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Pediatric Brain MR Perfusion Imaging

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A B S T R A C T

Magnetic resonance (MR) perfusion techniques are now easily implemented and have many clinically validated uses in brain imaging. A variety of techniques are now available to best suit particular individual patient and disease state indications. This review will present a conceptual overview of the underlying perfusion technical factors in addition to the clinically applicable facets related to patient preparation and the MR imaging appearance of various perfusion patterns in health and disease. A special focus on pediatric brain perfusion will be presented.

Introduction

The imaging assessment of brain perfusion can often augment the structural information obtained from conventional magnetic resonance imaging (MRI) using standard sequences, such as T1-weighted, T2-weighted, fluid-attenuated inversion recovery (FLAIR), and the other more mainstream physiological magnetic resonance (MR) sequence, diffusion-weighted imaging (Choi et al., 2016; Eilaghi et al., 2016; Gerstner et al., 2016; Hu et al., 2012; Patel et al., 2016). Brain MR perfusion sequences belong to the growing category of advanced imaging techniques, which attempt to better characterize the functional aspects of cerebral tissue in hopes of improving the evaluation and surveillance of neurological disease (Barlow et al., 2016). Relatively, few barriers to their use now exist for routine implementation wherever MRI is performed. The current perfusion techniques can be readily performed on all commercially available modern MRI scanners, at both 1.5 T and 3 T field strengths. MR sequence options for both gadolinium (Gd)-based contrast and noncontrast perfusion are also available, which can be of additional value in the imaging of children. In this review, we will broadly describe the concepts underlying the current brain MR perfusion techniques with an emphasis on the application of these techniques in pediatric populations. A rigorous description of the technical details related to imaging physics and mathematical models that underpin the MR perfusion methods will not be given. Interested readers are referred to a number of excellent literature references for further details (Griffith & Jain, 2015; Jackson, O'Connor, Thompson, & Mills, 2008). A brief overview of basic cerebrovascular physiology will be given to assist readers who may be unfamiliar with this topic as this knowledge will allow readers an improved conceptual understanding of nature and use of MR perfusion imaging.

Basic Cerebrovascular Physiology

The brain is a highly metabolic organ that receives a lot of blood flow, requiring approximately 50 to 60 mL/min/100 g of tissue. That flow is quickly moved in and out of the brain, with a mean transit time (MTT) of 4 s by a high-density capillary network. As a result, the overall baseline blood volume is relatively low, approximately 2 to 5 mL/100 g of tissue. Similar to other situations of fluid moving in and out of a space, there is an equation that describes this; cerebral blood flow (CBF) = cerebral blood volume (CBV)/MTT. Knowledge of this equation is helpful in better conceptualizing MR perfusion imaging findings (Jahng, Li, Ostergaard, & Calamante, 2014).

The critical facet of cerebrovascular physiology and perfusion are the local control mechanisms that exist to manipulate blood flow under various normal and pathological conditions. This mechanism is commonly referred to as autoregulation. Cerebral autoregulation describes the ability of the brain to maintain CBF over a wide range of potential cerebral perfusion pressures, which are primarily driven by mean arterial pressure. Autoregulatory control in the brain is controlled by manipulations of the diameter of small arterioles. Under conditions of low CBF, the resistance of these arterioles will increase to preserve an appropriate level of CBF. These conditions can range from the everyday changes in body position (standing up) to pathological conditions causing

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Table 1
Three primary methods of brain perfusion MRI and their primary characteristics

Characteristic	DSC	DCE	ASL
Dynamic time-resolved MRI scan	Yes	Yes	Not usually
Gd contrast agent	Yes	Yes	No
Primary method of blood signal contrast	T2 or T2*-weighted relaxation induced by Gd—causes magnetic susceptibility and blood to decrease in signal	T1-weighted relaxation induced by Gd—causes T1 shortening and blood to increase in signal	Pair-wise subtracted images showing radiofrequency-labeled blood magnetization
Primary quantitative endpoints	CBF, CBV, MTT, TTP	CBF, CBV, MTT, TTP, and permeability	CBF

MRI = magnetic resonance imaging; DSC = dynamic susceptibility contrast; DCE = dynamic contrast-enhanced; ASL = arterial spin labeling; Gd = gadolinium; CBF = cerebral blood flow; CBV = cerebral blood volume; MTT = mean transit time; TTP = time to peak.

significant cerebrovascular arterial stenosis. If the extent of reduced CBF overwhelms cerebral autoregulatory capabilities, clinical symptoms usually appear, and the imaging of brain perfusion can be of critical importance in patient management (Essig et al., 2013; Wang et al., 2014).

Overview of MR perfusion techniques

The MR brain perfusion techniques can be grouped into those that require intravenous (IV) MRI Gd-based contrast and those that can be performed without contrast. The technical background of each of these techniques will be described (Table 1) along with discussion of the advantages and disadvantages and pediatric clinical applications in neuroimaging.

Dynamic Susceptibility Contrast Perfusion MRI

Dynamic susceptibility contrast (DSC) is an IV contrast-based high temporal resolution MR perfusion technique. Using T2-weighted spin echo echo planar imaging (EPI) or T2*-weighted gradient-echo EPI pulse sequences, this technique follows contrast agent passage dynamically through brain tissue. The susceptibility effect of the first pass of IV Gd-based contrast agent results in a loss of MR signal intensity in each pixel over time (Figure 1), which is then converted into a time-tissue Gd concentration curve. From this curve, the main calculated perfusion metrics—CBV, MTT, CBF, and time to peak (TTP)—can be calculated (Paulson & Schmainda, 2008; Tasker, 2013; Welker et al., 2015; Willats & Calamante, 2012) (Figure 2). These calculations are performed by the MRI computer and are available largely without significant operator input. These parameters can be presented graphically, as radiographic images (Figure 3), or can be used to produce semiquantitative values that radiologists can evaluate to comment on the patient's brain perfusion.

Among the MR perfusion techniques, the greatest clinical experience is with DSC. This technique possesses a number of advantages, including short scan time, high signal-to-noise ratio, and straightforward calculation models for outputting perfusion data for interpretation. The major disadvantage is the requirement for IV contrast (Calamante, 2010; Markus, 2004; Schmainda et al., 2014; Shiroshi et al., 2015; Stokes & Quarles, 2016). This requirement basically negates any ability to perform repeated perfusion acquisitions during a single MR scanning session and can potentially be contraindicated in patients with severe renal disease at risk for

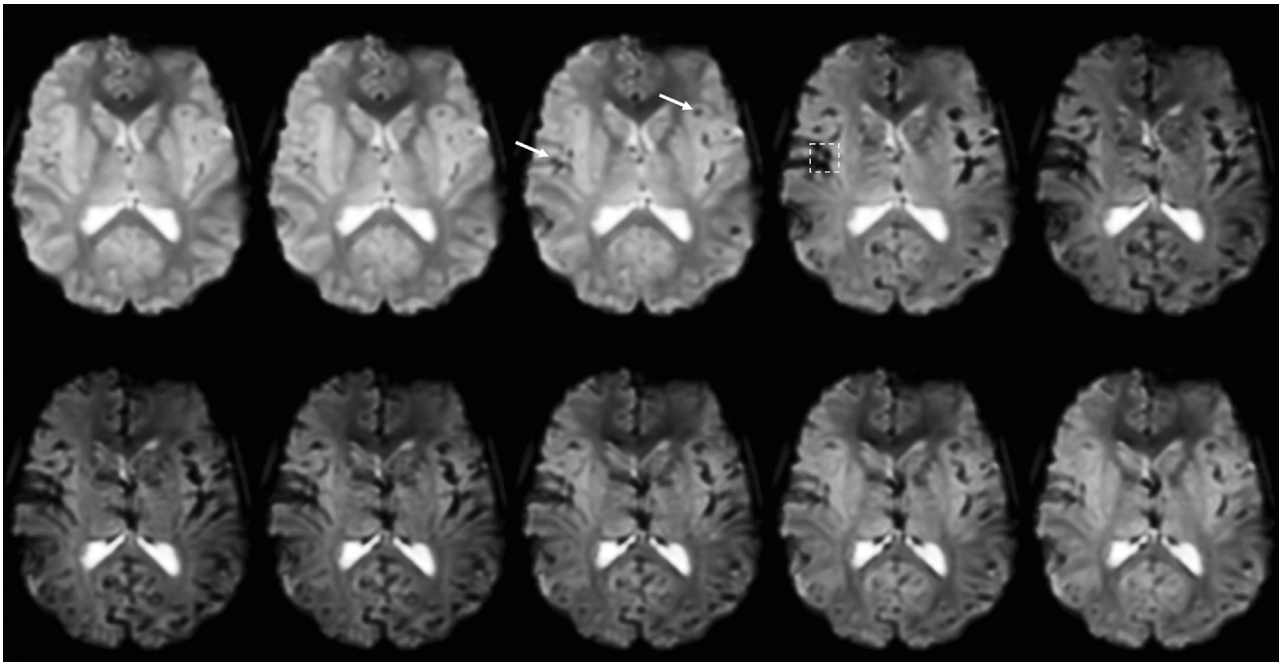

Figure 1. Representative images from a 6-year-old patient from our institution acquired with 2D multislice T2*-weighted gradient-echo echo planar imaging at 3 T demonstrating the dynamic susceptibility contrast technique. Ten consecutive time frames are shown, with a temporal resolution of 2 s between successive frames. Gadolinium arrival can be clearly observed from the third time frame onward as the blood vessels become darker in signal intensity (*arrows*) because of the local magnetic susceptibility changes caused by the contrast agent. If one plots the signal intensity within a voxel (e.g., *dashed box*) frame by frame, a time course of the signal evolution can be obtained, allowing calculations of parameters such as cerebral blood volume, mean transit time, and time to peak. See Figure 2 for further details.