The 10th ISNVD Annual Meeting on
Vascular Contributions to Healthy Aging and Dementia

Age Dependent Changes of Water Exchange Rate across the Blood-Brain Barrier

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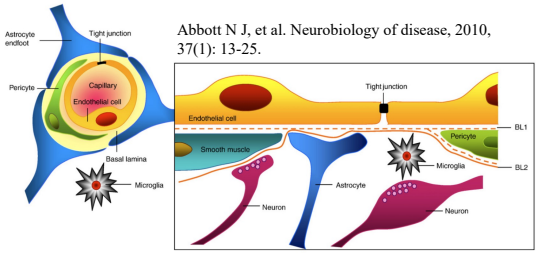
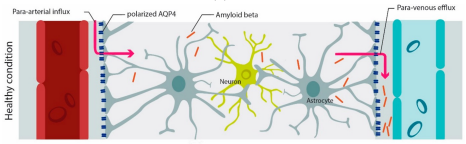
Age dependent kw changes

Xingfeng Shao



Abbott N J, et al. Neurobiology of disease, 2010, 37(1): 13-25.



Mader S, et al. Cells, 2019, 8(2): 90.

Blood-brain barrier (BBB):

- Tight junction of endothelial cell: restricts the para-cellular diffusion of macromolecules [1].
- Pericyte
- End-foot of astrocyte

Aquaporin-4 (AQP4): the water channel

- Along the end-foot of astrocytes.
- AQP4 provides a more efficient pathway for water exchange.
- Maintain brain homeostasis.
- Glymphatic function and clearance of deleterious proteins.

AQP4 redistribution slows the waste clearance through the glymphatic system.

[1] W M Pardridge. NeuroRx , 2(1):3{14, 2005.

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Age dependent kw changes

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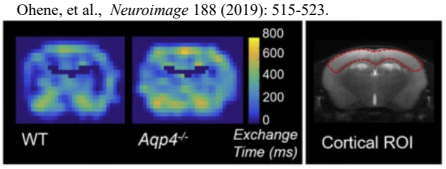
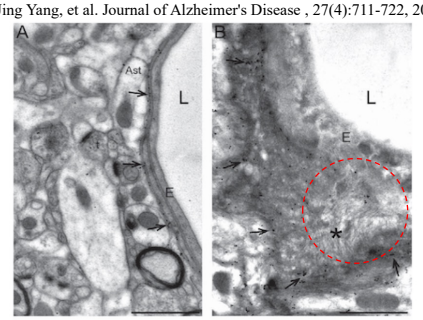
Ohene, et al., *Neuroimage* 188 (2019): 515-523.



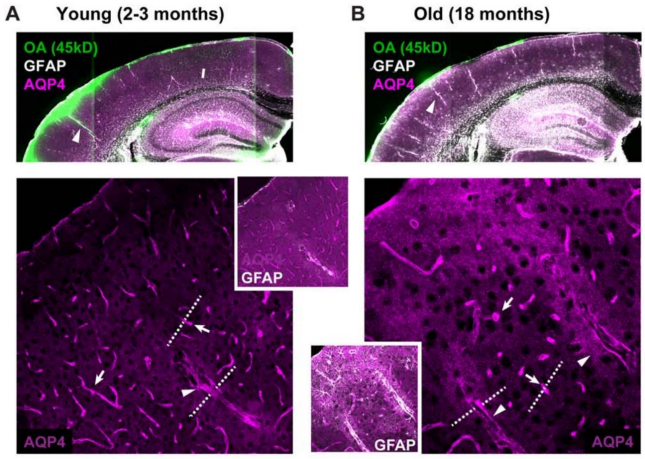
Increased water exchange time or decreased exchange rate in AQP4-deficient mice.

Jing Yang, et al. Journal of Alzheimer's Disease , 27(4):711-722, 2011.



Amyloid deposits is associated with AQP4 redistribution/loss of polarization.

Benjamin T Kress, et al. Annals of neurology, 76(6):845-861, 2014.



Widespread loss of AQP4 with aging

Goal: To study age dependent kw change with a wide range of age groups.

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Age dependent kw changes

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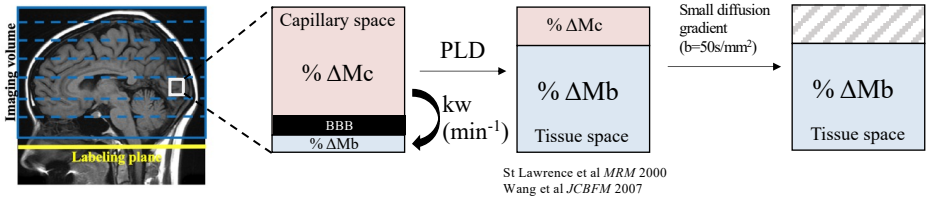
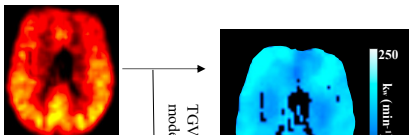
Arterial spin labeling (ASL)

- Traces the blood originated from outside of the voxels and *monitors the exchange of blood across the BBB.*



St Lawrence et al *MRM* 2000
Wang et al *JCBFM* 2007
St Lawrence et al *MRM* 2012



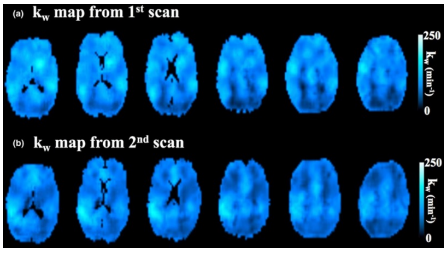
Perfusion image at PLD of 1800 ms

Vascular component nulled by diffusion weighting

TGV regularized SPA modeling (Shao et al, 2019)

kw map

12 axial slices
RES = 3.5×3.5×8 mm^3
*Single-shot acquisition



Good 2-month test/retest reliability (ICC=0.75)

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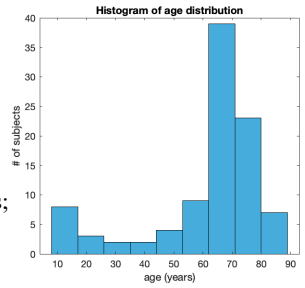
MRI experiments (3T Siemens Prisma scanner):

- **FOV = 224mm, 12 slices (10% oversampling), single-shot acquisition, resolution = 3.5×3.5×8mm^3, TE=36.5ms, TR=4000ms, label/control duration= 1500ms.**

- **A 2-stage approach for ATT and k_w measurement (10 mins)[1-4]:**
  - (1) PLD=900ms and b=0,14 s/mm^2 (VENC=7.5mm/s) to estimate ATT (FEAST method) (15 measurements each b-value);
  - (2) PLD=1800ms and b=0,50 s/mm^2 for kw measurement (20 measurements each b-value).

Human subjects:

- **All subjects are cognitive normal.**
- **97 subjects (53 males) from 5 age groups (data sets):**
  1. Pediatric subjects: N=9, age=13±2.9 (range 8-17) years, 6 males;
  2. Young adults: N=5, age=25.2±2.5 (23-29) years, 4 males;
  3. Elderly Latinx subjects: N=8, age=67.6±3.6 (64-70) years;
  4. Mid-Elderly African American subjects: N=39, age=63.9±10.2 (40-81) years, 24 males;
  5. Elderly Caucasian subjects: N=38, age=72.8±3.2 (67-86) years.



[1] Wang et al *JCBFM* 2007; [2] St Lawrence et al *MRM* 2012; [3] DJJ Wang, et al. MRM, 49(5):796{802, 2003. [4] Shao et al, MRM 2019

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kw map from sevens subjects across different ages

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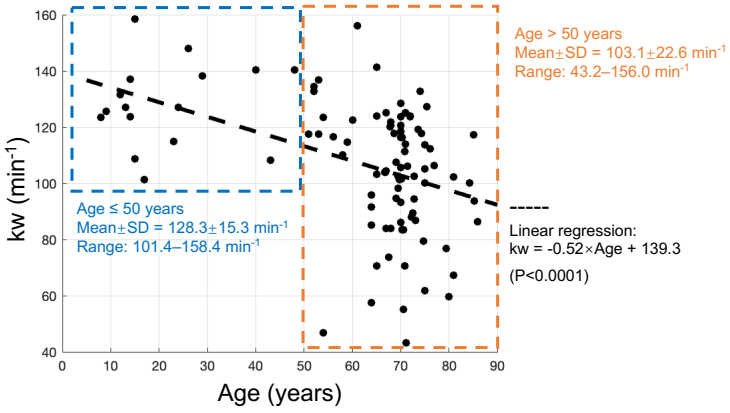
Age dependent kw changes — **Xingfeng Shao**

Scatter plot of kw versus age



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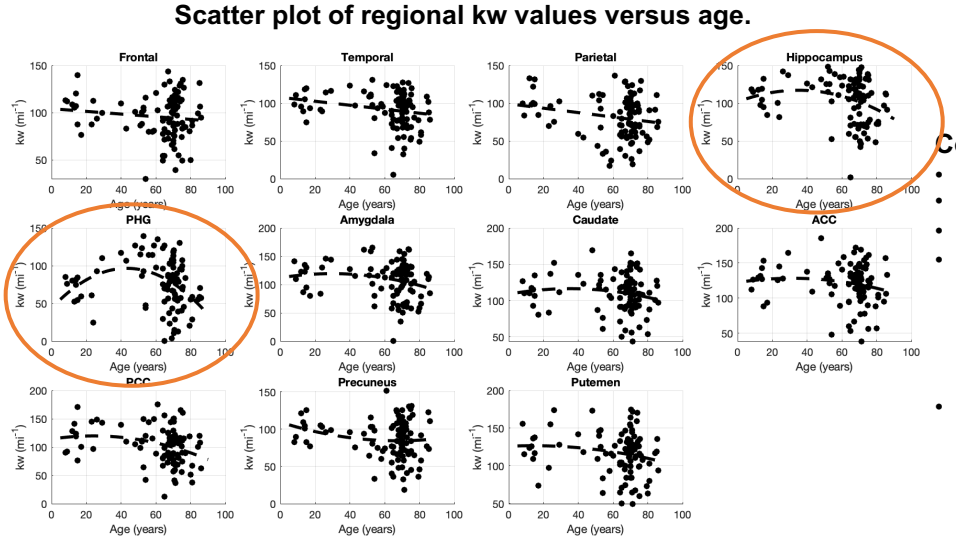
Age dependent kw changes — **Xingfeng Shao**

Scatter plot of regional kw values versus age.



Conclusion:

- 97 subjects.
- Age 8 to 86 years.
- **kw decreases with age.**
- **Large spread of kw values when >50 yrs.**
  - Slower waste clearance.
  - Compromised BBB.
  - Not all subjects :D
- **Inverted U-shape?**
  - **Hippocampus**
  - **PHG**

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