Age-related Cerebral Medullary Artery Tortuosity Revealed by USPIO-Enhanced 7T MRI

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1

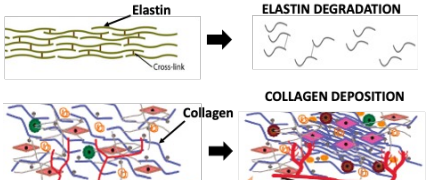
Introduction

- Vascular tortuosity changes are commonly seen in the aged population;
  - Occur in both extracranial large arteries and intracranial small arteries
  - May have impacts on the cerebral blood flow, small vessel disease (SVD), and cognitive function.
- Ultra-small superparamagnetic iron oxide (USPIO) contrast agent has shown great potential in enhancing contrast among small vessels that are invisible in conventional MRI.
  - Conventional SWI has capacity of visualizing sub-voxel veins.
  - USPIO increases the susceptibility within both arteries and veins, making small arteries imaged by SWI.

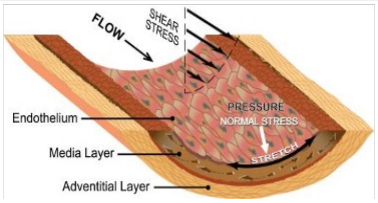
2

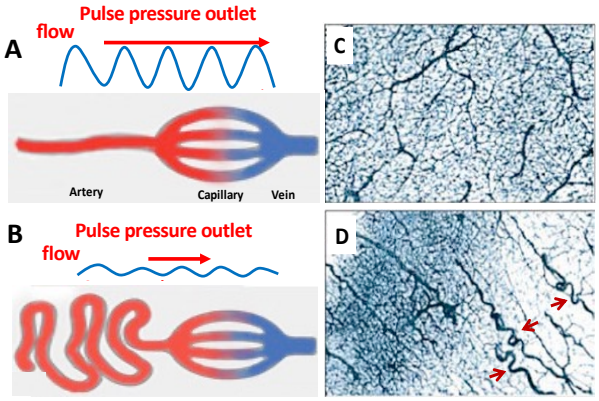
Age-related Vascular Wall Remodeling

- **Structural factors** (extracellular matrix)
  - Elastin degradation
  - Collagen deposition



- **Mechanical factors**
  - Pulsation pressure
  - Wall shear stress





Han HC. J Vasc Res (2012); Brown WR et al., Neuropathol Appl Neurobiol (2011)

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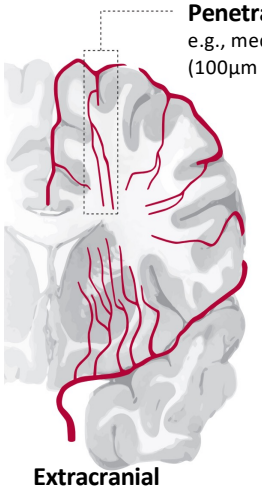
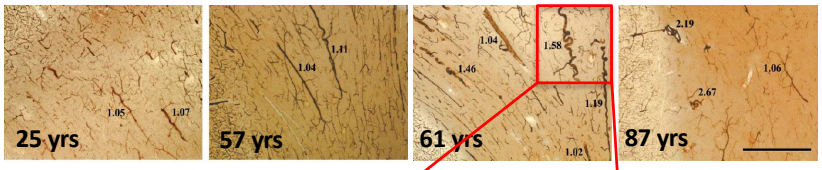
3

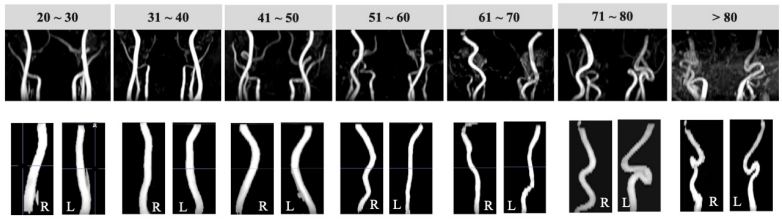
Vascular Tortuosity with Aging



Alkaline phosphatase-stained arterioles within WM



Tortuosity usually begins abruptly as the arteriole passes from the cortex into the white matter. WM is less dense than GM, so that there's enough space for arterioles twisted in cavities.



Thore CR. et al. (2007); Brown WR. et al. (2011); Sun et al. Frontier Neurology. (2022)

4

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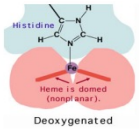
Study Aim: The purpose of this study is to use USPIO-enhanced 7T high resolution SWI to visualize the tortuosity changes of intracranial penetrating arteries (medullary arteries).

5

USPIO-Enhanced SWI

Venous blood



(**paramagnetic**)
Unpaired electrons produce local magnetic susceptibility gradients

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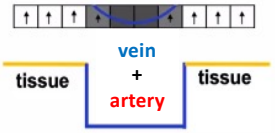
Ferumoxytol

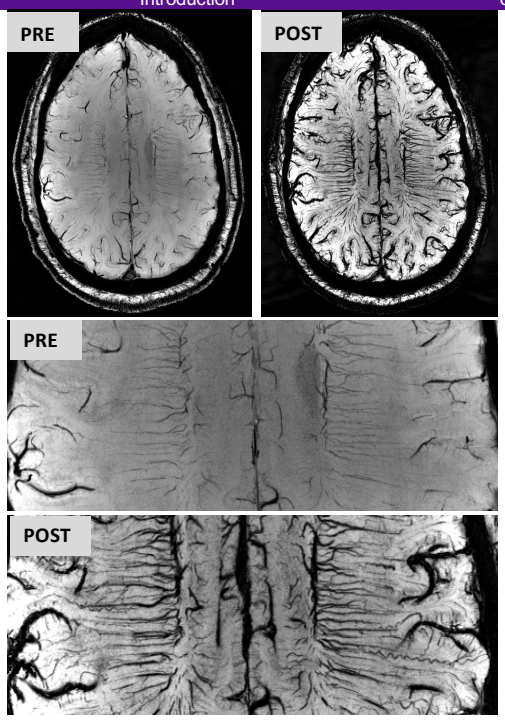
Super-paramagnetic

$$\Delta\emptyset = -\gamma \cdot \Delta\chi_{vt}\uparrow\uparrow \cdot \boldsymbol{B_0} \cdot \boldsymbol{TE}$$



- Ferumoxytol introduces magnetic susceptibility into the arterial system, so that **arteries** are visible at post-contrast images
- **Veins** show significant blooming effect. (e.g., Imaging with 100μm resolution could reveal veins on the order of 25μm)[1].
- Significant improvement for micro-vasculature to be seen at post contrast images.

Xu Y, Haacke EM. MRI (2006)



6

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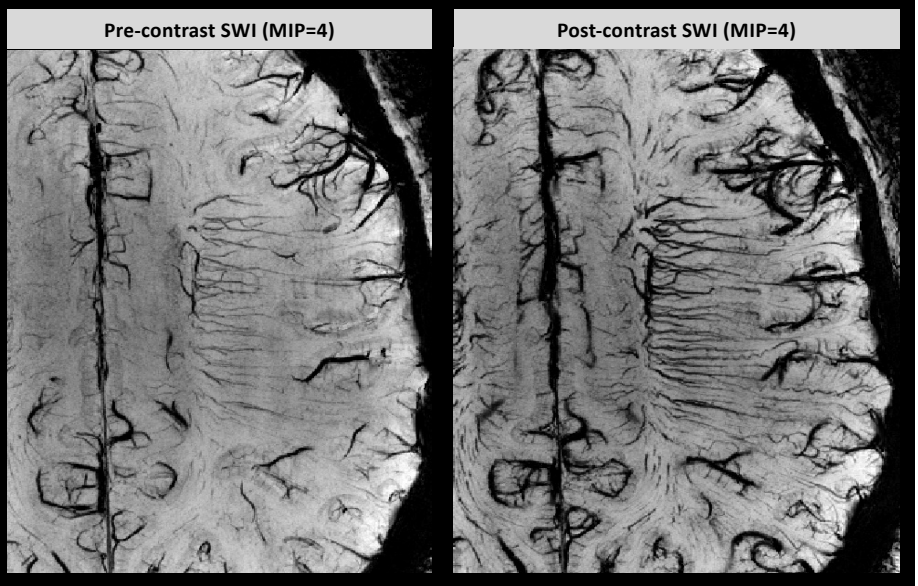
7

Methods

Imaging Acquisition

- Dual echo GRE sequence[1] with TE1/TE2/TR = 7.5/15/22ms
- Voxel = 0.25x0.25x1
- Ultrasmall super-paramagnetic iron oxide (Ferumoxytol) is administrated at 2mg/Kg through a 15-minute IV infusion.
- 96x96 high-pass filtered phase images were used to remove background phase. Combined with magnitude image, the acquired phase mask was used to generate SWI image.

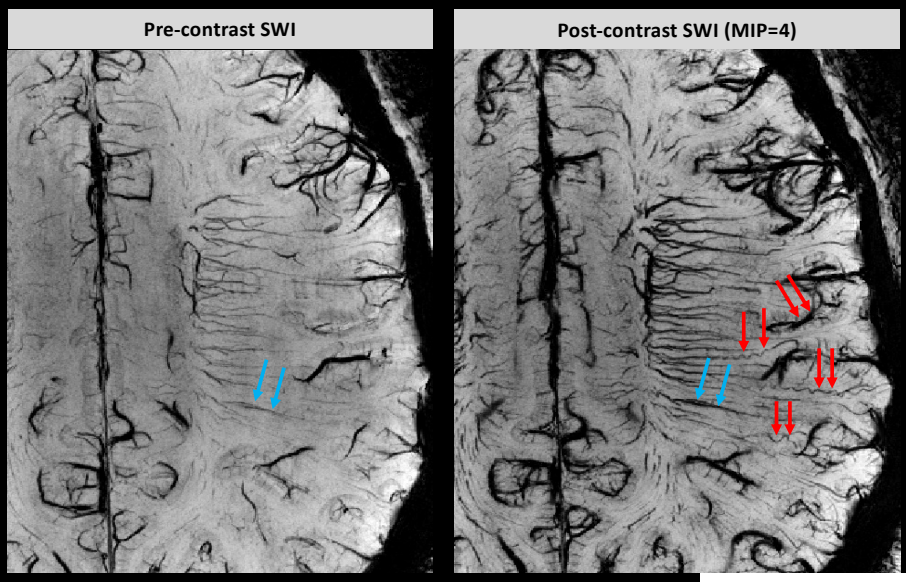


8

Methods

Differentiate **arteries** from **veins**

- Referring to the pre- and post-USPIO vessel contrast;
- Anatomical course: penetrating from pial surface (GM) to the deep WM.
- Characteristic corkscrew shape.
- Vessel tracking from large arteries



Small arteries (**red**) and veins (**blue**) on pre- and post-USPIO SWI

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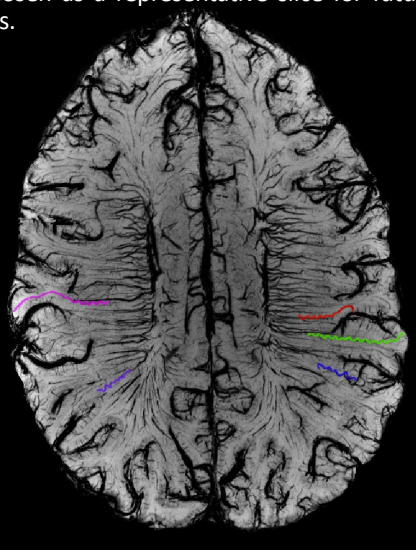
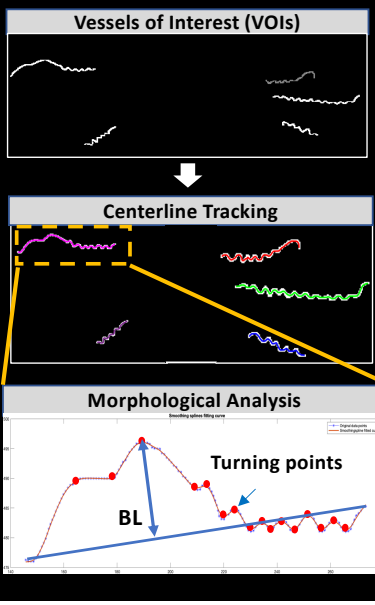
9

- By examining minimum intensity projection (mIP) SWI slices, the number of tortuous medullary arteries were counted.
- Slice with maximum number of tortuous arteries was chosen as a representative slice for future analysis.



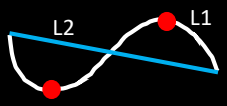
Tortuosity Quantitative Measurements



Tortuosity index = L1/L2

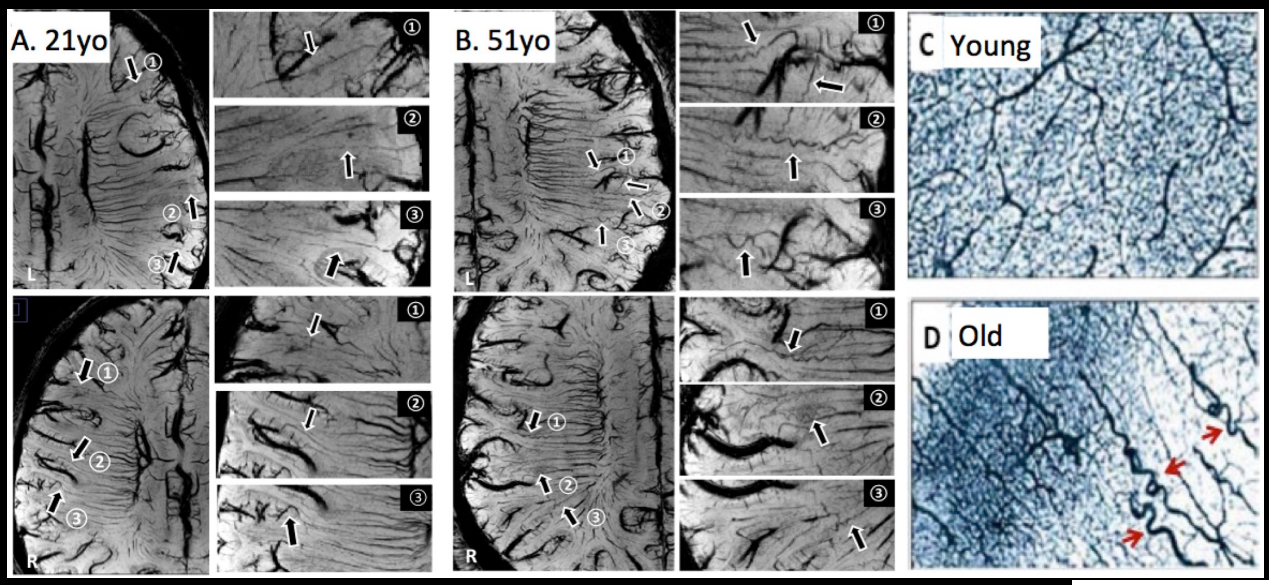
Bending length is the maximum distance between L2 to the curve

Inflection count metric = turning points x (L1/L2)



10

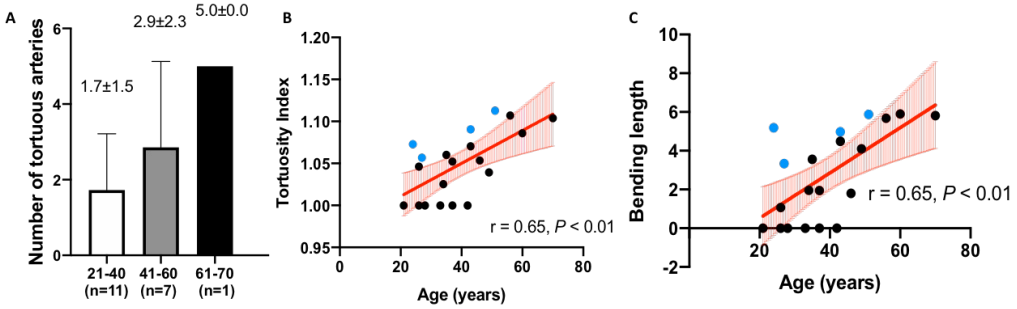
Results



11

Results

- 20 subjects (13 males/7 females; age=39.40±13.10; Systolic BP = 121.5±11.11; Diastolic BP = 71.95±13.52).
- With aging, there are more tortuous vessels within the brain, especially at the regions of centrum semiovale.
- Tortuosity index and bending length are positively correlated with age. The blue dot outside of the 95% confidence interval are subjects with high BMI **(>=29).**



12

Conclusions

- It is feasible to directly visualize the age-related corkscrew appearance of cerebral medullary arteries in vivo with USPIO-enhanced SWI on 7T.
- More tortuous **medullary arteries** can be observed in aged population, which might be the basis of hypoperfusion within the brain, especially within the region of **centrum semiovale**.
- Subjects with high BMIs demonstrated higher tortuosity measurements regardless of age.
- **Future directions**
  - To recruit more subjects, especially aged and dementia population.
  - To differentiate arteries from veins using quantitative susceptibility map.
  - To investigate the cross-talk between large arteries and intracranial small arteries.

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13

Acknowledgement

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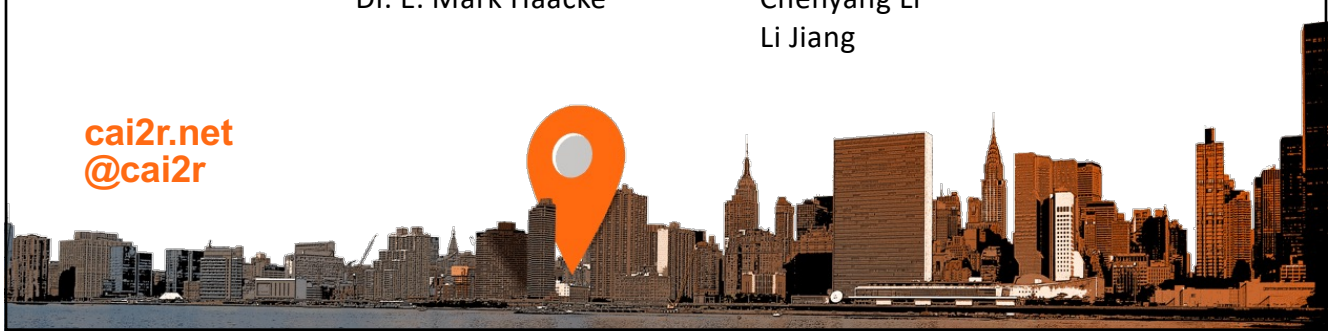

14