

# Connecting Arterial Blood Flow to Tissue Perfusion for In Silico Trials of Acute Ischaemic Stroke

September 27th, 2019

Raymond Padmos



UNIVERSITY  
OF AMSTERDAM



This project (INSIST; [www.insist-h2020.eu](http://www.insist-h2020.eu)) has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 777072.



# Acute Ischaemic stroke

- Most common type of stroke:  $\approx 87\%$
- 3 million deaths per year
- “Time is brain”



# Acute Ischaemic stroke



Patient enters the hospital

Treatment is given



Thrombolysis

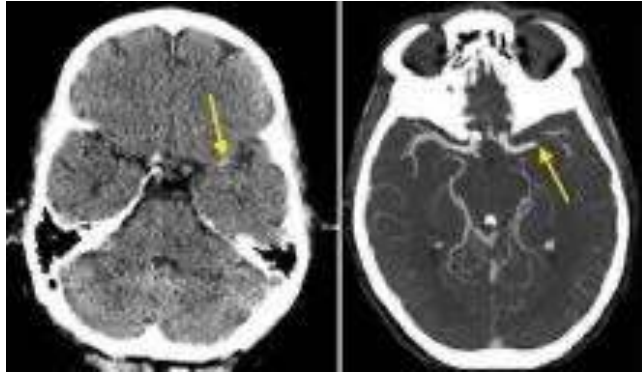


Thrombectomy

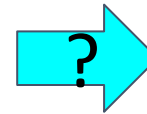


Follow-up  
6 months later

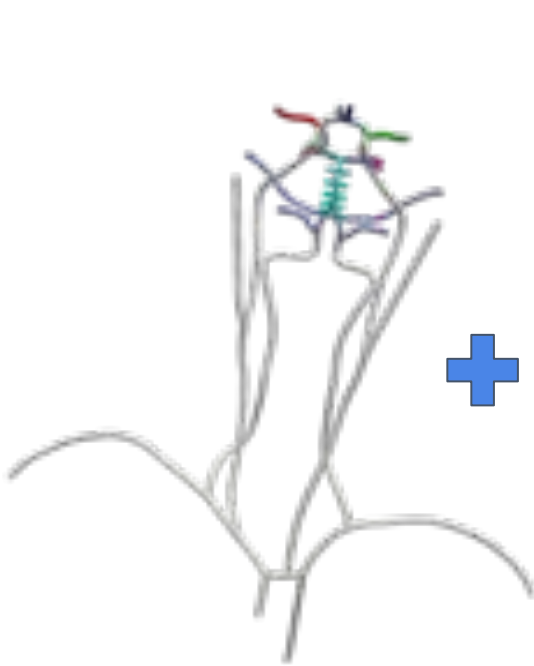
# Predicting Infarct volume



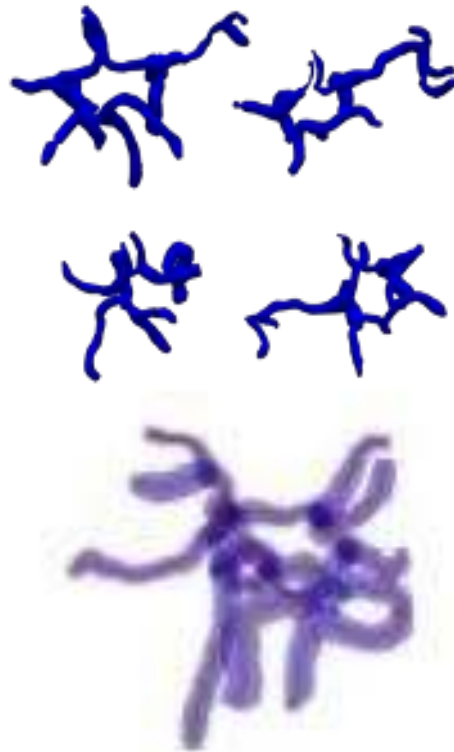
Patient enters the hospital



# Extending the Vasculature



Large Arteries



Major Cerebral Arteries

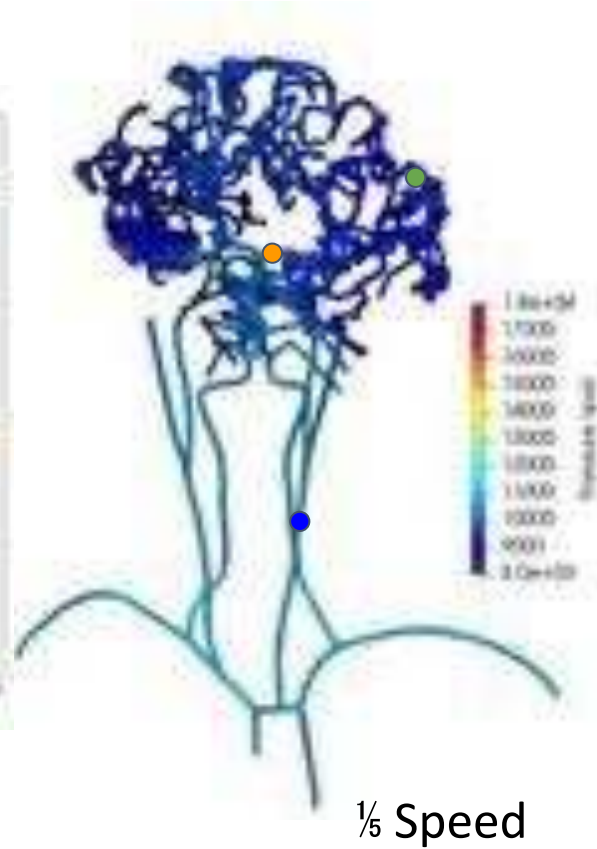
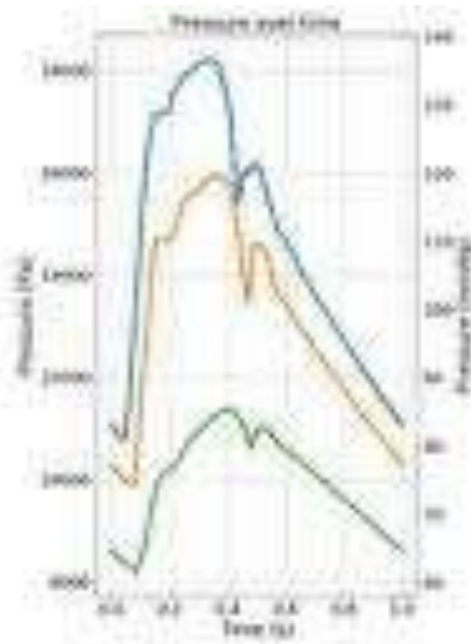
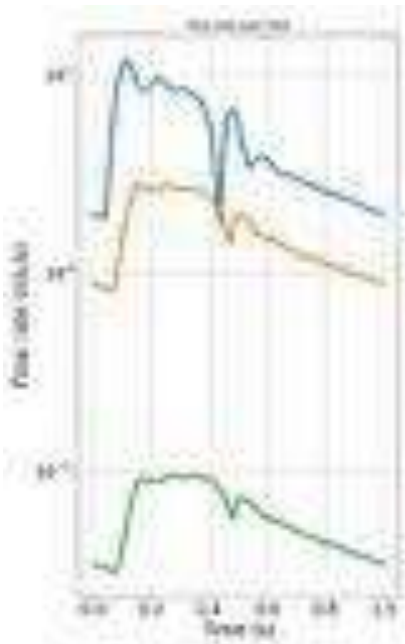


Small Arteries  
See Wright2013

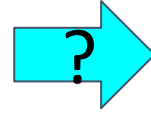
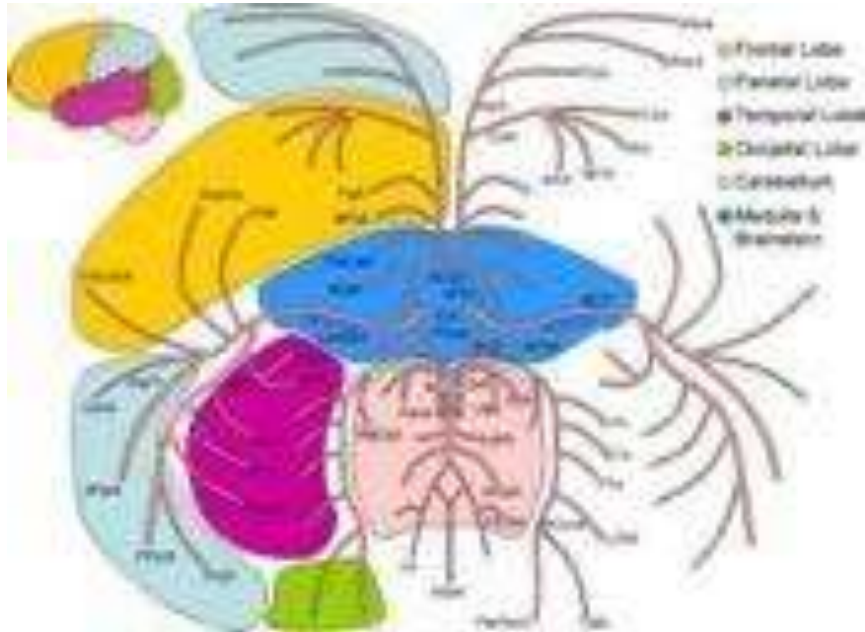
# Blood Flow Simulations



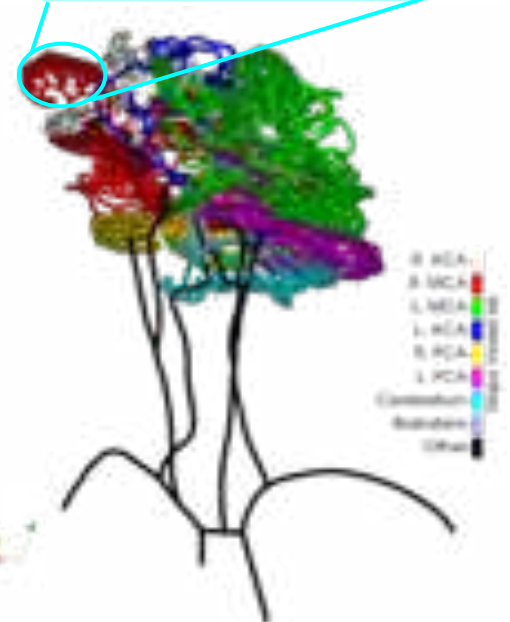
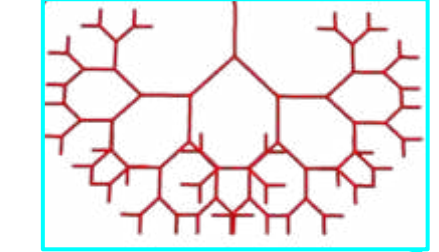
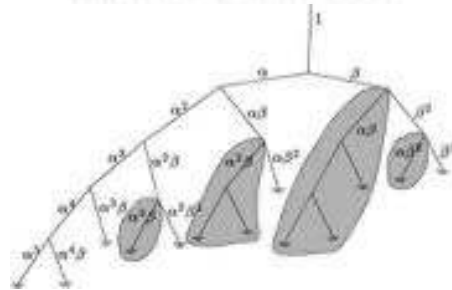
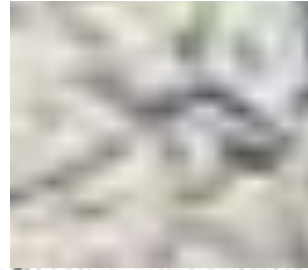
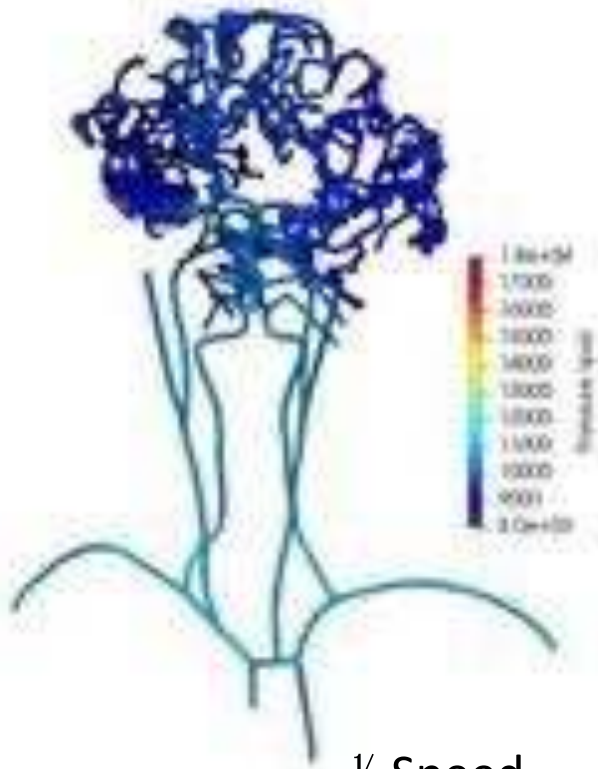
## 1-D Blood flow simulation



# Perfusion territories



# Estimating Perfusion Territories



Bifurcating trees

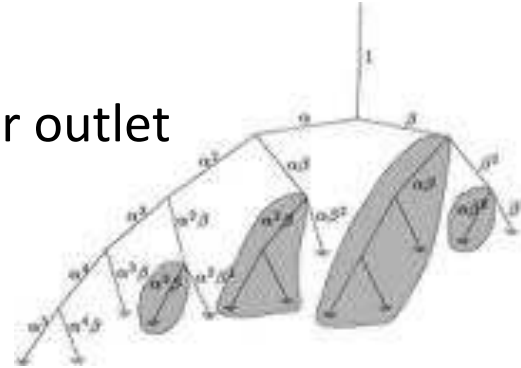


# Estimating Perfusion Territories



Based on the k-means clustering algorithm

1. Generate a bifurcating tree at each outlet.
2. Cut-off radius sets the number of coupling points per outlet
3. Project outlet to the pial surface -> root
4. Find the closest set of points to the root -> cluster
5. Minimize the root-point distance within the clusters
6. Update the root
7. Convergence or max iteration reached?
  - a. Yes -> done
  - b. No -> go to step 4
8. Repeat for each major region.



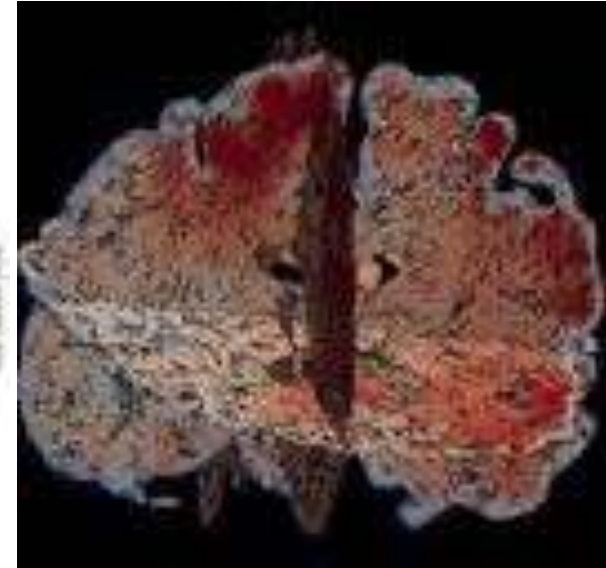
# Input to the perfusion model



Estimated Perfusion territories



1-D blood flow simulation



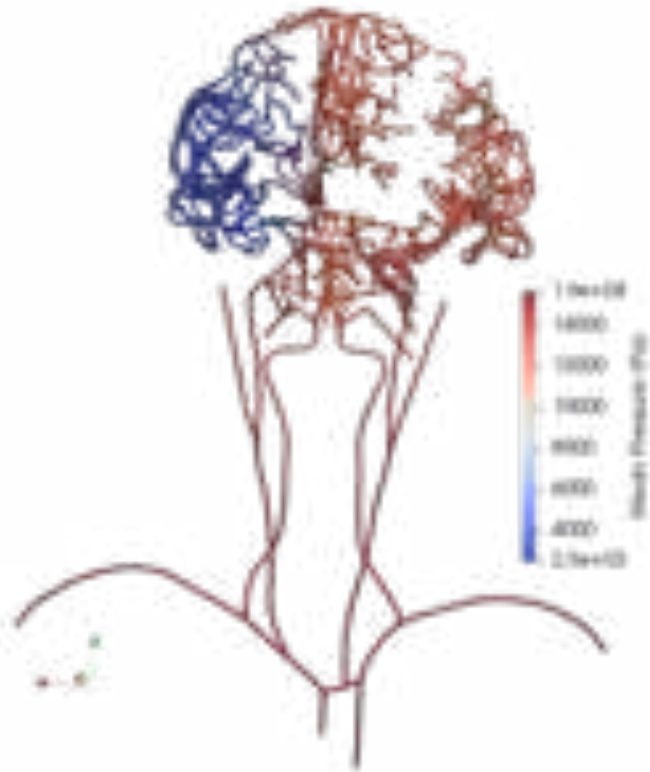
Perfusion model

Work By Tamás Jozsa et al.

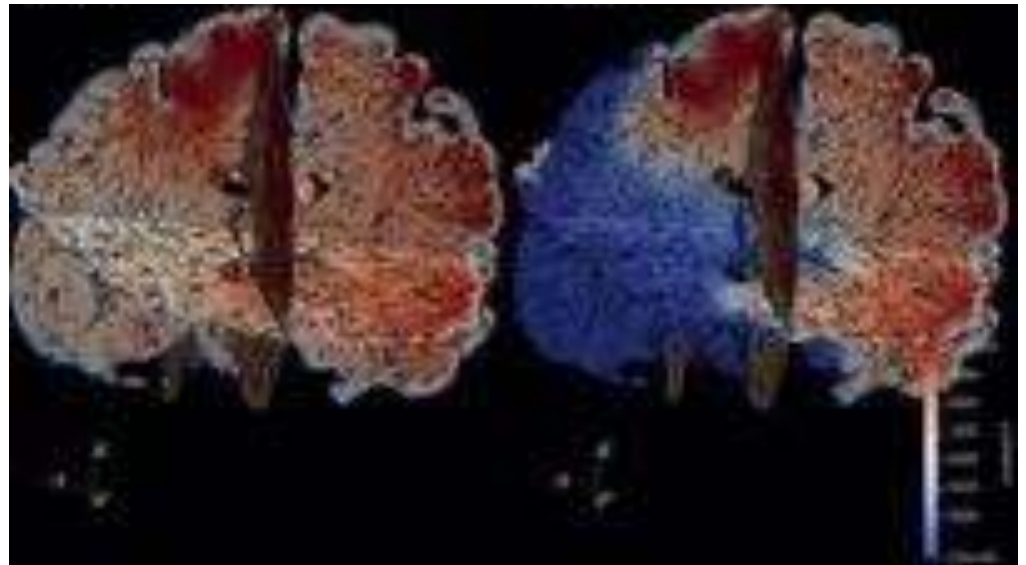
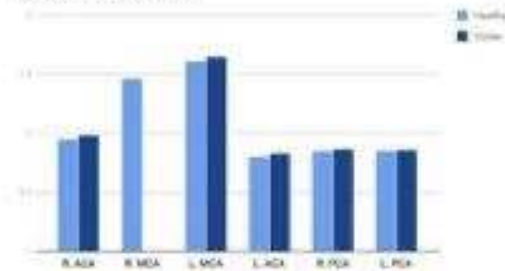
A cerebral circulation model for in silico clinical trials of ischaemic stroke

Presented 25th September at 11:35.

# Stroke modelling



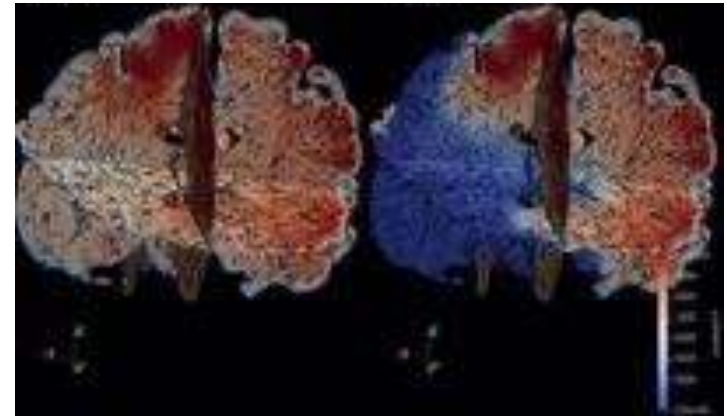
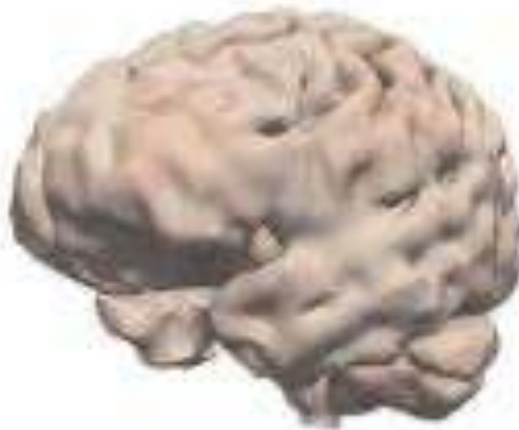
Healthy vs Stroke, R MCA



# Summary

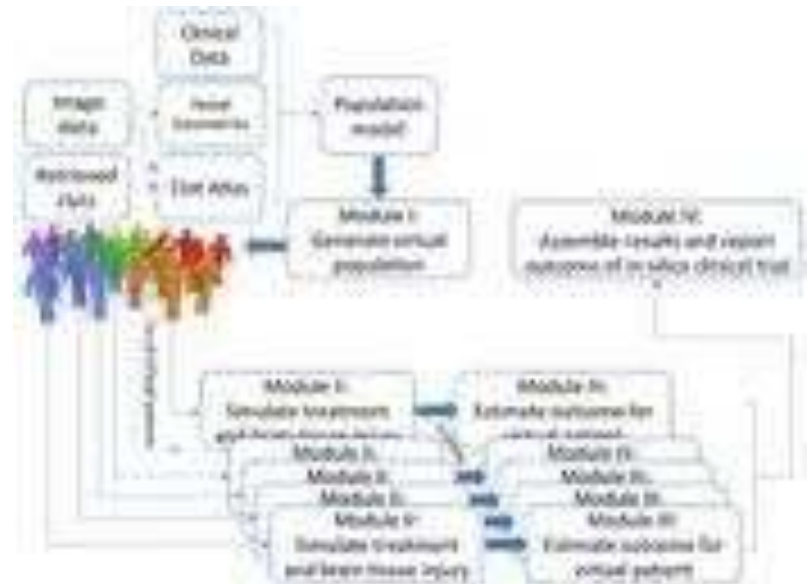
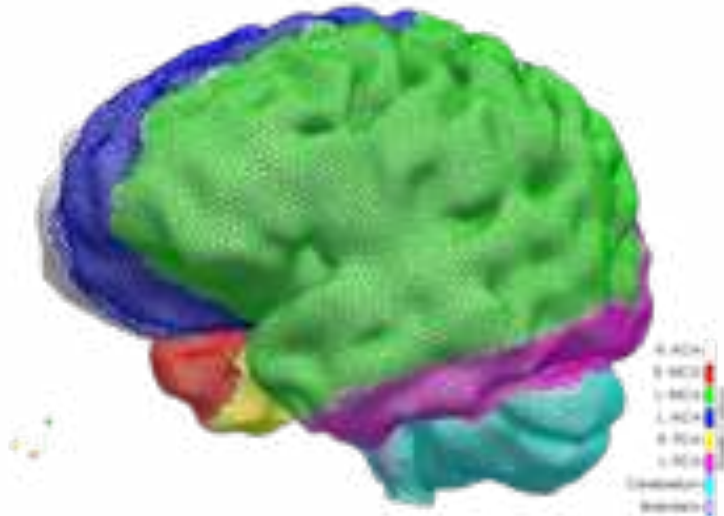
---

- Multiscale patient-specific model
- Estimating perfusion territories
- Stroke and infarct volume modelling



# Future plans

- Two-way coupling
- *In Silico* trial integration
- Pial surface network
- VVUQ



Thanks for listening!  
Questions?



# In Silico Clinical Trials for Treatment of Acute Ischemic Stroke (INSIST)



[Insist-h2020.eu](http://Insist-h2020.eu)





# References



- Wright**, S. N., Kochunov, P., Mut, F., Bergamino, M., Brown, K. M., Mazziotta, J. C., ... Ascoli, G. A. (2013). Digital reconstruction and morphometric analysis of human brain arterial vasculature from magnetic resonance angiography. *NeuroImage*, 82, 170–181. <https://doi.org/10.1016/j.neuroimage.2013.05.089>
- Sobotta**, J., Atlas and Text-book of Human Anatomy Volume III Vascular System, Lymphatic system, Nervous system and Sense Organs
- David**, T., & Moore, S. (2008). Modeling perfusion in the cerebral vasculature. *Medical Engineering and Physics*, 30(10), 1227–1245. <https://doi.org/10.1016/j.medengphy.2008.09.008>
- Liebeskind**, D. S. (2003). Collateral circulation. *Stroke*, 34(9), 2279–2284. <https://doi.org/10.1161/01.STR.0000086465.41263.06>
- Winship**, I. R., Armitage, G. A., Ramakrishnan, G., Dong, B., Todd, K. G., & Shuaib, A. (2014). Augmenting collateral blood flow during ischemic stroke via transient aortic occlusion. *Journal of Cerebral Blood Flow and Metabolism*, 34(1), 61–71. <https://doi.org/10.1038/jcbfm.2013.162>
- Duvernoy**, H. M., Delon, S., & Vannson, J. L. (1981). Cortical blood vessels of the human brain. *Brain Research Bulletin*, 7(5), 519–579. [https://doi.org/10.1016/0361-9230\(81\)90007-1](https://doi.org/10.1016/0361-9230(81)90007-1)
- Hirsch**, S., Reichold, J., Schneider, M., Székely, G., & Weber, B. (2012). Topology and Hemodynamics of the Cortical Cerebrovascular System. *Journal of Cerebral Blood Flow & Metabolism*, 32(6), 952–967. <https://doi.org/10.1038/jcbfm.2012.39>
- Schmid**, F., Barrett, M. J. P., Jenny, P., & Weber, B. (2019). Vascular density and distribution in neocortex. *NeuroImage*, 197, 792–805. <https://doi.org/10.1016/j.neuroimage.2017.06.046>
- Karch**, R., Neumann, F., Neumann, M., & Schreiner, W. (2000). Staged Growth of Optimized Arterial Model Trees. *Annals of Biomedical Engineering*, 28(5), 495–511. <https://doi.org/10.1114/1.290>
- Olufsen**, M. S. (1999). Structured tree outflow condition for blood flow in larger systemic arteries. *American Journal of Physiology-Heart and Circulatory Physiology*, 276(1), H257–H268. <https://doi.org/10.1152/ajpheart.1999.276.1.H257>
- <http://www.svuhradiology.ie/case-study/occluded-middle-cerebral-artery-ct-angiography/>
- <https://en.wikipedia.org/wiki/Stroke>
- <https://radiopaedia.org/>

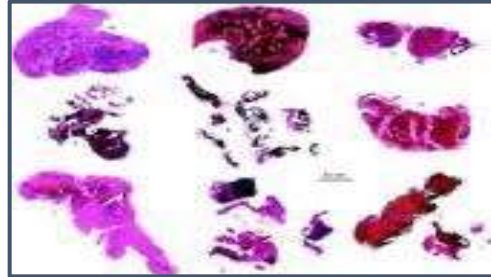
# INSIST Research Projects



Population Model



Clot properties



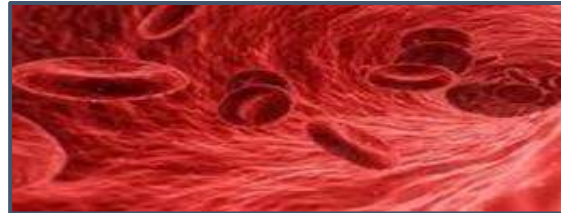
Thrombosis and thrombolysis



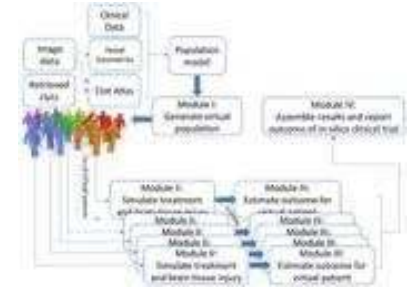
Thrombectomy



Blood flow and perfusion



Integration



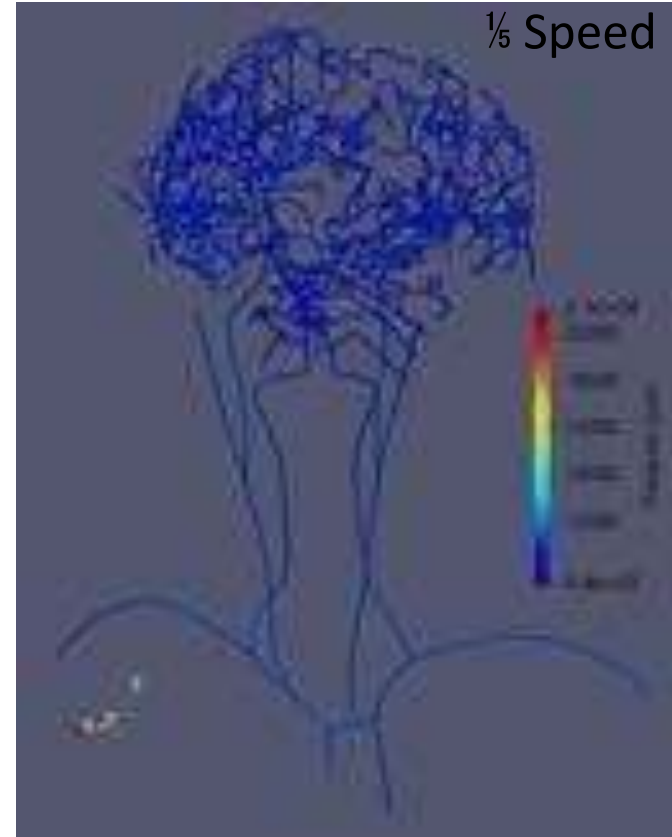
## 1-D Blood flow simulation

- Elastic tubes
- Incompressible fluid
- Detailed flow profiles
- Computational inexpensive

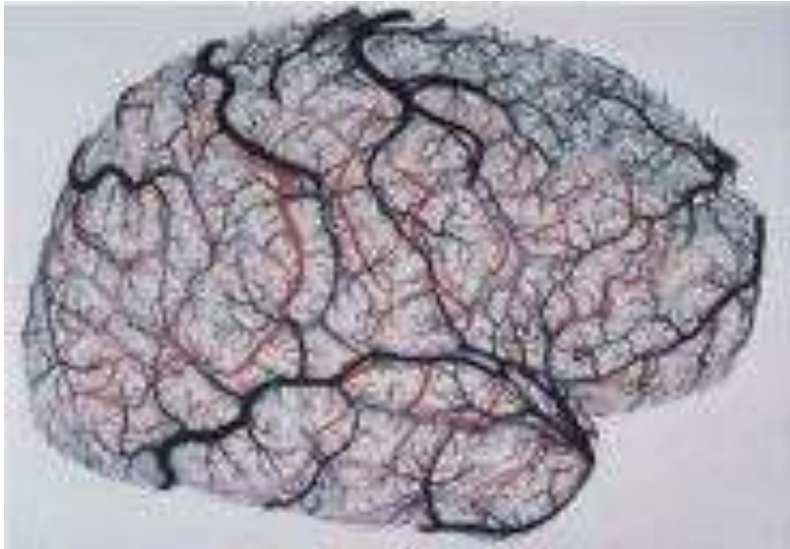
$$\frac{\partial \bar{v}_x}{\partial t} + (2\alpha - 1)\bar{v}_x \frac{\partial \bar{v}_x}{\partial x} + (\alpha - 1) \frac{\bar{v}_x^2}{A} \frac{\partial A}{\partial x} + \frac{1}{\rho} \frac{\partial p}{\partial x} = -2 \frac{\alpha}{\alpha - 1} \nu \pi \frac{\bar{v}_x}{A}$$

$$\frac{\partial A}{\partial t} + \frac{\partial(\bar{v}_x A)}{\partial x} = 0$$

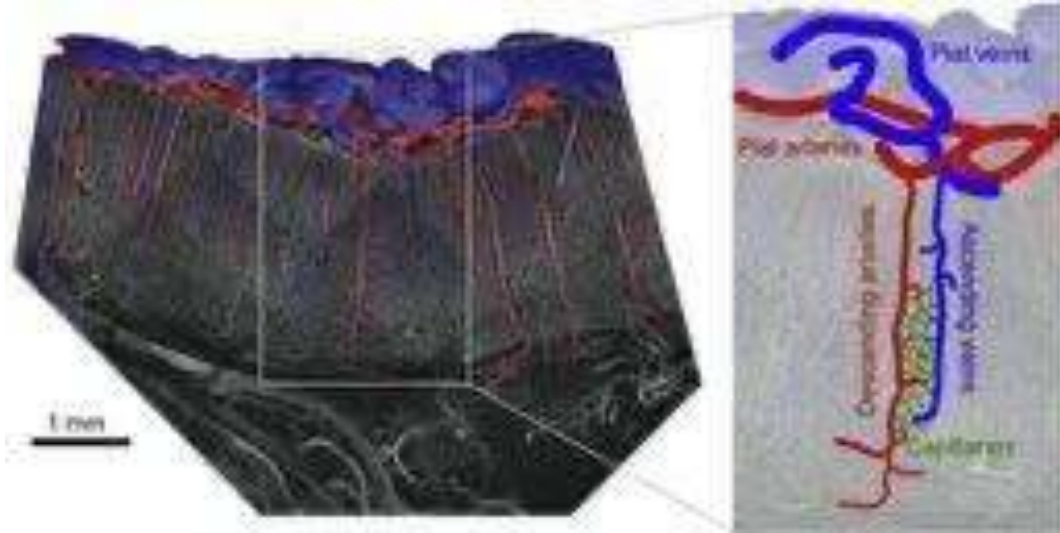
$$p = p_{ext} + \frac{\beta}{A_0} (\sqrt{A} - \sqrt{A_0})$$



# Pial Surface

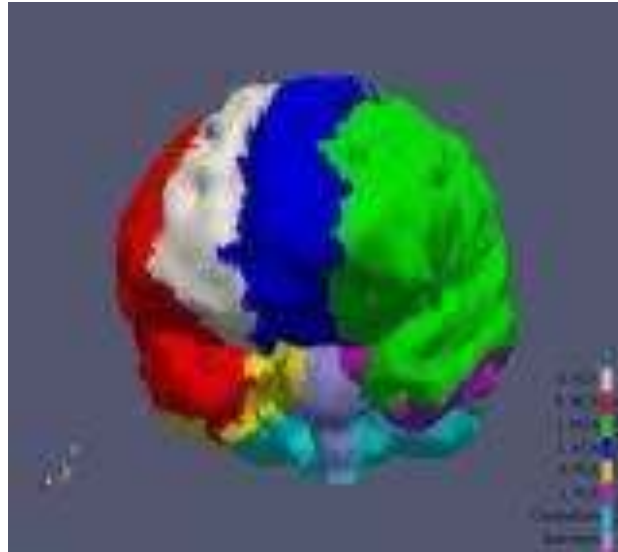
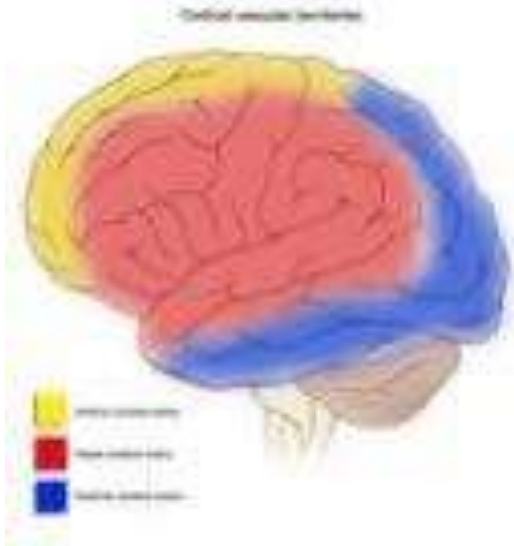


Pial surface vessels

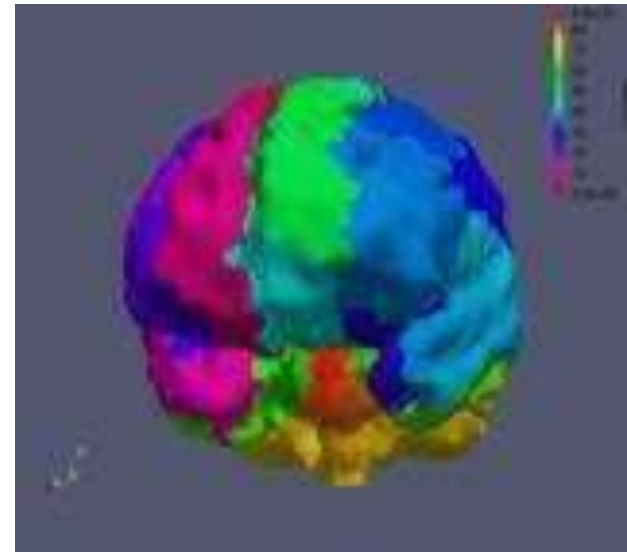


Penetrating vessels

# Estimating Perfusion Territories



Major Regions



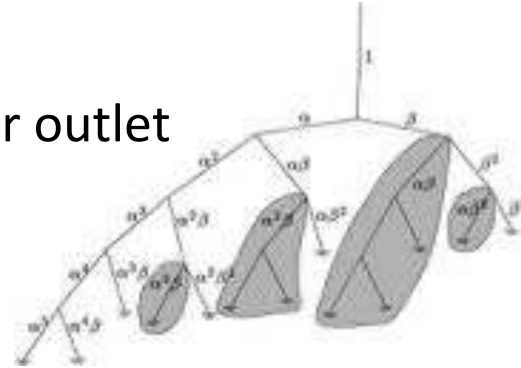
Detailed Regions

# Estimating Perfusion Territories



Based on the k-means clustering algorithm

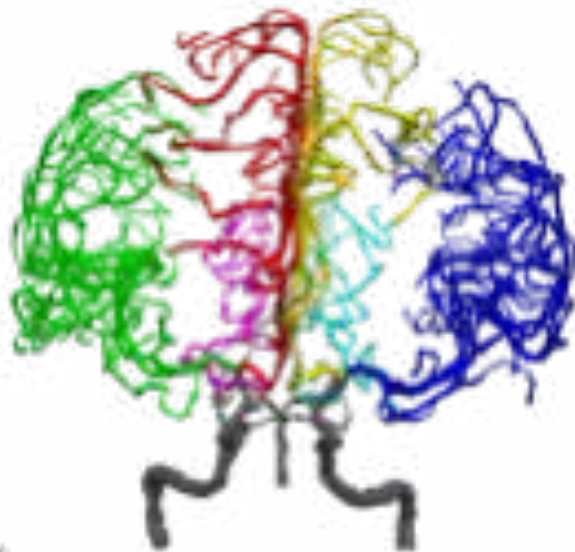
1. Generate a bifurcating tree at each outlet.
2. Cut-off radius sets the number of coupling points per outlet
3. Project outlet to the pial surface -> root
4. Find the closest set of points to the root -> cluster
5. Minimize the root-point distance within the clusters
6. Update the root
7. Convergence or max iteration reached?
  - a. Yes -> done
  - b. No -> go to step 4
8. Repeat for each major region.



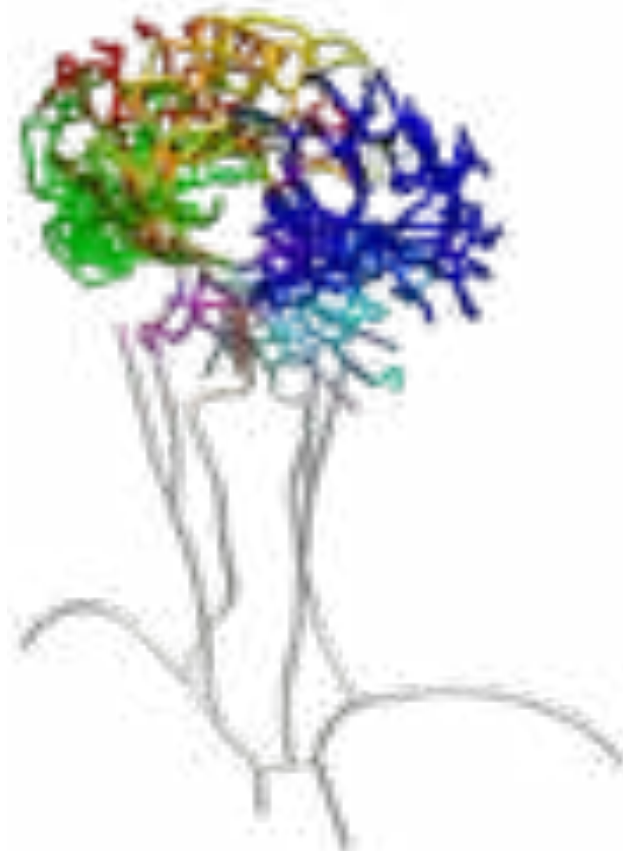
# Patient Vasculature



Large Arteries



Cerebral Arteries



Merged Network

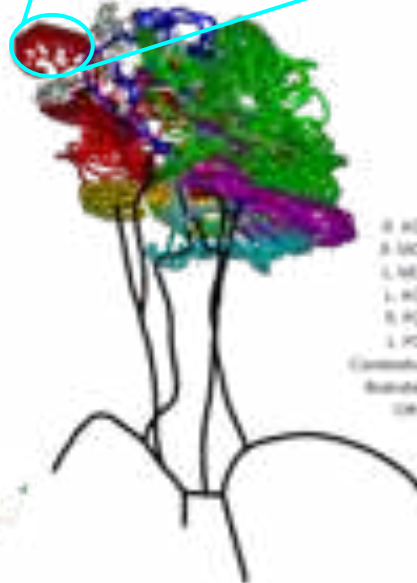
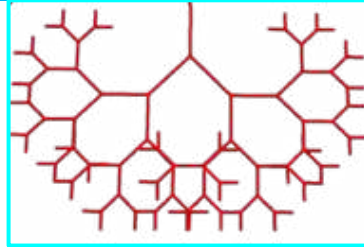
# Model Scales



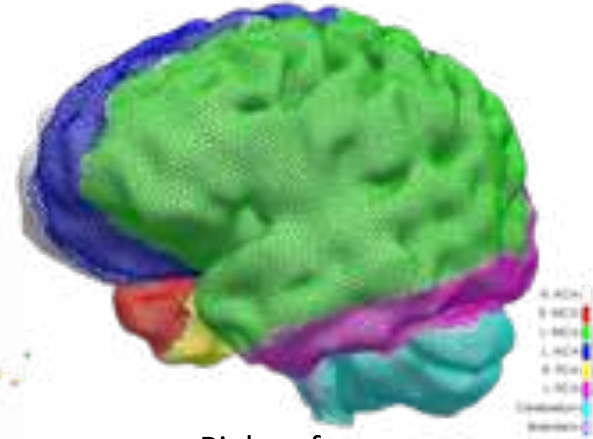
Large Arteries



Cerebral Arteries



Bifurcating trees



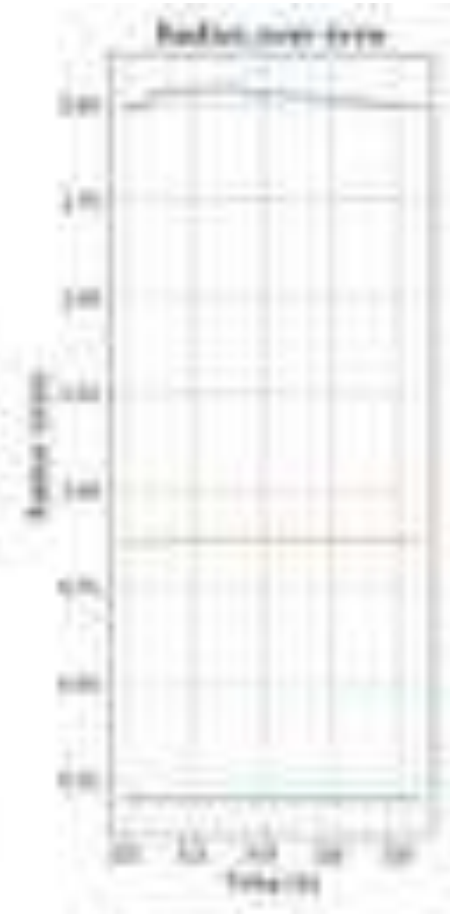
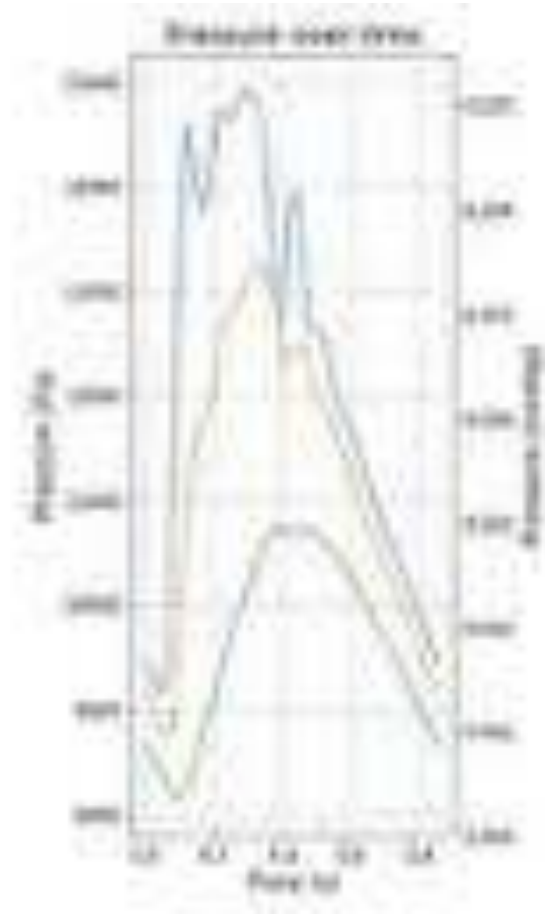
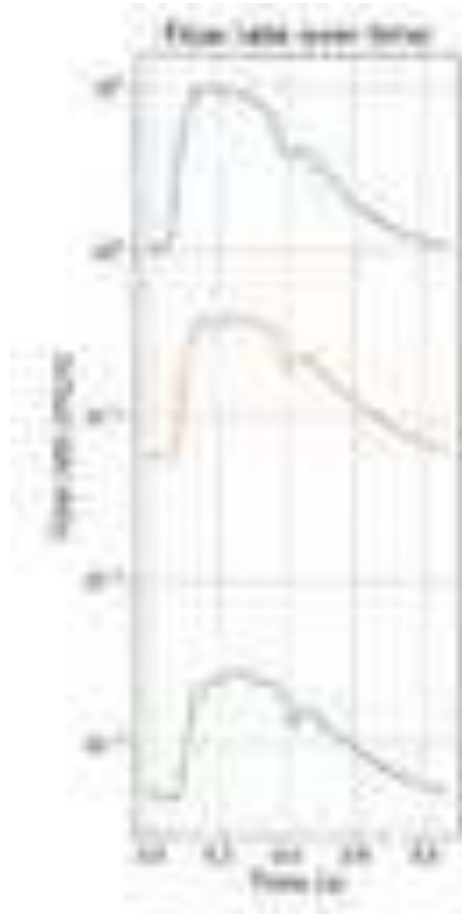
Pial surface



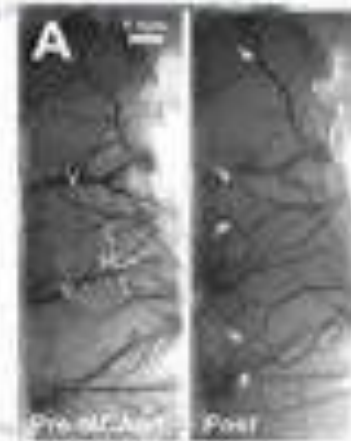
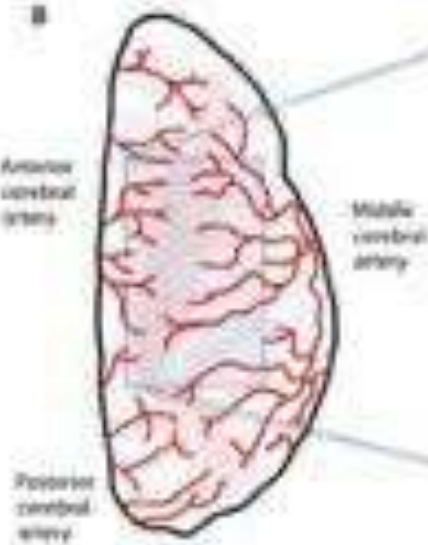
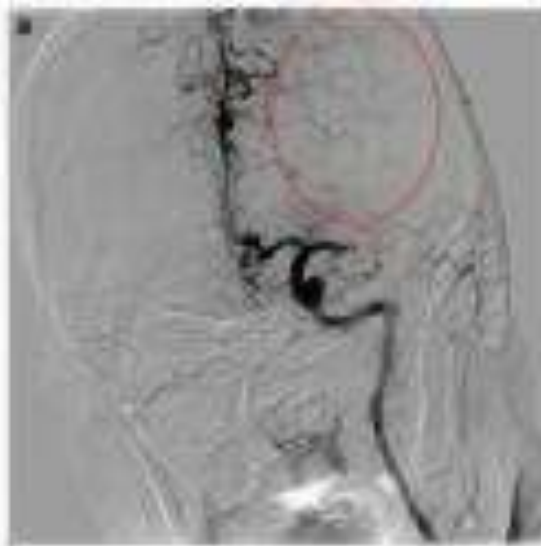
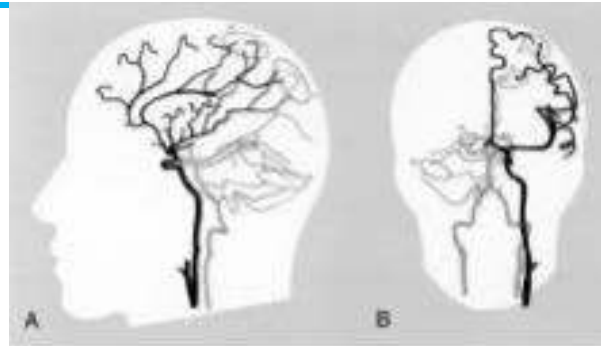
Penetrating arteries



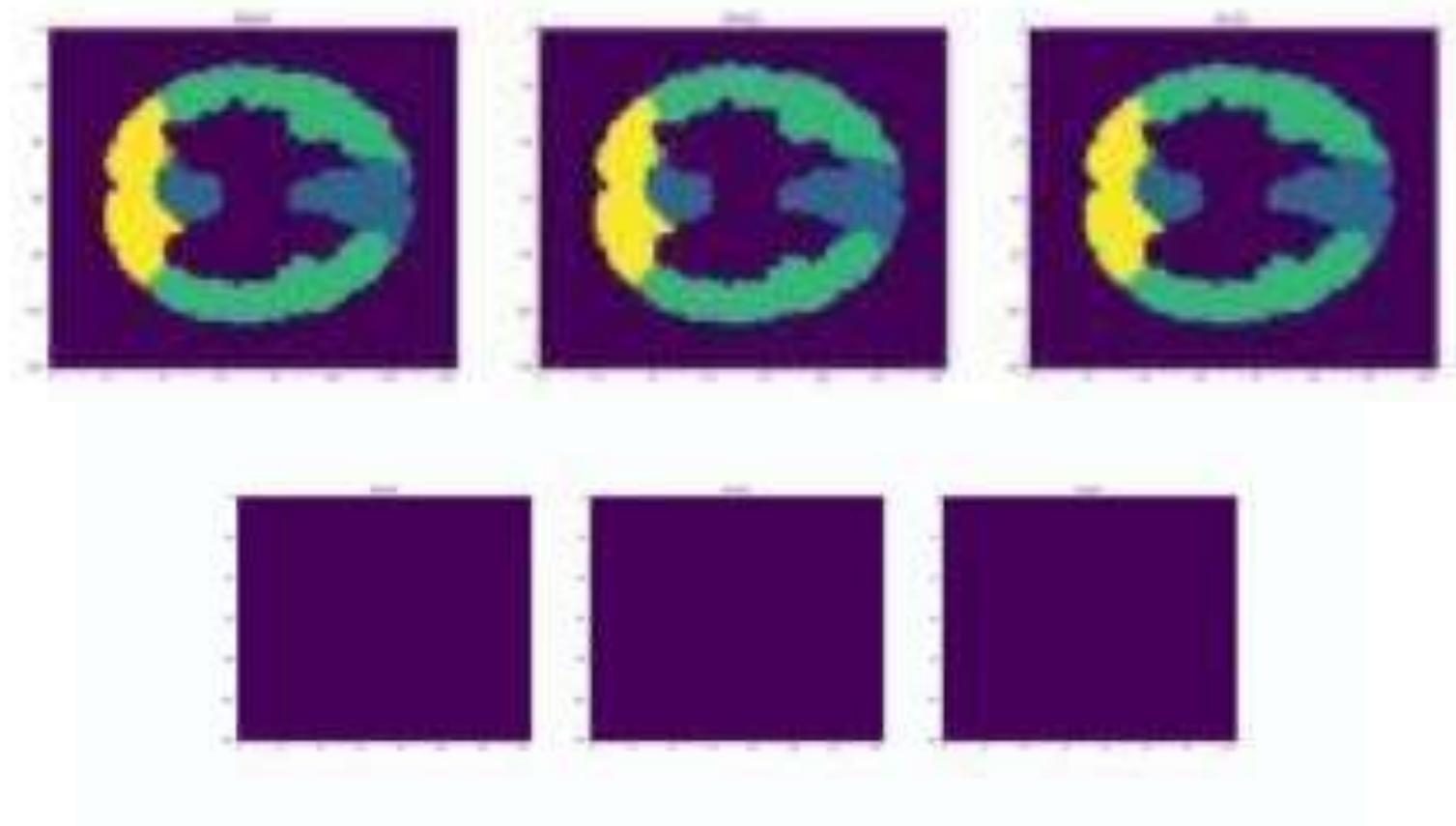
# 1-D blood flow results



# Collaterals

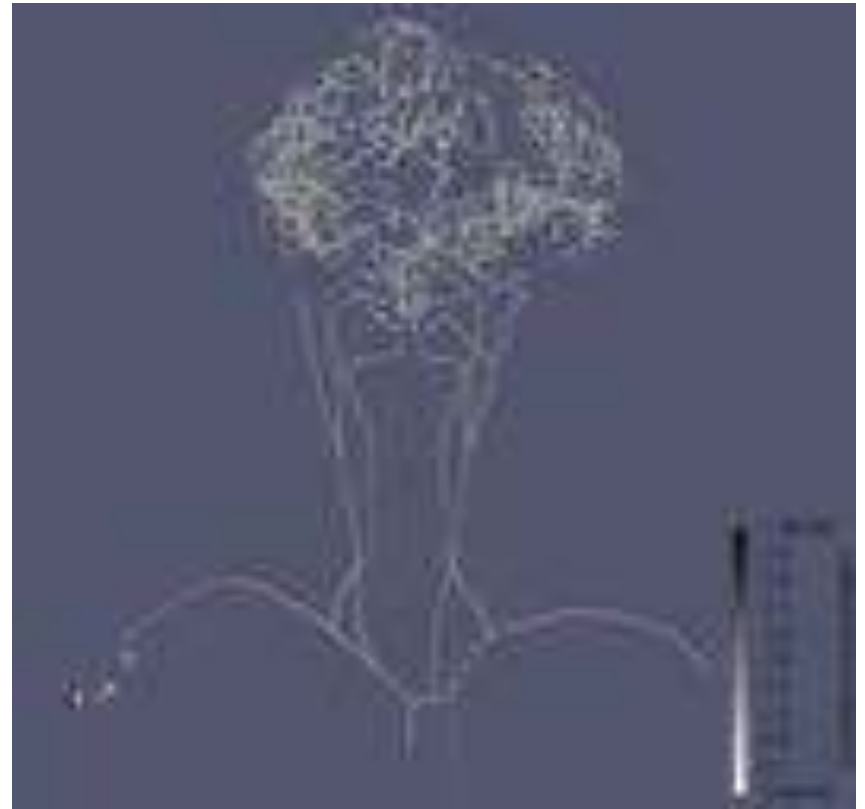


# Arterial Spin labelling data



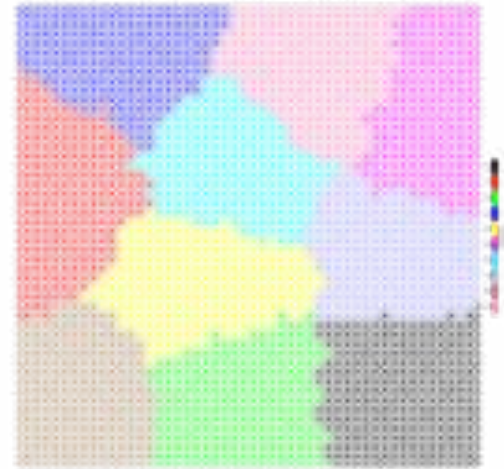
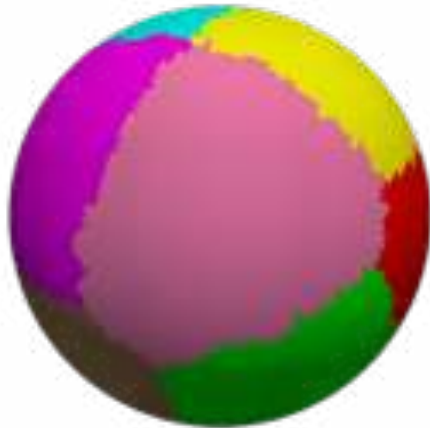
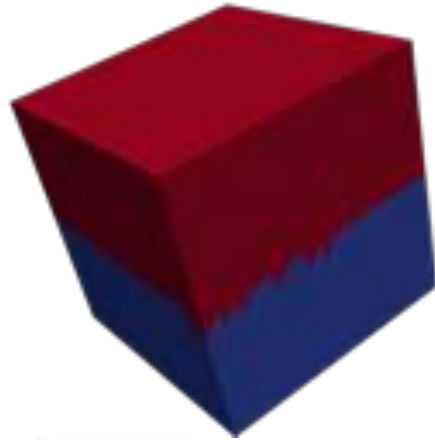
# Contrast advection model

---

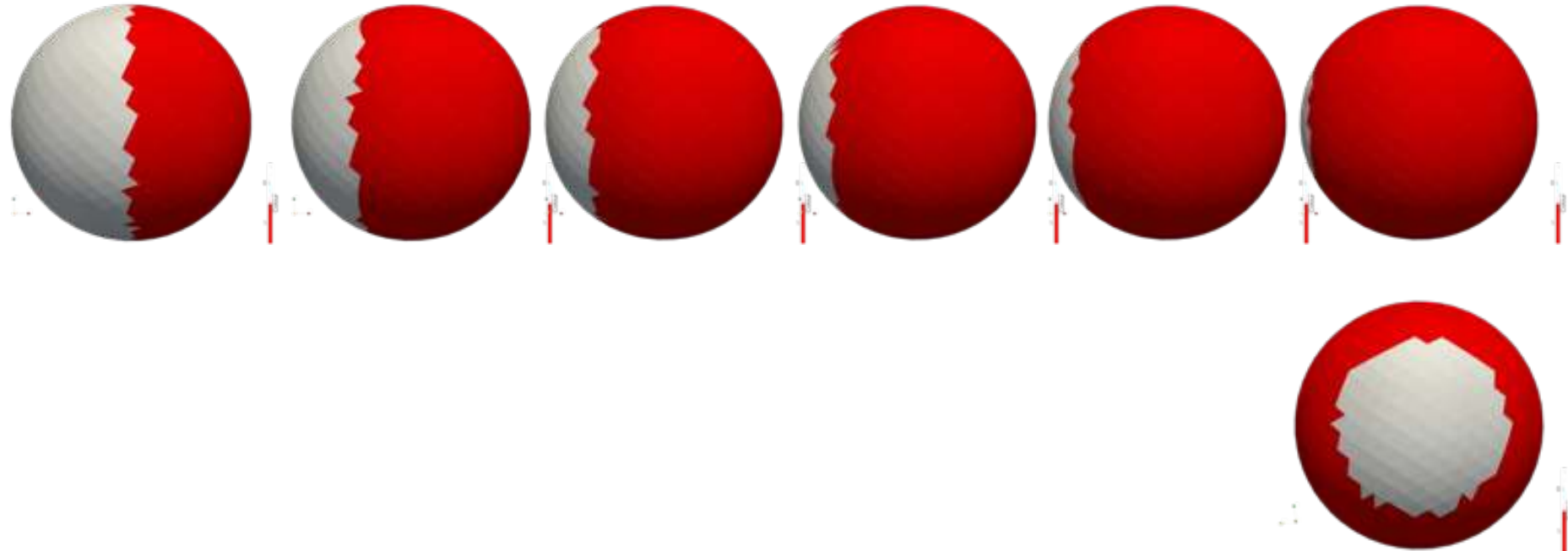


# Verification

---



# Clustering on a sphere with different ratios



# Cerebral Circulation

