Perfusion Imaging in Neuro-Oncology

Basic Techniques and Clinical Applications

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KEYWORDS

• MR perfusion • CT perfusion • DCE-T1 • DSC-T2* • ASL • Cerebral blood volume

KEY POINTS

- Perfusion imaging allows for assessment of changes occurring at the tumor microvasculature level.
- Perfusion-based parameters have the potential to serve as important quantitative imaging biomarkers, providing information not routinely available with standard morphologic imaging.
- Perfusion imaging is increasingly used for neuro-oncologic applications, including brain tumor grading, directing biopsies or targeted therapy, and evaluation of treatment response and disease progression.
- Perfusion-based quantitative biomarkers, when used in conjunction with standard morphologic imaging, have the potential to provide early indication of treatment failure or treatment response.
- Increased use of perfusion MR in the routine surveillance imaging of brain tumors allows for evaluation of relative cerebral blood volume (rCBV) trends, which may bolster its effectiveness as an imaging biomarker.

WHAT IS PERFUSION IMAGING?

Perfusion imaging is a method for assessing the flow of blood occurring at the tissue level.[1] Depending on the modality (eg, MR, CT) and method (eg, dynamic contrast enhanced [DCE], arterial spin labeled) used, several perfusion parameters can be evaluated, both qualitatively and quantitatively. These parameters include those related to the volume of blood within a given region of tissue, as well as those describing the movement of blood through that region over time. In addition to assessing blood volume and flow, these techniques also allow for the quantitative assessment of vessel leakiness through the measurement of vascular permeability.

WHAT IS MEASURED AND HOW IS IT USED?

Blood Volume and Blood Flow

Blood volume (BV), mean transit time (MTT), and blood flow (BF) are all parameters used to describe the flow of blood within a particular region of tissue.

- BV refers to the total volume of blood flowing within a given area of tissue and is measured in milliliters of blood per 100 g of tissue (mL/100 g).
- BF refers to the volume of blood flowing within a given area of tissue per unit time and is measured in milliliters of blood per 100 g of tissue per minute (mL/100 g/min).
- MTT refers to the average time blood takes to traverse through a given area of tissue and is measured in seconds (s).

Measuring the volume and flow of blood in a particular region of brain can have important clinical implications. In the setting of acute ischemia, measurement of CBV, MTT, and CBF helps in differentiating the "core" of irreversibly infarcted brain tissue from the ischemic, but potentially salvageable, brain tissue (ie, penumbra).[1] Similarly, CBV

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has also been used successfully to identify patients with hemodynamic impairment in the setting of major arterial occlusive disease,[2] as well as in evaluating cerebrovascular reserve in patients with Moya-Moya.[3] In addition, assessment of CBV has been used extensively in neuro-oncologic applications, including for brain tumor grading and directing biopsies or targeted therapy, as well as for the evaluation of treatment response and disease progression.[4,5] These neuro-oncologic applications of perfusion imaging are the focus of this article.

Vessel Permeability

In addition to parameters describing the volume and flow of blood within a particular region of brain, perfusion imaging also allows for assessment of vessel permeability. This is particularly important for applications involving the brain, given the role of the blood–brain barrier (BBB), which serves as a physical barrier to the entry of lipophobic substances into the brain and can be disrupted by a number of disease processes, including brain tumors. This breakdown of the BBB, which accounts for the contrast enhancement seen on standard imaging, also provides a potential surrogate imaging marker. Various methods have been developed to quantify this vessel "leakiness," most notably by measurement of the permeability surface-area product (PS), which characterizes the diffusion of contrast agent from the blood vessels into the interstitial space, or by the transfer constant (K_{trans}).[6]

METHODS

CT Perfusion

CT perfusion (CTP) allows for the assessment of CBV and permeability with a single acquisition. The greatest advantage of CT perfusion is the linear relationship between iodine concentration and attenuation on CT. This easy conversion allows for a direct measurement of vascular parameters.

CTP protocols vary depending on the manufacturer and scanner model used, as well as depending on the reason for the examination (eg, tumor volume protocol vs acute stroke imaging). However, as a general concept, CTP is based on the principle of sequential acquisition of CT images during the washin and washout of iodinated contrast material from brain parenchyma (**Fig. 1**)[7] with the goal being to observe the distribution of contrast agent within tissues over time.

How Is It Done?

- Before obtaining the perfusion scan, a low radiation dose noncontrast CT head study can be performed.
- For the perfusion scan at our institution, 50 mL of nonionic contrast is injected at a rate of 4 to 5 mL/s through an intravenous line using an automatic power injector.
- A cine scan is then initiated at 5 seconds into the injection, using the following parameters: 80 kV (peak), 100 to 120 mÅ, and 1 second per rotation for a duration of 50 seconds. After the initial 50-s cine scan, 8 additional axial images are acquired, 1 image every 15 seconds for an additional 2 minutes, resulting in a total acquisition time of 170 seconds to assess delayed permeability.[8]
- Perfusion maps can then be obtained through the use of a number of commercially available software applications with the superior sagittal sinus generally used as the venous output function and the artery with the greatest peak and slope on the time–attenuation curves as the arterial input function.[8]

MR Perfusion

The measurement of vascular parameters with MR perfusion can be accomplished with both contrast-enhanced and non–contrast-enhanced (arterial spin labeling [ASL]) techniques. Dynamic contrast-enhanced MRI utilizes 2 techniques—a T1-weighted acquisition (DCE MR) and a T2*-based acquisition (DSC MR). Although the methods used by these techniques in quantifying cerebral perfusion differ, both rely on a trace of contrast agent concentration over time to estimate blood volume and permeability.[9] In contrast to these contrast-enhanced methods, evaluation of perfusion with ASL is accomplished through the use of magnetically labeled arterial blood water as a freely diffusible tracer.

In contrast with CT perfusion, which directly images the iodinated contrast agent, contrast agents utilized in MR perfusion are not imaged directly and instead rely on signal intensity to provide an estimate of CBV. However, regardless of the technique used, MR perfusion offers 2 major advantages over CT perfusion. First, MR perfusion requires no radiation, which is very important in oncologic imaging, because patients often require frequent imaging for tumor surveillance. Second, particularly in neuro-oncologic imaging, MR is the standard of care for assessing treatment response or progression of disease. Therefore, the acquisition of perfusion parameters with MR perfusion requires only additional sequences to be obtained rather than an entirely separate examination as in the case of CT perfusion.