DEVELOPMENT OF MRI BIOMARKERS FOR IMPROVED DIAGNOSIS OF TBI

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Conflicts of Interest

- Research support from the DoD for TBI
- President of MR Innovations, Inc
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Aim 1: Compare advanced MRI methods to conventional imaging methods in their ability to detect mTBI in the acute setting.

Aim 2: Apply susceptibility weighted imaging and mapping (SWIM) to quantify and monitor evolution of pathological changes in mTBI.

Aim 3: Explore the role of perfusion weighted imaging as a means to diagnose hemodynamic abnormalities.

Outcomes: The major findings presented here is that SWI is a means to detect microvascular damage, and this is particularly the case in the venous system for mild TBI.
High resolution MR angiography

Small arteries around 250 microns are beginning to become visible even without a contrast agent (0.5mm isotropic resolution).
Susceptibility Weighted Imaging

- Enhances the presence of ferritin, hemosiderin and deoxyhemoglobin
- Exquisite images from which brain damage, microbleeding and increases in deoxyhemoglobin can be diagnosed

Venous Thrombosis: before treatment and after thrombolysis

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Low concentration iron is still seen on 7 slices with SWI and barely discernable on FLAIR!
Stroke with almost imperceptible bleeding

SWI shows the bleed  
short TE GRE T1
Stroke case for a young woman in her mid 30s

FLAIR  PWI (1st)  SWI mIP  MRA

CBV  CBF  MTT  TTP
The data collected for SWI can also be reprocessed to produce whole brain maps of oxygen saturation.

Haacke EM et al. Susceptibility mapping as a means to visualize veins and quantify oxygen saturation. JMRI 2010;32:663-76.
A 57 year old male patient with left limb weakness was scanned 144 hours after onset.

MR perfusion shows delayed TTP corresponding to the area of APCV, which can be associated with the penumbra of the right hemisphere.
It is now believed that up to 35% of dementia cases may be caused by vascular dementia.

We see microhemorrhages as a means to predict who will get Alzheimer’s disease.

These may lead to “cognitive strokes”.

Hopefully this work will lead to collaborations with the pharmaceutical industry to come up with neuroprotective drugs that will strengthen the vessel wall or help to prevent its degeneration.
Cerebral amyloid angiopathy

50µm objects can manifest as 1mm³ objects
time to go sailing
Using caffeine decreases blood flow to the brain.

two cups of coffee and you will have a major change of blood flow to the brain.

maybe we should approach Starbucks for funding.

at least it is a relatively harmless contrast agent to use to study the brain and a heck of a lot cheaper.
MinIP of caffeine/Gd over 28 slices with 4 phase multiplications
SWIM images pre/post caffeine injection

Increased susceptibilities indicated by yellow arrows

Mipped over 8 slices (16mm).
Conventional imaging (T1, T2, FLAIR, DWI)
SWI for visualizing vascular abnormalities
SWIM for quantifying oxygen saturation
PWI for evaluating local tissue flow
Motorcycle trauma: medullary vein involvement
Major venous and medullary vein involvement
SWI reveals MVD
SWIM of cerebral microbleeds in TBI

Maximal Intensity Projection (MIP) over 8mm

Maximal Intensity Projection (MIP) over 32mm
Medullary vein involvement (severe TBI)
mTBI studies to date

- Abnormal Transmedullary Veins
  - 3/22 patients – mTBI
  - 11/62 patients – mTBI

- Microvascular damage and particularly medullary vein and pial vein damage may take place in roughly 15% of mTBI cases

- These findings could help understand why some mTBI cases continue to have long term problems and at least represents direct evidence that there was brain damage
Patients with traumatic brain injury (TBI) are at an increased risk of developing venous thromboembolic events (VTE).

Pharmacological thromboprophylaxis (PTP) is routinely delayed because of concerns of exacerbating intracranial hemorrhage (ICH).

Based on the available literature, we can tentatively conclude that early PTP (< 72 h) reduces the risk of VTE without affecting progression of ICH.

However, much work is yet to be done to better clarify ICH subtypes at risk of progression and the implementation of evidence-based guidelines backed up with randomized control trial level evidence.
Conclusions

Venous flow abnormalities are an important aspect of neurodegenerative disease.

SWI and SWIM are important methods for assessing venous abnormalities and microbleeds.

Perfusion should be part and parcel of studying neurodegenerative disease including TBI.

These observations call for more studies in this direction and could lead to improved treatment for patients with venous thrombosis.