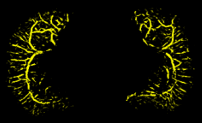
WAYNE STATE UNIVERSITY

In vivo Vascular Mapping of the Human Hippocampus Using MICRO Imaging



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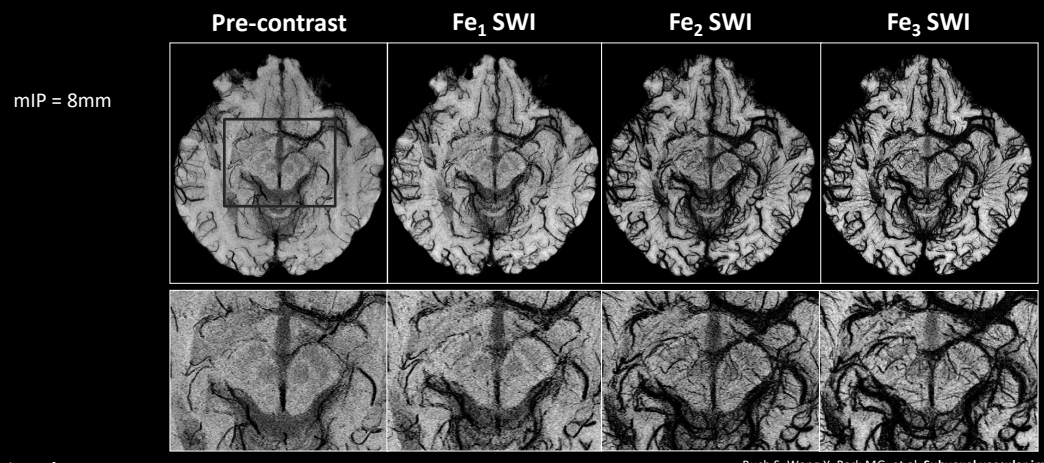
1

MICRO Protocol for Acquiring USPIO-enhanced SWI

(*M*icrovascular *I*n-vivo *C*ontrast *R*evealed *O*rigins)

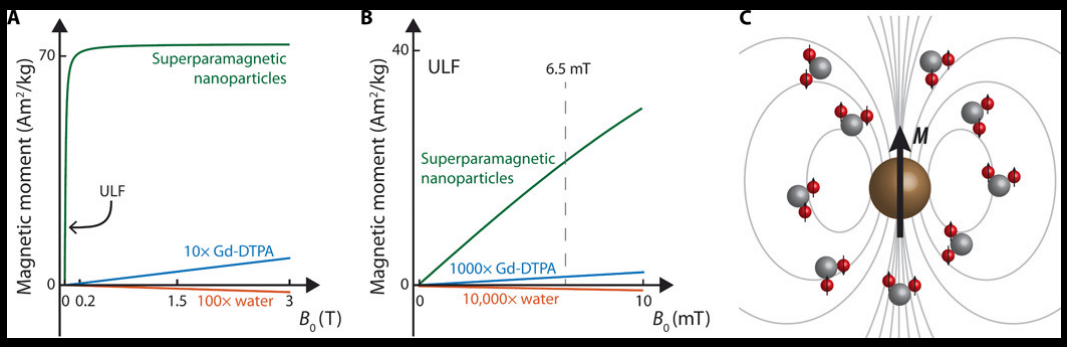


Imaging parameters:
$TE_1/TE_2/TR$ = 7.5/15/27ms, Bandwidth = 180Hz/pxl, number of slices = 96,
flip angle = 12°; voxel size = 0.22×0.44×1mm^3
Acquisition time for each sequence = 11 mins, GRAPPA = 2/36
Final **Ferumoxytol** dose = 4mg/kg, Dose delivery time = 21-23 mins

Buch S, Wang Y, Park MG, et al. **Subvoxel vascular imaging of the midbrain using USPIO-Enhanced MRI.** *Neuroimage*. 2020 Oct 15;220:117106.

2

Imaging properties of Ferumoxytol and GdDTPA

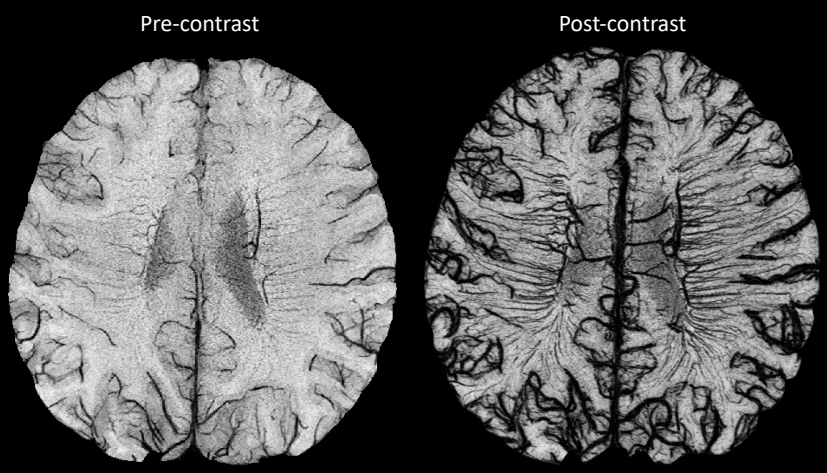


- USPIO is saturated at low fields and so it does not change its properties above roughly 0.5T to 1T.
- USPIOs possess much higher sensitivity than Gadolinium

Waddington et al., Science Advances. 2020: 6(29), eabb0998

3

Ferumoxytol enhanced MRAV on 3T



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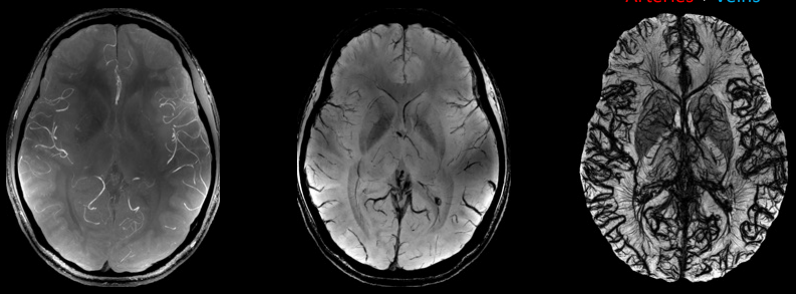
Imaging the Arteries and Veins with MICRO

MRA pre-contrast = Arteries

mIP pre-contrast = Veins

mIP post-contrast SWI = Arteries + Veins



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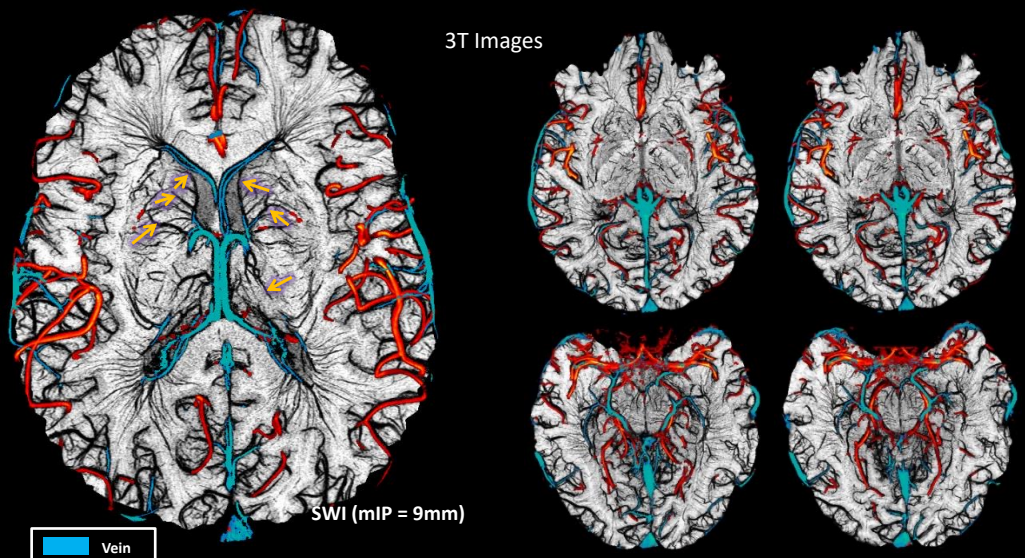
Mapping Cerebral Vessels

3T Images



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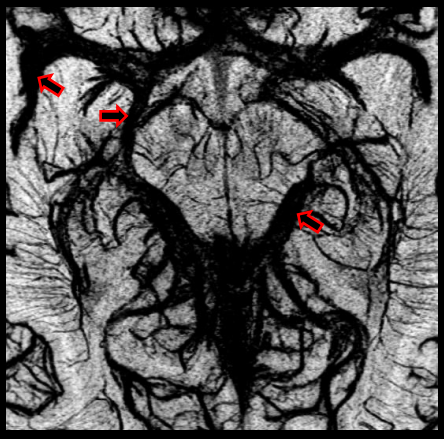
Dynamic Combination of USPIO-SWI data

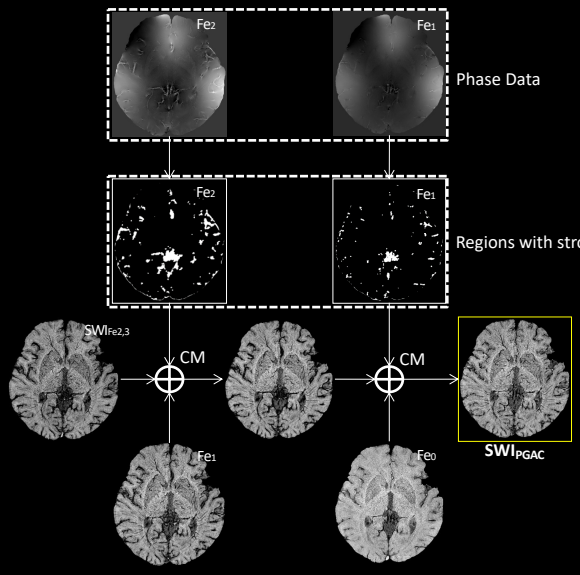
Post contrast SWI (mIP = 8mm)



Buch S, Wang Y, Park MG, et al. **Subvoxel vascular imaging of the midbrain using USPIO-Enhanced MRI**. *Neuroimage*. 2020;220:117106.

7

Dynamic Combination of USPIO-SWI data



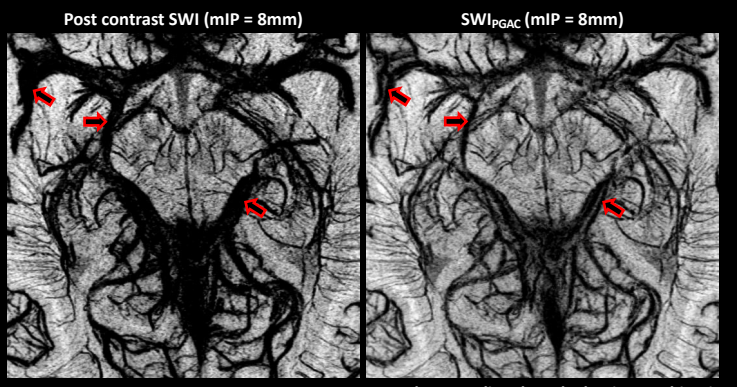
PGAC = Phase gradient based adaptive combination

Buch S, Wang Y, Park MG, et al. **Subvoxel vascular imaging of the midbrain using USPIO-Enhanced MRI**. *Neuroimage*. 2020;220:117106.

8

Dynamic Combination of USPIO-SWI data

To reduce the blooming artifact and better identify vessels



PGAC = Phase-gradient based adaptive combination

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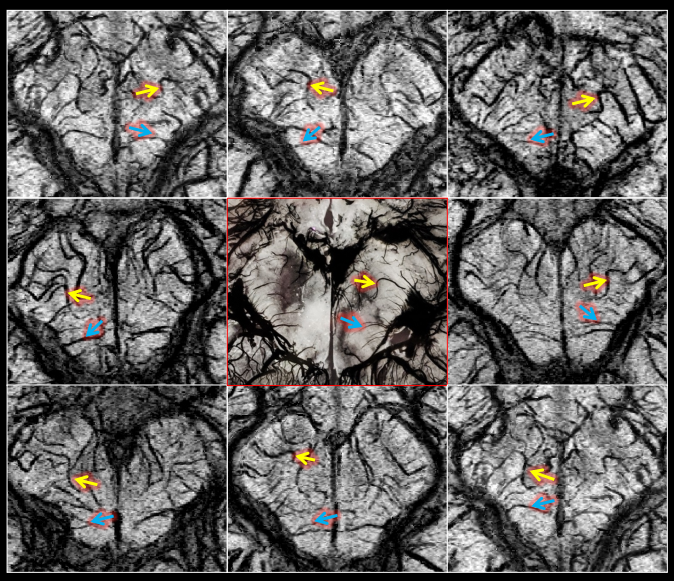
Comparison of MICRO and Cadaver brain dye injection

3T SWI (mIP = 8 mm)



Peduncular artery
Collicular artery

Center image:
***In vitro* angiogram**

Georges Salamon; J M Corbaz
Atlas de la vascularisation arterielle du cerveau chez l'homme

Buch S *et al.,* Subvoxel vascular imaging of the midbrain using USPIO-Enhanced MRI. *Neuroimage*. 2020;220:117106.

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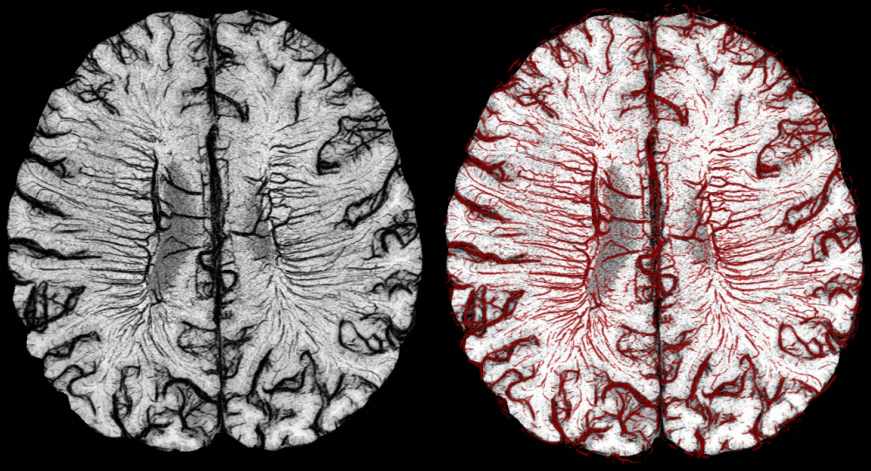
Extracting the Cerebral Vasculature

3T SWI (mIP = 5 mm)

SWI

SWI + Vessel overlay



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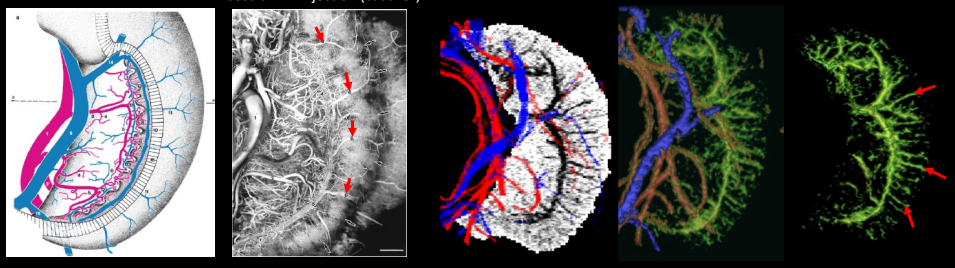
Hippocampal Macro- and Micro-vasculature

Illustration of Hippocampal vascularization

Vascular ink injection (cadaver)

MICRO SWI (Ferumoxytol)

3T Images



Duvernoy et al., The Human Hippocampus: Functional Anatomy, Vascularization and Serial Sections with MRI. 2013, 4th edition, Springer-Verlag Berlin Heidelberg, pg. 74 and 99.

→ Subependymal intra-hippocampal veins

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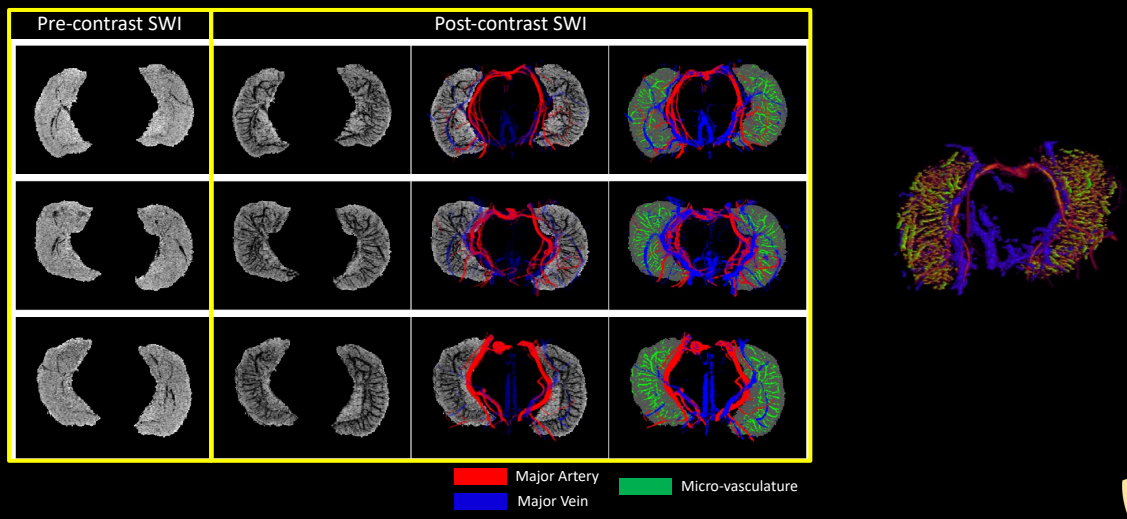
Hippocampal Macro- and Micro-vasculature



Buch S *et al.*, Vascular mapping of the human hippocampus using Ferumoxytol-enhanced MRI. *Neuroimage*. 2022 Feb 2;250:118957. doi: 10.1016/j.neuroimage.2022.118957

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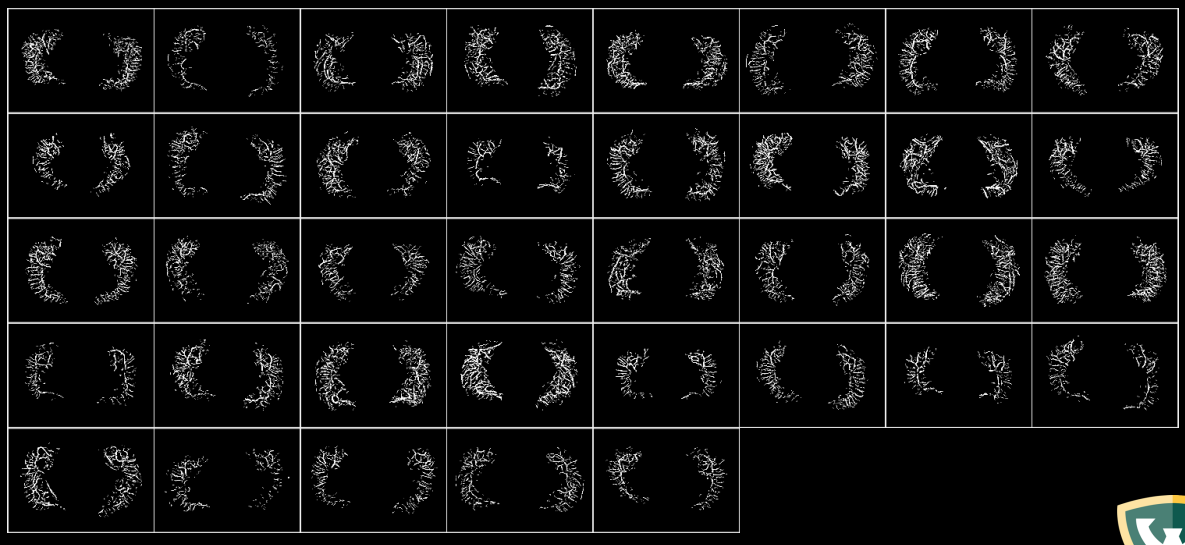
Mean Vessel Density in Different Hippocampal Subfields



Buch S *et al.*, Vascular mapping of the human hippocampus using Ferumoxytol-enhanced MRI. *Neuroimage*. 2022 Feb 2;250:118957. doi: 10.1016/j.neuroimage.2022.118957

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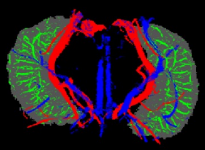
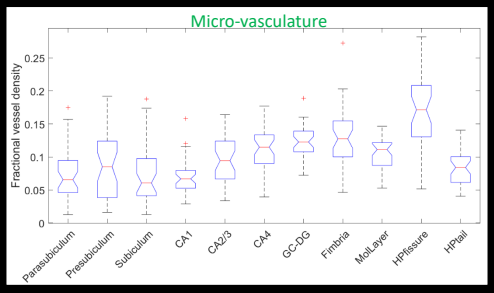
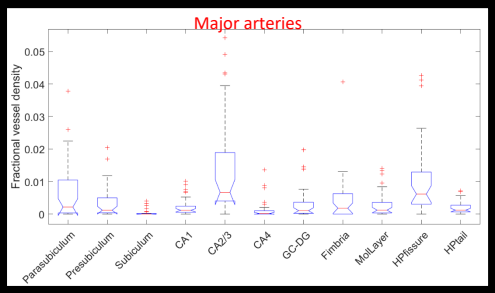
Mean Vessel Density in Different Hippocampal Subfields

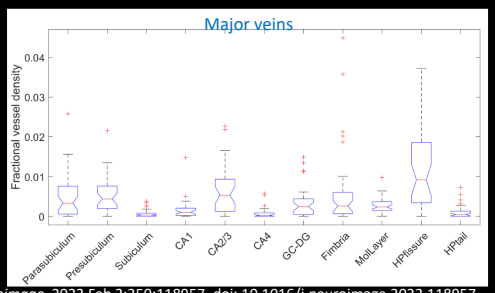


Fractional vessel density = $\frac{Vessel\ volume}{Total\ volume}$



GC-DG = Granule cell layer of the dentate gyrus,
MolLayer = Molecular layer of HP





Buch S *et al.*, Vascular mapping of the human hippocampus using Ferumoxytol-enhanced MRI. *Neuroimage*. 2022 Feb 2;250:118957. doi: 10.1016/j.neuroimage.2022.118957

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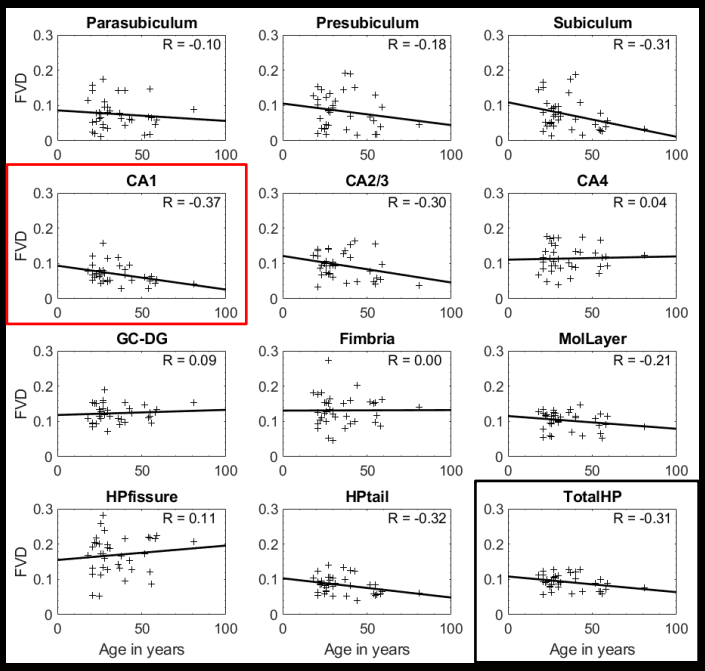
Age vs *Vascular Density*

There was a strong reduction in fractional vessel density (FVD) as a function of age for:

- Presubiculum
- Subiculum
- Cornu ammonis layer (***CA1***, CA2/3)
- Hippocampal tail
- ***Whole hippocampus***



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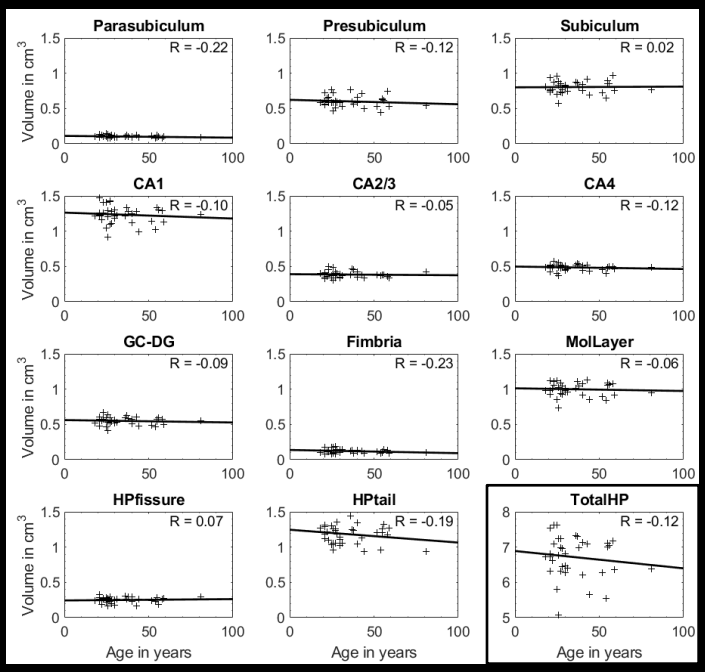
Age vs *Tissue Volume*

Tissue volume showed a weakly negative or lack of correlation as a function of age



Buch S *et al.*, Vascular mapping of the human hippocampus using Ferumoxytol-enhanced MRI. *Neuroimage*. 2022 Feb 2;250:118957. doi: 10.1016/j.neuroimage.2022.118957

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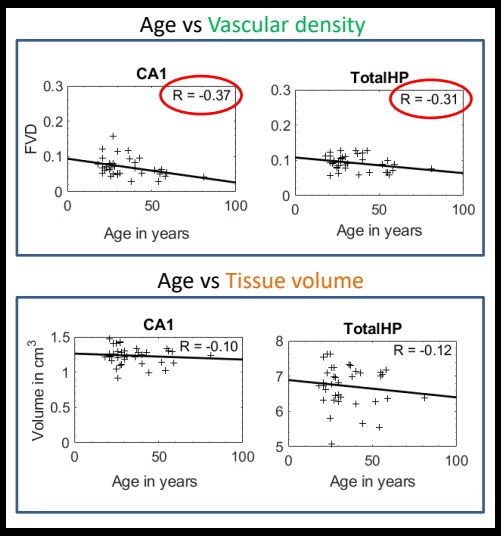

Buch S *et al.*, Vascular mapping of the human hippocampus using Ferumoxytol-enhanced MRI. *Neuroimage*. 2022 Feb 2;250:118957. doi: 10.1016/j.neuroimage.2022.118957

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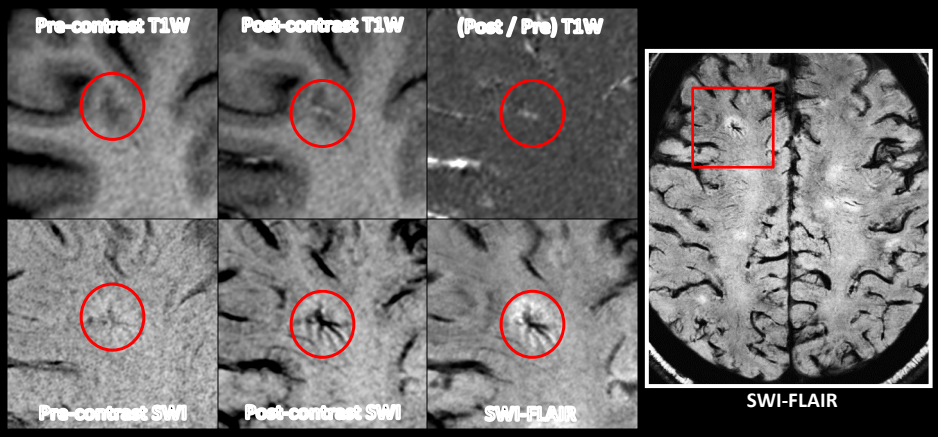
MICRO Imaging: MS patient

T_1 enhancement vs T_2* induced signal loss



Buch S *et al*., Revealing vascular abnormalities and measuring small vessel density in multiple sclerosis lesions using USPIO. *Neuroimage Clin*. 2021;29:102525. doi: 10.1016/j.nicl.2020.102525.

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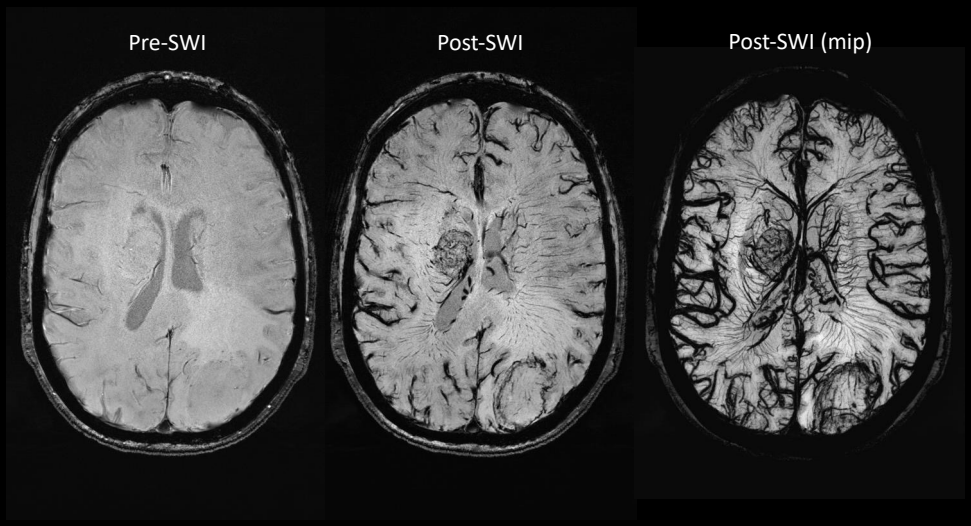
MICRO Imaging of Tumors at 3T

mIP/MIP = 12 mm



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Conclusions

- With this USPIO-induced increase in susceptibility, comes the potential to study the cerebral micro-vasculature using high-resolution SWI
- There was a strong negative correlation of the hippocampal FVD (especially in CA1) with age
- FVD reduction was more prominent than volume reduction vs. age
  => vascular atrophy may precede reductions in tissue volume
- Mapping the hippocampal vasculature has immediate implications for understanding the effects of normal aging and the etiology of many neurovascular diseases.
- MICRO imaging brings us into the decade of imaging the microvasculature of the entire human body

I would like to thank my colleagues from the USPIO imaging team:

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Yulin Ge

Li Jiang, Chenyang Li, Zhe Sun

More collaborators

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Mandar Jog and Soumya Sharma (Western University, Canada)
Eleuterio Toro, Lucan Muller, Beatrice Ghitti (University of Trento, Italy)

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