Hong Kong J Radiol. 2016;19:154-65 | DOI: 10.12809/hkjr1615389

REVIEW ARTICLE **CME**

Application of Advanced Neuroimaging in the Assessment of Cerebral White Matter and Cerebral Perfusion in Paediatric Patients

BMH Lai, EMW Man*, KYK Tang, WKW Leung, SSW Lo, WWC Wong, JLS Khoo

Department of Radiology, Pamela Youde Nethersole Eastern Hospital, Chai Wan, Hong Kong

* EMW Man is currently at the Department of Diagnostic & Interventional Radiology, Hong Kong Sanatorium & Hospital, Happy Valley, Hong Kong

ABSTRACT

The article reviews and illustrates the use of advanced neuroimaging techniques in paediatric patients, focusing particularly on magnetic resonance spectroscopy, diffusion tensor imaging, and magnetic resonance perfusion and their applications in the diagnosis, assessment, and treatment planning of neurological conditions.

中文摘要

先進神經影像學在審視小兒患者的腦白質和腦灌注中的應用

賴銘曦、萬民偉、鄧業勤、梁錦榮、盧成瑋、黃慧中、邱麗珊

本文回顧及展示如何在兒童患者中使用先進神經影像學技術用於診斷、評估和治療神經系統疾病，討論側重於磁共振波譜、彌散張量成像和磁共振灌注成像。

INTRODUCTION

Recent advances in neuroimaging have introduced new techniques that enable a better understanding of the pathologies that affect cerebral white matter (WM) and also offer less-invasive methods for assessment of cerebral perfusion. This article reviews the use of these imaging techniques, focusing particularly on the use of magnetic resonance spectroscopy (MRS), diffusion tensor imaging (DTI), and magnetic resonance (MR) perfusion in paediatric patients. We sought to illustrate how these imaging techniques can help in the diagnosis, assessment, and treatment planning of neurological conditions.

MAGNETIC RESONANCE SPECTROSCOPY

Paediatric patients are particularly vulnerable to WM insults. This, in part, is due to the high metabolic activity from active myelination during the first few years of life. There is also a wide variety of leukodystrophies, metabolic and mitochondrial disorders, and demyelinating conditions that affect paediatric WM. Differentiating between different disease entities on imaging is often difficult because many appear similar on conventional magnetic resonance imaging (MRI). MRS can aid in their differentiation by identifying changes in the brain tissue metabolic profile that occur

Correspondence: *Dr Billy Lai, Department of Radiology, Pamela Youde Nethersole Eastern Hospital, 3 Lok Man Road, Chai Wan, Hong Kong.*
Email: billylai@gmail.com

Submitted: 18 Dec 2015; Accepted: 5 Jan 2016.

Disclosure of Conflicts of Interest: All authors have disclosed no conflicts of interest.

in specific diseases.

Technical Aspects of Magnetic Resonance Spectroscopy

Most clinically available MRS softwares are based on the MR of the hydrogen proton (^{1}H). The abundance of various metabolites within the interrogated nervous tissue is represented graphically in the form of peaks that are deviations from the baseline. Identification of individual metabolites is based on the differences in MR frequencies, represented on the X-axis of the graph, with a scale in parts per million (ppm).

The time-to-echo (TE) chosen for the MRS has important implications in determining the metabolites that can be detected. Protocols can be classified as: short-TE (20-30 ms), intermediate-TE (135-144 ms), and long-TE (270-280 ms). Short-TE MRS protocols have the advantage of detecting more metabolites than long-TE protocols. They are also more prone to contamination by water and lipid, however, and hence produce more variable baselines that may undermine accurate interpretation. Long-TE protocols are insensitive to lipids and macromolecules, producing a flatter baseline, but are limited in the types of metabolites that they can detect. The choice of TE-protocol depends on the clinical scenario and practices vary among centres. Our routine MRS protocol begins with an intermediate-TE sequence with a short-TE sequence added in selected cases if deemed appropriate.

Choosing the appropriate anatomical site for performing MRS and deciding between single-voxel spectroscopy (SVS) and multi-voxel spectroscopy (MVS) are also important issues to consider when designing the MRS protocol. The three most common reasons for performing MRS for children in our practice are: suspected metabolic / syndromal disease, developmental delay, and suspected brain tumour. For the first two indications, we routinely perform MRS on the basal ganglia and peri-ventricular WM and selected areas of abnormal signal change seen on conventional MRI. For tumours, the choice is dictated by the site of the mass lesion. SVS and MVS each have their own advantages and disadvantages and differ with respect to scan time and spatial coverage.[1] SVS is mainly based on PRESS (Point-RESolved Spectroscopy) or STEAM (STimulated Echo Acquisition Mode) techniques, while MVS relies on chemical shift imaging.[2] For most machines, SVS allows faster scanning time. It is also less susceptible to artefacts for lesions near bone or fat, and this may be advantageous when assessing posterior fossa lesions. In contrast, MVS provides greater spatial coverage, a choice of retrospective voxel shift and the ability to produce spectral and metabolic maps over a wide area of the lesion and surrounding normal tissue. This may be useful when analysing large heterogeneous lesions and in cases where comparison with normal tissue is necessary.

Interpretation of Magnetic Resonance Spectroscopy in Paediatric Patients

N-acetylaspartate (NAA), creatine, and choline (Cho) peaks are seen on MRS in normal brain matter regardless of the TE protocol used. Myo-inositol, glutamine, and glutamate peaks can only be visualised on short-TE MRS. Lactate and lipid peaks are not typically seen in normal brain tissue and may signify the presence of anaerobic glycolysis and cell breakdown. The significance and resonance of these metabolites are listed in Table 1.

Several points require special attention when interpreting MRS for paediatric patients. First, in adults, the NAA peak is normally higher than the Cho peak. In neonates, however, the Cho peak is normally higher than the NAA peak at birth. This is thought to be due to active myelination and a lower abundance of mature neurons.[3,4] Hence, whereas a reverse of NAA:Cho peak ratio in adults and older children may signify increased

Table 1. Important metabolites on magnetic resonance spectroscopy.

Metabolite	Resonance (parts per million)	Significance
Lipids	0.9-1.4	Marker of tissue breakdown
Lactate	1.3	Marker of anaerobic glycolysis
N-acetylaspartate	2.0	Marker of viable neurons
Glutamate and Glutamine	2.1-2.6	Neurotransmitters
Choline	3.2	Marker of cell membrane turnover and cellular proliferation
Creatine	3.0 (and 3.9)	Marker of cellular energy
Myo-inositol	3.5	Glial marker

cellular turnover and possible underlying neoplastic change, in a newborn, this may be a normal finding. This pattern (i.e. Cho peak higher than NAA peak) usually reverses at around 3 to 6 months of age in normal infants.[3,5] Second, lactate may be seen in normal preterm infants. This finding alone does not necessarily signify hypoxic ischaemic encephalopathy or metabolic disease. Interpretation should be made in conjunction with the clinical context and other imaging findings. Lactate is also seen in the cerebrospinal fluid of term and preterm neonates. Meticulous technique is needed to ensure exclusion of cerebrospinal fluid from the voxel to avoid over-diagnosis. Lastly, proprane-1,2-diol, a solvent for anticonvulsants, produces a doublet peak at 1.1 ppm. Care must be taken to avoid misinterpretation as a lactate doublet peak that occurs at 1.3 ppm.

Clinical Applications of Magnetic Resonance Spectroscopy in Paediatric Patients

An important application of MRS in paediatric patients is identification and differentiation of metabolic diseases / leukodystrophies, as many appear similar on conventional MRI. Sjögren-Larsson syndrome (SLS) is one such example. SLS is an autosomal recessive condition associated with a deficiency in fatty aldehyde dehydrogenase, causing an inborn error in fatty alcohol oxidation. Clinically, patients present with ichthyosis, spastic paraplegia, and mental retardation. Conventional MRI of SLS demonstrates diffuse T2-weighted (T2W) hyperintensity in the bilateral cerebral WM (Figure 1a). This is non-specific and can commonly be seen in many paediatric metabolic and syndromal disorders. On MRS, SLS is characterised by sharp elevated lipid peaks at 1.3 ppm and 0.9 ppm on short-TE MRS (Figure 1b). These peaks correspond to the methylene and methyl proton spins from abnormal accumulated lipids, respectively. The sharp lipid peak at 1.3 ppm is reported to be characteristic of SLS in patients with suspected metabolic disease.[6,7]

Canavan disease is another condition that presents with non-specific periventricular T2W hyperintensity on conventional MRI. On MRS, it differs from other syndromes in that it shows markedly elevated NAA levels on MRS. This is caused by a deficiency in N-aspartoacylase, leading to abnormal accumulation of NAA. As NAA is normally a marker of neuronal viability, in most other syndromes affecting the central nervous system, the NAA peak on MRS would be reduced due to neuronal destruction or either remain unchanged rather than being increased as in Canavan disease.

Creatine is an important compound in energy metabolism. Creatine deficiency, although rare, is an important condition to consider in developmental delay, as certain forms of the disease are treatable by dietary supplementation. Conventional MRI findings

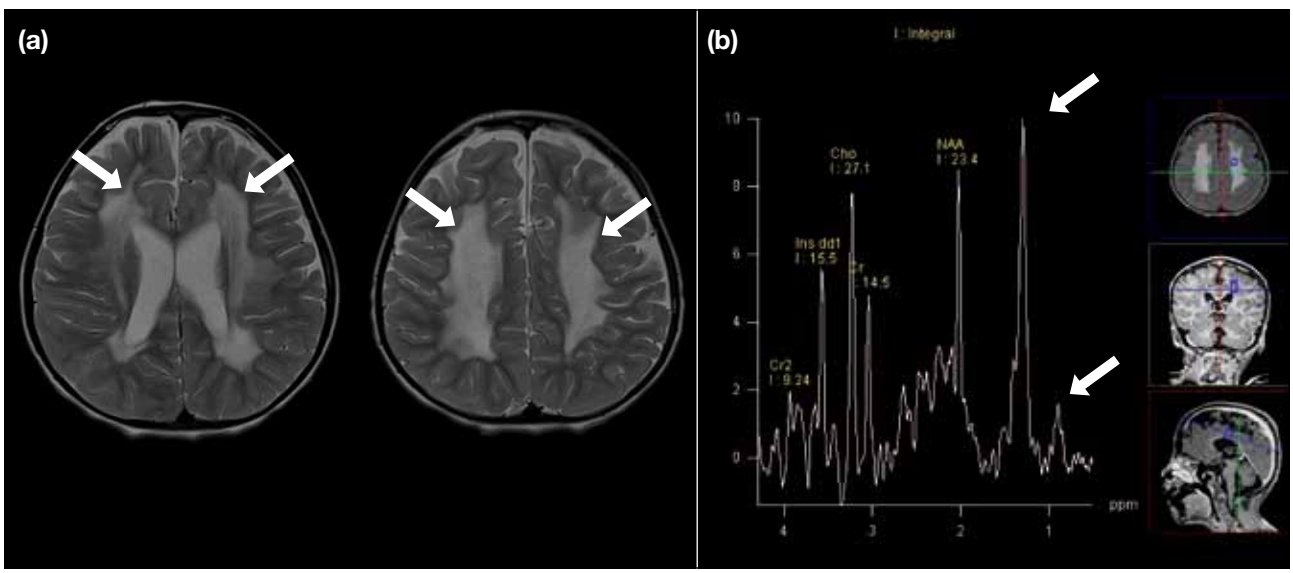

Figure 1. (a) T2-weighted hyperintensity seen in bilateral periventricular white matter in a patient with Sjögren-Larsson syndrome (SLS) [arrows]. (b) Magnetic resonance spectroscopy (TE = 30 ms) demonstrating elevated lipid peaks (at 1.3 ppm and 0.9 ppm) in SLS (arrows).

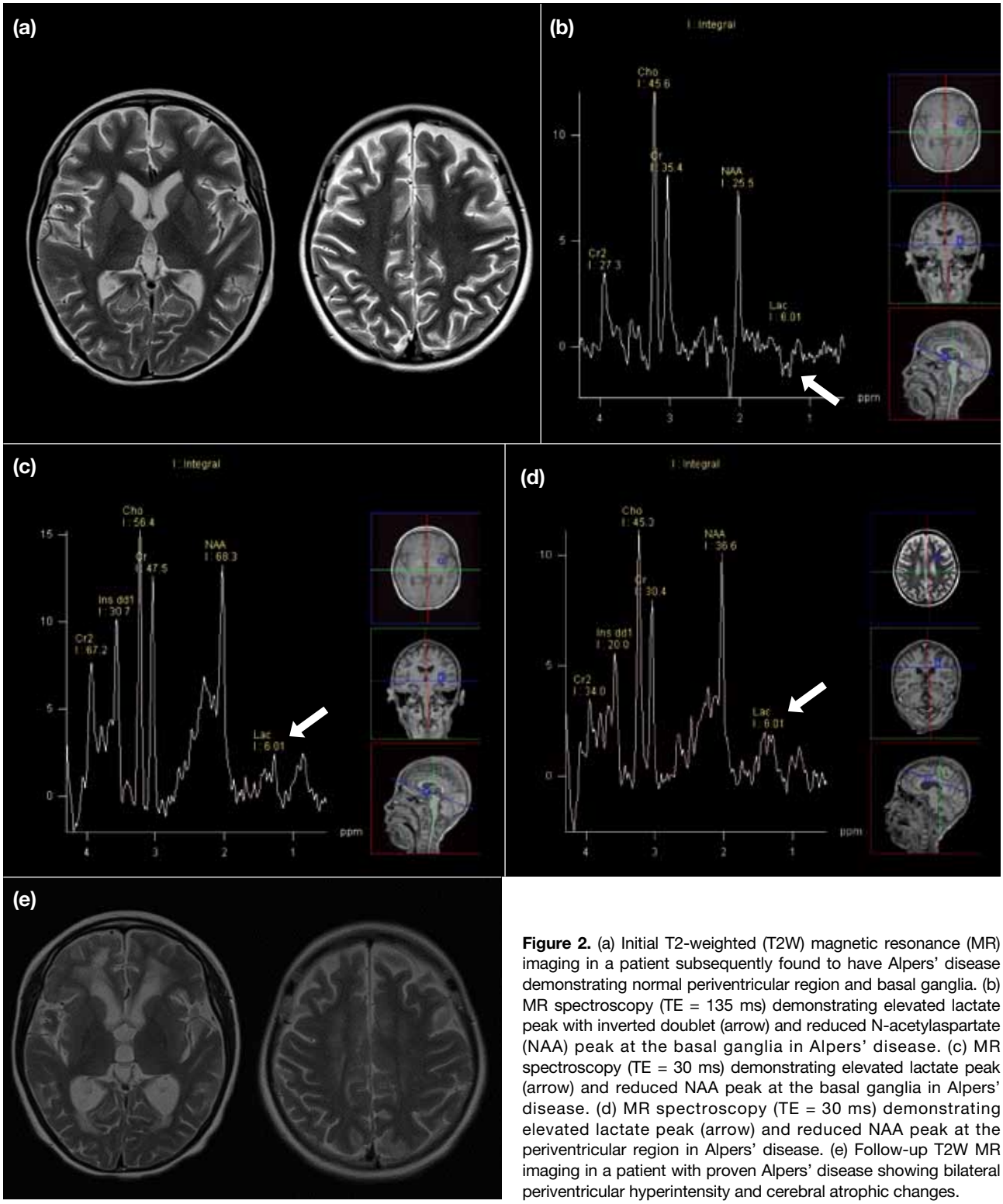

Figure 2. (a) Initial T2-weighted (T2W) magnetic resonance (MR) imaging in a patient subsequently found to have Alpers' disease demonstrating normal periventricular region and basal ganglia. (b) MR spectroscopy (TE = 135 ms) demonstrating elevated lactate peak with inverted doublet (arrow) and reduced N-acetylaspartate (NAA) peak at the basal ganglia in Alpers' disease. (c) MR spectroscopy (TE = 30 ms) demonstrating elevated lactate peak (arrow) and reduced NAA peak at the basal ganglia in Alpers' disease. (d) MR spectroscopy (TE = 30 ms) demonstrating elevated lactate peak (arrow) and reduced NAA peak at the periventricular region in Alpers' disease. (e) Follow-up T2W MR imaging in a patient with proven Alpers' disease showing bilateral periventricular hyperintensity and cerebral atrophic changes.

are usually unremarkable but MRS shows characteristic absence of the creatine peaks and is diagnostic of this disease. MRS also plays a role in monitoring treatment response. Presence of a creatine peak on MRS is seen during follow-up scanning of these patients who are responsive to treatment.

The lactate peak is an important marker of potential

disease on MRS. It is observed in a number of diseases including hypoxic ischaemic encephalopathy, abscesses, necrotic tumours, and a range of metabolic diseases. Detection of lactate is useful in early diagnosis of mitochondrial diseases such as Leigh syndrome, MELAS (mitochondrial myopathy, encephalopathy, lactic acidosis, and stroke-like episodes), Alpers' disease and Kearns-Sayre syndrome, as MRS changes may precede changes on conventional MRI.[8] Figure 2a shows the initial conventional T2W images of a patient who presented with seizures and was noted to have cognitive and developmental regression during the episode of admission. Findings at the basal ganglia and periventricular regions were normal on initial conventional MRI sequences. Nonetheless, the MRS at the basal ganglia and periventricular region showed elevated lactate peak and reduced NAA peak (Figures 2b to 2d), signifying anaerobic glycolysis and neuronal loss. The patient tested positive for *POLG* gene mutation, suggestive of Alpers' disease. Follow-up MRI 1 year later showed T2W hyperintensity at the periventricular regions and cerebral atrophy (Figure 2e), neither of which was evident on the initial MRI, confirming disease progress in Alpers' disease. For the detection of lactate peak, it is important to note that there is an overlap in the location of the lipid and lactate peaks on MRS (0.9-1.3 ppm). At intermediate-TE, lactate presents as a characteristic inverted doublet peak, whereas with short- and long-TE, it presents as an upright doublet peak (Figures 2b and 2c). Conversely, lipid peak presents as a single peak on short-TE scans and is not detectable on long-TE sequences.

DIFFUSION TENSOR IMAGING

The cerebral WM consists of a vast number of intercrossing tracts that enable communication between different parts of the brain. Conventional MRI is limited in its ability to identify individual WM tracts and the WM is seen only as a single conglomerate entity. Microscopically, WM displays anisotropy and impedes diffusion in the direction perpendicular to its axon fibres, while diffusion is relatively unhindered in the direction parallel to its fibres. Based on this property, DTI produces fractional anisotropy maps of the WM that can be colour-coded to indicate the direction of the diffusion tensor. With the help of fibre-tractography, this information can be used to produce a 3-dimensional map of WM tracts of the brain.

The most commonly used technique for DTI is pulsed-gradient-spin-echo with echo-planar imaging readout. The quality of the DTI is affected by the number of directions, number of averages, and the voxel size (Figure 3). The minimal number of directions is six. Increasing the number of directions and number of averages increases the accuracy of the DTI, but this also increases scan time. Increasing the voxel size can increase signal-to-noise ratio of the DTI, but this comes at a cost of reduced spatial resolution.

Fibre-tractography is used to identify individual WM tracts based on data from DTI. Methods of fibre-tractography are mainly based on either deterministic or probabilistic algorithms. Limited ability in resolving regions of crossing fibres is one of the pitfalls of fibre-

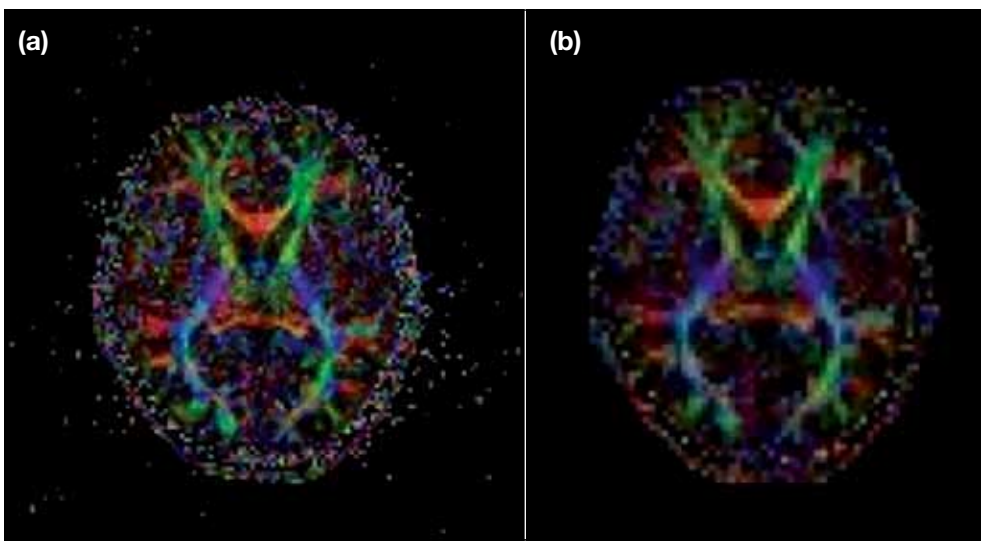

Figure 3. Difference in image quality for coloured-fractional anisotropy maps for diffusion-tensor imaging by varying imaging protocols: (a) 2-mm iso-voxel, 3 averages, 20 directions (scan time: approximately 7 minutes); (b) 3-mm iso-voxel, 2 averages, 20 directions (scan time: approximately 5 minutes).

tractography. Post-processing is also quite time-consuming, relative to the DTI scan time. Nonetheless, with continuing technological improvements, software with more user-friendly interfaces and faster data manipulation capabilities are becoming increasingly available for localisation of WM tracts. In practice, reconstruction of a number of major projectional (e.g. corticospinal tract), association (e.g. arcuate fasciculus, which connects Broca's area with Wernicke's area), and commissural pathways (e.g. corpus callosum) is now achievable using fibre-tractography (Figure 4). Many systems also allow integration of the tractography data into neuro-navigation and radiotherapy-planning systems for guiding surgery and radiotherapy planning to minimise damage to critical structures.

Besides treatment planning, DTI also has a role in assessing functional impairment of disease. This is

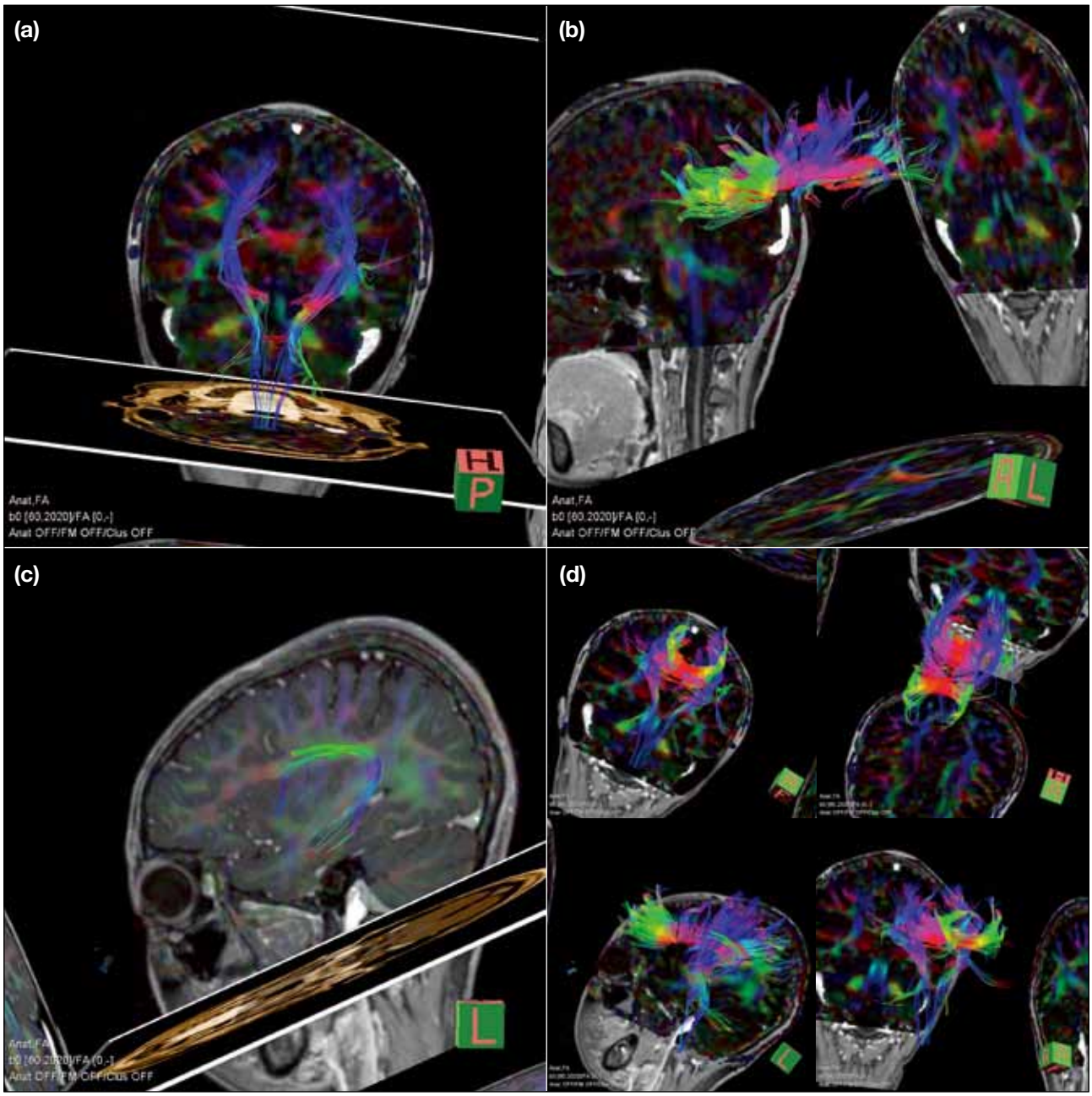

Figure 4. Diffusion tensor imaging fibre-tractography showing (a) the corticospinal tract, (b) the corpus callosum, (c) the arcuate fasciculus, and (d) the anatomical relationships of the corticospinal tract, corpus callosum, and arcuate fasciculus.

particularly useful in paediatric patients, as some of them may be too young to effectively communicate their symptoms and the physical examination findings may be non-revealing. Figure 5a shows a case of an infant with suspected incontinentia pigmenti who initially presented with haemorrhagic necrosis of the brain, a known association of the condition. Follow-up imaging showed a decrease in T1-weighted (T1W) hyperintensity of the haemorrhagic lesions. DTI showed involvement of bilateral corticospinal tracts and left

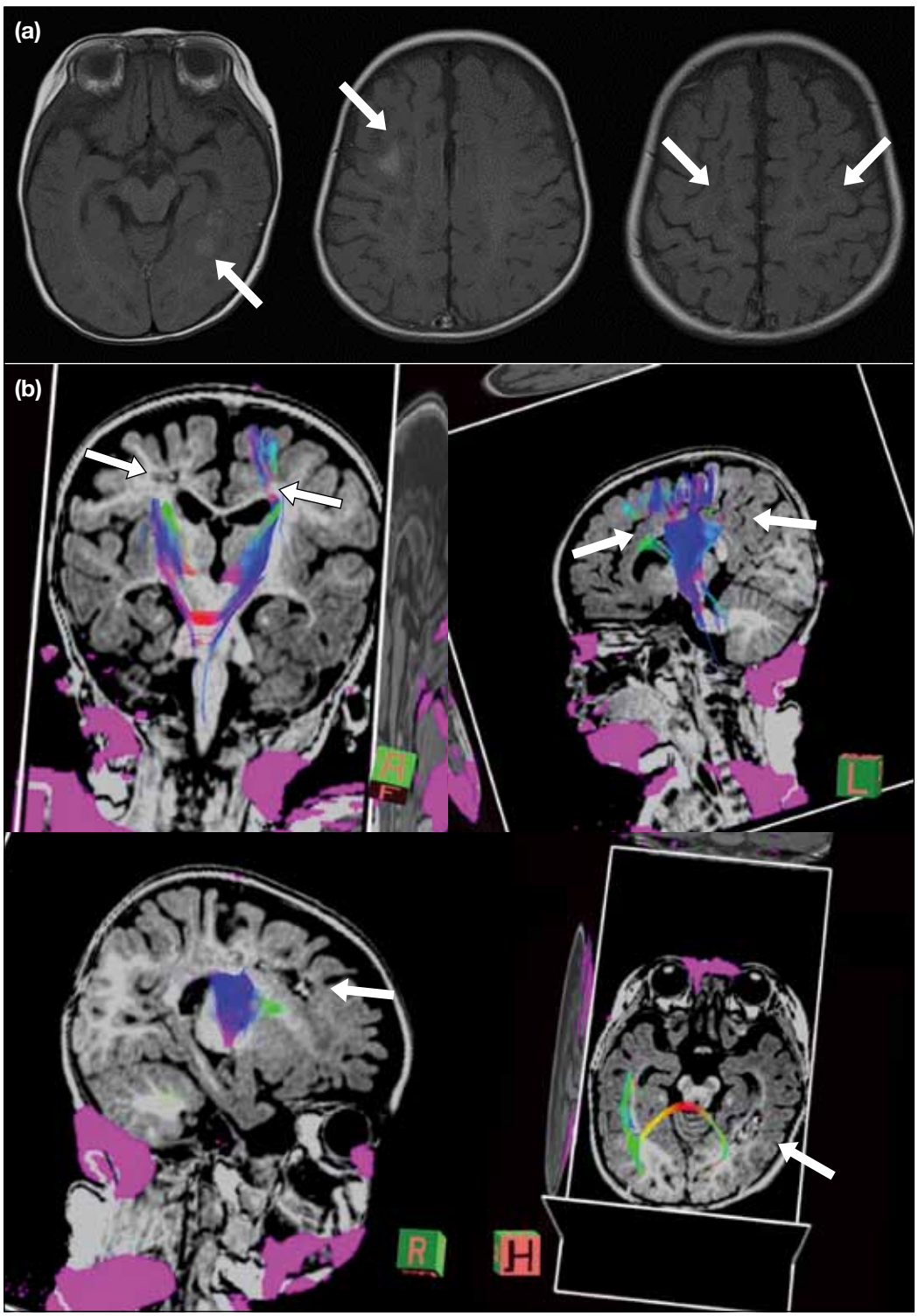

Figure 5. (a) T1-weighted images of a patient with suspected incontinentia pigmenti showing haemorrhagic necrosis (arrows). (b) Fibre-tractography showing involvement of bilateral corticospinal tracts and left inferior longitudinal fasciculus which is composed partly from the optic radiation (arrows).

inferior longitudinal fasciculus that constitutes part of the optic pathway (Figure 5b). Detection of potential involvement of the optic pathway was important in this young patient as this would have been difficult to detect clinically at this early age and the patient would not have been able to volunteer the relevant clinical symptoms to initiate further investigation. The finding on DTI alerted the clinician to the need for formal ophthalmological assessment and follow-up.

Involvement of the corticospinal tract fibres to foot homunculus was seen in our case. Unfortunately, fibres to the hand and oral homunculus could not be assessed on fibre-tractography due to an abundance of crossing fibres in this region. This is a well-known pitfall of clinical DTI. Hopefully, continuing research and development of more advanced diffusion techniques such as Q-ball, HARDI (high-angular-resolution diffusion imaging), and diffusion kurtosis imaging will help to provide improved resolution of crossing fibres in the future.

MAGNETIC RESONANCE CEREBRAL PERFUSION

Assessment of cerebral tissue perfusion is important for paediatric cerebral vascular conditions such as Moyamoya disease and stroke. Some of these patients may require frequent follow-up imaging, hence MRI is an ideal imaging modality due to the lack of radiation.

Magnetic Resonance Perfusion Techniques

MR perfusion can be performed with or without intravenous (IV) contrast. Techniques that require IV contrast include dynamic susceptibility contrast (DSC) MRI and dynamic contrast enhanced (DCE) MRI. These are performed at high contrast flow rates (3-5 ml/s), necessitating large-bore IV access (preferably 18G), hence their use in paediatric cases is usually limited to older children and adolescents.

DSC MR, also known as perfusion-weighted imaging, assesses cerebral perfusion based on T2* signal loss due to the susceptibility effect of gadolinium on the brain parenchyma. From this, information on relative cerebral blood flow (rCBF), mean transit time (MTT), and relative cerebral blood volume (rCBV) is derived. Because DSC is a T2*-based technique, inherent inaccuracies occur near areas with susceptibility artefacts, such as blood, calcification, metal, bone, and air. Errors related to contrast leakage are also concerns for DSC when the blood-brain-barrier is disrupted, such as in high-grade tumours. Leakage correction is required in such cases.

DCE MR, also known as permeability imaging, is a T1-based method assessing the contrast wash-in, plateau, washout, and the permeability characteristics of the brain parenchyma. Derived parameters including Ktrans (transfer constant), Kep (rate constant), and Ve (fractional volume of the extravascular space) are useful in neuro-oncological assessment. T1 DCE is less sensitive to effects of susceptibility artefacts compared with T2* DSC and provides higher spatial resolution. Complex pharmacokinetic modelling, however, is required to derive the permeability measurements and errors may be introduced due to multiple assumptions made during pharmacokinetic modelling and longer scan time needed compared with DSC.

Currently, arterial spin labelling (ASL) is the only technique available for assessing cerebral perfusion without IV contrast. This is suitable for neonates and young children in whom obtaining large-bore IV access is difficult. The basis of ASL perfusion relies on magnetically tagging arterial blood water protons before they enter the brain. The brain parenchyma is then imaged in the labelled and control (i.e. unlabelled) state. The difference reflects the CBF of the brain tissue. The two most common approaches for ASL include pulsed-ASL and continuous-ASL. Differences in the two techniques are summarised in Table 2. Although ASL is desirable in that it is entirely non-invasive,

Table 2. Differences between common arterial spin labelling (ASL) techniques.

	Pulsed-ASL	Continuous-ASL
Method	Short RF pulses to label a thick slab of spins in tagging plane	Long continuous RF pulses with a constant gradient field to induce flow-driven labelling in narrow plane of spins
Advantages	Higher labelling efficiency Lower SAR	Higher SNR Shorter transit delay

Abbreviations: RF = radiofrequency; SAR = specific absorption rate; SNR = signal-to-noise ratio.

there are disadvantages compared with IV-contrast MR perfusion techniques. First, ASL has significantly lower signal-to-noise ratio, temporal, and spatial resolution. It also requires a longer scanning time, which increases the risk of motion artefacts. ASL may underestimate CBF in patients with severe ischaemia due to relaxation of spin label in cases of prolonged arterial transit times. Lastly, CBF is the only parameter that can be derived from ASL. Other parameters obtainable from contrast MR perfusion, such as MTT and CBV, are not currently available for clinical use, although there is a lot of ongoing research in this area. Hopefully, these parameters will become available in the future.

Application of Magnetic Resonance Perfusion in Cerebral Vasculopathies

ASL and DSC are valuable tools for evaluating disease progress, the need for surgery, and the treatment response in cerebral vasculopathies. Figure 6a shows the time-of-flight MR angiography (TOF-MRA) of a young child with Moyamoya syndrome associated with neurofibromatosis. ASL permitted assessment of perfusion without the need for IV access or contrast and was ideal for a patient of this young age (Figure 6b). TOF-MRA showed multifocal narrowing and occlusion over bilateral terminal internal carotid arteries and middle cerebral arteries (MCAs), more severe on the left side. Development of collaterals from the lenticulostriate branches and posterior circulation was noted, signified by regions of relative hyperperfusion on the left basal ganglia and periventricular regions on ASL. A region of hypoperfusion, nonetheless, was still noted over the high left parietal region despite collaterals. After discussion, the case was thought to warrant surgery and subsequently synangiosis was performed for this patient.

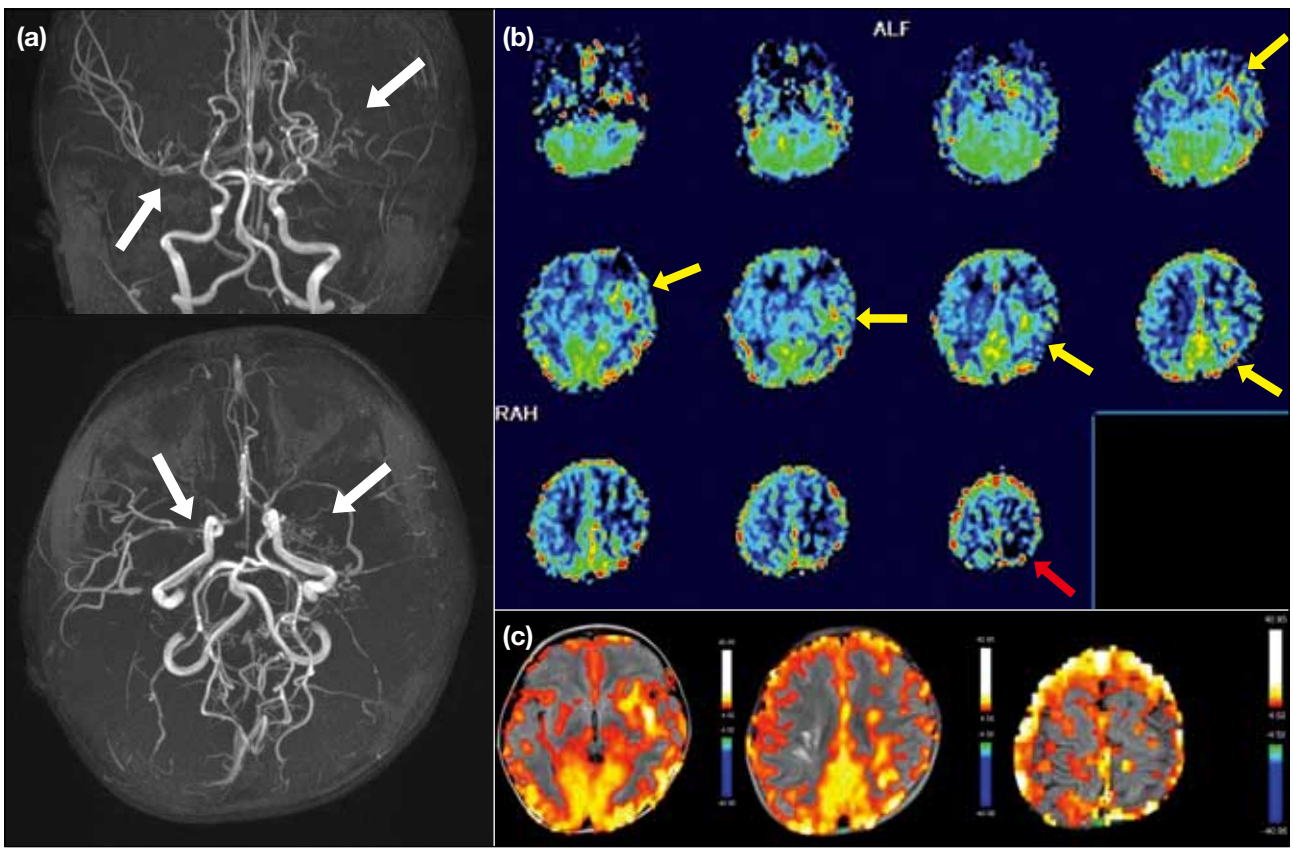

Figure 6. (a) Time-of-flight magnetic resonance (MR) angiography of a patient with Moyamoya syndrome due to underlying neurofibromatosis showing occlusion and narrowing over bilateral terminal internal carotid arteries and middle cerebral arteries with development of collaterals (arrows). (b) Arterial spin labelling (ASL) perfusion MR showing hyperperfusion at left basal ganglia and periventricular region due to collaterals (yellow arrows) and persistent hypoperfusion at high left parietal region (red arrow). (c) Fusion of ASL perfusion with fluid-attenuated inversion recovery images demonstrating findings described in Figure 6b. In addition, fusion images allow better appreciation of hypoperfusion over the chronic infarct in the right periventricular region.

When conducting MR perfusion study, it is important to perform concurrent MRA and other structural MR sequences for anatomical correlation. This is essential for correct interpretation of the MR perfusion study and avoiding pitfalls such as susceptibility artefacts, altered perfusion due to arteriovenous malformations, stroke, or other concurrent pathology. Fusion of MR perfusion parametric maps with anatomical imaging can be performed and may be helpful for better understanding of pathology (Figure 6c). When appropriate, acetazolamide challenge can be performed for DSC or ASL[9] and is useful for evaluation of cerebral vascular reserve and aids in clinical decision-making for surgery.

Other Applications of Magnetic Resonance Perfusion in Paediatric Patients

The invention of ASL provides a promising method for assessment of hypoxic ischaemic injury (HII) in neonates, in whom vascular access is difficult. Studies have shown that patients having HII demonstrate hyperperfusion at regions of restricted diffusion.[10] Together with MRS, ASL has also been shown to be a predictor of clinical outcome.[11] Furthermore, it has been suggested that ASL may have a role in stratifying the use of hypothermic therapy and adjunctive neuroprotective therapy for patients with HII.[10]

Stroke is another important potential application of

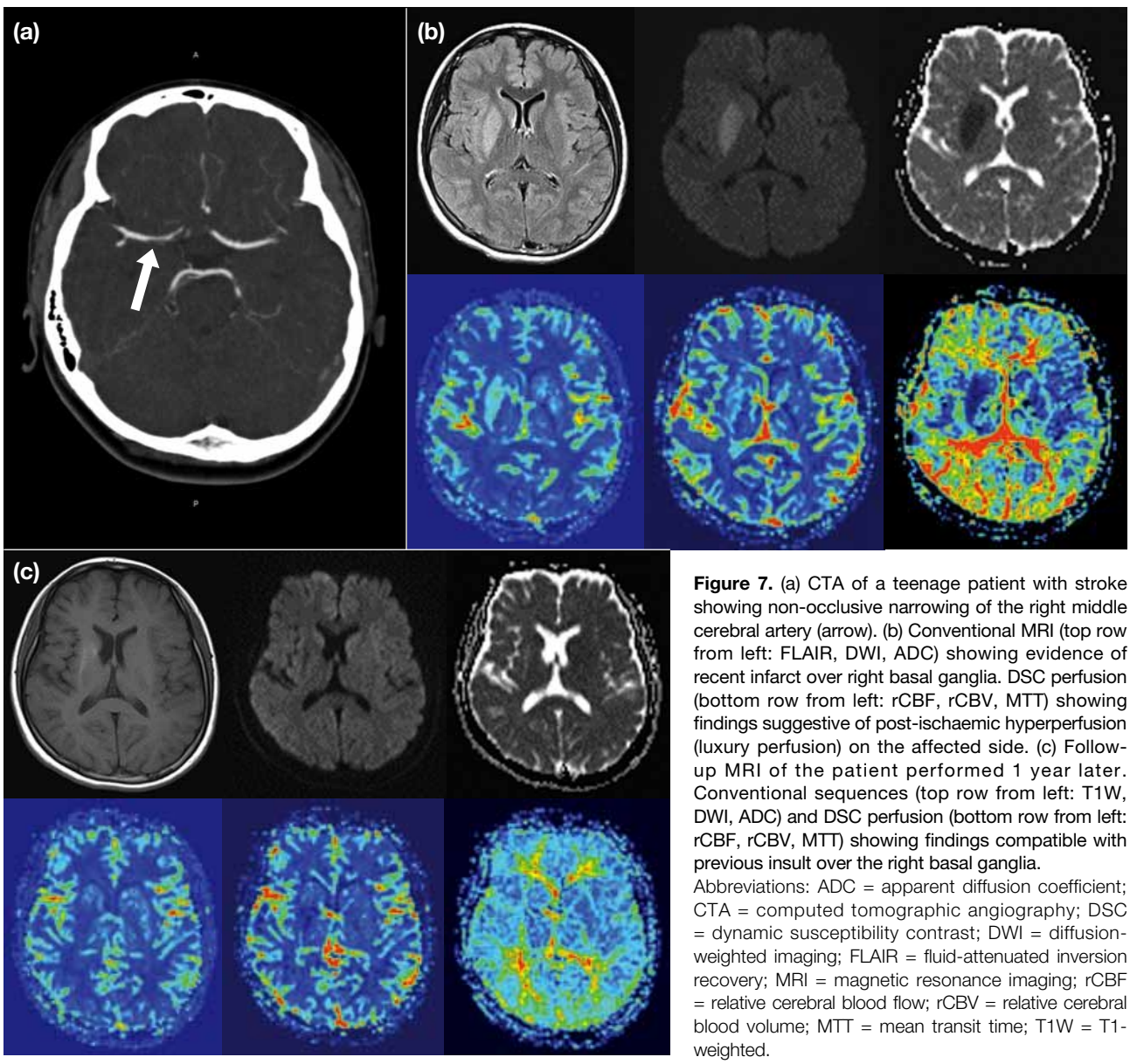

Figure 7. (a) CTA of a teenage patient with stroke showing non-occlusive narrowing of the right middle cerebral artery (arrow). (b) Conventional MRI (top row from left: FLAIR, DWI, ADC) showing evidence of recent infarct over right basal ganglia. DSC perfusion (bottom row from left: rCBF, rCBV, MTT) showing findings suggestive of post-ischaemic hyperperfusion (luxury perfusion) on the affected side. (c) Follow-up MRI of the patient performed 1 year later. Conventional sequences (top row from left: T1W, DWI, ADC) and DSC perfusion (bottom row from left: rCBF, rCBV, MTT) showing findings compatible with previous insult over the right basal ganglia.
Abbreviations: ADC = apparent diffusion coefficient; CTA = computed tomographic angiography; DSC = dynamic susceptibility contrast; DWI = diffusion-weighted imaging; FLAIR = fluid-attenuated inversion recovery; MRI = magnetic resonance imaging; rCBF = relative cerebral blood flow; rCBV = relative cerebral blood volume; MTT = mean transit time; T1W = T1-weighted.

MR perfusion. Figure 7 shows the imaging findings of a teenage patient who presented with left limb weakness. Computed tomographic angiography showed non-occlusive narrowing of the right MCA (Figure 7a). MRI demonstrated restricted diffusion over the right basal ganglia, compatible with recent infarction (Figure 7b). DSC perfusion showed findings suggestive of post-ischaemic hyperperfusion (luxury perfusion) as evidenced by raised rCBF, rCBV and normal-to-reduced MTT. The patient was treated with medication. Subsequent digital subtraction angiography and MRA showed interval reduction in MCA narrowing. The patient recovered without significant deficit. Follow-up MRI performed 1 year later showed T1W hyperintensity and reduced rCBF and rCBV over the right basal ganglia, compatible with prior insult (Figure 7c). In adults, MR / computed tomography perfusion have established roles in determining the treatment of acute stroke. The size of the infarct core versus the tissue at risk (ischaemic penumbra) has implications for the benefits and risks (reperfusion haemorrhage) of revascularisation therapy. Compared with adults, stroke is a relatively rare condition in the paediatric population. The aetiologies, ability for vascular collateralisation and neuroplasticity may differ between paediatric and adult subjects.[12] MR perfusion may help to increase our understanding of paediatric stroke. Further research is needed to elucidate the role of MR perfusion and its relevance in guiding management in this age-group.

MR perfusion may also help in the assessment of epileptic conditions. It has been demonstrated that in conditions such as mesial temporal epilepsy, the epileptogenic side displays decreased CBF during the interictal phase MRI and increased CBF during the ictal phase of the seizure.[13] In terms of technique, both ASL and DSC display a high degree of correlation for lateralisation of the epileptic focus in temporal lobe epilepsy.[14] With advances in spatial resolution of MR perfusion and fusion techniques, this additional functional information will be useful for determining the site of epileptic focus in cases where conventional MRI is indeterminate.

Another potential application of MR perfusion in children is tumours. In adults, DSC and DCE have well-established roles in tumour grading, detection of tumour recurrence, and differentiation from post-radiotherapy changes. The literature on perfusion studies of cerebral tumours in paediatric-specific populations is relatively sparse. This may be related to difficult IV access, thus limiting the use of contrast-based perfusion methods. As a relatively new technique, ASL currently lacks parameters comparable with DSC such as CBV although these are under development.[15,16] Some reports have suggested that there may be potential roles of MR perfusion in detecting tumour recurrence after radiation treatment[17] and planning biopsy routes.[16,18] More research is needed to elucidate the role of MR perfusion in children, as the spectrum of tumours that occur in the paediatric population is diverse and distinct from that of the adult population. The location of tumours in children is also significantly different, with tumours occurring more abundantly in the posterior fossa compared with adults. Studies of differences in tumour biology and the need for modifications in imaging technique in relation to tumour location may be necessary to obtain optimal results for assessment.

CONCLUSION

Advanced neuroimaging techniques including MRS, DTI, and MR perfusion are useful to increase our understanding of cerebral WM pathology and evaluation of cerebral perfusion. These are useful aids for diagnosis and treatment planning in paediatric patients.

REFERENCES

1. Hourani R, Horská A, Albayram S, Brant LJ, Melhem E, Cohen KJ, et al. Proton magnetic resonance spectroscopic imaging to differentiate between nonneoplastic lesions and brain tumors in children. J Magn Reson Imaging. 2006;23:99-107. cross ref
2. Horská A, Barker PB. Imaging of brain tumors: MR spectroscopy and metabolic imaging. Neuroimaging Clin N Am. 2010;20:293-310. cross ref
3. Kimura H, Fujii Y, Itoh S, Matsuda T, Iwasaki T, Maeda M, et al. Metabolic alterations in the neonate and infant brain during development: evaluation with proton MR spectroscopy. Radiology. 1995;194:483-9. cross ref
4. Kendall GS, Melbourne A, Johnson S, Price D, Bainbridge A, Gunny R, et al. White matter NAA/Cho and Cho/Cr ratios at MR spectroscopy are predictive of motor outcome in preterm infants. Radiology. 2014;271:230-8. cross ref
5. Robertson NJ, Cox IJ. Magnetic resonance spectroscopy of the neonatal brain. In: Rutherford MA, editor. MRI of the neonatal brain. London: WB Saunders; 2002. p 295-313.
6. Mano T, Ono J, Kaminaga T, Imai K, Sakurai K, Harada K, et al. Proton MR spectroscopy of Sjögren-Larsson's syndrome. AJNR Am J Neuroradiol. 1999;20:1671-3.
7. Willemsen MA, Van Der Graaf M, Van Der Knaap MS, Heerschap A, Van Domburg PH, Gabreëls FJ, et al. MR imaging and proton MR spectroscopic studies in Sjögren-Larsson syndrome: characterization of the leukoencephalopathy. AJNR Am J Neuroradiol. 2004;25:649-57.
8. Saneto RP, Friedman SD, Shaw DW. Neuroimaging of mitochondrial disease. Mitochondrion. 2008;8:396-413. cross ref
9. Deibler AR, Pollock JM, Kraft RA, Tan H, Burdette JH, Maldjian JA. Arterial spin-labeling in routine clinical practice, part 2: hypoperfusion patterns. AJNR Am J Neuroradiol. 2008;29:1235-

41. cross ref
10. Wintermark P, Hansen A, Gregas MC, Soul J, Labrecque M, Robertson RL, et al. Brain perfusion in asphyxiated newborns treated with therapeutic hypothermia. AJNR Am J Neuroradiol. 2011;32:2023-9. cross ref
11. De Vis JB, Hendrikse J, Petersen ET, de Vries LS, van Bel F, Alderliesten T, et al. Arterial spin-labelling perfusion MRI and outcome in neonates with hypoxic-ischemic encephalopathy. Eur Radiol. 2015;25:113-21. cross ref
12. Amlie-Lefond C, Sébire G, Fullerton HJ. Recent developments in childhood arterial ischaemic stroke. Lancet Neurol. 2008;7:425-35. cross ref
13. Wolf RL, Alsop DC, Levy-Reis I, Meyer PT, Maldjian JA, Gonzalez-Atavales J, et al. Detection of mesial temporal lobe hypoperfusion in patients with temporal lobe epilepsy by use of arterial spin labeled perfusion MR imaging. AJNR Am J Neuroradiol. 2001;22:1334-41.
14. Oner AY, Eryurt B, Ucar M, Capraz I, Kurt G, Bilir E, et al. pASL versus DSC perfusion MRI in lateralizing temporal lobe epilepsy. Acta Radiol. 2015;56:477-81. cross ref
15. Koob M, Girard N. Cerebral tumors: specific features in children. Diagn Interv Imaging. 2014;95:965-83. cross ref
16. Yeom KW, Mitchell LA, Lober RM, Barnes PD, Vogel H, Fisher PG, et al. Arterial spin-labeled perfusion of pediatric brain tumors. AJNR Am J Neuroradiol. 2014;35:395-401. cross ref
17. Ball WS Jr, Holland SK. Perfusion imaging in the pediatric patient. Magn Reson Imaging Clin N Am. 2001;9:207-30, ix.
18. Cha S. Dynamic susceptibility-weighted contrast-enhanced perfusion MR imaging in pediatric patients. Neuroimaging Clin N Am. 2006;16:137-47, ix. cross ref