Dynamic Magnetic Resonance Perfusion Imaging of Brain Tumors

DIEGO J. COVARRUBIAS, a BRUCE R. ROSEN, b MICHAEL H. LEV a

aDepartment of Radiology, Neuroradiology Division and bMGH-NMR Center, Massachusetts General Hospital and Harvard Medical School, Boston, Massachusetts

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LEARNING OBJECTIVES

After completing this course, the reader will be able to:

1. Understand the rationale and validity of using MR perfusion techniques for selecting the optimal biopsy site for brain neoplasms.

2. Understand the rationale and validity of using MR perfusion techniques to differentiate tumor recurrence from radiation necrosis.

3. Understand the technical difficulties and limitations of this technique in the setting of high-grade neoplasms with severe blood-brain barrier breakdown, as well as the multiple methods available to address this problem.

INTRODUCTION

Conventional magnetic resonance imaging (MRI) is widely used in the diagnosis and follow-up of brain tumor patients, owing to its high sensitivity and exquisite delineation of anatomic relationships. Nonetheless, conventional MR techniques are often nonspecific and provide limited information on tumor physiology. Thus, conventional MRI, which provides a “snapshot” in the time course of contrast conventional methods. We will scrutinize the use of MR perfusion for assessing true lesion extent, in contrast to conventional MR imaging and other MR techniques. We will discuss the role of MR perfusion in differentiating treatment effects, such as radiation necrosis, from tumor recurrence. Finally, the future potential applications of this technology in the setting of novel antiangiogenic therapies for brain tumors will be addressed. The Oncologist 2004;9:528-537
enhancement, is largely inadequate to guide biopsy or treatment of brain tumors. Indeed, the degree of contrast enhancement of glioblastomas has a relatively poor correlation with tumor grade and is not a reliable marker for distinguishing recurrent glioma from radiation necrosis.

As novel therapies for patients with brain tumors are being developed, the role of imaging has begun to shift to provide information on tumor physiology, as well as anatomy. Perfusion methods are ideally suited to such physiological imaging. Multiple studies have shown that perfusion MR techniques can noninvasively estimate tumor grade preoperatively [1-4]. This can in turn help guide stereotactic biopsy, by directing the surgeon to the most aggressive portions of the tumor [1, 2]. MR perfusion also holds promise in providing a better delineation of tumor margins than conventional techniques, which can similarly assist in surgical and radiation planning [5, 6]. MR perfusion is also useful in the follow-up of brain tumor patients by allowing differentiation between radiation effects and recurrent tumor [7, 8]. Perfusion changes also hold promise as surrogate markers of response to therapy in clinical trials of newer antiangiogenic pharmaceuticals [2-4]. In addition to the “first-pass” dynamic perfusion techniques, which are well described in the literature, newer, more prolonged, delayed permeability measurements also hold great promise for tumor assessment. MR or computed tomography (CT) perfusion imaging can be implemented using technology that is widely available in most contemporary scanners [2].

Other radiological techniques to evaluate tumor physiology, such as MR spectroscopy and 18F-flurodeoxyglucose positron-emission tomography (FDG-PET), deserve mention here. MR spectroscopy (MRS) relies on detection of metabolites within tumor tissue. Although useful in the differential diagnosis of brain tumors, MRS often can be nonspecific and suffers from low spatial resolution [5]. MRS may be more accurate, however, than MR perfusion or conventional MRI for determining tumor margins [9].

FDG-PET is based on tumor glucose metabolism and is limited in both sensitivity and specificity in the setting of post-radiated tumors and low-grade tumors [1, 2]. Automated coregistration between PET and CT datasets is gaining clinical acceptance as a technique for improving anatomic localization of highly metabolic regions. Newer compounds, such as methionine, tyrosine, and choline, offer the potential of higher accuracy but are costly, unproven, and not yet widely available [1].

In this paper, we discuss the value of perfusion-weighted imaging in the diagnosis and follow-up of patients with brain neoplasms.

**Physiologic Principles**

A growing body of basic science research underscores the importance of the angiogenesis pathway in the treatment of brain tumors. Recent data suggest that tumor response to radiotherapy in mice is mediated by microvascular damage [10]. Numerous antiangiogenic drugs are currently in development that specifically target angiogenic cytokines to disrupt their function and inhibit tumor growth [11]. Hence, disruption of angiogenesis plays a role in established treatment modalities as well as in cutting-edge treatment options for brain neoplasms.

The overall principle of MR perfusion oncologic imaging is that as a tumor grows its metabolic demands increase due to rapid cell growth and increased cell turnover. Cellular hypoglycemia and hypoxia lead to the production of angiogenic cytokines, such as vascular endothelial growth factor (VEGF), which leads to new blood vessel formation, or angiogenesis [4]. Capillary density in the tumor milieu increases, which in turn leads to higher blood volume and blood flow in the tumor bed [4].

The net result of angiogenesis is a complex network of abnormal vessels in the peritumoral space. Histological studies have shown that tumor vessels are composed of immature vessels with large endothelial cell gaps, an incomplete basement membrane, and absent smooth muscle layers, rendering them more permeable [3]. It is also thought that angiogenic cytokines can have an additional modulating effect on the microvasculature to increase permeability [4]. Direct damage to the blood-brain barrier by the tumor also leads to increased leakiness out of the intravascular compartment. Tumor vessels are more tortuous than normal vessels, which affects the distance that blood must traverse as it moves through the tumor. Hence, it is not just increased vessels within the tumor that lead to the observed perfusion abnormalities, but the presence of abnormal vessels that react differently to their environment and are arranged very differently than their normal counterparts elsewhere in the brain.

The higher vascularity of brain neoplasms is most commonly quantified with perfusion MR techniques in terms of the cerebral blood volume (CBV) of the tumor. CBV is defined as the total volume of blood traversing a given region of brain, measured in milliliters of blood per 100 grams of brain tissue (ml/100 g). Cerebral blood flow (CBF) is defined as the volume of blood traversing a given region of brain per unit time, measured in milliliters of blood per 100 grams of brain tissue per minute (ml/100 g/min). The definition of mean transit time (MTT) is more complex, but it can be thought of as the average time it takes for blood to traverse between arterial inflow and venous outflow, measured in seconds (s). MTT will therefore depend on the path taken by the blood to travel from artery to vein, and as such will depend on local tissue hemodynamics, such as shunts and vessel tortuosity. The concepts of CBF and MTT have not been as fully studied in the context of oncologic imaging as has CBV, despite their widespread application in stroke imaging.
CBV, CBF, and MTT are related to each other according to the central volume principle, which states that MTT = CBV/CBF. CBV can be directly estimated from the integral of the signal intensity versus time curve (the so-called time-density curve) resulting from the passage of contrast through the tumor. Calculation of CBF and MTT requires knowledge of an arterial input function; hence, the imaging planes through the tumor are chosen to contain a major intracranial artery feeding the neoplasm (typically the ipsilateral paracarotid internal carotid artery or middle cerebral artery). A deconvolution algorithm is used to post-process the data, typically at a separate workstation, to create CBF and MTT maps.

Quantification of the increased permeability of abnormal tumor vessels is more complex and depends on the imaging techniques employed and the specifics of the mathematical models used. In the studies of Roberts et al. using gradient-recalled T1-weighted MR perfusion, a bidirectional two-compartment kinetic model was employed that yields an estimate of the transendothelial transfer constant $k_{PS}$ (ml/100 cm$^3$/min) [2]. In this model, the signal decay for blood as a function of time is fitted to the following biexponential function:

$$S_{\text{blood}} = A_1 e^{-b_1 t} + A_2 e^{-b_2 t}$$

which yields four intermediary parameters $A_1$, $A_2$, $b_1$, and $b_2$, which are then inserted into the equation:

$$S_{\text{tissue}} = fBV \left[ \frac{A_1 k_1}{b_1-k_1} + \frac{A_2 k_1}{b_2-k_2} \right] e^{-b_1 t} + A_1 \left[ 1 - \frac{k_1}{b_1-k_2} \right] e^{-b_2 t}$$

where fBV is the fractional blood volume (analogous to CBV), $k_1$ is the efflux rate from plasma to interstitium (permeability), and $k_2$ reflects the reflux rate from interstitium back to the plasma. The above equation is then solved using nonlinear regression analysis.

**Techniques and Methods**

There are three main techniques used to perform MR perfusion imaging: T2*-weighted dynamic susceptibility, T1-weighted dynamic contrast-enhanced perfusion, and arterial spin labeling techniques. All three of these techniques involve repetitive serial imaging through the tumor during the passage of blood that has been labeled with either contrast material or with an endogenous magnetic tracer label.

The most established method of MR perfusion is T2*-weighted dynamic susceptibility imaging [3, 12, 13]. This technique exploits the T2* susceptibility effects of gadolinium, rather than the T1 shortening effects routinely associated with contrast enhancement on conventional imaging. A double-dose of gadolinium (0.2 mmol/Kg) is typically injected via an 18- or 20-gauge i.v. catheter at a high rate (3-7 ml/sec) using a power injector, to allow for a tight bolus of contrast material. Successive images are then acquired during the first pass of contrast material through the brain. The drop in T2* signal caused by the susceptibility effects of gadolinium is computed on a voxel-by-voxel basis and used to construct a time-versus-intensity curve [12]. The degree of signal drop is then assumed to be proportional to the tissue concentration of gadolinium, so that relative concentration-time curves can be obtained (delta R2 curves). Relative cerebral blood volume (rCBV) can then be obtained by calculating the area under the concentration-time curves, normalized to a contralateral, uninvolved region. “Relative” refers to the fact that an arterial input function is not used in the calculation of CBV, and therefore, precise quantitation of cerebral blood volume is not performed. Repeating this process on a voxel-by-voxel basis, one can construct an rCBV map of brain sections through the tumor. Limitations of the MR hardware may not allow for full brain coverage, but typically 10-11 axial sections can be obtained in this fashion.

A representative rCBV map from a patient with a high-grade pontine glioma is shown in Figure 1. Gray matter structures are seen to have higher blood volume values than white matter. Typically, high-grade tumors have rCBV values that are equal to or greater than those of gray matter. To simplify comparisons among different patients, many authors will normalize tumor rCBV data against normal-appearing white matter in the contralateral side.

Both gradient-echo and spin-echo acquisitions can be used, but rapid spin-echo imaging capable of dynamic perfusion measurements is only practical with echo-planar systems [1]. Spin-echo techniques have been shown to be selectively sensitive to small vessels that are less than 20 µ in diameter, whereas gradient-echo images incorporate signals from larger tumor vessels as well as the microvasculature [14]. For this reason, some have argued that spin-echo sequences are more specific, as they reflect the tumor physiology at the capillary level [14]. Others have shown that a stronger correlation between tumor grade and blood volume is observed with gradient-echo technique than with spin-echo technique, suggesting that the former is more sensitive [15, 16]. Regardless, both methods have been used successfully in the evaluation of brain neoplasms.

A potential problem arises in regions of severe blood-brain barrier breakdown, as is often seen in the setting of a high-grade neoplasm. High permeability in these regions leads to extravasation of contrast material into the interstitium, which increases signal above baseline due to the T1 shortening effects of gadolinium (i.e., enhancement). Since the algorithm for calculation of rCBV assumes a constant
baseline, the area above baseline is interpreted by the algorithm as negative blood volume, and subtracted from the area below baseline caused by the drop in T2* signal. This leads to significant underestimation of rCBV [1, 14].

Multiple methods exist to address this problem. One approach is to use non-gadolinium-based contrast agents, such as sprodiamide (dyspropium), which have stronger T2* effects than gadolinium but negligible T1 shortening effects [1], although this is not a practical solution today as dyspropium is an orphan drug. Newer contrast materials, such as gadobenate dimeglumine and monocrystalline iron oxide nanoparticles, which can act as “blood pool” agents, may play a role in addressing this problem in the future. A second approach is to increase the repetition time (TR), which reduces T1 effects but leads to increased scan times, lower temporal resolution, and decreased brain coverage. A third approach is to preinject a small dose of gadolinium (0.05 mmol/Kg) to presaturate the interstitium, effectively elevating the baseline before the dynamic acquisition. However, preloading doses are also impractical in routine in clinical practice [3]. A fourth approach is limited integration, where the computation of CBV is altered by excluding the portion of the curve above baseline, which has been used with some success in practice [6]. Nonetheless, this method still underestimates CBV, since leakage of contrast material will occur during the early phase of the injection before the signal reaches baseline.

At Massachusetts General Hospital, a more rigorous computational approach is used, originally proposed by Weisskoff et al., in which the image is mathematically corrected to account for leakiness of contrast material in regions of blood-brain barrier breakdown [17]. The premise of this model is that the observed concentration can be divided into intravascular and extravascular components, and that the intravascular component is proportional to the vascular signal in a normal nonleaky region, such as normal gray matter [3, 14]. The model allows generation of a K2 map, which provides an estimate of permeability within regions of blood-brain barrier breakdown and can be used to correct rCBV. An example of this method in practice is presented in Figure 2.

An entirely different approach to MR perfusion is dynamic T1-weighted contrast imaging, where the main focus is on estimating tumor permeability. A lower dose of gadolinium is administered, typically a single dose of 0.1 mmol/Kg [2], although even lower doses of 0.02 mmol/Kg have been used [13]. The injection is typically administered at a lower rate, such as 2 ml/sec, and repetitive acquisitions are then made through the tumor at longer intervals, typically every 15 to 26 seconds [2, 7]. Imaging is carried out over a much longer period of time than with T2*-based techniques, to allow for the contrast to leak out into the extravascular space and come into equilibrium over several passes of the contrast bolus through the tumor bed. The main advantage of T1-based techniques is that tumor leakiness is not an artifact to be corrected for, but the very information we are seeking.
Arterial-spin labeling (ASL) is an ingenious way of performing MR perfusion without the use of an intravenous contrast agent. With ASL, a powerful magnetic gradient is applied to inflowing blood to invert its magnetization, effectively tagging the blood flowing upstream. Preliminary data suggest that ASL provides similar information to the methods described above, and ASL flow maps may even be more conspicuous than their rCBV counterparts in detecting regions of disturbed vascularity [1]. ASL also has the advantage of being independent of tumor permeability, so that no corrections are needed. To date, long imaging times and decreased spatial resolution compared with gadolinium-based techniques have precluded widespread clinical application of ASL, but this technique may play an important role in the future of MR perfusion imaging of brain tumors.

CLINICAL APPLICATIONS

Preoperative Tumor Grading

Many groups have shown it is possible to estimate the histopathological grade of cerebral gliomas using dynamic susceptibility MR perfusion imaging [4, 14, 18]. Similar results have been found using dynamic T1-weighted MR perfusion [2, 7]. As a rule, high-grade gliomas have foci of higher cerebral blood volume and permeability within them than low-grade tumors (Figs. 3-4). An exception to this rule is oligodendroglioma, which can show foci of high cerebral blood volume irrespective of tumor grade (Fig. 5) [1, 19]. Similarly, highly vascular benign neoplasms such as meningioma often show high rCBV values (Fig. 6). Vascular metastases such as renal cell carcinoma and melanoma also have higher rCBV than normal gray and white matter [1]. Densely packed tumors such as lymphoma and medulloblastoma, on the other hand, tend to have low rCBV; however, this may be an artifact of steroid treatment, as some studies have shown increased rCBV in untreated lymphomas [1, 20]. Further studies are needed to elucidate the perfusion characteristics of untreated highly cellular neoplasms.

Because of the high level of histological variability within cerebral gliomas, rCBV maps of high-grade tumors are often heterogeneous, containing both high and low rCBV foci. Therefore, the focus of maximal CBV is taken to be representative of the tumor grade. Low-grade tumors, on
the other hand, tend to have homogenously low rCBV throughout the lesion [1, 14, 21]. Foci of maximal tumor rCBV have been associated with increased mitosis and vascularity in pathologic specimens, but not with cellular atypia, endothelial proliferation, necrosis, or cellularity [12, 22].

Because blood-brain barrier breakdown leads to underestimation of rCBV, as previously discussed, the presence of high rCBV foci in an uncorrected rCBV map will generally represent a true positive sign for high-grade neoplasm. Low rCBV values, on the other hand, require computation of the corrected CBV map to exclude neoplasm.

In our experience with untreated brain tumors undergoing dynamic spin-echo susceptibility MR perfusion imaging, normalized rCBV values greater than 1.5 are indicative of high-grade neoplasm. In a series of 30 patients with cerebral gliomas, all 13 histologically proven high-grade neoplasms had foci of maximal normalized rCBV values greater than 1.5 [19]. Conversely, homogeneously low normalized rCBV values less than 1.5 were seen in 7 of 9 histologically proven low-grade neoplasms. Sensitivity and specificity using this cut off value were 100% and 69%, respectively. Four of eight oligodendrogliomas in our series were high-grade, and all showed foci of elevated normalized maximal rCBV greater than 1.5. Among the four low-grade oligodendrogliomas, two had foci of elevated normalized rCBV greater than 1.5 and two had low rCBV foci [1, 19]. What is most significant about these results is that: A) no lesion with exclusively “low” rCBV foci proved to be high grade (no false negatives); B) half of all low-grade oligodendrogliomas had “high” CBV foci, and C) there was a much stronger relationship between rCBV and tumor grade/survival than between the degree of contrast enhancement and tumor grade/survival.

Jackson et al. showed a similar increase in mean rCBV for 27 untreated glioma patients [4]. This study furthermore showed that variations in the circulation characteristics of the contrast bolus, termed the relative recirculation (rR), were also correlated with tumor grade, and that both of these measures are independent of one another.

Other groups have found similar results using CBF to evaluate tumor grade. Shin et al. studied 17 untreated patients with biopsy-proven gliomas and found no significant difference between receiver operating characteristic curves using rCBV and rCBF maps [18]. In this study using spin-echo dynamic susceptibility MR perfusion, a cut off value of 2.9 for rCBV yielded a sensitivity and specificity of
91% and 83%, respectively, for distinguishing high- from low-grade tumors. A cut off value of 3.6 for rCBF yielded a sensitivity and specificity of 73% and 100%, respectively.

Good correlations between perfusion parameters and tumor grade have also been established using dynamic T1-weighted MR permeability imaging. In a group of 22 untreated gliomas, Roberts et al. showed a strong correlation between tumor grade and permeability ($r = 0.76$), which was even stronger when the reflux rate in the two-directional compartment model was included in the permeability calculations ($r = 0.83$) [2]. Differences in $k_{ps}$ values between grade 4 and grade 2 and 3 tumors were statistically significant; however, the difference in $k_{ps}$ values between grade 2 and grade 3 tumors was not significant. When the reflux rate is included in the calculations, the difference in mean total permeability became statistically significant between all tumor grades. Despite this, their data show overlap in permeability values between high-grade and low-grade tumors. A similar observation was made in a study by Provenzale et al. of first-pass tumor permeability using dynamic susceptibility MR perfusion in 22 patients, which included both treated and untreated patients [3]. In this study, there was overlap in first-pass permeability (K2) values between different tumor grades. Their data suggest that a cut off of 0.03 in permeability separates low- from high-grade tumors, with a positive predictive value of 90% and negative predictive value of 75%.

Biopsy Guidance

CT-guided stereotactic needle biopsy, a widely used method of evaluating brain neoplasms, relies on the assumption that the contrast-enhancing portion of the tumor corresponds to the most aggressive cell population. The problem with this approach is that contrast enhancement alone or the lack thereof is not a reliable indicator of tumor grade. Up to 38% of anaplastic astrocytomas do not enhance with gadolinium, and it is estimated that up to 25% of brain tumors are under-graded at stereotactic biopsy [1, 23].

MR perfusion imaging may offer a more accurate way of choosing a biopsy site. High-grade tumors have been shown to demonstrate foci of high rCBV even in the absence of gadolinium enhancement. In our experience with untreated brain
tumors, MR perfusion CBV maps suggested additional biopsy sites in nonenhancing portions of astrocytomas in 7 of 13 patients with high-grade gliomas (54%), and correctly categorized all 13 of the high-grade lesions preoperatively. Three of these tumors did not show gadolinium enhancement [19].

Tumor Margins

It is well known that the enhancing margins of cerebral gliomas do not reflect the true boundaries of these lesions, which typically extend into and even beyond the visualized area of T2 abnormality surrounding the enhancing tumor. Indeed, Earnest et al. found histological evidence of abnormal tumor cells not only outside the region of enhancing tumor, but beyond the surrounding T2 lesion volume [24]. It stands to reason that a noninvasive method to reliably and accurately evaluate tumor borders would be of clinical value for surgical and radiation treatment planning.

The utility of MR perfusion techniques for mapping tumor extent has shown mixed results. Henry et al. found a good correlation between rCBV maps and MR spectroscopy data for delineating tumor margins, both of which were more sensitive than conventional MRI [5]. MR spectroscopy, however, was superior to rCBV mapping for delineating tumor involving cortex, possibly due to the high background rCBV values in gray matter. Other investigators have had even less encouraging results with pediatric brain tumors, with no evidence of rCBV abnormality beyond the enhancing tumor margin, even for cases in which MR spectroscopy detected such foci [9].

Radiation Necrosis Versus Tumor Recurrence

The distinction of radiation necrosis from tumor recurrence is a particularly challenging problem in neuro-oncology, as treatment is radically different for the two entities, yet radiological differentiation is not reliable using conventional contrast-enhanced MR or CT scanning. Damage to the blood-brain barrier induced by radiation results in leakage of gadolinium into the interstitium, which produces a ring-enhancing lesion that can mimic tumor recurrence. The chronicity of the changes is often not helpful, as radiation necrosis can occur from 6 months to many years following radiation therapy—the same time period during which recurrence is most likely. The problem is confounded by the fact that these conditions frequently coexist, with at least microscopic tumor frequently present in most post-treatment tissue beds.

First-pass MR perfusion imaging, although more accurate than conventional MRI for differentiating between these entities, remains imperfect. Radiation necrosis typically shows decreased rCBV, whereas tumor recurrence results in high rCBV (Fig. 7) [14]. Using gradient-echo dynamic susceptibility perfusion MR imaging, Sugahara et al. studied 20 patients with enhancing lesions after radiation and found that an rCBV greater than 2.6 was always indicative of tumor recurrence, and that an rCBV of less than 0.6 was always consistent with radiation necrosis [8]. Unfortunately, there was a significant degree of overlap between the two groups, so that further studies, such as thallium 201 or PET, were often necessary to allow differentiation.

More encouraging results have been obtained using more delayed, T1-weighted MR permeability methods, which image beyond the first-pass circulation of contrast, sometimes

Figure 7. Radiation necrosis. A) Axial T1-weighted image (TR 450, TE 20, NEX 1, 0.2 mmol/Kg gadolinium at 5 cc/s) obtained 18 months following resection of an anaplastic oligoastrocytoma shows an enhancing abnormality posterior to the deep margin of the resection cavity. B) FDG-PET shows subtle foci of increased glucose metabolism corresponding to the foci of enhancement, greater than the adjacent white matter but less than adjacent grey matter. This was felt to represent tumor recurrence by the interpreting PET specialist. C) Corrected CBV revealed reduced blood volume within the lesion (arrow), consistent with radiation necrosis (perfusion raw data obtained at TR 500, TE 65, 5-mm thick, 6-mm skip, 0.2 mmol/Kg gadolinium at 5 cc/s). Resection of the abnormality confirmed radiation effect without evidence of tumor.
for as long as 10-15 minutes. In a group of 95 patients, Hazle et al. were able to reliably distinguish between tumor recurrence, radiation necrosis, or a combination of both factors, using an empiric model to study the rate of contrast enhancement [7]. They found that radiation and tumor enhance at different rates, with mean maximal enhancement rates (max dI/dt) of 5.85 in recurrent tumor (1.78 standard deviation [SD]), 1.90 in radiation necrosis (0.78 SD), and 2.79 in cases of mixed radiation necrosis and tumor (1.03 SD). This allowed differentiation among these lesions preoperatively. The difference among the three groups was statistically significant (p < 0.001) across all pairs, with 95% confidence interval or better.

**Future Applications**

The development of novel antiangiogenesis therapies is closely linked to the future of MR perfusion techniques. Jayson et al. showed rapid increases in capillary permeability within less than 24 hours following administration of an antibody directed against the angiogenic cytokine VEGF [4, 25]. The ability of MR perfusion techniques to reveal changes in tumor microvasculature so quickly is likely to accelerate the process of development and testing of new antiangiogenic compounds. Dynamic susceptibility MR perfusion is also being used to monitor antiangiogenic therapy in the clinical setting for recurrent glioma patients treated with thalidomide and carboplatin [26].

CBV measurements have been shown to be more useful than volumetric measurements in predicting response to radiotherapy in patients with cerebral metastasis treated with radiosurgery [19]. In our experience, patients with normalized CBV values of less than 1.5 at presentation showed a clear trend towards longer survival following treatment [19]. Further studies will be needed to assess the full prognostic utility of perfusion-weighted imaging in the diagnosis and follow-up of cerebral neoplasms.

A word of caution is needed in interpreting the literature on MR perfusion of brain tumors, as the confounding effect of steroid use has been consistently ignored in the literature. Steroids have been shown to decrease CBV using both MRI perfusion and PET [27-29] in both humans and a rat model. Increased permeability of the blood-tumor barrier with steroid use has also been observed [27]. The data are less clear on the effect on CBF, which was shown to be unchanged using MR perfusion [27] and decreased using PET [28]. The mechanism for the steroid effect on CBV is poorly understood but is probably mediated by cerebral blood vessel vasoconstriction [28].

**Conclusions**

MR perfusion is an exciting imaging tool that allows assessment of both tumor anatomy and physiology in one setting. Multiple studies have shown that preoperative grading of brain tumors is not only possible using MR perfusion methods, but is more accurate than that using conventional MRI scanning alone. This can, in turn, be used to guide the surgeon to perform biopsy on the most aggressive portions of a tumor. In the future, it is also possible that MR perfusion could be used to more accurately delineate tumor margins, in order to better plan resection and radiation treatment of brain neoplasms. MR perfusion imaging, most notably the delayed T1-weighted permeability methods, may also be valuable in distinguishing radiation necrosis from tumor recurrence, thus sparing patients from unnecessary treatment. Finally, MR perfusion methods, as a surrogate marker for treatment outcome, are likely to play a central role in the development of new antiangiogenic compounds. As advances in MR technology take place, the role of MR perfusion in the care of neuro-oncologic patients is likely to increase, and may eventually permit reliable, noninvasive assessment of a patient’s prognosis and response to therapy.

**References**


