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Perfusion MR imaging: basic principles and clinical applications

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Dynamic contrast-enhanced perfusion MR imaging of the brain provides hemodynamic information that complements the anatomic information attainable with conventional MR imaging. Contrast-enhanced perfusion MR imaging methods exploit signal changes that accompany the passage of a paramagnetic contrast agent through the cerebrovascular system and can be used to derive information on blood volume and flow [1-6]. Dynamic perfusion MR imaging data analyzed using the radiotracer kinetic theory yields quantitative estimates of cerebral blood volume that reflect the underlying microvasculature and angiogenesis. Hence, this quick and robust technique is increasingly used as a research tool with which to evaluate and understand intracranial disease processes and as a clinical tool for diagnosis, management, and understanding of intracranial mass lesions, especially brain tumors. The vascularity of intracranial lesions, such as gliomas [1,2,7], cerebral lymphomas [8], and tumor-mimicking demyelinating lesions [4], has been assessed with perfusion MR imaging. Other studies [1-3] have shown that maps of estimated cerebral blood volume (ie, relative cerebral blood volume) correlate with the histopathologic microvascularity of glial tumors and are a valuable guide for stereotactic biopsy. With the increasing number of applications of perfusion MR imaging, under-

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standing the principles underlying the technique is important. In this article, the essential physics and methodology underlying dynamic contrastenhanced susceptibility-weighted perfusion MR imaging are described. In addition, the clinical applications of perfusion MR imaging-derived maps of cerebral blood volume in the diagnosis of brain tumors and tumor-mimicking lesions and the pitfalls and limitations of the technique are discussed.

Technical considerations

Susceptibility contrast and radiotracer kinetic theory

As a paramagnetic agent such as gadopentetate dimeglumine passes through the cerebrovascular system, it produces T2* signal loss because of local magnetic susceptibility, a phenomenon also known as susceptibility-induced T2* shortening. The radiotracer kinetic theory of a nondiffusible radiotracer (ie, an agent assumed to remain in the vascular bed) such as gadopentetate dimeglumine allows relative measurements of cerebral blood flow and volume to be obtained. The passage of gadopentetate dimeglumine through the brain can be followed by way of changes in the relaxation rates of brain water protons. When gadopentetate dimeglumine compartmentalized into a confined space, its dominant effect of on MR imaging is its susceptibility contrast from T2 and T2* signal loss. In the radiotracer kinetic model, the MR signal change must be expressed in terms of changes in the

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concentration of the local contrast agent. Empiric data and kinetic modeling have shown that a linear relationship exists between the concentration of the contrast agent and the rate of T2 signal change. Therefore, the T2* shortening during the bolus tracking of gadopentetate dimeglumine can be converted to a tissue contrast agent concentration-time curve, which can then be used to determine tissue microcirculatory measurements, such as blood volume or blood flow, from the appropriate kinetic modeling of the data. It is beyond the scope of this article to discuss in detail the principles underlying measurement of tissue perfusion using MR contrast agents; however, the author outlines the ways in which such techniques can be applied in clinical MR imaging and discuss the essential technical elements involved and their applicability in the acute clinical environment.

Contrast agents for perfusion MR imaging

The basis for perfusion MR imaging is the exploitation of signal changes that accompany the passage of a radiotracer as it passes through the cerebrovascular system. The radiotracer can be either endogenous (arterial water) or exogenous (deuterium oxide or gadopentetate dimeglumine) and can be either freely diffusible (arterial water or deuterium oxide) or nondiffusible (gadopentetate dimeglumine). In each case, the analysis is based on the indicator dilution methods originally developed for the radioisotope measurements of blood flow and volume [9]. In endogenous or arterial spin-labeling techniques (ie, echoplanar MR imaging and signal targeting with alternating radiofrequency [EPISTAR] and flow-sensitive alternating inversion recovery [FAIR]), blood spins are magnetically labeled upstream from the imaging slice with either inverting or saturating radiofrequency pulses. In this approach, the regional changes in signal intensity are determined by an interaction between blood flow and T1 relaxation. Comparison of images acquired with and without labeling allows calculation of tissue perfusion [10-14]. Arterial spin labeling does not require injection of exogenous contrast agent, can be performed without additional hardware, and, in principle, yields fully quantitatifiable measurements of cerebral blood flow. (For a detailed description of arterial spin-labeling methods, interested readers are referred to several excellent sources). Exogenous radiotracers such as gadopentetate dimeglumine are used far more commonly in perfusion MR imaging in a clinical setting because these radiotracers have relatively short imaging times and require image processing tools that are widely available. The focus of this article is dynamic contrast-enhanced pMR imaging using a gradient echo echoplanar technique in clinical applications for imaging brain tumors.

Sequence consideration and imaging protocol

For measurements of cerebral blood flow, several images are acquired at intervals of approximately 1 second before, during, and after the bolus injection of contrast agent. Longer intervals may be feasible, but the measurement of the signal time curve would then be less accurate. Rapid gradient-echo imaging is capable of generating approximately two T1-weighted slices per second, which are not generally sufficient to cover a large heterogeneous tumor. Echo-planar imaging is capable of generating approximately 10 slices every second and is ideal for rapid dynamic imaging. The following MR sequence parameters are used for perfusion MR imaging: TR/TE, 1250/ 54; flip angle, 30°; number of slices, 7; thickness of slice, 4 mm; gap, 0; field of view, 26 cm; matrix, 128×128 ; in-plane voxel size, 1.8×1.8 mm; and bandwidth, 120 kHz. The passage of gadopentetate dimeglumine causes changes in both T2 and T2* so that both gradient-echo echoplanar and spin-echo MR imaging sequences provide robust measurements of cerebral blood volume. However, gradient-echo echoplanar sequences are much more sensitive than are spin-echo sequences. When a paramagnetic contrast agent such as gadopentetate dimeglumine passes through the cerebral vascular system, the contrast agent induces differences in local magnetic susceptibility between vessels and the surrounding tissue. Although the vascular space is a small fraction (4%-5%) of the total tissue blood volume, this compartmentalization of the contrast agent causes targeted paramagnetism in the intravascular spins and in the surrounding spins in a given voxel. Thus, both intra and extravascular spins experience a reduction of T2* that leads to a large transient signal loss of approximately 25% in normal white matter with a standard dose of the contrast agent (0.1 mmol/kg of body weight). T2weighted spin-echo MR images are less sensitive than gradient-echo MR images and require double or even quadruple the dose of contrast agent to provide substantial signal changes during the passage of the bolus. On the other hand, gradient-echo MR imaging sequences are more

prone to magnetic susceptibility artifacts. Thus, when imaging lesions near interfaces of brain, bone, and air—such as in the temporal lobes or posterior fossa—where these artifacts are more pronounced, spin-echo sequences may be preferable. However, artifacts in gradient-echo MR images can be overcome to a large extent by reducing the slice thickness [15].

Image processing

If recirculation and contrast leakage are assumed to be negligible, the cerebral blood volume is proportional to the area under the contrast concentration time curve [9]. Concentration of gadopentetate dimeglumine is proportional to the change in the relaxation rate (ie, the change in the reciprocal of T2*), which is DR2* and can be calculated from the signal using the following equation [16]: $DR2^* = -\ln n$ S(t)/S(0)/TE, where -ln is negative natural log, S(t) is pixel intensity at time t, S(0) is baseline pixel intensity before injection of contrast agent, and TE is echo time. This equation is valid only if the T1 enhancement associated with the disruption of the blood-brain barrier has a negligible effect on signal intensity, which is ensured if a long TR, a low flip angle, or a combination of the two is used to reduce saturation. Generally, the assumptions concerning negligible recirculation and contrast leakage are violated. The effects of such a disruption can be reduced by fitting a gamma-variate function to the measured DR2* curve [17]. The gamma-variate function approximates the curve that would have been obtained without recirculation or leakage. Cerebral blood volume can then be estimated from the area under this fitted curve rather than from the original data. In the author's experience, however, the gamma-variate fit is unstable: small variations in the initial parameter estimates produce wide variations in the results. This instability occurs even with data averaged over regions of interest in areas of high perfusion and seems to be inherent to the procedure. In practice, satisfactory fits can often be found only by repeating the procedure with several different initial estimates until a set is found that causes the fitting algorithm to converge. This approach can be applied to fit contrast concentrationtime curves from multiple regions of interest because each fit takes only a short time. However, because the approach is not suited for pixel-by-pixel calculations of maps of the cerebral blood volume, using alternative corrections for leakage is preferable when mapping cerebral blood volume. The simplest method is to estimate the end of the bolus and to calculate the area under the bolus alone, although this method results in a systematic overestimate of cerebral blood volume in areas in which the blood-brain barrier is damaged. Alternatively, having estimated the beginning and end of the bolus, a baseline can be subtracted from under the curve. The area under the corrected contrast concentration-time curve is proportional to the cerebral blood volume and does not vield an absolute measurement. Therefore, the measurement must be expressed as relative to a standard reference of measurement, which is usually obtained in the contralateral white matter. The author refers to this estimation as relative cerebral blood volume. For image processing, the source images are first transferred to an offline workstation and inspected for overall image quality and the presence of motion artifacts.

A single region of interest is placed over the contralateral unaffected centrum semiovale white matter, and the relative cerebral blood volume maps are generated. Cerebral blood volume maps can then be calculated on a pixel-by-pixel basis and displayed as a grayscale image. Fig. 1 shows raw data images with changes in tissue signal intensity before, during, and after the passage of intravascular gadopentetate dimeglumine. However, small but important variations in the cerebral blood volume are not always apparent from these maps. An alternative method is to use a color overlay on the raw image in which the abnormal cerebral blood volume values are often more apparent. Setting a threshold for the color overlay at a cerebral blood volume of approximately 50% greater than the unaffected (normal) white matter allows visualization of underlying anatomy that can be helpful in interpretation. The cerebral blood volume measurements of the lesion are generally calculated relative to region of interest values in contralateral normal white matter.

Technical pitfalls and limitations

Several important limitations are associated with dynamic contrast-enhanced gradient echo perfusion MR imaging. First, because the technique is susceptibility weighted, it is exquisitely sensitive to structures or lesions that induce strong magnetic field inhomogeneity (eg, blood



Fig. 1. Forty-three-year-old man with left frontal meningioma. Series of transverse dynamic perfusion MR images (TR/ TE, 1250/54; flip angle 30°) obtained using gradient-echo echoplanar technique show tumor before bolus IV injection of gadopentetate dimeglumine (*A*), at peak arrival time (in this case, 10 seconds after contrast injection, (*B*), and 50 seconds after injection (*C*). In peak arrival image (*B*), tumor displays marked signal intensity drop (*black arrows*). In later image (*C*), signal intensity in tumor returns to baseline except in areas of disrupted or absent blood–brain barrier (*white arrows*) where leakage has occurred. (*D*) Contrast-enhanced transverse T1- weighted MR image (600/14) shows avid contrast enhancement of tumor (*small black arrows*) because of absence of blood–brain barrier.

products, calcium, melanin, metals, or lesions located near the brain-bone-air interfaces, such as the middle and anterior cranial fossa) One simple way to reduce inhomogeneity and susceptibility artifacts is to decrease the thickness of slice sections, although such a reduction also reduces the signal-to-noise ratio and slice coverage. If slice coverage is insufficient to cover the tumor, the interslice gap can be increased. This solution does carry the risk of missing small vascular regions but even with thicker slices, such small regions may be missed because of volume averaging. Second, the cost of imaging hardware can be high because perfusion MR imaging requires high performance gradients and ultrafast echoplanar imaging sequences. Finally, the calculation of relative cerebral blood volume can be grossly inaccurate in lesions such as glioblastomas multiforme or meningiomas, which cause a severe breakdown or absence of the blood-brain barrier [18]. One should bear in mind that relative cerebral blood volume measurements are not absolute quantifications of blood volume.

Clinical applications

Intracranial neoplasms

Vascular morphology and the degree of angiogenesis are important elements in evaluating different tumor types and determining the biologic aggressiveness of intracranial neoplasms [19]. Tumor angiogenesis [1] can be indirectly assessed using perfusion MR imaging-derived in vivo maps of cerebral blood volume that depict the overall tumor vascularity. MR imaging measurements of relative cerebral blood volume have been shown to correlate with both conventional angiographic assessments of tumor vascular density and histologic measurements of tumor neovascularization [1-3]. Increased tumor vascularity, however, is not synonymous with malignancy. Several intracranial neoplasms, especially those that are extraaxial such as meningiomas or choroid plexus papillomas, can be vascular but benign in biologic behavior. In patients receiving antiangiogenesis cancer therapies that directly attack tumor vessels [20-24], perfusion MR imaging is a noninvasive method to assess changes in the relative cerebral blood volume of the tumor during treatment and thus can be used to monitor the efficacy of therapy. Conventional MR imaging is limited by its nonspecificity and inability to allow differentiation between tumor recurrence and therapy related necrosis. Findings of perfusion MR imaging have been shown to correlate better with clinical responses of patients undergoing antiangiogenic therapy [25].

Gliomas

In primary high-grade gliomas, vascular morphology is a critical parameter in determining the potential for malignancy and for survival. Glioma grading is important for determining both prognosis and therapy. Several studies have found a statistically significant correlation between the relative cerebral blood volume in the tumor and glioma grading and between relative cerebral blood volume in the tumor and tumor vascularities determined using conventional catheter angiography [1–3]. Vascular morphology and degree of angiogenesis are important histopathologic features that determine the malignancy and grade of glial neoplasms. Because MR imaging can be used to quantitatively assess tumor vascularity, contrast-enhanced perfusion MR imaging can be used to measure cerebral blood volume of the tumor, which reflects underlying tumor vascularity. Therefore, perfusion MR imaging-derived relative cerebral blood volume measurements can serve as noninvasive surrogate markers of tumor angiogenesis and malignancy. Low-grade astrocytomas have significantly lower mean relative cerebral blood volume than anaplastic astrocytomas or glioblastomas [1,2,7]. As shown in Fig. 2, low-grade astocytomas show little or no elevation in the cerebral blood volume in the tumor compared with the contralateral uninvolved brain. Anaplastic astrocytomas tend to have a higher relative cerebral blood volume than low-grade astrocytomas but lower relative cerebral blood volume than glioblastomas. The progressive increase in relative cerebral blood volume

from low-grade to high-grade tumors is consistent with studies showing that microvascular density in low-grade astrocytomas is significantly lower than in anaplastic astrocytomas or glioblastomas, with glioblastomas being the most vascularized type of tumor (Fig. 3). Not only do the measurements of relative cerebral blood volume in different glioma grades overlap, but also relative cerebral blood volume measurements can and do vary considerably because of the inherent extreme histologic heterogeneity of gliomas. Therefore, maps of relative cerebral blood volume of gliomas should not be interpreted without a concomitant evaluation of conventional MR images, which can provide other valuable information such as the integrity of the blood-brain barrier or the degree and characteristics of T2 abnormality. Biopsy remains the definitive method of determining tumor type and grade. The sampling error rate in biopsies of high-grade gliomas is well known and is caused in part by the extreme geographic heterogeneity within a single tumor [26,27]. Ideally, the grading of gliomas should be based on histologic evaluation of tissue from the most malignant area in the tumor. Identifying this region can be difficult, however. In most biopsies, the imaging modality used for guidance is contrast-enhanced T1-weighted MR imaging or CT [28], which depict areas of blood-brain barrier breakdown that may not correspond with the most malignant or most vascular portion of the tumor. Selecting a biopsy target based on contrastenhanced T1- weighted MR imaging alone may be quite challenging. Maps of cerebral blood volume can depict regions of increased vascularity that can serve as additional targets for stereotactic biopsy. At the author's institution, maps of relative cerebral blood volume are routinely used to select biopsy sites for enhancing and nonenhancing tumors and to help reduce sampling error and nondiagnostic biopsies. The relative cerebral blood volume map is particularly useful in patients with nonenhancing tumors, because the map can be used to locate the "hot" area or the presumed site of increased tumor vascularity.

Differentiation between radiation necrosis and recurrent tumor carries obvious therapeutic implications. Patients with recurrent tumors may benefit from undergoing a second operation and receiving adjuvant chemotherapy or targeted high dose radiotherapy, whereas patients with radiation necrosis may be treated conservatively with steroids. Currently, the only definitive means of differentiating between radiation necrosis and



Fig. 2. Enhancing right superior frontal lobe low-grade glioma in a 30-year-old woman. (A) Contrast-enhanced transverse T1-weighted MR image (TR/TE, 600/14) shows a heterogeneously enhancing right superior frontal tumor (*arrows*). (B) Relative cerebral blood volume map displays no evidence of increased tumor vascularity. Patient underwent surgical resection, and final pathologic examination revealed low-grade fibrillary astrocytoma.



Fig. 3. Nonenhancing right frontal glioblastoma multiforme in a 34-year-old man. (*A*) Contrast-enhanced transverse T1-weighted MR image (TR/TE, 600/14) displays no evidence of contrast enhancement in right frontal tumor (*arrows*). (*B*) Relative cerebral blood volume map clearly shows increased vascularity (*arrows*) within tumor.



Fig. 4. Delayed radiation necrosis in a 67-year-old man who underwent surgery and external beam radiation therapy 12 months before for clival chordoma. (*A*) Contrast-enhanced axial T1-weighted MR image (TR/TE, 600/14) shows heterogeneously enhancing left temporal lobe mass (*arrows*). (*B*) Relative cerebral blood volume map displays no evidence of increased vascularity (*arrows*) in left temporal lobe mass. Surgical resection revealed radiation necrosis with no evidence of tumor.

recurrent tumor is histologic evaluation of tissue from biopsy or resection. However, surgical manipulation of areas of radiation necrosis can cause further damage to the adjacent brain parenchyma.

Delayed radiation necrosis usually is indistinguishable from recurrent tumors clinically and radiologically. Clinically, patients with either entity can present with progressive focal neurologic deficits and signs of increased intracranial pressure. On imaging, both entities can appear as a mass lesion with surrounding edema [29-33]. Conventional contrast-enhanced CT or MR imaging cannot be used to reliably distinguish radiation necrosis from recurrent tumor. Both processes can cause extensive edema and varying degrees of disruption in the blood-brain barrier that result in mass effect and abnormal contrast enhancement, respectively. Pathologically, however, radiation necrosis and recurrent tumor are dissimilar. Although the exact pathogenesis of delayed radiation necrosis remains obscure, a consistent pathologic feature is extensive endothelial injury and ultimate fibrinoid necrosis; in contrast, recurrent tumor is characterized by vascular proliferation [34,35]. MR imaging-derived cerebral blood volume maps can show the pathologic differences in vascularity between therapy-induced necrosis and recurrent tumor. Our preliminary results have shown such maps to be useful tools with which to differentiate the two entities [36]. Fig. 4 shows a patient with clival chordoma who was treated with surgery and external beam radiation therapy and who presented with a large rim-enhancing necrotic mass in the left temporal lobe 8 months following the completion of irradiation. The features on conventional MR imaging were nonspecific, but perfusion MR imaging showed low relative cerebral blood volume in the left temporal lesion. Surgical biopsy revealed radiation necrosis with no evidence of tumor.

Metastases

Metastatic tumors, which make up almost 50% of all brain tumors, enter the central nervous system either hematogenously or by direct extension and induce neovascularization as they grow and expand. The newly formed capillaries resemble those of the primary systemic tumor with fenestrated membranes and open endothelial junctions, all of which differ from normal brain capillaries that possess a well developed blood–brain barrier with tight junctions, a continuous

basement membrane, and astrocytic foot processes [37]. Intracranial metastases tend to be multiple lesions that enhance avidly on enhanced T1-weighted images with varying degrees of associated edema; they characteristically are located near the junction of the gray and white matter. Hence, differentiating a metastatic brain lesion from a primary glioma usually presents no diagnostic dilemma. However, when a metastatic brain tumor presents as a solitary lesion, it can have an appearance similar to that of a glioma on both enhanced T1-weighted MR images and on relative cerebral blood volume maps. Perfusion MR imaging may be useful in differentiating a solitary metastasis from a primary glioma based on the difference in the measurements of peritumoral relative cerebral blood volume [38]. This difference in the blood volume can, in part, be explained by the difference in pathophysiology: in metastatic tumors, the peritumoral edema (defined as the area of hyperintensity on T2-weighted images in immediate contact with the enhancing tumor margin) is a vasogenic edema that is caused by the increased interstitial water from leaky capillaries [39]. In metastatic tumors, there is no histologic evidence of tumor beyond the outer contrast enhancing margin of the tumor, and the peritumoral region represents the reaction of the surrounding intrinsically normal but edematous brain parenchyma. In high-grade gliomas, on the other hand, the peritumoral region represents a variable combination of vasogenic edema and tumor cells infiltrating along the perivascular spaces [40]. It has been shown that neoplastic cells can be found in some high-grade gliomas not only outside the contrast-enhancing margin but also well beyond the outer edge of the peritumoral zone visualized on T2-weighted MR images [28]. By exploiting the pathophysiologic difference in peritumoral region, perfusion MR-derived blood volume measurements may help differentiate tumor infiltrated edema (in case of high-grade gliomas) from purely vasogenic edema (in case of metastasis).

Primary cerebral lymphomas

Over the last 2 decades, the incidence of primary cerebral lymphomas has substantially increased in both immunocompromised and immunocompetent individuals—a phenomenon that cannot be entirely explained by changes in tumor classification, the increased prevalence of AIDS, or the growing number of organ

transplantations [41,42]. Primary cerebral lymphoma histopathologically shows angiocentric growth with neoplastic cells forming multiple thick layers around blood vessels. Tumor cells are found in the perivascular space and within the vessel walls [43], but hypervascularity is not observed. Lymphomas generally appear as avascular on angiography [44,45]. Radiologic diagnosis, however, remains a challenge. Conventional MR imaging findings of primary cerebral lymphoma can be similar to those for other intracranial tumors or even demyelinating lesions. Lymphomas often have an appearance similar to glomerular basement membranes. The capability of perfusion MR imaging to reveal and allow quantification of tumor angiogenesis could potentially be useful in differentiating glioma from lymphoma based on their differences in tumor vascularity. This distinction is important because unlike other high-grade intracranial neoplasms, lymphomas are treated with combined high-dose chemotherapy and radiation therapy without radical surgery. Surgical intervention is usually limited to biopsy for obtaining tissue for pathologic diagnosis [46-48]. Finding a minimally invasive technique that can provide an accurate diagnosis of primary cerebral lymphoma is therefore an important goal that could clearly alter disease management and reduce risk to the patient. A relative decrease in relative cerebral blood volume in lymphoma detectable on perfusion MR imaging [49] therefore can be useful in differentiating between the two tumor types that are treated and managed quite differently.

Meningiomas

Meningiomas are vascular, extraaxial tumors that derive blood supply mostly from meningeal arteries with tumor capillaries that completely lack blood-brain barrier. Angiographically, meningiomas appear as hypervascular extraaxial masses that exhibit diffuse, homogeneous, and prolonged staining. Similarly, meningiomas are hypervascular on perfusion MR imaging, as shown in Fig. 1. Because of the lack of a blood-brain barrier within the tumor, the capillaries of meningioma are leaky and permeable. This phenomenon is apparent during the first-pass contrast agent bolus when there is immediate contrast agent leakage without any substantial recovery of T2* signal loss back to the baseline. Therefore, the perfusion MR imaging-derived relative cerebral blood volume measurements of meningiomas may be grossly over or underestimated because of firstpass leakage, which essentially renders the intravascular compartmentalization of contrast agent impossible.

Tumor-mimicking lesions

A few nonneoplastic lesions of the brain cerebral infections, tumefactive demyelinating lesions, and, less commonly, infarcts—may be confused with and misdiagnosed as brain tumors. The conventional MR imaging appearance of these lesions can be nonspecific and pose a serious challenge in differentiation from brain tumors. Even with the use of a contrast agent, the



Fig. 5. Demyelinating lesion in a 44-year-old woman. (A) axial fluid-attenuated inversion recovery (FLAIR; TR/TE/ inversion time, 10,000/148/2200) image reveals a hyperintense lesion with surrounding edema (*arrows*) in the left periatrial white matter. (B) Contrast-enhanced axial spoiled gradient recalled image (TR/TE, 8.5/1.6) shows a thin rim of peripheral enhancement (*arrows*). (C) Relative cerebral blood volume map displays lack of increased vascularity within the lesion (*arrows*).

distinction can be difficult because any process that disrupts the integrity of blood-brain barrier can result in enhancement. Potentially, perfusion MR imaging offers a different mechanism of differentiation by assessment of variations in vascularity of these lesions.

Tumefactive demyelinating lesions

Tumefactive demyelinating lesions are large demyelinating lesions that can mimic high-grade glial tumors. Histopathologically, tumefactive demyelinating lesions consist of perivascular inflammatory infiltration and demyelination, but hypervascularity is uncommon [50]. Angiography of tumefactive demyelinating lesions has been described only infrequently; however, one case series found that normal angiograms were obtained for four tumefactive demyelinating lesions [51]. Multiple dilated medullary veins with early drainage into subependymal veins within the area of demyelination have been shown on angiography [52]. Tumefactive demyelinating lesions can mimic intracranial neoplasms and pose a diagnostic dilemma on both clinical presentation and conventional MR imaging. On imaging, tumefactive demyelinating lesions and high-grade intracranial neoplasms can both display contrast enhancement, perilesional edema, varying degrees of mass effect, and central necrosis [50,51,53]. Furthermore, tumefactive demyelinating lesions can be confused with high-grade glial neoplasms at histopathologic evaluation because of the presence of hypercellularity and atypical reactive astrocytes with mitotic figures [50]. Single dominant tumefactive demyelinating lesions, in particular, are often misdiagnosed as brain tumors, leading to unnecessary, and possibly harmful, biopsy or even resection. The literature reports a few cases in which patients with tumefactive demyelinating lesions were subjected not only to surgery but also to radiation therapy for a mistaken diagnosis of lymphoma or glioma [50,53]. In light of this diagnostic dilemma, several reports in the pathology literature have stressed the need for special stains to be used for myelin and axons to make the correct diagnosis of tumefactive demyelinating lesions [50,54–56]. The radiology literature also has numerous reports that address the topic of tumefactive demyelinating lesions masquerading as brain tumors, which leads to unnecessary surgery [51,53,56,57]. One of the key histopathologic differences between tumefactive demyelinating lesions and high-grade brain tumors is the absence of frank angiogenesis in the former. The blood vessels within areas of demyelination do not elaborate evidence of neovascularization in contrast to the angiogenesis seen in tumors [4,50]. Therefore, pMR imaging can aid in the differentiation of tumefactive demyelinating lesions from tumors by depicting differences in lesion vascularity. Fig. 5 depicts a large demyelinating lesion lacking evidence of increased blood volume on pMR imaging.

Summary

Dynamic contrast-enhanced perfusion MR imaging provides hemodynamic information that complements traditional structural imaging and is increasingly used in clinical practice to diagnose, manage, and understand brain tumors. Relative cerebral blood volume maps derived from perfusion MR imaging data provide quantifiable estimates of regional blood volume that can be used to grade gliomas, differentiate different brain tumor types, and distinguish tumors from nonneoplastic lesions. There are a few minor limitations of the dynamic contrastenhanced perfusion MR imaging technique-susceptibility artifacts, relative rather than absolute quantification of cerebral blood volume, and the inaccurate estimation of cerebral blood volume in patients in whom the blood-brain barrier has been severely disrupted or destroyed. Despite the minor potential pitfalls of the technique, inclusion of perfusion MR imaging as part of a routine evaluation of brain tumors can lead to improved diagnostic accuracy, understanding of tumor pathophysiology, and detection and quantification of tumor angiogenesis. With further work, perfusion MR imaging could be used to assess existing and novel cancer therapies that target blood vessels.

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