The Role of Neuroimaging in the Clinical Management of Concussion and Traumatic Brain Injury: Current Status and Future Directions

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Pan Am Concussion Program
2017 UHN TBI Meeting
Disclosures

• Funding sources: Pan Am Clinic Foundation, Manitoba Health Research Council, HSC Foundation, Manitoba Public Insurance, University of Manitoba Department of Surgery, Thorlakson Fund

• No additional disclosures.
Objectives

• To discuss the clinical role of conventional neuroimaging in the evaluation and management of concussion and TBI

• To review the potential role of novel neuroimaging assessment tools in the evaluation and management of concussion and TBI

• To identity obstacles that must be overcome for novel neuroimaging tools to bridge the gap between understanding and managing concussion
Case

• 15 year old female athlete
• Cycling accident
• +LOC, post-traumatic amnesia
• 5 months later presents with global headaches, dizziness, and fatigue
• Physical examination:
  – Normal: no evidence of vestibulo-ocular dysfunction or cervical spine injury
• Management? Neuroimaging?
**Neuroimaging**

**Conventional neuroimaging:**
- Computerized tomography
- Magnetic resonance imaging

**Advanced neuroimaging**
- Diffusion tensor imaging
- Functional MRI
- Cerebrovascular imaging
Computerized tomography (CT):

**Strengths**
- Widely available
- Short acquisition time
- Easy to interpret

**Limitations**
- Exposure to radiation
- Poorer contrast resolution compared to MRI
Common Findings in TBI

## Marshall CT Classification of Brain Injury

<table>
<thead>
<tr>
<th>Diffuse Injury Grade</th>
<th>CT Findings</th>
<th>Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Normal</td>
<td>9.6%</td>
</tr>
<tr>
<td>II</td>
<td>Cisterns present, midline shift&lt; 5mm</td>
<td>13.5%</td>
</tr>
<tr>
<td>III</td>
<td>Cisterns compressed/absent, midline shift&lt; 5mm</td>
<td>34%</td>
</tr>
<tr>
<td>IV</td>
<td>Midline shift&gt; 5mm</td>
<td>56.2%</td>
</tr>
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</table>
Rotterdam CT Classification

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Basal cisterns</td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>0</td>
</tr>
<tr>
<td>Compressed</td>
<td>1</td>
</tr>
<tr>
<td>Absent</td>
<td>2</td>
</tr>
<tr>
<td>Midline shift</td>
<td></td>
</tr>
<tr>
<td>No shift or shift ≤5 mm</td>
<td>0</td>
</tr>
<tr>
<td>Shift &gt;5 mm</td>
<td>1</td>
</tr>
<tr>
<td>Epidural mass lesion</td>
<td></td>
</tr>
<tr>
<td>Present</td>
<td>0</td>
</tr>
<tr>
<td>Absent</td>
<td>1</td>
</tr>
<tr>
<td>Intraventricular blood or subarachnoid hemorrhage</td>
<td></td>
</tr>
<tr>
<td>Absent</td>
<td>0</td>
</tr>
<tr>
<td>Present</td>
<td>1</td>
</tr>
<tr>
<td>Sum score</td>
<td>+1</td>
</tr>
</tbody>
</table>

In the Rotterdam scoring system, 1 point is added as a sum score to make the Rotterdam grade numerically total 6 points, consistent with the motor score of the Glasgow Coma Scale and the Marshall classification. From Maas AI, Hukkelhoven CW, Marshall LF, Steyerberg EW. Prediction of outcome in traumatic brain injury with computed tomographic characteristics: a comparison between the computed tomographic classification and combinations of computed tomographic predictors. Neurosurgery. 2005;57(6):1173–1182.
Mild TBI

CATCH: a clinical decision rule for the use of computed tomography in children with minor head injury

Martin H. Osmond MD CM, Terry P. Klassen MD, George A. Wells PhD, Rhonda Correll RN, Anna Jarvis MD, Gary Joubert MD, Benoit Bailey MD, Laurel Chauvin-Kimoff MD CM, Martin Pusic MD, Don McConnell MD, Cheri Nijssen-Jordan MD, Norm Silver MD, Brett Taylor MD, Ian G. Stiell MD; for the Pediatric Emergency Research Canada (PERC) Head Injury Study Group

- GCS 13-15, LOC, amnesia, disorientation, vomiting or irritability
- 3866 pediatric patients enrolled
- 159 (4.1%) had CT evidence of brain injury
- 24 (0.6%) underwent a neurosurgical intervention

Osmond et al., CMAJ, 2010
Prevalence of abnormal CT-scans following mild head injury

GRANT L. IVERSON†, MARK R. LOVELL‡, STANLEY SMITH§ and MICHAEL D. FRANZEN§

• GCS 13-15
• 912 adult patients enrolled
• 59% MVA
• 16-21% had positive CT findings
Children

CT of the head is required only for children with minor head injury* and any one of the following findings:

**High risk (need for neurologic intervention)**
1. Glasgow Coma Scale score < 15 at two hours after injury
2. Suspected open or depressed skull fracture
3. History of worsening headache
4. Irritability on examination

**Medium risk (brain injury on CT scan)**
5. Any sign of basal skull fracture (e.g., hemotympanum, “raccoon” eyes, otorrhea or rhinorrhea of the cerebrospinal fluid, Battle’s sign)
6. Large, boggy hematoma of the scalp
7. Dangerous mechanism of injury (e.g., motor vehicle crash, fall from elevation ≥ 3 ft [≥ 91 cm] or 5 stairs, fall from bicycle with no helmet)

Note: CT = computed tomography.
*Minor head injury is defined as injury within the past 24 hours associated with witnessed loss of consciousness, definite amnesia, witnessed disorientation, persistent vomiting (more than one episode) or persistent irritability (in a child under two years of age) in a patient with a Glasgow Coma Scale score of 13–15.

Osmond et al., CMAJ, 2010

Adults

**Canadian CT Head Rule**
CT head is only required for minor head injury patients with any one of these findings:

**High Risk (for Neurological Intervention)**
1. GCS score < 15 at 2 hrs after injury
2. Suspected open or depressed skull fracture
3. Any sign of basal skull fracture*
4. Vomiting ≥ 2 episodes
5. Age ≥ 65 years

**Medium Risk (for Brain Injury on CT)**
6. Amnesia before impact ≥ 30 min
7. Dangerous mechanism ** (pedestrian, occupant ejected, fall from elevation)

*Signs of Basal Skull Fracture
- hemotympanum, “raccoon” eyes, CSF otorrhea/rhinorrhea, Battle’s sign
** Dangerous Mechanism
- pedestrian struck by vehicle
- occupant ejected from motor vehicle
- fall from elevation ≥ 3 feet or 5 stairs

Rule not applicable if:
- Non-trauma cases
- GCS ≥ 13
- Age < 10 years
- Cerebral or bleeding disorder
- Obvious open skull fracture

Summary

Computerized tomography:

• Most commonly used neuroimaging tool used in initial evaluation of TBI patients

• Abnormal findings observed in 4-30% of mTBI patients

• Use of CT should be restricted to the emergency room setting

• Recommended use according to evidence-based clinical decision-making rules
Magnetic resonance imaging (MRI):

**Strengths**
- Superior resolution

**Limitations**
- Less accessible
- Longer acquisition time
- Contraindications
- Greater cost
Gradient recalled echo & susceptibility-weighted imaging:

- Enhanced sensitivity to cerebral micro-hemorrhages previously undetected on conventional sequences
Magnetic Resonance Imaging Improves 3-Month Outcome Prediction in Mild Traumatic Brain Injury

Esther L. Yuh, MD, PhD, Pratik Mukherjee, MD, PhD, Hester F. Lingsma, PhD, John K. Yue, BS, Adam R. Ferguson, PhD, Wayne A. Gordon, PhD, Alex B. Valadka, MD, David M. Schnyer, PhD, David O. Okonkwo, MD, PhD, Andrew I. R. Maas, MD, PhD, Geoffrey T. Manley, MD, PhD, and the TRACK-TBI Investigators

• GCS 13-15
• 135 adult patients enrolled
• Day of injury CT, early MRI (mean= 12 days)

• More sensitive than CT for DAI and contusions
• Presence of any contusion or ≥4 hemorrhagic foci on MRI associated with multivariate odd ratio of 3.5 for poorer 3-month outcome after controlling for demographic, clinical, and socioeconomic factors

Ann Neurol, 2013
Structural Neuroimaging Findings in Mild Traumatic Brain Injury

Erin D. Bigler, PhD,*† Tracy J. Abildskov,* Naomi J. Goodrich-Hunsaker, PhD,* Garrett Black, BS,* Zachary P. Christensen, BS,*† Trevor Huff, BS,*† Dawn-Marie G. Wood, MS,† John R. Hesselink, MD,‡ Elisabeth A. Wilde, PhD,§ and Jeffrey E. Max, MBBCh‡||

- Pediatric mTBI Study
- 131 mTBI: GCS 13-15; 66 Orthopedic injured controls
- MRI at 6 month post-injury
- Hemosiderin deposition (3 patients), encephalomalacia (2 patients), white matter changes (4 patients), prominent Virchow-Robin spaces (5 patients)
Conventional CT and MR-imaging is typically normal in SRC patients, and therefore, “contributes little to concussion evaluation.”
Post-concussion syndrome (PCS) in a youth population: defining the diagnostic value and cost-utility of brain imaging

Clinton D. Morgan¹ · Scott L. Zuckerman¹ · Lauren E. King² · Susan E. Beaird² · Allen K. Sills¹ · Gary S. Solomon¹

- 52 PCS patients (imaging obtained in 23 patients)
- 77% sports-related concussion
- 1/8 (13%) CT studies demonstrated skull fracture
- 1/19 (5.3%) MRI studies demonstrated multiple punctate foci within the bilateral frontal, temporal, and parietal lobes
- Clinical indication for imaging- persistent symptoms
151 patients (mean age=14 years, 59% female) were included in this study. Overall, 24% of patients underwent neuroimaging studies (CT, MRI) of which 78% were normal.

11% of neuroimaging studies demonstrated traumatic abnormalities.
Neuroimaging

Arachnoid cyst

Cavum septum pellucidum

Chiari I malformation
Retirement-from-sport considerations following pediatric sports-related concussion: case illustrations and institutional approach

Michael J. Ellis, MD, FRCSC,1,2,5,9 Patrick J. McDonald, MD, MHS, FRCSC,9-11
Dean Cordingley, MSc,9 Behzad Mansouri, MD, PhD, FRCP(C),4,7,9
Marco Essig, MD, PhD, FRCP(C),3,7,9 and Lesley Ritchie, PhD5,7,9

- Abnormalities on neuroimaging
- Focal neurological deficits and abnormalities on clinical exam
- Cumulative or prolonged effects of concussion
## TABLE 1. Summary of our current institutional approach to RTP and retirement considerations in children and adolescents with structural brain abnormalities

<table>
<thead>
<tr>
<th>Clinical Indication</th>
<th>Institutional Approach/RTP Consideration</th>
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<tbody>
<tr>
<td>Traumatic structural brain injury</td>
<td>Retirement from future contact &amp; collision sports participation</td>
</tr>
<tr>
<td>Skull fractures &amp; prior craniotomy for nontraumatic brain lesions</td>
<td>Individualized approach. RTP considered following radiographic evidence of bone healing</td>
</tr>
<tr>
<td>Craniotomy for traumatic lesions (e.g., subdural hematoma, intraparenchymal hemorrhage, second-impact syndrome)</td>
<td>Retirement from future contact &amp; collision sports participation</td>
</tr>
<tr>
<td>Transsphenoidal, endovascular, endoscopic approaches to intracranial lesions</td>
<td>Individualized approach</td>
</tr>
<tr>
<td>Cavum septum pellucidum</td>
<td>No contraindication to safe RTP</td>
</tr>
<tr>
<td>Arachnoid cyst</td>
<td>Individualized approach. Patient must be informed of risk of intracystic hemorrhage, subdural hematoma/hygroma. RTP considered in patients w/ small, asymptomatic, or incidental arachnoid cysts (&lt;5 cm) w/ no or minimal mass effect</td>
</tr>
<tr>
<td>Hydrocephalus</td>
<td>Individualized approach. Patient must be informed of risk of shunt malfunction, hardware damage, subdural hematoma/hygroma. RTP considered in patients treated w/ endoscopic third ventriculostomy</td>
</tr>
<tr>
<td>Chiari Type I malformation</td>
<td>Individualized approach. RTP considered for patients w/ asymptomatic or minimal tonsillar herniation w/ no syrinx. RTP considered in patients w/ foramen magnum decompression w/o associated spinal malformation &amp; instability</td>
</tr>
</tbody>
</table>
Magnetic resonance imaging: Considered in patients with:

- Focal neurological deficits (weakness, numbness, monocular visual deficits)
- Post-traumatic seizures
- Abnormalities on initial CT
- Persistent symptoms that do not respond to conservative management or treatment
- Deficits on formal neuropsychological testing
Future studies are needed…

• To identify which patients benefit from neuroimaging (i.e. clinical indications)

• To evaluate the prognostic value of MRI findings on patient outcomes

• Evidence-based recommendations regarding sports participation in patients with abnormalities detected on conventional MRI
Remember..

- Just because an MRI study is normal does not mean it doesn’t provide value to the patient, their family, and the treating physician.
• 15 year old female athlete
• Cycling accident
• +LOC, post-traumatic amnesia
• PMHx: 3 previous concussions
• 5 months later presents with global headaches, dizziness, and fatigue
• Physical examination:
  – Normal: no evidence of vestibulo-ocular dysfunction or cervical spine injury
• Management? Neuroimaging?
Neuroimaging

Conventional neuroimaging:
• Computerized tomography
• Magnetic resonance imaging

Advanced neuroimaging
• Diffusion tensor imaging
• Functional MRI
• Cerebrovascular imaging
Case

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Clinical Value

Advanced neuroimaging

• Must be able to provide clinically meaningful information that can *not* otherwise be obtained by clinical history & physical examination

• Must provide information about an *individual* patient basis

• Ideally, provides reliable *quantitative* biomarkers that can be used in cross-sectional and longitudinal assessment
Potential uses of advanced neuroimaging in concussion and mTBI:

• Assist diagnosis
• Confirm recovery
• Quantify extent of injury
• Prediction of outcomes
Neuroimaging

Conventional neuroimaging:
- Computerized tomography
- Magnetic resonance imaging

Advanced neuroimaging
- Diffusion tensor imaging
- Functional MRI
- Cerebrovascular imaging
Diffusion tensor imaging (DTI):

- Diffusion is constrained by tissues in the brain and that assessment of this diffusion can provide information about the white matter microstructure.

- Based on assessment of diffusion, a number of quantitative biomarkers can be calculated.

- Fractional anisotropy (FA), radial diffusivity (RD), mean diffusivity (MD), axial diffusivity (AD), trace.
• One of key pathophysiological mechanisms underlying TBI is shear injury to white matter tracts and resultant cerebral micro-hemorrhages, termed diffuse axonal injury.

• DAI has been found in TBI patients of all severities

Adams et al., Histopathology, 1989
• One of key pathophysiological mechanisms underlying TBI is shear injury to white matter tracts and resultant cerebral micro-hemorrhages, termed diffuse axonal injury.

• DAI has been found in TBI patients of all severities
A Longitudinal Diffusion Tensor Imaging Study Assessing White Matter Fiber Tracts after Sports-Related Concussion

- Varsity athletes with SRC vs. normal controls
- DTI within 2 days, 2 weeks, and 2 month post-injury
- ↑ RD and ↓ FA within right hemisphere WMT within 72 hours of injury followed by recovery that may extend beyond 2 weeks.
• Collegiate athletes with SRC vs. normal controls
• DTI within 6 days of injury and at 6 months post-injury
  • ↑ FA and AD ↓ MD within the corpus callosum and right corticospinal tract and right hemisphere WMT compared to controls.
• ↑ FA was found to persist at 6 months
Female athletes with SRC vs. normal controls

DTI at 7 months post-injury

↑ MD within diffuse white matter tracts but no differences in FA.
Diffusion tensor imaging findings are not strongly associated with postconcussional disorder 2 months following mild traumatic brain injury. (Lipton et al., J Head Trauma Rehabil, 2012)

- mTBI patients vs. orthopedically injured controls
- DTI of the corpus callosum at 6-8 weeks post-injury
- No group differences any DTI measures
- No group differences between mTBI patients meeting the ICD-10 criteria for post-concussion syndrome
Longitudinal Assessment of White Matter Abnormalities Following Sports-Related Concussion

Timothy B. Meier, Maurizio Bergamino, Patrick S. F. Bellgowan, T. K. Teague, Josef M. Ling, Andreas Jeromin, and Andrew R. Mayer

• Longitudinal DTI in collegiate SRC patients vs controls
• Imaged at mean 1.64, 8.33, & 32.15 days
• Group and subject-specific analysis demonstrated ↑ FA within several WMT
• No evidence of longitudinal recovery
Diffusion Tensor Imaging Alterations in Patients With Postconcussion Syndrome Undergoing Exercise Treatment: A Pilot Longitudinal Study

Paul Polak, MAsc; John J. Leddy, MD, FACSM, FACP; Michael G. Dwyer, PhD; Barry Willer, PhD; Robert Zivadinov, MD, PhD, FAAN

- 8 patients with PCS, 15 controls
- 4 treated with sub-maximal exercise prescription and 4 treated with stretching
- ↓ FA and ↑ RD and MD within the corpus callosum among PCS group compared to controls
- Despite clinical improvements in exercise tolerance and symptoms in patients treated with exercise there were no longitudinal group differences in DTI indices.
Neuroimaging

Soccer Heading Is Associated with White Matter Microstructural and Cognitive Abnormalities

- Observed ↓ FA within the temporo-occipital white matter in amateur soccer players that were associated with poorer memory scores and a soccer “heading” threshold of 1800/year.
White matter microstructure abnormalities in pediatric migraine patients

Roberta Messina¹,², Maria A Rocca¹,², Bruno Colombo², Elisabetta Pagani¹, Andrea Falini³, Giancarlo Comi² and Massimo Filippi¹,²

- Observed ↓ MD, RD, AD and ↑ FA among pediatric migraine patients compared to controls
Summary

• DTI is capable of demonstrating group (and more recently individual) changes in white matter tracts following mTBI and concussion.

• The anatomical distribution of these changes are variable across studies.

• Natural history of quantitative biomarkers changes following concussion remains unclear.

• Similar changes have been observed in athletes with exposure to sub-clinical head impacts and in other neurological conditions to commonly co-exist among SRC patients.
Case

- 15 year old female athlete
- Cycling accident
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- PMHx: 3 previous concussions
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- Management? Neuroimaging?
Clinical Questions

Conventional neuroimaging:
• Computerized tomography
• Magnetic resonance imaging

Advanced neuroimaging
• Diffusion tensor imaging
• Functional MRI
• Cerebrovascular imaging
Functional MRI (fMRI):

- Spatial measurements of blood oxygen level-dependent (BOLD) MRI signal throughout the brain.
- Task-based: assessing activation patterns within networks that govern performance on behavioral and cognitive tasks.
Functional Brain Abnormalities Are Related to Clinical Recovery and Time to Return-to-Play in Athletes

- High school SRC patients
- fMRI during N-back working memory task within 1 week of injury and again following clinical recovery
- Decreased activation within posterior parietal network correlated with increased symptoms
- Activity within the medial premotor and supplementary motor region was associated with time to recovery
Functional abnormalities in normally appearing athletes following mild traumatic brain injury: a functional MRI study

Semyon M. Slobounov · K. Zhang · D. Pennell · W. Ray · B. Johnson · W. Sebastianelli

- Collegiate SRC patients imaged 30 days post-injury and normal controls
- “virtual corridor” spatial memory task
- No differences in task performance between groups
- SRC patients demonstrated larger activations involving the right dorsolateral prefrontal cortex and cerebellum.
Varsity athletes and controls

fMRI during N-back working memory task within 72 hours, at 2 weeks and at 2 months of injury injury

Persistent hyperactivation within the inferior parietal lobe for two weeks and within the dorsolateral prefrontal cortices for two months among SRC patients
Functionally-Detected Cognitive Impairment in High School Football Players without Clinically-Diagnosed Concussion

Thomas M. Talavage,1,2 Eric A. Nauman,1,3,4 Evan L. Breedlove,1 Umit Yoruk,2 Anne E. Dye,3 Katherine E. Morigaki,5 Henry Feuer,6 and Larry J. Leverenz5

- 11 male highschool football players
- Collision events (HIT system), neurocognitive testing (ImPACT) and fMRI during N-back task
- Baseline and in-season testing
Alterations in fMRI activation patterns among those with concussion and those without a concussion but with neurocognitive deficits.
FMRI activation patterns during a math processing task examined in healthy controls, PCS patients assigned to stretching, and PCS patients assigned to aerobic exercise prescription.

Exercise prescription resulted in improved resting HR and concussion symptoms, increased exercise tolerance, and normalization of activation patterns compared to PCS patients assigned to stretching.
Summary

• fMRI is capable of demonstrating group changes in brain activation patterns following mTBI and concussion.

• Differences in study samples and imaging paradigms limit comparisons between studies

• Changes have been observed in athletes with exposure to sub-clinical head impacts and in other neurological conditions to commonly co-exist among SRC patients.

• Use for longitudinal assessment shows promise
Case

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Clinical Questions

Conventional neuroimaging:
• Computerized tomography
• Magnetic resonance imaging

Advanced neuroimaging
• Diffusion tensor imaging
• Functional MRI
• Cerebrovascular imaging
The maintenance of CBF is one of the most important processes responsible for maintaining brain function during health, disease, and injury.
Cerebrovascular imaging

• Primary brain injury: biomechanical disruption of brain tissue at the time of injury
• Secondary brain injury: cellular, metabolic, inflammatory processes that result in further tissue edema, injury, and resultant neurological deterioration
• 90% of autopsy specimens from patients with fatal TBI show evidence of ischemia (Graham et al., 1971, 1989)

• Clinical studies in moderate and severe TBI demonstrate that alterations in resting global CBF are predictive of poor outcomes (Bouma et al., 1991; Coles et al., 2004; Wintermark et al., 2004).
Cerebrovascular imaging

Giza & Hovda, Journal of Athletic training 2001
Cerebrovascular imaging

Measurement of cerebral blood flow:

• Quantify global and regional cerebral blood flow.

• *Direct CBF measurement*: arterial spin labeling (ASL), pseudo-continuous ASL (pCASL)

• *Indirect CBF measurement*: blood oxygen level-dependent (BOLD) MRI
Pediatric Sports-Related Concussion Produces Cerebral Blood Flow Alterations

**AUTHORS:** Todd A. Maugans, MD, Chad Farley, MD, Mekibib Altaye, PhD, James Leach, MD, and Kim M. Cecil, PhD

- 12 SRC patients (11-15 years) vs controls
- ASL & DTI MRI and ImPACT testing <72 hours, 2 weeks, and >30 days post-injury
- No group differences in DTI indices over any time point or within any regions of interest
- Impaired mean resting CBF in the acute phase that persisted at 1 month despite resolution of symptoms and normalization of neurocognitive testing scores.

Pediatrics 2012;129:28–37
Recovery of Cerebral Blood Flow Following Sports-Related Concussion

Timothy B. Meier, PhD; Patrick S. F. Bellgowan, PhD; Rashmi Singh, PhD; Rayus Kuplicki, PhD; David W. Polanski, MS, ATC, LAT; Andrew R. Mayer, PhD

• 44 collegiate football players including 13-15 with a SRC
• Completed ASL MRI and depression and anxiety rating scales at T1(0-3 d), T2(6-13d), and T3(30 d) post-injury.
Recovery of Cerebral Blood Flow Following Sports-Related Concussion

Timothy B. Meier, PhD; Patrick S. F. Bellgowan, PhD; Rashmi Singh, PhD; Rayus Kuplicki, PhD; David W. Polanski, MS, ATC, LAT; Andrew R. Mayer, PhD

A. Regions exhibiting a significant main effect of time for the longitudinal analysis. The highlighted regions indicate the location of the clustered volume that had a significant main effect of time.

B. Five mm radius spherical regions of interest created at the 2 peak regions for the main effect of time including the right dorsal insular cortex (dmiC) and right superior temporal sulcus (STS). The red indicates the location of the regions of interest used in subsequent post hoc analyses.

C. Scatterplots of relative CBF are displayed for all healthy athletes (open circles) as well as concussed athletes (filled circles) at the 3 recovery points (T1 = 1 day; T2 = 1 week; T3 = 1 month) postinjury.
Cerebrovascular imaging

Cerebral blood flow alterations in acute sports-related concussion (Wang et al. J of Neurotrauma, 2016)

• 18 football players with SRC and 19 normal controls
• Completed ASL MRI and SCAT3 within 24 hours of injury and at 8 days post-injury.
• Significant reduction in resting CBF at 8 days compared to 24 hours post-injury despite normalization of SCAT3 scores.
Cerebrovascular reactivity: unit change in cerebral blood flow in response to a unit change in a vasodilatory (stress)
**FIGURE 2** The effect of a global vasodilatory stimulus on regional blood flow with normal vasculature and with impaired regional vascular response. (A) The normal state at normocapnia. The extent of red color in the vascular beds represents actual blood flow and blue color represents potential blood flow. “+++” beside vessels represents normal blood flow at rest (+) compared to the flow demand (+). This would be the case for normal vasculature and for vasculature that has branches with reduced vasodilatory capacity. (B) With normal vasculature, hypercapnia stimulates increase blood demand by the vascular beds. The vasodilatory demand of the vascular beds combined exceed that of the main feeding vessel (23), which is limiting, i.e., their flow (+) does not meet demand (+++). However, the dilatory response capability of each feeding vessel is symmetrical and so is their flow. (C) In the presence of a dysfunctional vessel, a hypercapnic stimulus results in the same demand in the healthy and dysfunctional vessel (i.e., +++). There is a strong vasodilation in the healthy (upper) branch and a weaker vasodilation in the dysfunctional (lower) branch. The inflow from the main vessel is still limiting (i.e., +++). The direct competition for flow between the vascular beds results in an increased proportion of the flow through the normal vessel (+++ “at the expense of the dysfunctional vessel [flow reduced from +++ in (B), to ++]. This is referred to as vascular ‘steal.’"
Cerebrovascular imaging

Figure 1 - End-tidal Gas Sequence
15 symptomatic adolescent PCS patients and 17 normal controls

CVR assessment using model-based prospective end-tidal CO$_2$ targeting and BOLD MRI

Patient-specific alterations in resting regional CBF and CVR
Cerebrovascular imaging

PCSS=0
> Voxel=0
< Voxel=0

PCSS=73
> Voxel=708
< Voxel=744

PCSS=42
> Voxel=9391
< Voxel=192
Cerebrovascular imaging

AUC=0.87
P=0.001

AUC=0.80
P=0.001

FIG. 5. The ROC curves for the greater-than (left) and less-than (right) responses to the control atlas at the p = 0.001 level for significant abnormal voxel counts.
• MRI-based techniques are capable of demonstrating group and individual differences in resting CBF and CVR following mTBI and concussion.
• Limited studies with small sample sizes published to date.
• Natural history of CBF and CVR changes following concussion require further study.
• CVR studies require rigorous methodological considerations to generate reliable results.
Case

- 15 year old female athlete
- Cycling accident
- +LOC, post-traumatic amnesia
- PMHx: 3 previous concussions
- 5 months later presents with global headaches, dizziness, and fatigue
- Physical examination:
  - Normal: no evidence of vestibulo-ocular dysfunction, cervical spine injury
- Management? Neuroimaging?
Case Illustration

- Graded aerobic treadmill testing
- Symptom limiting threshold = Physiological PCD
- MRI normal
- Brain stress test = abnormal
Case

- Sub-maximal aerobic exercise program
- 2 month later, transition to sports-specific RTP program
- 1 month later, cleared for return to full sports activities
Mutch WAC, et al.: Longitudinal brain magnetic resonance imaging CO2 stress testing in individual adolescent sports-related concussion patients. Frontiers of Neurology- Neurotrauma (published online) 2016
Brain magnetic resonance imaging CO₂ stress testing in adolescent postconcussion syndrome

*W. Alan C. Mutch, MD,1,6,10 Michael J. Ellis, MD,2,3,5,7,8,10 Lawrence N. Ryner, PhD,4,8,10 M. Ruth Graham, MD,1,10 Brenden Dufault, MSc,9,10 Brian Gregson, MD,1,10 Thomas Hall, BSc,10 Martin Bunge, MD,4,10 and Marco Essig, MD,4,8,10 for the Canada North Concussion Network, and Joseph A. Fisher, MD,1,12,14 James Duffin, PhD,11,12,14 and David J. Mikulis, MD,13,14 for the University Health Network Cerebrovascular Reactivity Research Group

Vestibulo-ocular PCD

Physiological PCD
Conclusions

• Conventional neuroimaging plays an important role in clinical management of moderate and severe TBI patients and selected patients with mild TBI and concussion.

• At present, there is no role for advanced neuroimaging techniques in the clinical management of concussion patients.
Conclusions

• For advanced neuroimaging techniques to contribute value to the clinical care of concussion patients in the future they must provide biomarkers:
  – Reliable
  – Disease-specific
  – Must provide information on an individual patient basis
  – Must provide information that is otherwise clinically unavailable
Thanks