Dynamic Contrast Enhancement of Intracranial Tumors with Snapshot-FLASH MR Imaging

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PURPOSE: To investigate whether exact evaluation of the dynamic contrast enhancement pattern within intracranial tumors can help to classify tumor histology and vascularity. **METHOD:** Forty-nine patients suffering from different intra- and extraaxial intracranial tumors underwent MR-examination in a 1.5-T superconductive whole body system. After rapid injection of Gd-DTPA, 48 images were acquired during the first 1.5 to 2 minutes of contrast enhancement within the tumors. A fast snapshot-FLASH imaging technique allowed measurement times of 1 second per image. Appearance of Gd-DTPA in a venous sinus served as a temporal reference point. Transformation of 48 discrete measurement points (mean signal values of the enhancing tumor region) into a continuous curve, using a cubic spline approximation, allowed calculation of the time of maximum signal increase (Tm1) and the following time of half maximum increase (Tm2). These time parameters were compared to histopathologic findings, especially the degree of tumor vascularization. **RESULTS:** Significantly different dynamic patterns of the early enhancement period were found for the different tumors. All eight neurinomas, typically less vascularized than most meningiomas, showed a characteristically prolonged contrast enhancement with a long Tm2. Histopathologic findings concerning the degree of vascularization showed two subtypes in meningiomas (n = 17) as well as in pituitary macroadenomas (n = 7). This was confirmed by dynamic evaluation in all cases, in the sense that short Tm1 and Tm2 were found in cases with higher degrees of vascularization. Negatives values of Tm1 were measured in two glomus jugulare tumors, reflecting the arterialization of these vascular tumors. In neuroepithelial tumors (n = 15), the glioblastomas (n = 7) showed very short Tm1 compared to the lower grade gliomas (n = 8). This is explained by histologic findings of pathologic vessels with arteriovenous shunts. **CONCLUSION:** The evaluated dynamic time parameters can be used to narrow differential diagnostic possibilities and to infer the degree of vascularization of intracranial tumors.

Index terms: Magnetic resonance, technique; Brain neoplasms, magnetic resonance

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The purpose of this study was to analyze whether an exact evaluation of dynamic contrast-enhancement patterns of different intracranial tumors using an ultrafast magnetic resonance (MR) imaging technique can help to classify tumor histology and vascularity. This so-called "snapshot-FLASH" technique combines T1 contrast with short measurement time of approximately 1 second per image on a conventional whole body system, if satisfactory spatial resolution (256 × 256 matrix size) is still required (1–6). After MR examination all patients underwent neurosurgery and all tumors were histopathologically confirmed, including a determination of the degree of vascularization. These histopathologic findings were compared with the results of the dynamic contrast-enhancement evaluation.

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Patients and Methods

In a prospective study, 49 patients with different intracranial tumors were evaluated by MR imaging. Thirty-four patients suffering from extraaxial tumors (17 meningiomas,

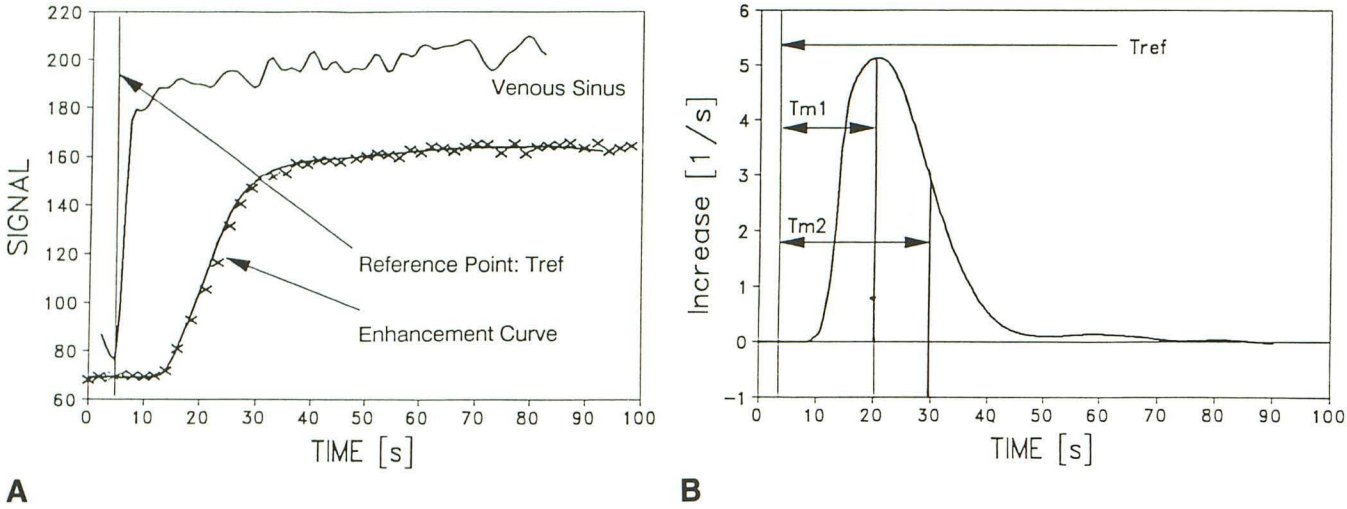


Fig. 1. Example for the evaluation of dynamic contrast enhancement.

A, Continuous approximated tumor enhancement curve with its original discrete measurement points. The temporal reference point (T_{ref}) is defined as the beginning of signal increase in the venous sinus.

B, Increase of the enhancement curve (first derivation) and the two time intervals between T_{ref} and the time of maximum (Tm1) and half maximum (Tm2) rate of contrast enhancement, respectively.

TABLE 1: Extraaxial tumors (n = 34)

Histologic Degree of Vascularization	Glomus Jugulare Tumors (n = 2)	Meningiomas (n = 17)	Neuromas (n = 8)	Adenomas (n = 7)
Highly vascularized	Tm1 [s] = −1.7 ± 0.5 Tm2 [s] = 2.7 ± 0.7	Tm1 [s] = 0.2 ± 0.2 Tm2 [s] = 3.7 ± 0.5		Tm1 [s] = 2.3 ± 0.3 Tm2 [s] = 5.3 ± 0.05
Normally vascularized		Tm1 [s] = 3.9 ± 1.3 Tm2 [s] = 11.2 ± 2.6	Tm1 [s] = 3.8 ± 0.3 Tm2 [s] = 27.8 ± 5.5	Tm1 [s] = 7.55 ± 1.7 Tm2 [s] = 15.1 ± 7.1

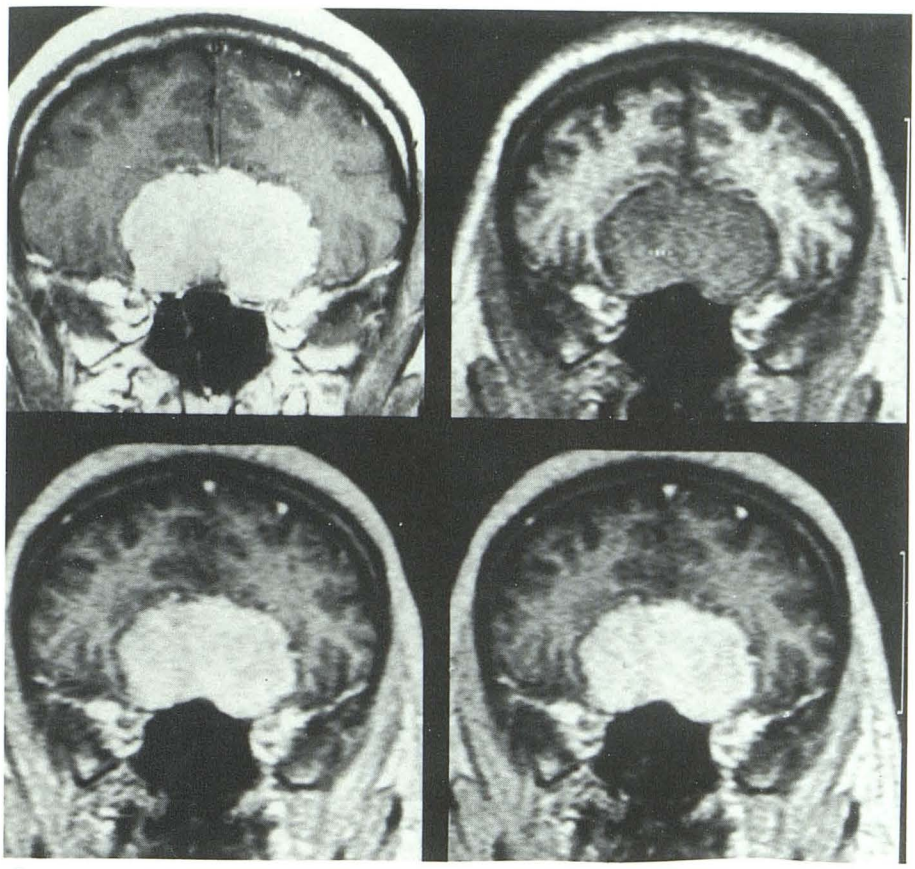
Note.—Mean values and standard deviation of time of maximum signal increase (Tm1) and following time of half-maximum increase (Tm2) for tumor-related typical ("normal") and atypically high degree of vascularization of extra-axial tumors.

eight neurinomas, seven adenomas, two glomus jugulare tumors) and 15 patients with intra-axial tumors (seven glioblastomas, three oligoastrocytomas, two oligodendrogliomas, three astrocytomas I-II) were examined on a 1.5-T whole body imager. All patients underwent neurosurgical resection, and all tumors were histopathologically confirmed and their degree of vascularization determined. Each kind of tumor was classified in two subgroups of tumor vascularization through independent graduation by two experienced senior neuropathologists, who rated the specimen subjectively as typically ("normally") or atypically ("highly") vascularized.

The MR examinations were performed according to a fixed protocol, including conventional T1- and T2-weighted precontrast spin-echo (SE) images to assess tumor localization, size, extent, and delineation from the perifocal edema. The cut plane with the largest tumor extent was chosen for the dynamic contrast-enhancement analysis. To monitor the contrast dynamics after contrast media administration within a range of seconds, we used a snapshot-FLASH technique, as described previously (4–6). This technique provides a T1-weighted image with a very short repetition time (TR = 8 msec, TE = 3.5 msec) with a low flip angle (FL = 7°). Measurement time for one image with satisfactory spatial resolution (256 × 256 matrix size, in plane resolution of 0.8 mm, section thickness of 4 mm) in conjunction with a half-Fourier space reconstruction technique was 1 second.

In every dynamic contrast enhancement series, three baseline snapshot images were acquired prior to contrast injection as a nonenhanced reference. Then, 48 snapshot images were acquired sequentially with a 1-second interscan delay, over a period of approximately 96 seconds immediately following the intravenous bolus injection over 10 seconds of 0.1 mmol Gd-DTPA per kg of body weight.

For exact temporal analysis of the enhancement curve a region of interest (ROI) was defined, containing the total tumor area in homogeneously enhancing tumors. In inhomogeneous lesions containing enhanced, well-vascularized portions, as well as nonenhanced portions, only the enhanced portions were analyzed. Best delineation of the different portions was possible during the early period of tumor contrast enhancement (see Fig. 7D), when less vascular parts, in comparison with the well-vascularized



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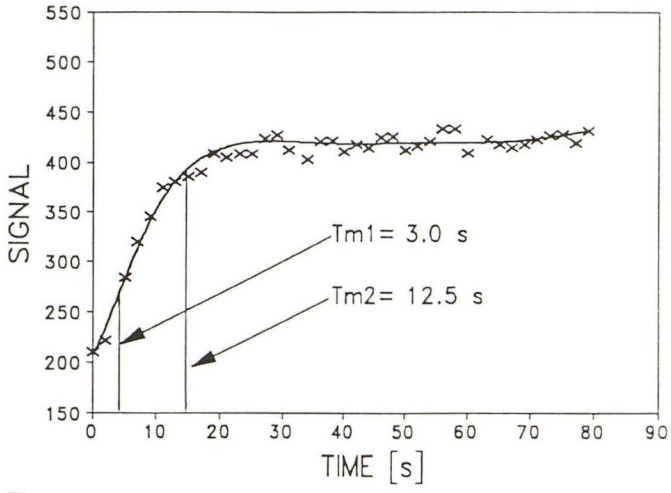

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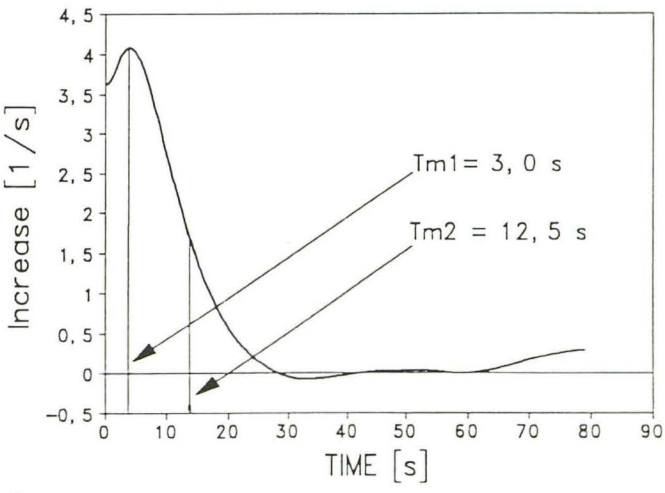

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Fig. 2. Meningioma.

A, On the upper left, a conventional postcontrast T1-weighted spin-echo image with good tumor delineation from surrounding tissue and an associated dural enhancement. From the *upper right* to the *lower left* and *lower right*, three snapshot-FLASH images of the early, intermediate, and late enhancement period.

B, Contrast enhancement curve of the illustrated case in *A*.

C, Corresponding signal increase curve (T_{ref} = 0): time of maximum increase (Tm1) and the following half maximum increase (Tm2).

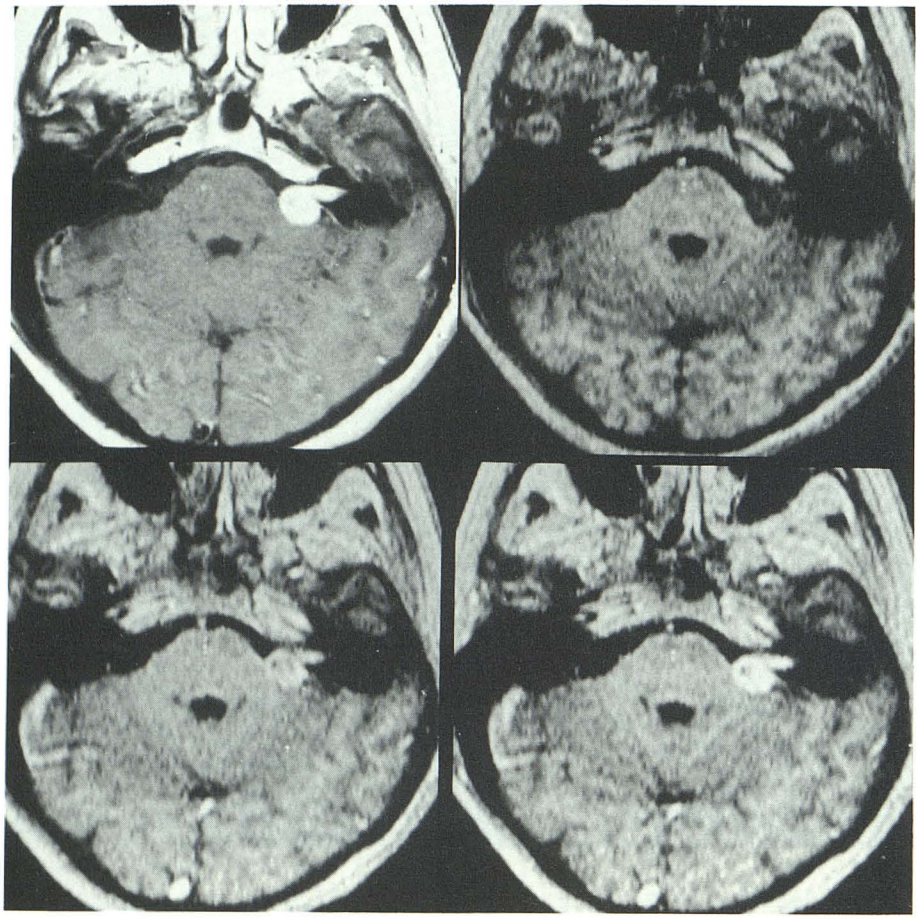
parts, do not yet show contrast enhancement (see Fig. 7A, upper right). At the end of the contrast-enhancement series (see Fig. 7A, lower right) or on the delayed conventional SE image (see Fig. 7A, upper left), delineation is more difficult or impossible since the Gd-DTPA has also reached the less vascular parts, probably due to disruption of the blood-brain barrier or diffusion from the vascular parts. Different ROIs of the same tumor, each containing early-enhancing tumor portions, were evaluated in five examples and no detectable difference of the dynamic behavior was found, so that all further evaluations were based on the largest ROI possible in each tumor, excluding its less vascular parts. The ROI size ranged from 1 cm^2 to 14 cm^2, depending on the size of the lesions. The mean ROI value of signal intensity for each of the 48 discrete measurements was then transformed into a continuous curve by application of a cubic spline approximation (Fig. 1A). The first derivation, representing the rate of increase of the signal curve (which is not directly related to the measured signal intensity on an individual image), was calculated for further

Fig. 3. Acoustic neurinoma.

A, Upper left: Postcontrast T1-weighted spin-echo image. The intrameatal part is best shown on this image. Three snapshot images (*upper right* to *lower right*) analogous to Figure 2A show lower spatial resolution and signal-to-noise ratio. Nevertheless the central regressive alterations (necrosis and cyst formation) of the tumor are best seen on the snapshot-FLASH image of the intermediate enhancement period (*lower left*).

B, Signal enhancement curve of the illustrated case in *A*.

C, Signal increase curve. Compared with meningeomas, there is a prolonged increase with a long Tm2 (see Fig. 2).



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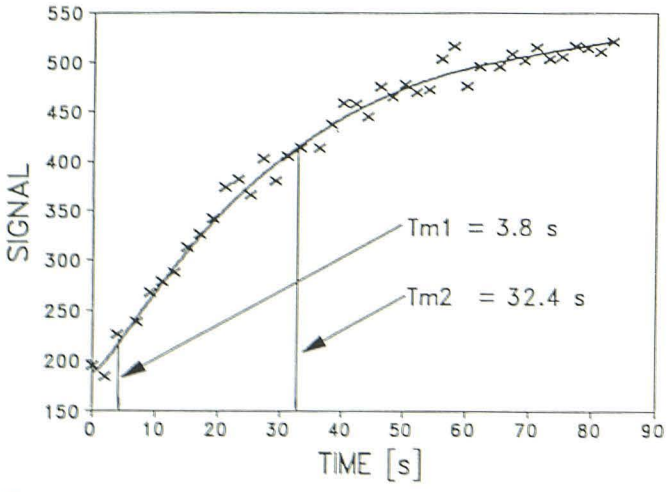

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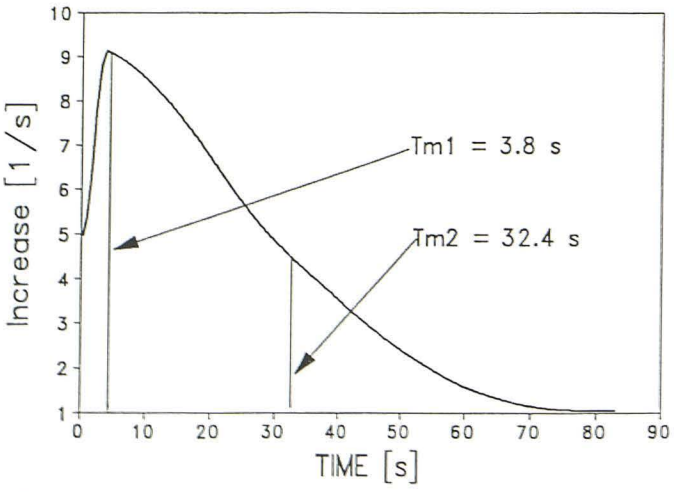

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evaluation (Fig. 1B). The time of maximum increase (Tm1) represents maximum rate of increase of contrast accumulation within the tumor, while the time of half maximum increase (Tm2) describes the point at which the rate of contrast increase has decreased to one half of the maximum rate of contrast accumulation (Fig. 1B).

The values Tm1 and Tm2 calculated on the first derivative curve were correlated with the histopathologic degree of vascularization. As seen in figure 1B, all time parameters are calculated as differences to a well-defined reference point T_{ref}, which was chosen to be the time when the bolus of contrast media appeared in the venous system (venous sinus); the venous sinus reference was chosen since in arteries no bolus-dependent signal increase can be seen due to strongly pulsating flow. No detectable differences were found, using the same venous sinus in various loca-

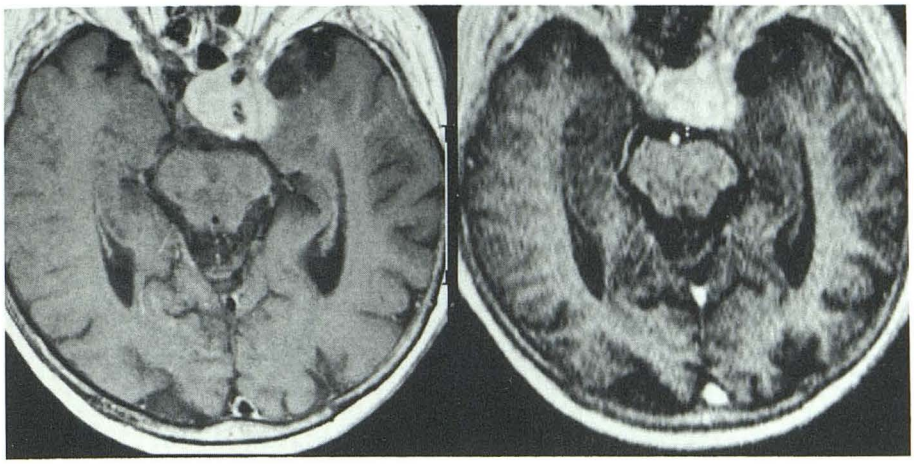

Fig. 4. Macroadenoma of the pituitary gland (normally vascularized).

A, Postcontrast spin-echo image (*left*) and snapshot-FLASH image (*right*).

B, and *C*, Contrast-enhancement and signal-increase curves corresponding to *A*. From dynamic aspects, the adenoma showed Tm1 and Tm2 values belonging to a histologically adenoma typical degree of vascularization ($T_{ref} = 0$).

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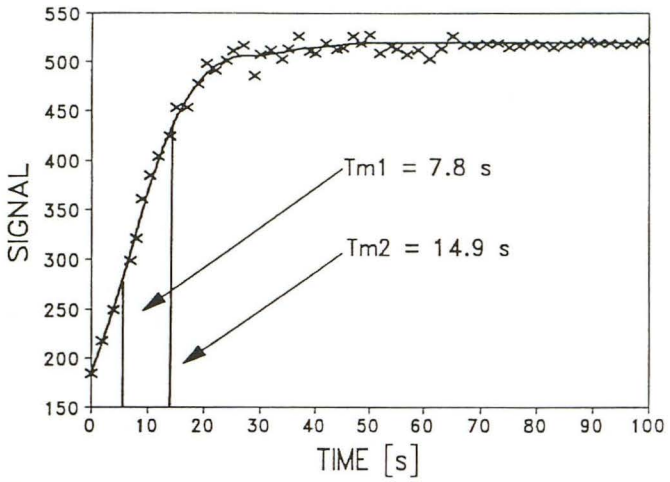

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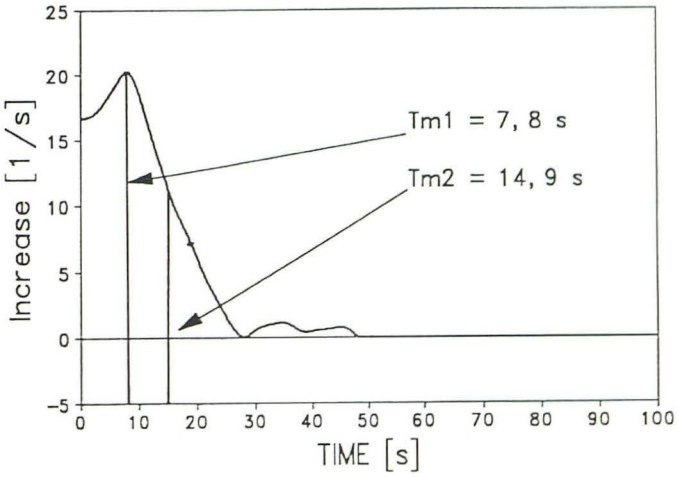

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tions, eg, the frontal or dorsal parts of the superior sagittal sinus. Even different sinuses (sagittal or transverse sinus) did not measurably vary in their dynamic contrast enhancement behavior, so that the cerebral venous system can be used as a valid reference system.

Results

Meningiomas

From the histopathologic aspect, the vast majority of meningiomas (n = 15) formed a homogeneous group with a typical pattern of vascularization. In these cases of "normally vascularized" meningiomas, a mean Tm1 of 3.9 seconds and a mean Tm2 of 11.2 seconds were found (Table 1). Two cases, however, showed a very short mean Tm1 of 0.2 seconds and a mean Tm2 of 3.7 seconds, corresponding to an atypically high degree of vascularization of the histologic specimen.

As already known from other studies (7–9), best tumor detection and delineation from surrounding tissue was possible with conventional T1-weighted postcontrast SE images (Fig. 2A), since on precontrast T1- and T2-weighted images meningiomas often appear isointense to neighboring gray matter.

Neurinomas

Similar to meningiomas, which often tend to have approximately the same T1 and T2 values as surrounding brain tissue, neurinomas, especially the intrameatal portions of acoustic neurinomas, are insufficiently delineated on precontrast T1-weighted SE images (3). On postcontrast images, however, all eight neurinomas, including their intrameatal parts, could be delineated. Four of them showed necrotic or cystic areas in their central portions, best seen on the snapshot-FLASH image of the intermediate enhancement period (Fig. 3A, lower left).

Concerning contrast dynamics, all neurinomas showed a relative prolonged increase of their contrast enhancement. Whereas the mean Tm1

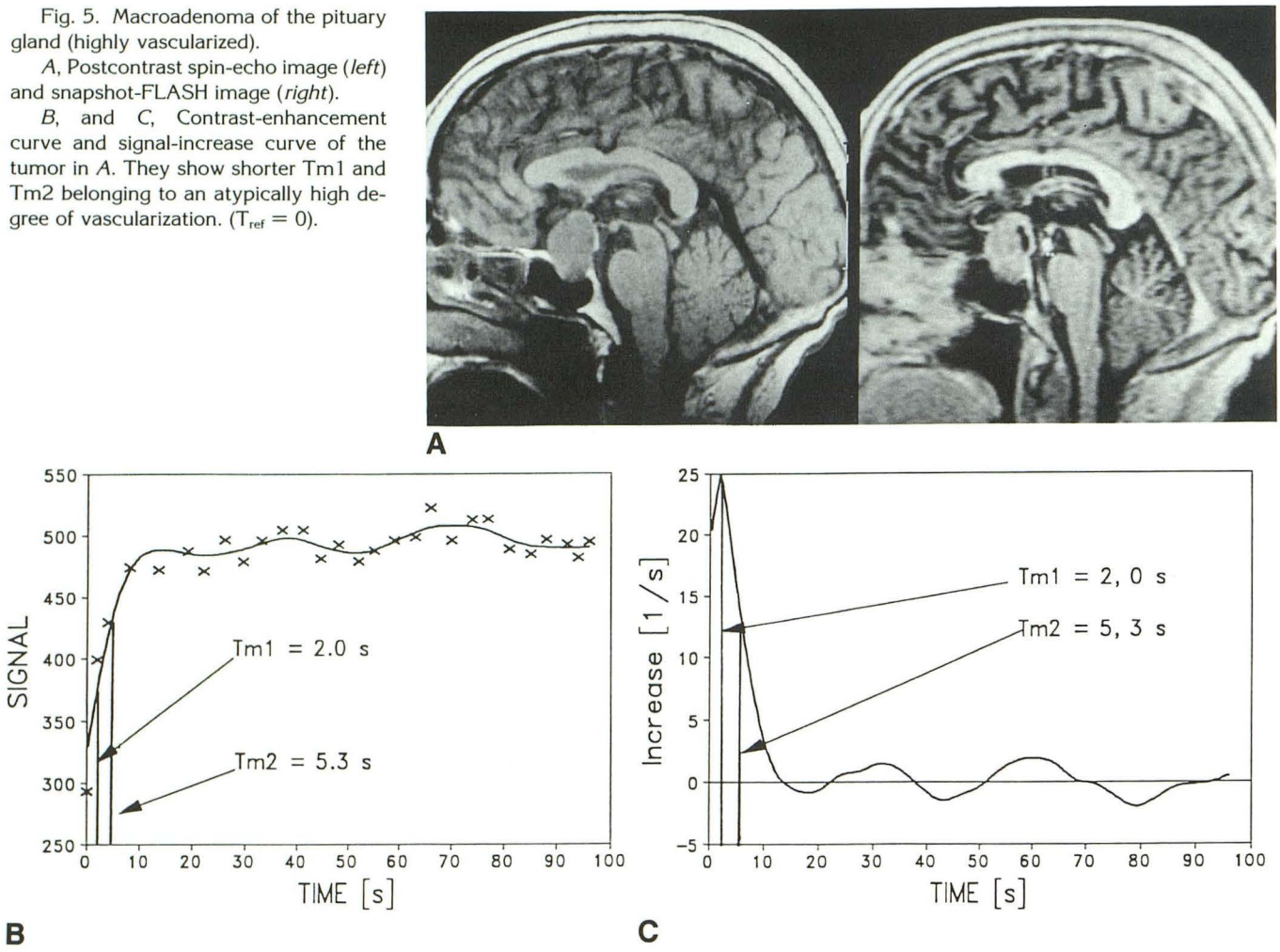

Fig. 5. Macroadenoma of the pituary gland (highly vascularized).

A, Postcontrast spin-echo image (*left*) and snapshot-FLASH image (*right*).

B, and *C*, Contrast-enhancement curve and signal-increase curve of the tumor in *A*. They show shorter Tm1 and Tm2 belonging to an atypically high degree of vascularization. ($T_{ref} = 0$).

of 3.8 seconds (Table 1) was almost identical with that of meningiomas, we found a significant longer mean Tm2 of 27.8 seconds, reflecting the slowly increasing contrast enhancement (Figs. 3B and 3C). Histopathologic findings confirmed, in all cases of neurinomas, a typical, rather low degree of vascularization.

Pituitary Adenomas

All seven macroadenomas of the pituitary gland (four nonfunctioning, three prolactin-producing) could be visualized without any difficulty on SE as well as on snapshot-FLASH images. From the dynamic aspect, in good correlation with histopathologic results, two groups could be distinguished. Four of the seven cases that turned out to be normally vascularized showed comparatively long mean Tm1 values of 7.6 seconds and mean Tm2 values of 15.1 seconds, indicating a rather modestly increasing contrast enhancement (Fig. 4). In three highly vascularized cases, however, Tm1 was found to be 2.3 seconds and Tm2 was 5.3 seconds, corresponding to an early onset and reach of the enhancement curve plateau (Fig. 5). No differences were found between hormone-producing and nonfunctioning tumors.

Glomus Jugulare Tumors

We examined two glomus jugulare tumors and found heterogeneous signal intensity on pre- and postcontrast SE images, containing signal extinctions caused by different flow velocities in the tumor, described in the literature as "salt and pepper" (10) (Fig. 6A). Evaluation of the dynamic data show the vascular nature of these tumors. Mean value of Tm1 was −1.7 seconds and mean value of Tm2 was 2.7 seconds. The Tm1 value was negative, as a result of the arterialization of glomus tumors (Figs. 6B and 6C).

Neuroepithelial Tumors

In five cases of lower grade gliomas, histologically confirmed as three astrocytomas of grade I-

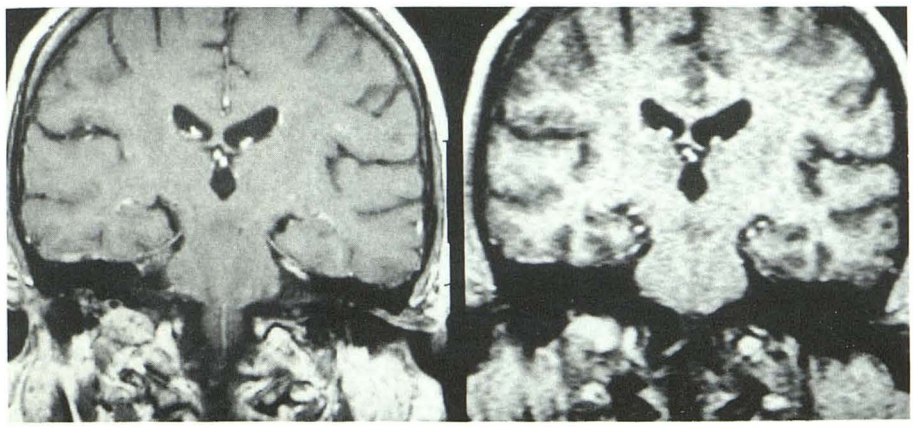

Fig. 6. Glomus jugulare tumor.

A, Spin-echo image (*left*) and snapshot FLASH image (*right*). Central signal extinctions due to high flow can be seen on the spin-echo image.

B and *C*, Contrast-enhancement curve and signal-increase curve of the tumor in *A* ($T_{ref} = 0$). Very early onset of the enhancement (negative Tm1) as a result of the high-grade vascularization and intratumorous arteriovenous shunting.

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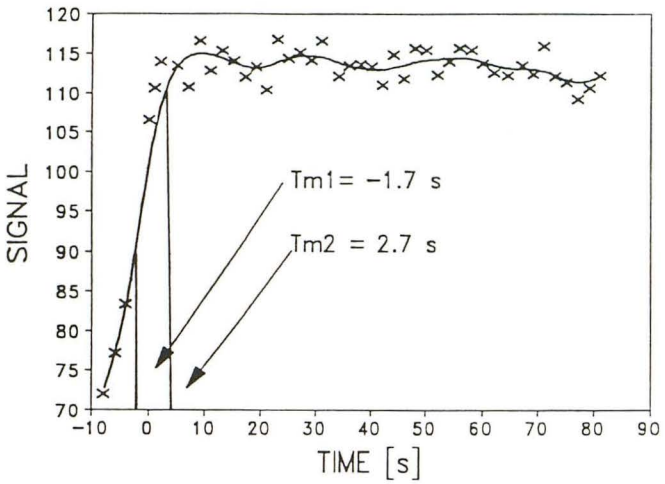

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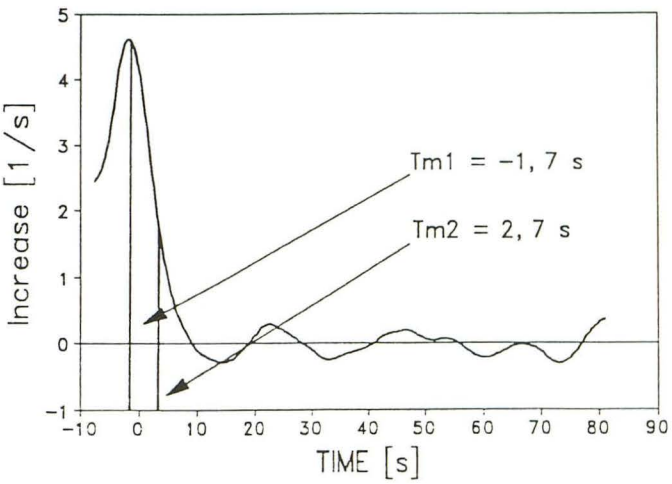

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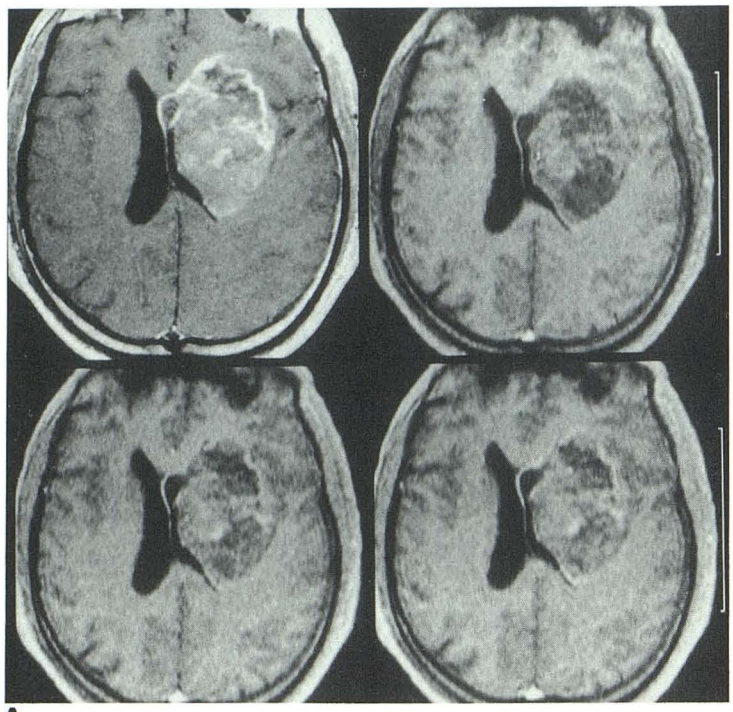
ll and two oligodendrogliomas, no contrast enhancement was found, which made dynamic analysis impossible. Enhancing intraaxial tumors showed differences in their dynamic enhancement behavior. All seven glioblastomas were enhancing fast with a mean Tm1 of 0.5 seconds and a mean Tm2 of 4.2 seconds (Fig. 7), whereas three mixed oligoastrocytomas showed late onset and prolonged increase, corresponding to a mean Tm1 of 13.6 seconds and Tm2 of 34.3 seconds (Table 2).

Discussion

Short measurement times of 1 second per image and a 1-second interscan delay result in a temporal resolution of 2 seconds per image with preservation of satisfactory spatial resolution. This technique permits dynamic analysis of the first 1–2 minutes of the tumor contrast enhancement (6). An apparent disadvantage of the snapshot-FLASH technique is the nonlinear relation between concentration of contrast medium and signal intensity, which depends on T1 as well as on T2. On the other hand, in dynamic CT studies profiting from this linearity (11, 12), techniques and data analysis for evaluation of perfusion and transit times are based on the assumption that there is an intact blood-brain barrier. Because this condition in brain tumors is rare, we focused our interest on the exact temporal analysis of the enhancement curve.

Although the number of analyzed cases of each tumor subcategory is limited as yet, and thus no statistical significance can be reached, we believe the preceding results to demonstrate that exact dynamic analysis of tumor contrast enhancement can give useful additional information to conventional pre- and postcontrast SE images in differential diagnosis of intracranial tumors. In our cases, dynamic contrast enhancement of neurinomas with their long Tm2 was quite characteristic, so that diagnosis of neurinoma could be given or excluded. Long Tm2 can be explained, assuming that in neurinomas, which are typically less vascularized than most meningiomas, absence of the blood-brain barrier is the main contribution to contrast enhancement. This would



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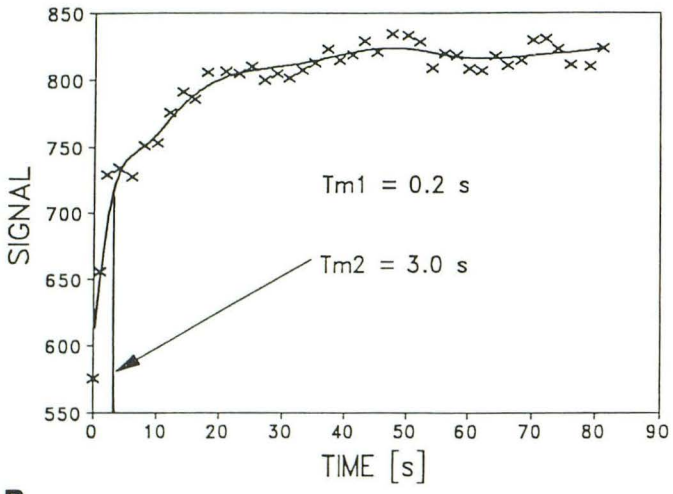

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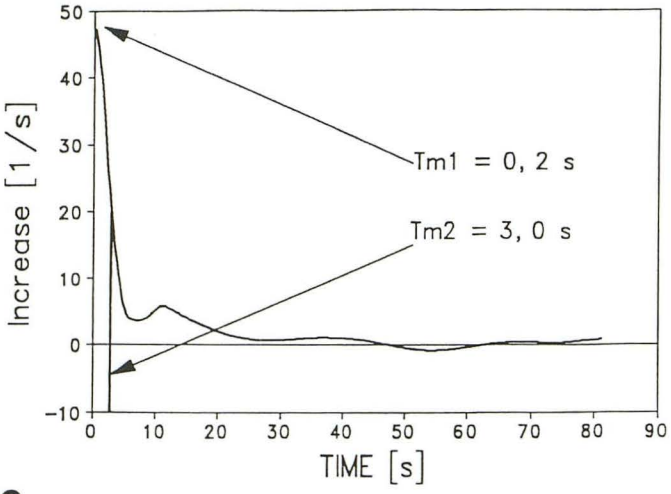

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Fig. 7. Glioblastoma multiforme.

A, Irregular marginal enhancement and central regressive changes best seen on the T1-weighted postcontrast spin-echo image (*upper left*). Snapshot-FLASH images of the early, intermediate, and late enhancement period from the *upper right* to the *lower right*.

B, Contrast-enhancement curve: very early onset and reach of the plateau due to arteriovenous shunts and high degree of neovascularization.

C, Corresponding signal increase curve ($T_{ref} = 0$) with short Tm1 and short Tm2.

D, ROI placement of the inhomogeneous lesion in *A*. Best delineation of vital, well-vascularized tumor parts from undergoing and necrotic parts, which were excluded from evaluation, is possible in the early enhancement period.

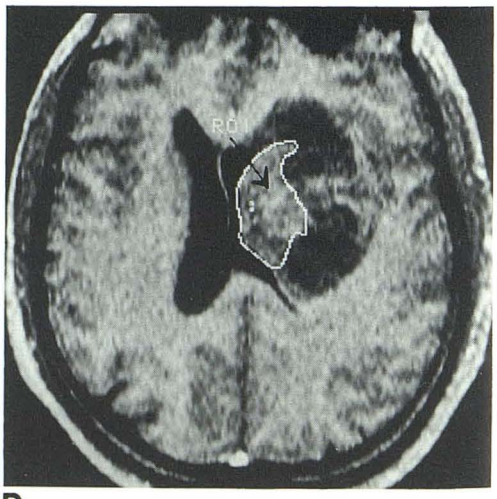

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TABLE 2: Intraaxial tumors (n = 15)

	Astrocytomas I–II (n = 3)	Oligodendrogliomas (n = 2)	Mixed Oligoastrocytomas (n = 3)	Glioblastomas (n = 7)
No contrast enhancement	3	2		
Contrast enhancement			Tm1 [s] = 13.6 ± 6.4 Tm2 [s] = 34.3 ± 14.7	Tm1 [s] = 0.45 ± 0.8 Tm2 [s] = 4.2 ± 1.5

Note.—Mean values and standard deviation of time of maximum signal increase (Tm1) and following time of half-maximum increase (Tm2) for intraaxial tumors.

also support electron microscopical findings, showing characteristic endothelial fenestration and gap junctions in capillaries of neurinomas, which favor extravasation of contrast medium (13).

Histopathologic degree of tumor vascularization is an important point, not only for differential diagnosis, but also for subclassification within a group of tumors. A good correlation of Tm1 and Tm2 to histopathologic findings concerning tumor vascularization (atypically highly vascularized tumors showed short Tm1 and Tm2 values, whereas moderately vascularized tumors showed longer Tm2 or both prolonged Tm1 and Tm2 values) made such subclassification possible in meningiomas and pituitary macroadenomas. A recent dynamic study of pituitary adenomas (11) showed two groups of macroadenomas with differing enhancement velocity. Although time parameters of that study cannot be directly compared with our results because an SE technique with a rather low temporal resolution of 20 seconds was used, nevertheless the subclassification into two groups can be supported by our results, in which three of seven cases with a high degree of vascularization showed a rapid dynamic contrast increase (Figs. 5B and 5C).

Glomus tumors are vascular tumors with a prominent arterialization, hence the main signal increase appears earlier in the tumor than even in the venous system, which consequently leads to a negative Tm1. Evaluation of intra-axial tumors showed the glioblastomas to have the earliest onset of the enhancement. Mean values Tm1 and Tm2 were characteristically shorter than in other enhancing lower grade gliomas. This result is compatible with our histopathologic finding of a high degree of neovascularization and arteriovenous shunts as demonstrated in angiography (14).

An important problem in correlating time parameters of the rate of contrast enhancement in intracranial tumors with the histopathologic degree of vascularization is the fact that the time parameters Tm1 and Tm2 are always affected by both degree of vascularization and disruption of blood-brain barrier. It is, however, reasonable to presume that the very early period of contrast enhancement, represented by Tm1 (approximately the first 10 seconds), is mainly influenced by the degree of vascularization, whereas in the later period, approximated by Tm2, the influence of the permeability of the blood-brain barrier increases. This assumption provides the basis of explanation for the good correlation observed between vascularization and the measured time parameters. In histopathology, vascularization plays an important role in tissue characterization. Therefore, we believe that this method with a correlation between time parameters Tm1 and Tm2 and histologic degree of vascularization represents an additional possibility for an MR tissue characterization, in addition to tissue characterization by relaxation parameters T1 and T2 (15, 16).

Additional studies are necessary not only because of the small number of cases of each subcategory that have been analyzed as yet, but also for further clarification of the role of an intact or disrupted blood-brain barrier in dynamic contrast enhancement of intracranial tumors. In summary, undoubtedly an analysis of dynamic enhancement curves alone cannot give accurate specific histopathologic information about intracranial tumors. Nevertheless, in our opinion, the time parameters evaluated in this study describing the dynamic contrast enhancement behavior of the tumors can be utilized in conjunction with other radiologic, anatomical, and clinical properties in order to narrow the differential diagnostic possibilities.

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