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Commentary

Harnessing Neuroimaging Capability in Pediatric Stroke: Proceedings of the Stroke Imaging Laboratory for Children Workshop

Nomazulu Dlamini MD, PhD [a,*], Max Wintermark MD [b], Heather Fullerton MD [c,d], Stephen Strother PhD [e], Wayne Lee MSc [a], Bruce Bjornson MD [f,g], Kristin P. Guilliams MD [h,i], Steven Miller MD [a], Adam Kirton MD [j,k], Christopher G. Filippi MD [l,m], Alexandra Linds MSc [a], Rand Askalan MD, PhD [a], Gabrielle deVeber MD [a]

[a] *Division of Neurology, Department of Pediatrics, The Hospital for Sick Children, University of Toronto, Toronto, Ontario, Canada*
[b] *Division of Neuroradiology, Department of Radiology, Stanford University, Stanford, California*
[c] *Department of Neurology, University of California, San Francisco, San Francisco, California*
[d] *Department of Pediatrics, University of California, San Francisco, San Francisco, California*
[e] *Department of Medical Biophysics, Rotman Research Institute at Baycrest, University of Toronto, Toronto, Ontario, Canada*
[f] *Department of Pediatrics, University of British Columbia, Vancouver, British Columbia, Canada*
[g] *Developmental Neurosciences and Child Health, Child and Family Research Institute, Vancouver, British Columbia, Canada*
[h] *Division of Pediatric Neurology, Department of Neurology, Washington University in St. Louis, St. Louis, Missouri*
[i] *Division of Critical Care Medicine, Department of Pediatrics, Washington University in St. Louis, St. Louis, Missouri*
[j] *Department of Pediatrics, Alberta Children's Hospital Research Institute, Cumming School of Medicine, University of Calgary, Calgary, Alberta, Canada*
[k] *Department of Clinical Neurosciences, Alberta Children's Hospital Research Institute, Cumming School of Medicine, University of Calgary, Calgary, Alberta, Canada*
[l] *Department of Radiology, Northwell Health, Manhasset, New York*
[m] *Department of Neurology, University of Vermont Medical Center, Burlington, Vermont*

ABSTRACT

On June 5, 2015 the International Pediatric Stroke Study and the Stroke Imaging Laboratory for Children cohosted a unique workshop focused on developing neuroimaging research in pediatric stroke. Pediatric neurologists, neuroradiologists, interventional neuroradiologists, physicists, nurse practitioners, neuropsychologists, and imaging research scientists from around the world attended this one-day meeting. Our objectives were to (1) establish a group of experts to collaborate in advancing pediatric neuroimaging for stroke, (2) develop consensus clinical and research magnetic resonance imaging protocols for pediatric stroke patients, and (3) develop imaging-based research strategies in pediatric ischemic stroke. This article provides a summary of the meeting proceedings focusing on identified challenges and solutions and outcomes from the meeting. Further details on the workshop contents and outcomes are provided in three additional articles in the current issue of Pediatric Neurology.

Keywords: pediatric, stroke, neuroimaging, MRI, diffusion, perfusion, cerebrovascular reactivity

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Introduction

Pediatric arterial ischemic stroke (AIS), defined by focal infarction within a vascular territory, occurs in one in 3500 live births and 1 to 3 per 100,000 children per year.[1,2] Pediatric AIS remains one of the top ten causes of death

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* Communications should be addressed to: Dr. Dlamini; Stroke Program; Division of Neurology; The Hospital for Sick Children; 555 University Avenue; Toronto, Canada.
E-mail address: nomazulu.dlamini@sickkids.ca

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and lifelong disability in childhood. The socioeconomic impact of pediatric stroke is significant.[3-5]

Brain injury because of AIS results from arterial occlusion, critical decrease in regional perfusion, and focal brain tissue ischemia. Within the focal ischemic zone complex molecular and tissue changes occur. After acute ischemic infarction, at least some functional recovery occurs related to compensatory brain rewiring and repair. Characterization of these mechanisms from infancy to adult years is an important area of research. Emerging research-based imaging techniques can further expand our understanding of the mechanisms underlying focal ischemic injury and repair within the developing brain. An enhanced understanding of these mechanisms will ultimately help us to develop novel treatment approaches aimed at minimizing injury and enhancing mechanisms of repair, thereby improving outcomes in pediatric AIS (Table).

Although similar clinical challenges (timely detection and targeted therapy) exist in AIS across pediatric and adult patients, differences in mechanisms of stroke pathogenesis, injury, and repair likely exist. Clinical management relies upon appropriate neuroimaging to provide specific diagnosis, etiological classification, and patient selection for possible therapies. Yet imaging strategies that are feasible in adults present specific challenges in infants and children. This workshop was convened to harness opportunities for developing systematic and collaborative research to address the unique aspects of imaging in the pediatric stroke population.

The Stroke Imaging Laboratory for Children (SILC) cohosted the meeting in collaboration with the International Pediatric Stroke Study.[6] SILC was recently established at the Hospital for Sick Children Research Institute to advance imaging research in pediatric stroke. Leveraging the latest imaging technology, SILC aims to employ synergistic neuroimaging techniques to provide new insights into pediatric stroke. Consistent with these aims, Part I of the workshop consisted of slide presentations that emphasized (1) acute practical imaging needs and solutions; (2) imaging of acute pathogenesis; (3) stroke lesion delineation; (4) imaging stroke impact: recovery and plasticity; and (5) building a collaborative network. Part II of the day consisted of breakout sessions with working groups focused on three main objectives: (1) establishing a group of experts to collaborate in advancing imaging; (2) developing consensus-based clinical and research magnetic resonance imaging (MRI) protocols; and (3) developing and sharing imaging-based research strategies in pediatric AIS. A major outcome of the workshop was the development of four complementary articles designed to address the aforementioned objectives. The current article presents the overview of the meeting and the framework from which the other more specific articles were developed.[7-10]

TABLE.
Imaging Stroke Mechanisms

Cerebral Artery Wall Pathology	Wall Imaging MRI
Cerebral artery lumen (e.g., occlusion)	MRA
Perfusion drop	Perfusion imaging, CVR, SWI
Brain tissue cell death	DWI, DKI
Recanalization	MRA
Reperfusion	Perfusion imaging, CVR
Blood-brain barrier breakdown	Gadolinium enhancement
Hemorrhagic conversion of bland infarct	SWI
Neuronal salvage	??
Reperfusion injury	DCE
Plasticity and repair	fMRI, MEG
Rewiring	DTI

Abbreviations:
CVR = Cerebrovascular reactivity
DCE = Dynamic contrast enhancement
DKA = Diffusion kurtosis imaging
DTI = Diffusion tensor imaging
DWI = Diffusion-weighted imaging
fMRI = Functional magnetic resonance imaging
MEG = Magnetoencephalography
MRA = Magnetic resonance angiogram
MRI = Magnetic resonance imaging
SWI = Susceptibility-weighted imaging
?? = Requires further research

Pediatric stroke: Overview, clinical challenges, and imaging solutions

Part I of the day consisted of presentations that outlined the challenges and potential imaging solutions to timely diagnosis, treatment selection, and recognition of the pathogenesis of pediatric AIS in the acute setting.

Imaging for stroke diagnosis—the acute infarct and penumbra

The differential diagnosis of acute onset focal neurological symptoms in childhood is broad, posing a challenge to accurate and timely diagnosis of pediatric AIS.[11,12] Specific imaging confirmation of stroke is necessary. In adults, the differential diagnosis of acute focal deficits is narrow and cranial computed tomography (CT) imaging to rule out bleeding is the standard initial imaging modality. However, CT has limited sensitivity for pediatric AIS, missing 50% to 80% of lesions verified by MRI.[13] Exposure to ionizing radiation is an additional consideration in the developing brain.[14] Accordingly, MRI has emerged as the modality of choice for the initial diagnosis of pediatric AIS. Diffusion-weighted imaging (DWI) utilizes the diffusion properties of water to interrogate cellular integrity and injury.[15,16] Animal and human studies have shown that ischemic injury and restricted diffusion become evident on diffusion-weighted MRI when cerebral blood flow (CBF) falls below 20 mL per 100 g/minute. Thus diffusion restriction on MRI in pediatric AIS is meant to represent irreversibly infarcted tissue or the ischemic core. Outside the ischemic core, where CBF reduction may not have reached this critical threshold, DWI remains normal but perfusion-weighted imaging (PWI) is abnormal. This finding is the neuroimaging equivalent of the penumbra, which is potentially viable, but vulnerable tissue that may provide a therapeutic target for recanalization and neuroprotective care in acute ischemic stroke.[17,18]

Identification of patients most likely to benefit from recanalization and neuroprotection care requires perfusion imaging. The main MR perfusion techniques used in adults, including T2* dynamic susceptibility contrast imaging and T1 dynamic contrast enhancement, require the use of gadolinium contrast agents. The invasive nature of the contrast