Functional Information on Meningiomas Through Perfusion Magnetic Resonance Imaging

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Abstract
This article focuses on the use of perfusion magnetic resonance imaging (MRI), and in particular dynamic susceptibility contrast-enhanced MRI (DSC-MRI), to assess hemodynamics in meningiomas. We first introduce the basic principles of DSC-MRI and the most popular imaging techniques and perfusion parameters for data analysis of DSC-MRI. We then review the blood supply characteristics of meningiomas and how perfusion MRI is applied in meningiomas to help the subtyping of different meningiomas and to differentiate between benign and malignant meningiomas. Our first-hand experiences are also included. We conclude that DSC perfusion MRI can provide critical information on the vascularity of meningiomas that is not available with conventional MRI. DSC perfusion MRI measurements are helpful in the pre-operative subtyping and grading of meningiomas.

Keywords
Perfusion, magnetic resonance imaging (MRI), meningioma, brain, tumors, diagnosis

Perfusion is defined as the steady-state delivery of nutrients and oxygen via blood to tissue per unit volume or mass and is typically measured in milliliters per 100g of tissue per minute.1 Because blood flow brings crucial nutrients, and because it is disturbed in many disease processes, monitoring of this key physiological parameter can often provide insight into disease.

The brain is an unusual organ in the hemodynamic sense, with a high metabolic rate that is sustained through high cerebral blood flow (CBF). CBF is defined as the volume of blood moving through a given brain region per unit time. Normal CBF is typically greater than 50–60ml/100g/min. Unlike other high-flow organs, the limited space inside the bony cranium requires an efficient regulation system, which is accomplished with a high capillary density but remarkably low cerebral blood volume (CBV). CBV is defined as the total volume of blood in a given region of the brain. CBV has units of milliliters of blood per 100g of brain tissue (ml/100g); normal CBV is 2–5ml/100g. Mean transit time (MTT) is a slightly more complex concept. Because the transit time of blood through the brain parenchyma varies depending on the distance traveled between arterial inflow and venous outflow, the MTT is defined as the average of the transit time of blood through a given brain region, integrated across these different paths. Mathematically, MTT is related to both CBV and CBF according to the central volume principle, which states that the MTT = CBV/CBF.13 Conceptually, MTT can be thought of as the time required for blood to cross from the arterial to the venous side of the circulation. MTT is typically measured in seconds.

While magnetic resonance imaging (MRI) has traditionally been used to evaluate anatomy, with its main application being the central nervous system (CNS), the recent application of MRI to visualize tissue physiology or function has met with great success. Indeed, a whole new field known as functional MRI has arisen to apply these techniques. Because blood flow is altered in many pathophysiological states, from abnormal cognition through stroke to brain tumors, use of MRI to study blood flow is one of the most clinically relevant of the many forms of functional MRI. Dynamic susceptibility contrast, arterial spin labeling (ASL), and methods to measure permeability are the three techniques that have been used to quantify the perfusion of brain in many research and clinical applications. Rather than surveying the entire field of brain perfusion imaging, this article focuses on the use of perfusion MRI and, in particular, dynamic susceptibility contrast-enhanced MR imaging (DSC-MRI) to assess hemodynamics in meningiomas.

Basic Theory and Data Analysis of Dynamic Susceptibility Contrast-enhanced Magnetic Resonance Imaging
DSC-MRI, first described in 1991 by Rosen et al.,4 uses rapid measurements of MRI signal change after the injection of a bolus of a paramagnetic MRI contrast agent.5 This is the most commonly employed perfusion MRI technique and has been studied extensively in clinical settings. Gadolinium chelates with high magnetic susceptibility were used as contrast agents in DSC-MRI. Given their size and low lipophilicility, they are constrained to the intravascular space by a normal blood–brain...
Applications of Perfusion Magnetic Resonance Imaging in Meningiomas

Brain tumors require a blood supply to grow and thus in turn require angiogenesis. More recently, angiogenesis has been recognized as a key element in the pathophysiology of tumor growth and metastasis. Once tumors grow beyond a diameter of 1–2 mm, passive diffusion is no longer sufficient to support the viability of malignant cells, and neovascularization becomes a necessity. Therefore, tumors that grow beyond the occult stage are capable of activating the ‘angiogenic switch.’ The new blood vessels formed are generally less organized than the normal vessels and hence have altered perfusion characteristics with increased blood flow and volume.

Meningiomas are highly vascular neoplasms and often show higher rCBV than other primary and metastatic brain tumors. Previous studies suggested that for meningiomas with atypical conventional MRI findings, calculation of rCBV ratios and construction of signal intensity–time curves may contribute to the differentiation of meningiomas from intra-axial tumors. Different meningioma subtypes also show different vascular characters. A study by Kimura et al. illustrated that among different subtypes of meningioma, perfusion values of angiomatous meningioma were the greatest and lowest for fibrous meningioma, and their results correspond to our experiences. By studying a group of 37 patients with newly diagnosed meningiomas, we found that the maximal rCBVs in both tumor parenchyma and peri-tumoral edema showed statistical differences between subtype meningiomas.

In our results, from highest to lowest, the maximal rCBVs in tumor parenchyma were ranked as angiomatous, anaplastic, meningiothelial, and fibrous meningioma. In the peri-tumoral region, the maximal rCBV of anaplastic meningioma was highest, followed by fibrous, meningiothelial, and angiomatous meningioma.

When comparing the mean rCBVs of the two subtypes, our results showed that the maximum rCBVs in tumor parenchyma of angiomatous meningioma and in the peri-tumoral region of anaplastic meningioma were statistically greater (p<0.05) than those of other subtypes. From these studies, we presumed that some common benign subtypes of meningioma such as meningiothelial and fibrous meningiomas cannot be differentiated from atypical or anaplastic meningiomas simply by evaluating their parenchyma rCBV values. However, rare benign subtypes such as angiomatous meningiomas might show different perfusion characteristics.

Differentiating between malignant and benign meningiomas before surgery is important for both treatment planning and the prognosis.
and peri-tumoral edema. While the maximal rCBV derived from the contralateral normal white matter and corresponding rMTE of peri-tumoral edema of malignant meningiomas were significantly greater than those of benign ones (p<0.05). The increase in rCBV in the peri-tumoral edema of malignant meningiomas might be attributed to tumor invasion and angiogenesis in the adjacent brain tissue. Our results were also supported by previous molecular studies of meningiomas, which have shown that FLT1- and VEGF-positive cells are increased in the endothelium of intratumoral vessels and are associated with microvascular proliferations in peri-tumoral brain tissue of anaplastic meningiomas.

Conclusion

DSC perfusion MRI can provide critical information on the vascularity of meningiomas that is not available with conventional MRI. DSC perfusion MRI measurements are helpful in the pre-operative subtyping and grading of meningiomas. Because of the limited patient numbers and the inconsistent results in published papers, perfusion MRI studies of meningioma with larger sample sizes are needed to investigate the reliability and reproducibility of this new technique before it can be used as clinical routine.