New MRI Techniques for Imaging Cerebrovascular Disease

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Vanderbilt University Institute of Imaging Science (VUIIS)

- Established 2002
- A trans-institutional center within Vanderbilt (strong links to other departments/centers)
- ~30 core faculty
- AIM: To develop world-class research program in imaging science and to support research imaging through collaborations
Our lab:

i. Develop new methods for evaluating brain function

ii. Implement methods in clinical environment

Methodology Development

Collaborations

VUIIS

Vanderbilt Medical Center
Stages of stroke imaging

I. Pre-stroke
Risk assessment

- Vascular disease
- Cerebrovascular reactivity
- Perfusion
  (Lots of time)

II. Acute stroke
Treatment stratification

- Perfusion
- Diffusion
  (pH-weighted imaging?)
- Very little time!

III. Post-stroke
Rehabilitation

- Vascular disease
- Cerebrovascular reactivity
- Perfusion
  (Lots of time)
- Plasticity?
- Therapy response?
  (Lots of time)
Evaluating stroke risk

Stroke risk factors:

- Cervical stenosis > 70%
  - Revascularized with carotid endarterectomy (CEA)
- Intracranial (IC) stenosis
  - 18% 2-yr stroke risk
  - Treatment course currently unclear

Goal: Use new MRI approaches to better stratify stroke risk in IC stenosis patients

Inform surgical intervention vs. medical management
How does vascular disease contribute to stroke risk?
- Need to image intravascular plaque (< 1 mm)
- Vessel wall (<< 1 mm)
- High spatial resolution: 7 Tesla
7 Tesla vessel wall imaging. L M1 Stroke (60yr/M)

Circle of Willis

Vessel Wall

Swati Rane, Anja van der Kolk, Megan Strother
Evaluating cerebrovascular reactivity using blood oxygenation level-dependent (BOLD) contrast
Changes in blood oxygenation influence MRI signal

**HbO$_2$: Diamagnetic**

Oxygenated RBC

**Hb: Paramagnetic**

De-Oxygenated RBC

Proton signal dephased by local fields: $\downarrow T_2(*)$
Changes in blood oxygenation arise due to changes in CBF, CBV, and CMRO2

↑ Cerebral blood flow (CBF)

↑ Cerebral blood volume (CBV)

↑ Cerebral metabolic rate of oxygen consumption (CMRO2)
Cerebrovascular reactivity (CVR): Ability of blood vessels to dilate to meet hemodynamic demand

- Challenge blood vessels with increased CO₂ (5% CO₂ / 95% O₂)
  - Increases cerebral blood volume (CBV)
  - Increases cerebral blood flow (CBF)
  - Measure using blood oxygenation level-dependent (BOLD) MRI

Megan Strother (Radiology), Lori Jordan (Neurology), Paul Clemmons (Nursing), Carlos Faraco (VUIIS), Lindsey Dethrage (VUIIS), VUMC Technologists, Respiratory Therapy, Nursing
Cerebrovascular reactivity in the clinic

Patients (n=50)
BOLD (5%CO2/95% O2)
3.0 Tesla

Moyamoya disease
Longitudinal monitoring of CVR
Non-invasive arterial spin labeling for CBF quantification

Separately label right internal carotid (RICA), left internal carotid (LICA), and vertebral/basilar artery (VBA)

Perfusion territory map

Label: (1) all vessels, (2) no vessels, (3) RICA, (4) VBA-1, (5) VBA-2
Flow-territory grouping: k-means clustering (Gevers S et al. AJNR 2012; Donahue MJ et al. JMRI 2013.)
Mechanisms of negative responses to vasodilatory stimuli
Mechanisms of negative responses to vasodilatory stimuli
Normalization of vascular response time after revascularization (Moyamoya patient; right EDAS)

Pre-surgery

Post-surgery
Normalization of blood arrival time following revascularization

Control

Intracranial Stenosis Patient (Moyamoya Disease)

Presurgery

6 mo. post

12 mo. post

Time delay of blood arrival at the cortex, in seconds, relative to the arrival at the center of the cerebellum, pre and post EDAS revascularization surgery on right side.

Blaise Frederick, PhD (Harvard University/McLean Hospital)
Novel imaging protocol to assess stroke risk in patients with intracranial (IC) stenosis

VAMMPRIS: Vanderbilt Assessment of Multi-modal MRI in Patients at Risk for stroke with Intracranial Stenosis

a. Perform 3T non-invasive MRI in IC stenosis patients (goal: 120 patients)
b. Patients monitored for two years
c. Assess correlations between novel imaging contrasts and stroke risk

- MRA
- T2w FLAIR
- T1w MPRAGE
- Hypercarbic Blood oxygenation level-dependent (BOLD)
- Normo and Hypercarbic Arterial spin labeling (ASL)
- Normo and Hypercarbic Vessel-encoded ASL

Duration: 31 min
Measuring cerebral blood flow with arterial spin labeling (ASL) MRI

CBF: rate blood is delivered to tissue

Redundancies in cerebral circulation.

CBF often maintained through collateral and angiogenic pathways

Indicator of hemodynamic impairment
Improving our understanding of stroke risk: flow territory mapping

Cerebral perfusion territories reflect route that blood is delivered to tissue
Study hypothesis

• Baseline flow territory heterogeneity is difficult to interpret owing to normal variants in circle of Willis

• Flow territories may adjust during hypercarbic stimuli if parenchyma is operating near cerebrovascular reserve
  – Flow territory adjustments may be more sensitive indicator of stroke risk than BOLD or CBF alone

• **Hypothesis:** Flow territories in patients with IC stenosis adjust significantly relative to controls in response to hypercarbia
  – Flow territory volume increases in unaffected hemisphere and decreases in affected hemisphere
Control results: no clear change in flow territories with hypercarbia
Patient results: reduction in flow territory volume with hypercarbia in affected hemisphere
Reduction in flow territory volume with hypercarbia in affected hemisphere

Controls (n=9)

Patients (n=12)

- Large coefficient of variation in patients relative to controls
- Flow territory adjustment potential indicator of stroke risk in patients
Fundamental question in acute stroke therapy: can we titrate therapy based on infarction risk?

- Tissue progressing to infarction: Positive on diffusion weighted imaging (DWI)
- Tissue at-risk for infarction: time-to-peak (TTP) lengthening
- Ischemic penumbra: DWI/PWI mismatch
- Benign oligemia: Abnormal on TTP, but low risk of progressing to infarction
Amide proton transfer (APT) CEST

1. **Saturate** labile N-H protons (3.5 ppm) with RF pulse

2. **Wait** for protons to exchange with detectable water protons

3. **Detect** attenuation in water signal
Improving infarction-risk characterization in ischemia

Moderate Ischemia
- Insufficient O₂ and Glc
- Inadequate energy supply

Severe
- Ion channel disruption
- Extrusion of CO₂ limited
- PCR reduction
- H⁺ buildup (↓ pH)

Advanced Ischemia
- Glu and Asp buildup
- Influx of water
- Advanced ion disruption

CBF ~ 30 ml/100g/min

CBF = 0 ml/100g/min
Results: patient example: 58 yr/M. 2-4 hrs

R M1 and R ICA Occlusion

Reduced acute CEST APT in tissue progressing to infarct

Consistent with acidosis
Multimodal MRI in acute stroke patients

**A**
- Large final infarct
- Hyperacute APT contrast (reduced)

**B**
- No final infarct
- No hyperacute APT contrast

**C**
- Small final infarct
- Hyperacute APT contrast (reduced)
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