lesions were recorded as metastases on the blinded readings of the noncontrast MR or postcontrast long TR sequence. In the final interpretation, since these lesions did not enhance in the postcontrast scans, they were not considered to be metastases. In six of the 24 cases, lesions missed on the blinded readings were unanimously agreed upon by all participants in the final interpretation. In the remaining 11 patients, uncertainties persisted and further validation was sought. In two patients, surgery was performed; one case proved positive for an adjacent lesion and one case proved negative. In six patients, follow-up CT or MR scans were used, proving the existence of possible metastases in four cases and documenting infarct in two cases. In one patient, autopsy confirmed the finding of metastases. In the two remaining patients, clinical neurological examination after 4 months without treatment suggested a lack of change in the clinical status that was considered inconsistent with metastatic disease.

Infarcts of various ages could usually be distinguished from metastases. Twenty-two of the 50 had foci of high signal in the basal ganglia or white matter that did not enhance on either contrast CT or contrast MR and were thought most likely to be the result of small-vessel ischemic disease or chronic infarct (Fig. 1). Five of the 50 had enhancing lesions most consistent with subacute infarcts. In three, the lesions were wedge-shaped, widening toward the gray matter. After contrast, gyral enhancement was visible.

Although differentiation of infarct from metastasis was usually not difficult, in three, including one patient with a subacute infarct, small foci of high signal in either the basal ganglia or white matter were shown to enhance after the administration of gadopentetate dimeglumine (Fig. 2). All three had no other evidence of intraparenchymal metastasis and these lesions were thought to represent subacute punctate infarcts. In two cases, follow-up scans and clinical assessment were negative. One case was associated with an occluded internal carotid artery.

Of the 27 patients with metastases, short TR contrast MR imaging showed more lesions than did contrast CT in eight cases. In three of these eight, CT missed posterior fossa lesions. In three other cases, CT did not detect primarily isodense hemorrhagic lesions. In these cases, metastases were either punctate or were primarily hemorrhagic with small foci of minimal contrast enhancement (Fig. 3). Short TR contrast MR, however, easily revealed these lesions, which were hyperintense on these sequences. The addition of MR contrast agents in these cases was often superfluous. In the two remaining cases, CT did not detect punctate enhancing supratentorial lesions seen on contrast MR. Contrast CT was never superior to contrast MR for intraparenchymal metastases.

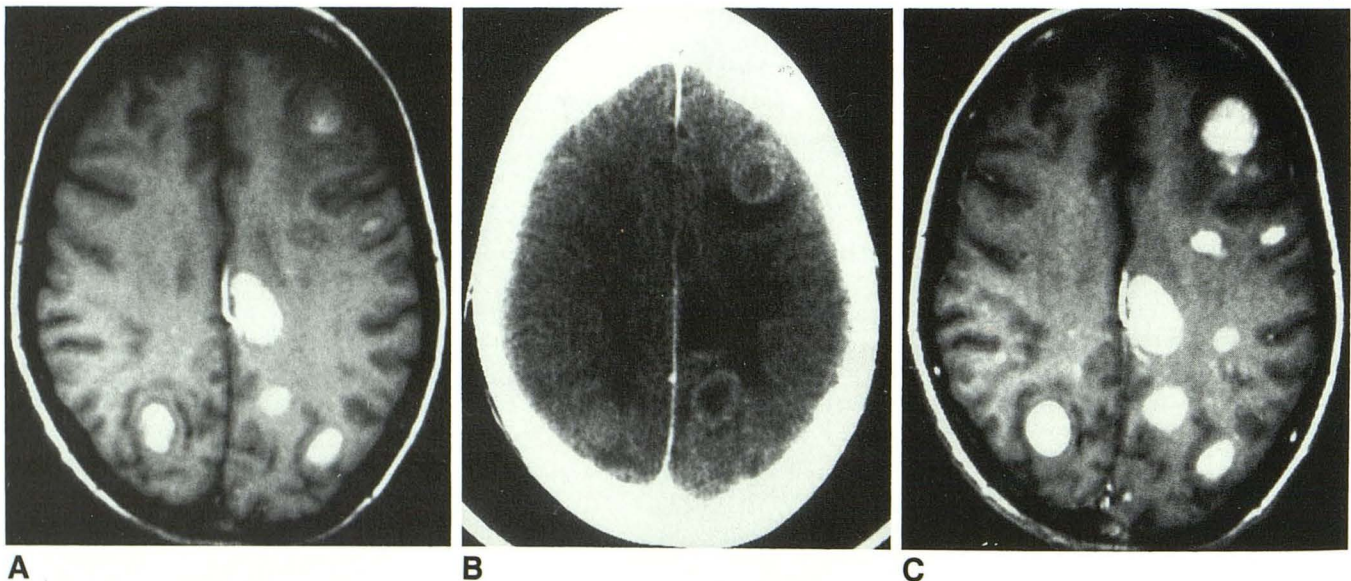


Fig. 3.—Hemorrhagic metastases.

A-C, 50-year-old woman with melanoma. Unenhanced short TR (400/20) MR image (A) shows many more hyperintense metastases than does contrast-enhanced CT scan (B). The use of contrast in MR revealed still more metastases in this case (C).

In six of the 27 cases with metastases, short TR contrast MR imaging detected metastases that were not seen on noncontrast MR, including the long TR acquisitions. In five cases, noncontrast MR was unable to detect lesions that were isointense under all sequence parameters and that lacked significant surrounding edema. Contrast MR easily detected these metastases, which were peripheral, gray matter lesions (Fig. 4). These lesions were not always small and punctate; they ranged up to 1½ cm. In one case, a small lesion adjacent to a large lesion was missed on account of copious edema surrounding the second lesion (Fig. 5).

In three of the 27 cases, short TR contrast-enhanced scans detected more metastases than did long TR contrast-enhanced scans. In these cases, punctate lesions identified in the short TR postcontrast scan were either not well visualized on the long TR postcontrast scan or were mistaken for punctate high-intensity artifact often seen in sulcal vessels when gradient-moment nulling techniques are employed. In the latter case, the true nature of these metastases was revealed, since the greater morphologic detail possible on the short TR sequence allowed differentiation between true enhancing lesions and sulcal vessels. Of course, owing to their

sensitivity to nonspecific white matter lesions, long TR scans detected a greater number of total lesions in most scans. In five of 27 cases, however, despite the previous administration of gadopentetate dimeglumine, differentiation of small metastases from white matter ischemic changes was difficult on long TR postcontrast scans.

In three of the 27 cases, long TR scans demonstrated lesions that were not identified well on the postcontrast short TR scan (Fig. 6). In two cases, the patients had small hemorrhagic metastases. On the long TR scan, whether pre- or postcontrast, these lesions were easily seen owing to their marked hypointensity. On the short TR scan, however, the lesions were nearly isointense, enhanced to only a mild extent, and were much less obvious. In one case, a patient with multiple intracranial metastases had several punctate non-hemorrhagic foci that were better seen on the long TR scan and identified only in retrospect on the postcontrast short TR scan. In addition, long TR scans were useful in two other cases to show edema and confirm the presence of lesions suspected on the postcontrast short TR scan.

In general, an equal number of metastases was detected on the immediate postcontrast short TR scan and on the

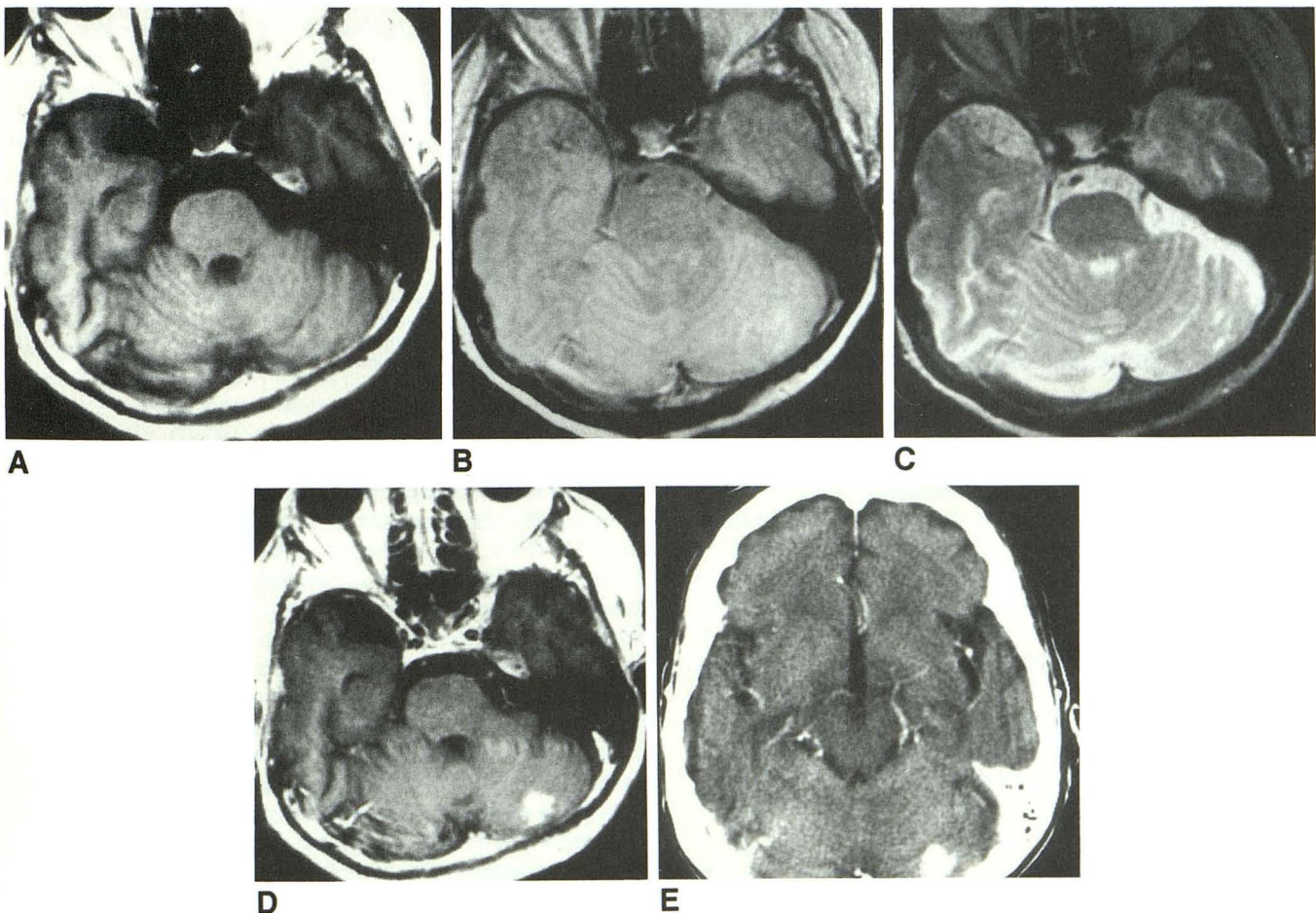


Fig. 4.—68-year-old woman with breast carcinoma and ataxia.

A–C, Unenhanced short TR (400/20) (A) and long TR (2000/35,70) (B and C) sequences fail to disclose any unequivocal posterior fossa lesion.

D, Postcontrast short TR (400/20) sequence shows a 1½-cm left cerebellar hemisphere lesion, located primarily in the gray matter.

E, Lesion is seen well on contrast CT scan.

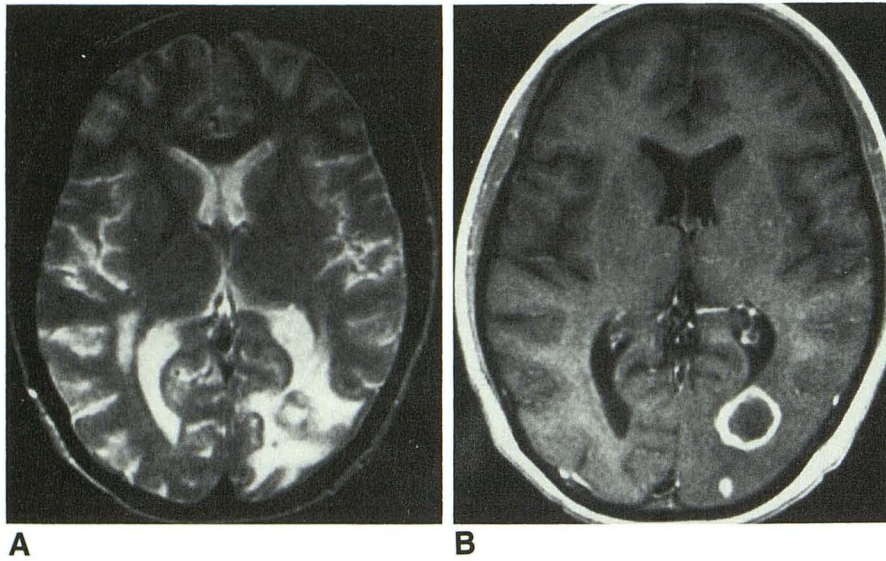


Fig. 5.—46-year-old woman with a history of breast carcinoma.

A, Unenhanced long TR (2000/70) scan shows a lesion in left occipital lobe.

B, Postcontrast short TR (400/20) scan discloses the presence of two separate lesions. The smaller lesion is hidden by the edema of the larger lesion on the noncontrast scans.

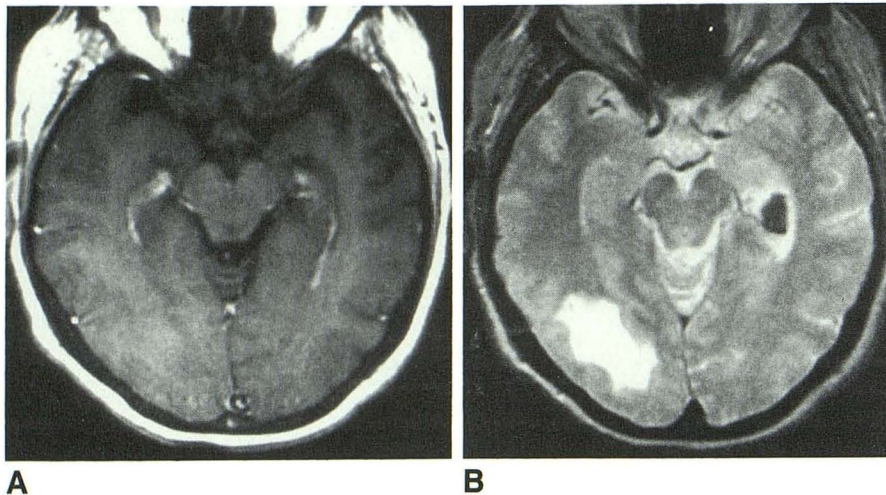


Fig. 6.—58-year-old woman with lung carcinoma.

A and B, Postcontrast short TR (400/20) scan (A) is less definitive than long TR (2000/70) scan (B). The hemorrhagic metastasis is better visualized on the long TR image owing to the striking magnetic susceptibility effect of the blood as compared with the subtle enhancement of the presumably small amount of tumor.

delayed postcontrast short TR scan. In three cases, lesions were well seen on the immediate postcontrast short TR scan but not on the delayed short TR scan. In two of the three cases, these lesions were very small and it was unclear if they actually ceased to enhance on the delayed scan or if they were averaged into the interslice gap caused by minimal patient motion. However, in four cases, metastases were seen better on delayed postcontrast scans. In three of the four cases, they could be identified on the immediate postcontrast scan, although detection was much easier in retrospect in a few small lesions. In one case, a small lesion was difficult to visualize on the immediate postcontrast scan.

Discussion

In this study, postcontrast short TR scans, either immediate or delayed, were the most accurate in the detection of intraparenchymal metastases. Contrast CT and noncontrast MR were roughly comparable. Postcontrast long TR sequences

were slightly better than contrast CT and noncontrast MR but not as accurate as postcontrast short TR sequences. While the long TR scans were not as accurate as the postcontrast short TR scans, they were still useful in questionable cases, in occasional hypointense hemorrhagic lesions (Fig. 6), and to detect other pathology. In addition, the use of the long TR scans following contrast administration provided a short delay prior to the short TR scans.

Because of the trends of our findings, we recommend that the evaluation of intraparenchymal metastases consist of a single postcontrast long TR scan followed by a single postcontrast short TR scan. These sequences should be very practical. In addition, a precontrast short TR scan is useful if bone lesions are suspected and in differentiating hemorrhage from enhancement. Because this study concerned intraparenchymal brain metastases, bone lesions were not included. Detection of skull metastases may benefit from noncontrast scans, since bone lesions in the skull base may enhance to isointensity with normal surrounding marrow and since enhancing skull vault metastases might be mistaken for marrow

fat if only postcontrast scans are obtained [6]. Clearly, the inclusion of this category might change the results to favor the addition of a precontrast short TR scan. In fact, on reviewing the bone windows of the CT scans in this study only three skull metastases were present in our patients and they were large enough to be detected easily on all scans.

With respect to hemorrhage, precontrast short TR scans may be useful to differentiate hemorrhage from enhancement when high-intensity methemoglobin is present in the precontrast sequence. However, tumor hemorrhage is often characterized by substantial areas of hypointensity. This is particularly true in such instances, since blood in a tumor bed evolves much more slowly than intraparenchymal blood not associated with a neoplasm [7, 8]. We have seen hemorrhagic metastases remain hypointense on all sequences for over 5 months. When the blood is hypointense, it will be correctly identified, particularly on long TR sequences, regardless of whether or not gadopentetate dimeglumine has been administered. Therefore, the identification of hemorrhage on contrast-enhanced MR scans is often not as difficult as on contrast CT scans. By the time the blood can evolve to a hyperintense phase, it is less likely that the question of hemorrhage will be clinically relevant. In addition, some visualization of hemosiderin deposition is usually possible at this point although it may be diminished, as is often typical of tumor hemorrhages.

If hemorrhagic metastases are specifically sought, gradient-echo sequences may be more sensitive [9], particularly on low or middle field strength units. However, the long TR scan is more sensitive to nonhemorrhagic disease. Whether the gradient-echo sequence will detect hemorrhagic metastases not seen on the postcontrast long and short TR scans is a matter for future study.

While punctate enhancing lesions often represent metastases, caution must be used when these foci are seen in the white matter or basal ganglia. The causes of these lesions appear to be diverse [10, 11]. Often, these foci may be punctate infarcts, and, in subacute cases, enhancement can occur (Fig. 2). Owing to the sensitivity of contrast MR, small white matter and basal ganglia infarcts are now noted to enhance much more often than with contrast CT. In questionable cases, follow-up scans should help differentiate them from punctate metastases.

While contrast MR appeared more successful than contrast CT, one important point must be kept in mind. Our patients received a single dose of 150 ml of 60% contrast or 42 g of iodine, followed by immediate scanning for CT. The literature, however, confirms the superiority of both high-dose and delayed scans [12, 13]. If double-dose delayed scans had been performed, contrast CT might well be close to equivalent to contrast MR for detecting intraparenchymal metastases. In addition, it would probably be more sensitive for many skull metastases.

In patients who have multiple lesions, demonstrated on either contrast CT or noncontrast MR, the finding of additional

metastases on contrast MR may be superfluous. In patients who have single lesions and who appear to be candidates for surgical removal of the metastasis, however, the finding of an additional lesion would be highly significant. Similarly, in patients with negative contrast CT scans or noncontrast MR scans, the increased sensitivity of contrast MR may also be important. Of our 50 patients, we did not have one in whom all studies except the contrast MR were negative in the final evaluation and in whom the contrast MR was the only method to detect a metastasis. Nevertheless, given the increased accuracy of contrast MR, we consider this a real possibility if an even larger series were to be performed.

In conclusion, for routine evaluation of suspected intraparenchymal metastases, a single long TR postcontrast scan followed by a single short TR postcontrast scan should be very accurate. The short delay of the long TR scan may improve the conspicuity of small lesions on the short TR scan. At the same time, the long TR scan provides additional information that may prove useful. Precontrast scans may also be helpful if bone lesions or hemorrhagic foci are clinically relevant, for example, in patients receiving anticoagulation therapy.

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