Correlation of MR Imaging–Determined Cerebral Blood Volume Maps with Histologic and Angiographic Determination of Vascularity of Gliomas

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OBJECTIVE. Our purpose was to evaluate the relationships between the ratio of maximum relative cerebral blood volume (rCBV) (rCBV ratio = rCBV[tumor] / rCBV[contralateral white matter]) and histologic and angiographic vascularities of gliomas using the gradient-echo echoplanar MR imaging technique. We also evaluated the usefulness of rCBV maps for grading gliomas.

SUBJECTS AND METHODS. We examined 30 patients with histologically verified gliomas. Gliomas were classified as glioblastoma, anaplastic glioma with enhancement, anaplastic glioma without enhancement, and low-grade glioma. The maximum rCBV ratio of each glioma was compared with both histologic and angiographic vascularities, and the relationship between the maximum rCBV ratios and each type of glioma was established.

RESULTS. The maximum rCBV ratios of the gliomas significantly correlated with both histologic and angiographic vascularities ($p < .001$). Mean values and SDs of maximum rCBV ratios of each type of tumor were 7.32 ± 4.39 for glioblastomas, 5.84 ± 1.82 for anaplastic gliomas with enhancement, 1.53 ± 0.75 for anaplastic gliomas without enhancement, and 1.26 ± 0.55 for low-grade gliomas. The maximum rCBV ratios of the glioblastomas were significantly higher than those of the anaplastic gliomas without enhancement ($p = .002$) and the low-grade gliomas ($p < .001$). The maximum rCBV ratios of the anaplastic gliomas with enhancement were higher than those of the anaplastic gliomas without enhancement and the low-grade gliomas, but the differences were not statistically significant ($p = .08$ and $p = .03$, respectively).

CONCLUSION. The results of perfusion-sensitive MR imaging with gradient-echo echoplanar technique correlated with both histologic and angiographic vascularities.

It is well known that the vasculature of tumors differs from that of normal tissues [1, 2]. Two types of vasculature typify malignant gliomas. The first is derived from existing vessels that the tumor takes over for its arterial supply and venous drainage. These vessels may become tortuous, possibly because blood flows through them more rapidly than normally or because adjacent tumor, necrosis, or edema presses on them [3, 4]. The second type of vasculature is new vessels induced by or developed for growth of the tumor. These consist mainly of wild tangles and irregular meshworks in viable portions of the tumor and in infiltrative tumors [3, 4]. Additionally, malignant gliomas contain muscularized veins, approximately 5 mm in diameter, which indicate arteriovenous shunting [3, 4]. Most histologic grading systems assess microvascular structures such as the proliferation of endothelial cells that line tumor capillaries, and the results of these grading systems when used for gliomas and other malignant tumors have been encouraging [5].

Aronen et al. [6] reported that the degree of vascularity of gliomas observed with a spin-echo echoplanar technique correlated well with histologic vascularity and that these results might show the ability of the spin-echo echoplanar technique to detect neovascularization at the capillary level. However, tumor angiogenesis is a complex process, and the existence of larger neovascular structures (such as feeding arteries and draining veins) associated with malignant tumors is not uncommon. A study documented that some tumors have average capillary diameters two to three times those of normal tissues [7].

The gradient-echo echoplanar technique produces hemodynamic maps by representing the effects of total blood volume from capillaries to large vessels and weighs all vessels approximately equally [8]. In addition, this technique, because of its greater sensitivity to

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the susceptibility effect, can provide a relative cerebral blood volume (rCBV) map with the use of a low-dose contrast medium [8]. Therefore, the gradient-echo echoplanar technique is expected to be suitable for evaluating brain tumors, especially those with large vessels.

The purposes of our study were, first, to produce the rCBV maps of gliomas using the gradient-echo echoplanar technique and to examine the relationship between the ratio of maximum rCBV (rCBV ratio = rCBV[tumor] / rCBV[contralateral white matter]) and the histologic and angiographic vascularities and, second, to evaluate whether the gradient-echo echoplanar imaging findings correlate with both small vessels and medium to large vessels that can be observed on conventional angiograms. We also evaluated the usefulness of rCBV maps for grading gliomas.

Subjects and Methods

Subjects

Thirty consecutive patients with intraaxial gliomas were prospectively entered into the study over a 22-month period between February 1996 and December 1997 to evaluate the grading of their tumors.

Fifteen of the patients were male, and 15 were female. They ranged in age from 8 to 68 years old (mean ± SD, 46 ± 13 years). The gliomas of 27 patients were verified by surgical resection, and the gliomas of the other three patients were verified by stereotactic biopsy. One patient with glioblastoma had been previously treated for anaplastic astrocytoma of the right occipital lobe with surgical resection followed by irradiation and chemotherapy. In this patient, a glioblastoma was found in the frontal lobe distant from the primary site 44 months after the first therapy. The remaining 29 patients had not undergone any major therapeutic interventions before the present MR examinations. All tumors were examined by a neuropathologist and graded according to the World Health Organization grading system [9]; grade 2 tumors were designated as low-grade gliomas, and grade 3 and 4 tumors were designated as anaplastic gliomas and glioblastomas, respectively. Therefore, the final diagnoses were 12 glioblastomas (11 glioblastomas and one gliosarcoma), 14 anaplastic gliomas (11 anaplastic astrocytomas, one anaplastic oligodendroglioma, and two anaplastic oligoastrocytomas), and four low-grade gliomas (four astrocytomas).

Methods

Imaging technique and rCBV maps.—All MR images were obtained with a 1.5-T superconducting system (Magnetom Vision; Siemens, Erlangen, Germany). Conventional MR images and rCBV maps were acquired during the same procedure to allow exact comparison of the results. In the initial six consecutive patients, rCBV maps were obtained with the gradient-echo echoplanar technique at a readout bandwidth of 980 Hz per pixel, a maximum amplitude of 15 mT/m, and a TE of 18 msec. In the remaining patients, rCBV maps were obtained with the gradient-echo echoplanar technique at a readout bandwidth of 926 Hz per pixel, a maximum amplitude of 25 mT/m, and a TE of 40 msec, because the echoplanar imaging gradient system was upgraded in the course of this study. Sagittal T1-weighted localizing images were acquired first. Unenhanced axial T1- and T2-weighted images were then obtained for each patient. Before the recording of rCBV maps, a 21-gauge IV needle was inserted in the vein of the right antecubital fossa. Axial sections were selected from the unenhanced images for dynamic MR imaging. A 0.1 mmol/kg bolus of gadopentetate dimeglumine (Magnevist; Nihon Schering, Osaka, Japan) was manually injected within 5 sec, followed by a 20-ml saline flush.

In this study, a series of images was obtained using a lipid-suppressed gradient-echo echoplanar technique before, during, and after each injection of contrast agent [6]. Lipid suppression was used for subcutaneous fat, which can be superimposed on the brain because of large chemical-shift artifacts seen with gradient-echo echoplanar imaging. All patients were examined using multisection data acquisition to record the tumors in their entirety. Five-section studies were acquired for nine patients, and nine-section studies were acquired for the other 21 patients. In all patients, 30 images of each section in 60-sec periods were obtained. Each section was collected using a section thickness of 5 mm, an intersection gap of 1 mm, a 256 × 128 matrix, a 20 × 22–28 cm field of view, and a TR of 2000 msec. After data collection, the rCBV maps were derived on a pixel-by-pixel basis from the dynamic image sets.

The start and end points of the first-pass transit of contrast agent through the brain were identified using the time–activity curve of the means of the signal magnitude of the pixels covering the whole-brain tissue on the section. Before the start point of the first-pass circulation (seen as a decrease in the signal intensity), a representative number of baseline points was selected and their average was calculated for each pixel as a baseline measure for signal intensity. On a pixel-by-pixel basis, the signal intensity was converted to changes in the T2* relaxation rate (Δ R2*) (Δ R2* = –ln (S/So) / TE, where ln is natural logarithm, S is signal intensity, and So is baseline signal intensity). Previous experiments and theoretical data have shown that Δ R2* is approximately linearly proportional to the concentration of contrast material in the tissue [10–12]. The rCBV maps were generated by the numeric integration of the relative concentration for the first-pass bolus through each voxel based on kinetic principles for nondiffusible tracers [13, 14]. The imaging process required approximately 30 min to integrate the functional time course data.

Because the rCBV mapping method yields a relative rather than an absolute value of cerebral blood volume, comparison of the patients was facilitated by reference to an internal contralateral standard. As in a positron emission tomography study [15], normal white matter in the contralateral hemisphere was used as a reference. For calculation of the maximum rCBV ratios of tumor:contralateral white matter, the regions of interest (ROIs) consisting of more than 20 pixels were carefully chosen by a radiologist who was unaware of the clinical diagnosis. To avoid the risk of calculating the rCBV from normal vessels such as cerebral arteries and veins, the radiologist initially investigated the serial Δ R2* maps from arterial to venous phases as well as conventional MR images and then located the ROIs within tumors. The Δ R2* maps clearly showed the rCBV from cerebral arteries or veins (Fig. 1), and the ROIs were easily defined without superimposition of those vessels. When a glioma had enhanced areas on the contrast-enhanced T1-weighted images, the ROIs were located within both the enhanced and the unenhanced areas. When a glioma had no enhanced areas, the ROIs were randomly located. When a stereotactic biopsy was performed, the ROIs were located within the biopsy sites. At least five ROIs were chosen in each enhanced, unenhanced, or biopsy site, and the areas of highest rCBV were identified.

Angiography.—Informed consent was obtained and conventional angiography performed for all patients to obtain diagnostic information and rule out incidental vascular anomalies before surgery. The perfusion-sensitive MR imaging and conventional angiography were performed within 27 days of each other. Four-vessel cerebral catheter angiography was performed using standard angiographic technique with a 5- or 5.5-French JB1 or JB2 catheter (Medikit, Tokyo, Japan) inserted through the femoral artery.

All angiograms were analyzed by another two radiologists who were unaware of the clinical diagnosis. Initial agreement was complete in the interpretation of 28 of 30 angiograms. The two initial disagreements in interpretation were resolved by consensus. The angiographic vasculature was assessed for the presence of tumor vessels, tumor stain, and early venous return. The findings for each evaluation were classified 0 (absence) or 1 (presence). The sum of the evaluation was calculated and defined as the angiographic vascularity.

Histology.—After the perfusion-sensitive MR imaging, histologic proof was obtained within 22 days. Histologic vascularity was analyzed by a neuropathologist and graded according to a system described previously [6]. The grading was on a scale of 1–3, with 1 being vascularity equal to that of the normal brain, 2 being moderately increased vascularity, and 3 being greatly increased vascularity characteristic of some glial tumors.

Image analysis.—The maximum rCBV ratios were recorded for each tumor. Simple linear regression was used to analyze the relationship between the maximum rCBV ratios and the histologic and angiographic vascularities. As in the analysis of the relationship between the maximum rCBV ratios and the grading of gliomas, anaplastic gliomas were divided into two groups—anaplastic gliomas with and without enhancement—and thus the gliomas were graded as

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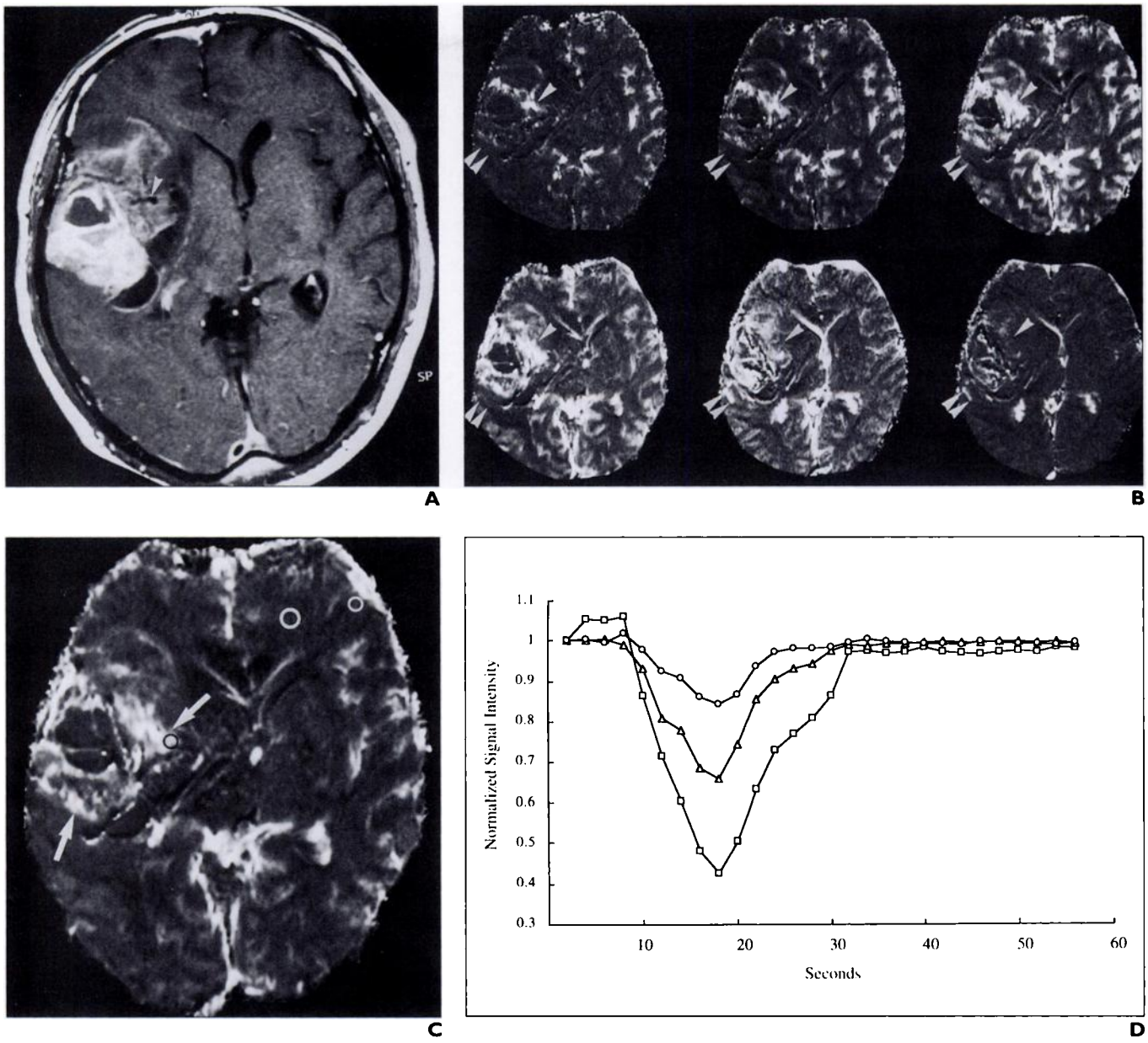

Fig. 1.—45-year-old man with anaplastic oligodendroglioma.
A, Contrast-enhanced T1-weighted MR image shows nonhomogeneously enhanced tumor in right frontoparietal lobe. Note flow void effects suggesting that branch of right middle cerebral artery is displaced by mass effect (*arrowhead*).
B, Serial maps of changes in T2* relaxation rate (Δ R2*) proceeding from arterial to venous phases show, in arterial phase (top left), high-signal-intensity areas reflecting relative cerebral blood volume (rCBV) from cerebral arteries (*single arrowhead*). At this point, no contribution to overall rCBV is seen at expected location of cerebral veins (*double arrowhead*). Δ R2* map of venous phase (bottom right) shows high-signal-intensity areas reflecting rCBV from cerebral veins (*double arrowhead*). Regions of interest located within tumors must be carefully placed so as not to be superimposed on normal vessels.
C and **D**, rCBV map (**C**) shows inhomogeneously highly vascular cerebral blood volume areas within tumor (*arrows*). Graph (**D**) shows signal intensity curves during transit of contrast material through patient's brain for regions of tumor (*black circle*, **C**; ■, **D**), gray matter (*small white circle*, **C**; ▲, **D**), and white matter (*large white circle*, **C**; ●, **D**).

glioblastoma, anaplastic gliomas with enhancement, anaplastic gliomas without enhancement, or low-grade gliomas. The mean and SD of the maximum rCBV ratios of each tumor grade were calculated, and the relationship between the maximum rCBV ratios and tumor grade was analyzed using Student's t test. The findings were considered significant when the p value was less than .01.

Results

Relationship Between the Maximum rCBV Ratios and Histologic and Angiographic Vascularities

All 12 glioblastomas had enhanced areas, and all four low-grade gliomas had no enhanced areas. Among the 14 anaplastic gliomas, 10 had enhanced areas and four did not. The enhanced regions, when present, did not necessarily coincide with the maximum rCBV regions. All glioblastomas, four anaplastic gliomas with enhancement, and one anaplastic glioma without enhancement had a histologic vascularity rating of 3. Six anaplastic gliomas with enhancement and one anaplastic glioma without enhancement had a histologic vascularity rating of 2. Two anaplastic gliomas with-

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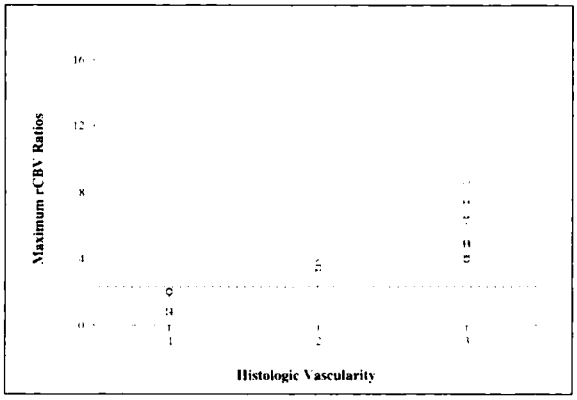

Fig. 2.—Graph shows relationship between maximum relative cerebral blood volume (rCBV) ratio and histologic vascularity. Significant correlation was seen between these parameters ($p < .001$). When maximum rCBV ratio was more than 2.5, histologic vascularity was always rated as 2 or 3, except for one anaplastic oligoastrocytoma. $y = -1.43 + 2.81x$; $r = .40$.

out enhancement and all low-grade gliomas had a histologic vascularity rating of 1. Ten glioblastomas and five anaplastic gliomas with enhancement had an angiographic vascularity rating of 1 or more. Two glioblastomas, five anaplastic gliomas with enhancement, four anaplastic gliomas without enhancement, and all low-grade gliomas had no abnormal angiographic vasculature and thus were given an angiographic vascularity rating of 0. The rCBV maps clearly depicted the highly vascular areas, which were not always consistent with the enhanced areas on contrast-enhanced T1-weighted images.

The maximum rCBV ratios correlated significantly with the histologic vascularities ($p < .001$) (Figs. 2–5). Except for one anaplastic oligoastrocytoma for which the maximum rCBV ratio was 1.58 and the histologic vascularity rating was 3, the gliomas with maximum rCBV ratios of more than 2.50 had a histologic vascularity score of 2 or 3. Among the glioblastomas or anaplastic gliomas with a histologic vascularity score of 3, the maximum rCBV ratios varied from 1.53 to 16.24 (Fig. 2).

The maximum rCBV ratios also correlated significantly with angiographic vascularities (Fig. 6). Interestingly, when the maximum rCBV ratio of a glioma was more than 4.30, the angiographic vascularity was classified as 1 or more (Fig. 4).

Relationship Between the Maximum rCBV Ratios and Tumor Grade

Figure 7 summarizes the relationship between maximum rCBV ratio and grade of glioma. The maximum rCBV ratio of each tumor grade was as follows: glioblastomas, 4.00:16.2 (mean, 7.32 ± 4.39); anaplastic gliomas with enhancement, 2.59:7.93 (mean, 5.84 ± 1.82); anaplastic gliomas without enhancement, 0.98:3.84 (mean, 1.53 ± 0.75); and low-grade gliomas, 0.64:2.01 (mean, 1.26 ± 0.55).

The maximum rCBV ratios of the glioblastomas were significantly higher than those of the anaplastic gliomas without enhancement ($p = .002$) and low-grade gliomas ($p < .001$). Although the difference in the maximum rCBV ratios between the glioblastomas and the anaplastic gliomas with enhancement did not reach significance ($p = .04$), the maximum rCBV ratios of the glioblastomas were higher than those of the anaplastic gliomas with enhancement. The maximum rCBV ratios of the anaplastic gliomas with enhancement were higher than those of the anaplastic gliomas without enhancement and low-grade gliomas, but the differences did not reach statistical significance ($p = .08$ and $p = .03$, respectively). Differences in the maximum rCBV ratios between anaplastic gliomas without enhancement and low-grade gliomas were not statistically significant (Figs. 3 and 8).

Discussion

Monte Carlo simulations on susceptibility contrast mechanisms have shown that a relationship exists between Δ R2 and R2* and the average vessel size and that Δ R2 / R2* is proportional to the average value of $1 / r^2$, where r is the average vessel size [8]. These simulations have also shown that spin-echo sequences are maximally sensitive to compartments with dimensions roughly equal to normal capillary diameters, whereas gradient-echo sequences are equally sensitive to all vessel sizes (Dennie J et al., presented at the International Society of Magnetic Reso-

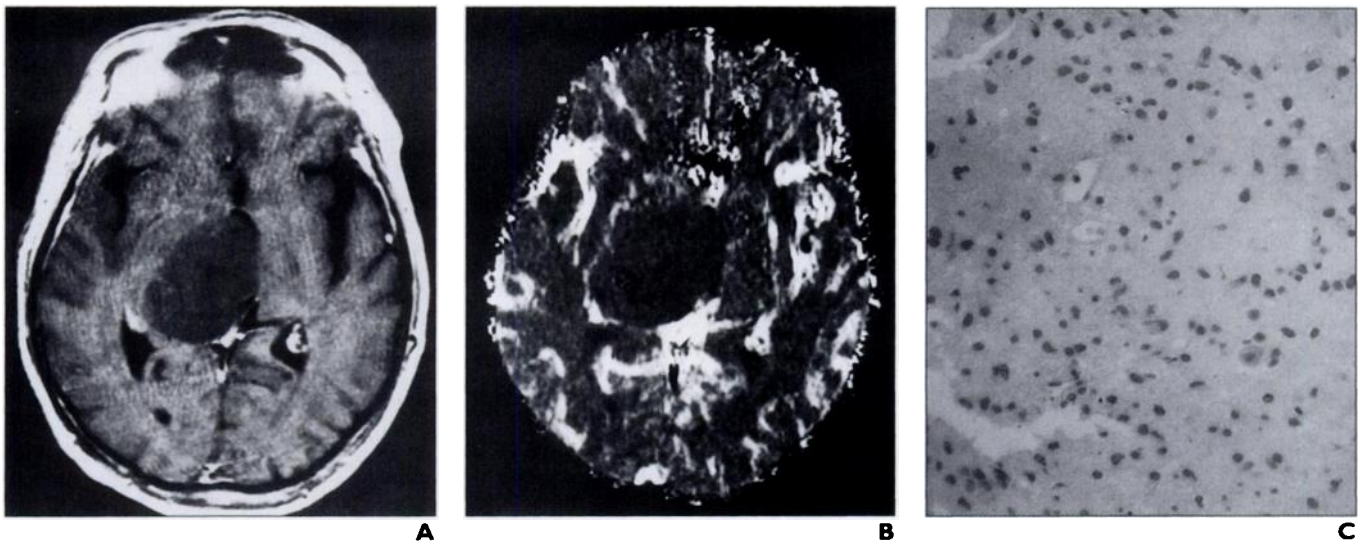

Fig. 3.—66-year-old woman with low-grade glioma in right thalamus.
A, Contrast-enhanced T1-weighted image. Enhancement was not observed within tumor.
B, Relative cerebral blood volume (rCBV) map. Tumor was shown as hypovascular. Maximum rCBV ratio was 0.64. No abnormal vessels were observed on conventional angiography.
C, Histologic specimen. Tumor vascularity was poor, and histologic vascularity was rated as 1. (H and E, ×120)

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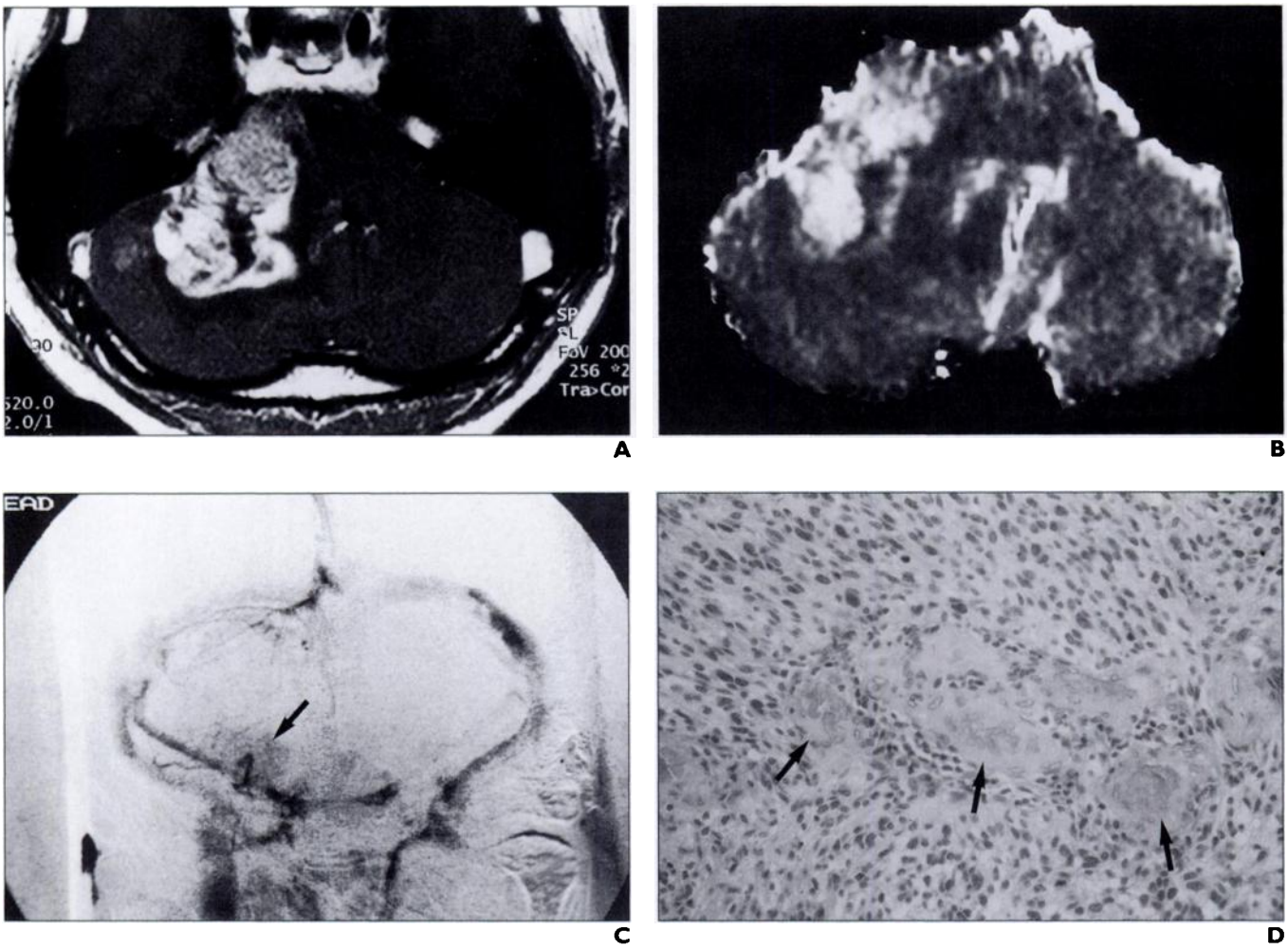

Fig. 4.—50-year-old woman with glioblastoma in right cerebellum extending to middle cerebellar peduncle.
A, Contrast-enhanced T1-weighted image. Nonhomogeneous enhancement was observed within tumor.
B, Relative cerebral blood volume (rCBV) map. Hypervascular areas within tumor were clearly shown. Maximum rCBV ratio was 4.3.
C, Conventional angiogram. Tumor stains (*arrow*) without feeding artery or early venous return were observed in venous phase, and angiographic vascularity was classified as 1.
D, Histologic specimen. Tumor vessels of large diameter and endothelial proliferation (*arrows*) were observed, and histologic vascularity was classified as 3. (H and E, ×120)

nance in Medicine meeting, April 1997). On the basis of these results and the finding that tumors frequently have large vessels [1], one would expect a difference in relaxation time ratios between spin-echo and gradient-echo acquisitions in the evaluation of tumors. A group of researchers recently described a study of glial tumors inoculated in Fisher rat brains. The tumors had vessels 1.9 times larger than those of the gray matter, and the glial tumor:gray matter ratio of Δ R2*/R2 was 2.3 (Dennie J et al., ISMRM meeting, April 1997). The close agreement between those results leads one to expect that more highly vascular areas within gliomas would be more clearly depicted with the gradient-echo than the spin-echo technique.

We found a correlation between histologic vascularity and the maximum rCBV ratios measured with the gradient-echo echoplanar technique. These results illustrate the usefulness of this technique for evaluating tumor angiogenesis at the capillary level. The mean maximum rCBV ratio of the high-grade gliomas, including both glioblastomas and anaplastic gliomas, was 6.00 ± 3.79, whereas Aronen et al. [6] produced rCBV maps with the spin-echo echoplanar technique and showed that the mean maximum rCBV ratio of high-grade gliomas was 3.64 ± 1.59. Our mean maximum rCBV ratio of high-grade gliomas is 1.6 times as large as that found by Aronen et al. This difference may be due to a difference in sensitivity for tumor vessels, especially those larger than capillaries, and may indicate that the gradient-echo echoplanar technique is indeed more sensitive than the spin-echo echoplanar technique in detecting highly vascular areas within tumors. On the other hand, the mean maximum rCBV ratio of the low-grade gliomas in our study was 1.26 ± 0.55 and that in the Aronen et al. study was 1.11 ± 0.08. Our values were only 1.1 times as large as those of Aronen et al., possibly because low-grade gliomas generally do not have vessels as large as those observed in high-grade gliomas. In fact, low-grade gliomas have neither histologically high vascularity nor angiographically abnormal vessels such as feeding arteries, tumor stains, or early venous return.

We also found correlations between the maximum rCBV ratios and angiographic vascularity. This result is not surprising because the gradient-echo echoplanar technique is inherently sensitive to total vascular beds [8], such as large vessels observed in angiography. Interestingly, when the gliomas had a maximum rCBV ratio of more than 4.30, the abnormal vascularity could be observed by angiography in all cases. When the gliomas (except for one anaplastic oligoastrocytoma) had a maximum rCBV ratio of more than

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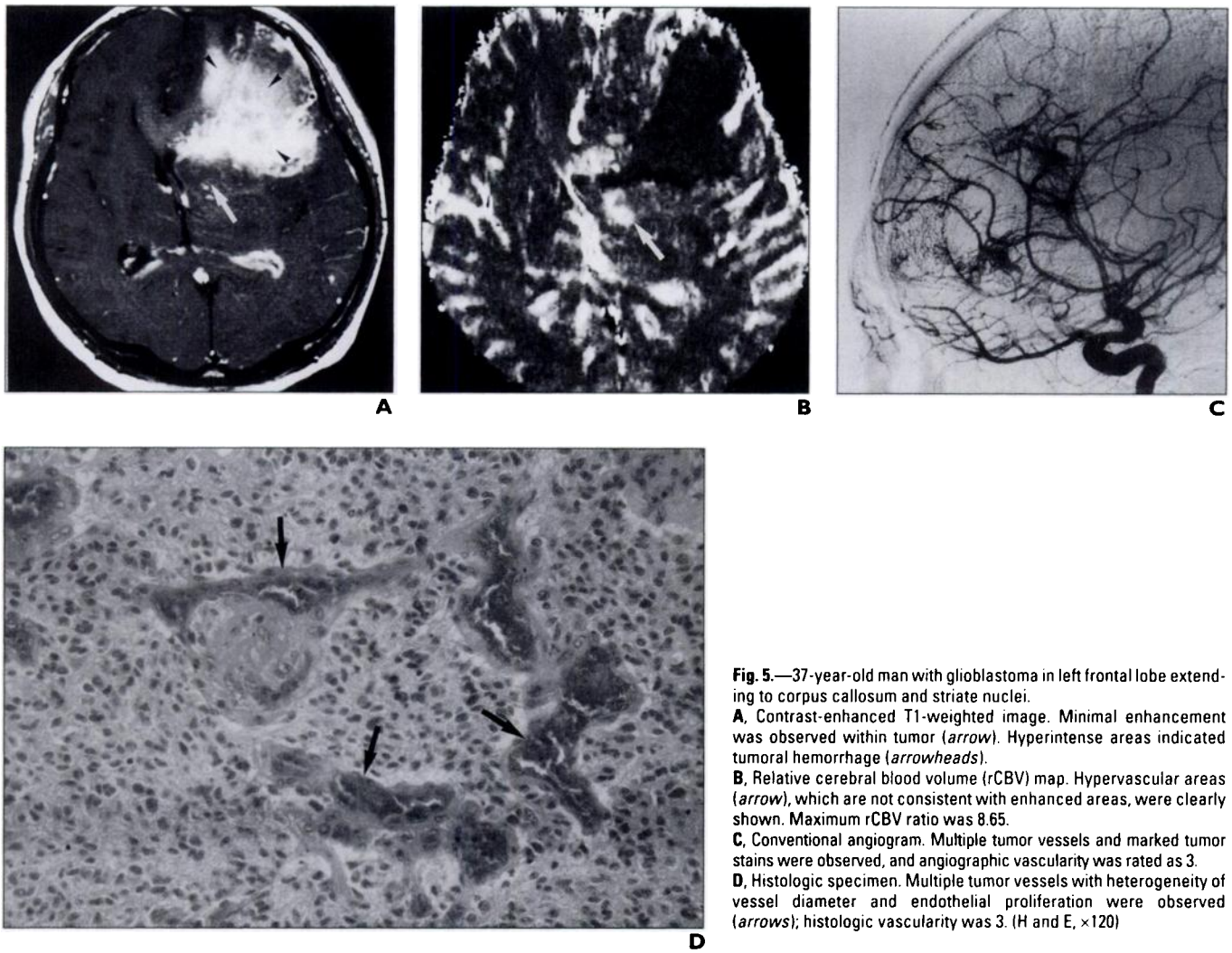

Fig. 5.—37-year-old man with glioblastoma in left frontal lobe extending to corpus callosum and striate nuclei.
A, Contrast-enhanced T1-weighted image. Minimal enhancement was observed within tumor (*arrow*). Hyperintense areas indicated tumoral hemorrhage (*arrowheads*).
B, Relative cerebral blood volume (rCBV) map. Hypervascular areas (*arrow*), which are not consistent with enhanced areas, were clearly shown. Maximum rCBV ratio was 8.65.
C, Conventional angiogram. Multiple tumor vessels and marked tumor stains were observed, and angiographic vascularity was rated as 3.
D, Histologic specimen. Multiple tumor vessels with heterogeneity of vessel diameter and endothelial proliferation were observed (*arrows*); histologic vascularity was 3. (H and E, ×120)

2.50, the histologic vascularity score reached 2 or 3. In other words, when the maximum rCBV ratio exceeded 4.30, the gliomas might have had large tumor vessels that could be observed with angiography. When the maximum rCBV ratio exceeded 2.50, the histologic vascularity increased. These results indicate that the maximum rCBV ratios of the gliomas without abnormal vasculature in angiography were affected by only histologically abnormal vascularity, whereas those of the gliomas with abnormal vasculature in angiography were affected by both histologically and angiographically abnormal vascularity. Therefore, perfusion-sensitive MR imaging with the gradient-echo echoplanar technique can be used for predicting both histologic and angiographic vascularities.

Treatment of anaplastic gliomas substantially increases the average length of survival, to a range of 2–5 years. Multitechnique treatment such as surgical debulking, radiotherapy, or chemotherapy is therefore recommended [16, 17]. Glioblastomas, however, have an unfavorable prognosis, with most patients surviving less than 15 months even with intensive therapy. Despite recent developments in MR imaging technology, differentiating between anaplastic gliomas and glioblastomas remains difficult even when a contrast medium is used. Generally, increased malignancy is said to be associated with increased vascularity [3, 4], and thus we thought that perfusion-sensitive MR imaging could potentially differentiate between anaplastic gliomas with enhancement and glioblastomas. In our study, the difference in maximum rCBV ratios between these tumor types did not reach significance ($p = .04$), although the maximum rCBV ratios of the glioblastomas were higher than those of the anaplastic gliomas with enhancement. However, a maximum rCBV ratio exceeding 8.00 was observed for glioblastoma only. We conclude that a high maximum rCBV ratio (>8.00) suggests glioblastoma.

In two of the four anaplastic gliomas without enhancement, the histologic specimens showed no increased vascularity (rated 1), whereas all other high-grade gliomas showed histologic vascularity (rated 2 or 3). These two gliomas were diagnosed as anaplastic by the neuropathologist because of the existence of mitosis alone. These results suggest that a lack of neovascularity within a tumor may not always mean the tumor is benign. An anaplastic status cannot be confirmed in mitotic gliomas with neither blood–brain barrier disruption nor increased vascularity.

Perfusion-sensitive MR imaging may be less clinically useful for grading than is conventional contrast MR imaging, because gliomas with enhanced regions are usually high-grade and gliomas without enhanced regions are low-grade. However, we observed one anaplastic oligoastrocytoma that had high rCBV regions on the rCBV maps but no enhanced regions on MR images. This type of discrepancy has been reported before [6, 10, 18]. In addition, the enhanced regions did not necessarily coincide with the high rCBV regions, and the rCBV

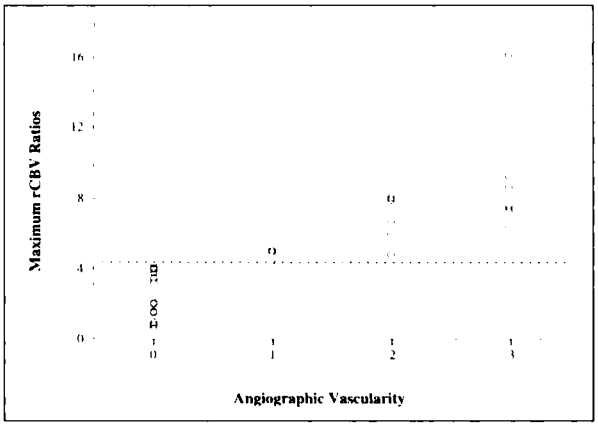

Fig. 6.—Graph shows relationship between maximum relative cerebral blood volume (rCBV) ratio and angiographic vascularity. Significant correlation was seen between these parameters ($p < .001$). When maximum rCBV ratio was more than 4.3, angiographic vascularity was always rated 1 or more. $y = 0.18 + 2.36x$, $r = .70$.

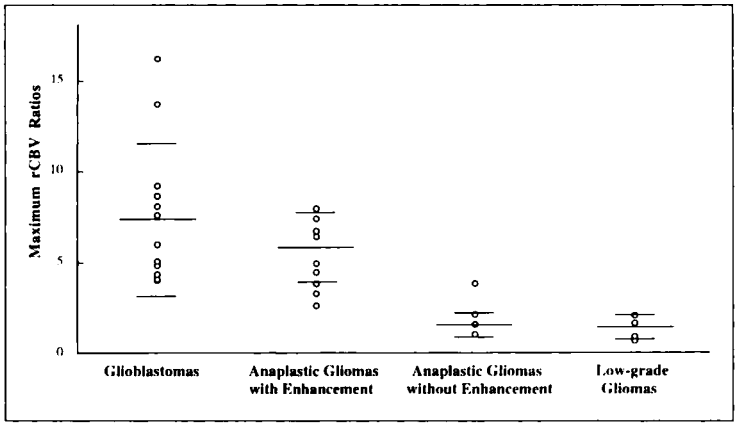

Fig. 7.—Graph shows relationship between maximum relative cerebral blood volume (rCBV) ratios and gliomas. Maximum rCBV ratios of glioblastomas were significantly higher than those of anaplastic gliomas without enhancement ($p = .002$) and low-grade gliomas ($p < .001$). Maximum rCBV ratios of glioblastomas (mean = 7.32 ± 4.39) were higher than those of anaplastic gliomas with enhancement (mean = 5.84 ± 1.82), although difference did not reach statistical significance ($p = .04$). Maximum rCBV ratios of anaplastic gliomas with enhancement were higher than those of anaplastic gliomas without enhancement (mean = 1.53 ± 0.75) and low-grade gliomas (mean = 1.26 ± 0.55), but not significantly so ($p = .08$ and .03, respectively). No significant difference was found between anaplastic gliomas without enhancement and low-grade gliomas in this regard ($p = .68$).

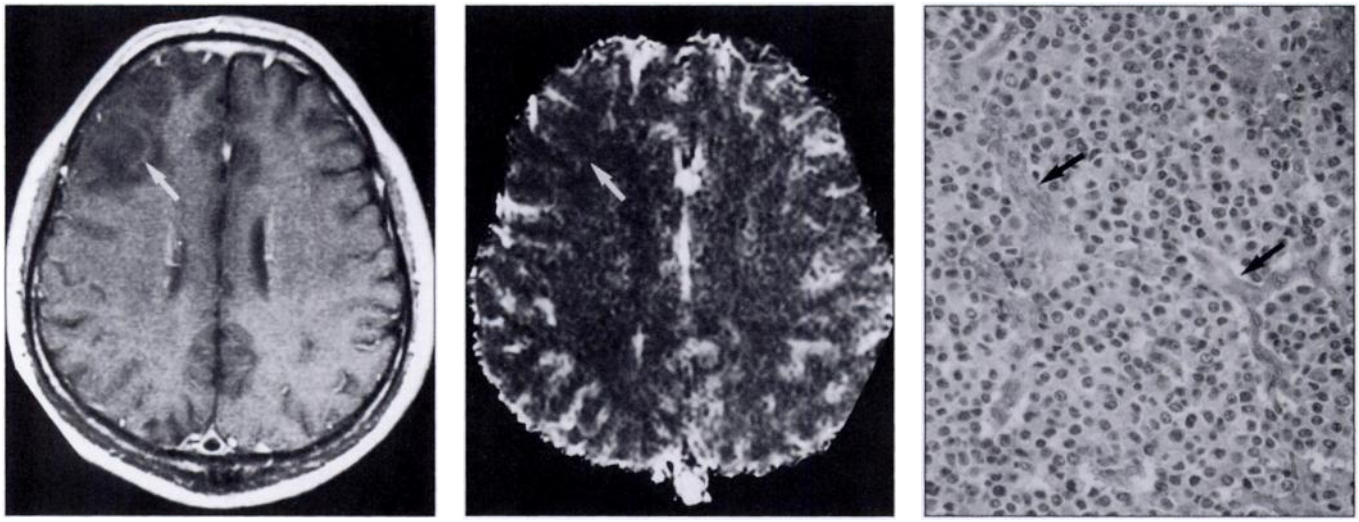

Fig. 8.—47-year-old man with anaplastic oligoastrocytoma in right frontal lobe.
A, Contrast-enhanced T1-weighted image. Enhanced area was not observed within tumor (*arrow*).
B, Relative cerebral blood volume (rCBV) map. Vascularity within tumor (*arrow*) was almost same as that of white matter and less than that of gray matter. Maximum rCBV ratio was 1.53.
C, Histologic specimen. Multiple tumor vessels (*arrows*) were observed, and histologic vascularity was rated as 2. (H and E, ×120)

maps could reveal the highly vascular active areas within the tumors. Therefore, perfusion-sensitive MR imaging should be performed in the evaluation of gliomas.

One should attend to the choice of areas of maximum rCBV when the gradient-echo echoplanar technique is used for rCBV maps. Because the gradient-echo echoplanar technique is sensitive to susceptibility effects from total vascular beds, normal arteries and veins at the surface of brain tissue and ventricles might be mistaken for tumor vessels. If highly vascular areas within gliomas are adjacent to the surface of brain tissue, identification of areas of maximum rCBV may be difficult. However, confusion between gliomas and normal brain tissue can be avoided with a detailed investigation of serial $\Delta R2^*$ maps and conventional MR images. The vascularity of an infratentorial tumor may be distorted and difficult to evaluate because the gradient-echo echoplanar technique is especially affected by susceptibility artifacts [19]. However, we were able to obtain images of sufficient quality to calculate the rCBV of infratentorial tumors (Fig. 6), and this technique can therefore be used in the whole brain for the evaluation of vascularity.

Gradient-echo echoplanar imaging requires a half dose of contrast agent rather than the full dose that spin-echo echoplanar imaging requires to obtain perfusion-sensitive MR imaging [6, 19]. This difference may be the most important one from an economic

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standpoint. Additionally, the smaller bolus adds the advantage of being narrower and better defined. This property is important in extracting information on regional cerebral blood flow from first-pass data.

In conclusion, perfusion-sensitive MR imaging using the gradient-echo echoplanar technique reveals both histologic and angiographic vascularities. Because tumor vessels are complex and might vary in size, this technique should be included when evaluating gliomas.

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