Low frequency oscillating gradient spin-echo sequences improves sensitivity to axon diameter

An experimental validation study in viable nerve tissue

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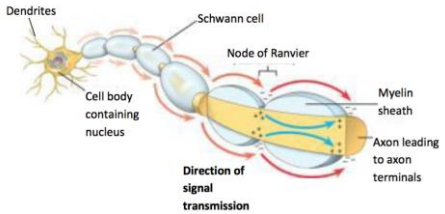
Declaration of Financial Interests or Relationships

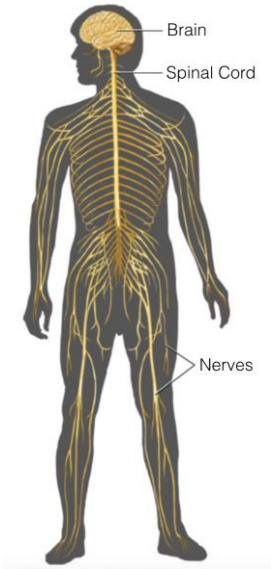
Speaker Name: Lebina Shrestha Kakkar

I have no financial interests or relationships to disclose with regard to the subject matter of this presentation.

Importance of axon diameter

- Axon diameter is directly proportional to conduction velocity
  - In central nervous system **(CNS)**
    - Performance of white matter pathways
  - In peripheral nervous system **(PNS)**
    - Axon regeneration





Radcliff (2015)

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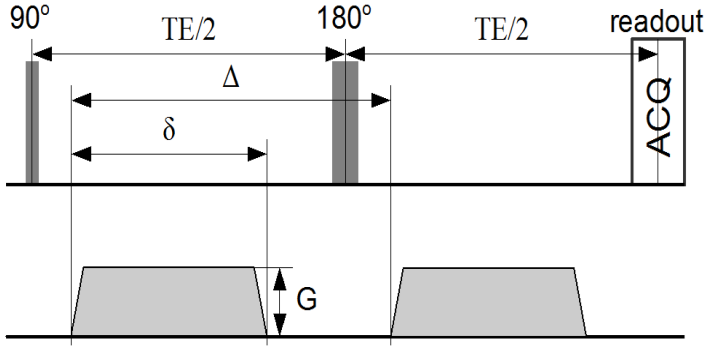
Imaging axon diameters

Spin echo readout sequence

Pulsed gradient spin echo (**PGSE**)



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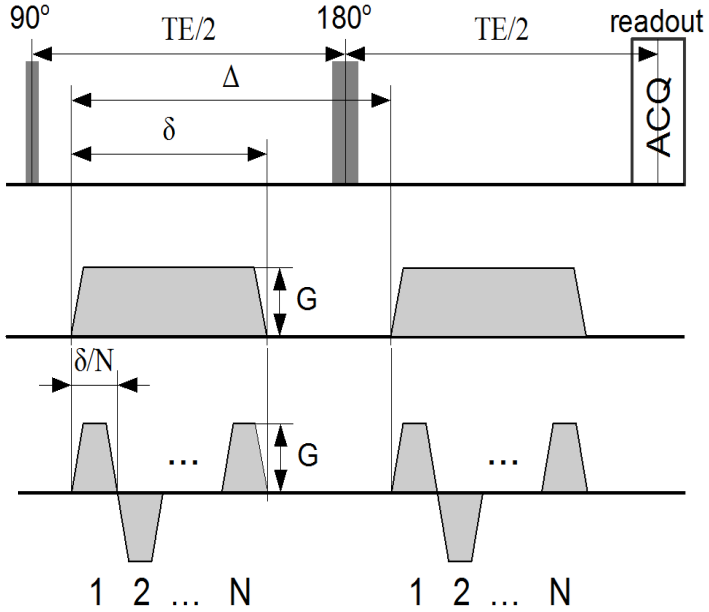
Imaging axon diameters

Spin echo readout sequence

Pulsed Gradient Spin Echo (**PGSE**)

Oscillating Gradient Spin Echo (**OGSE**)



Parsons et al (MRM 2006); Drobnjak et al (JMR 2010,2011); Xu et al (NeuroImage 2014);

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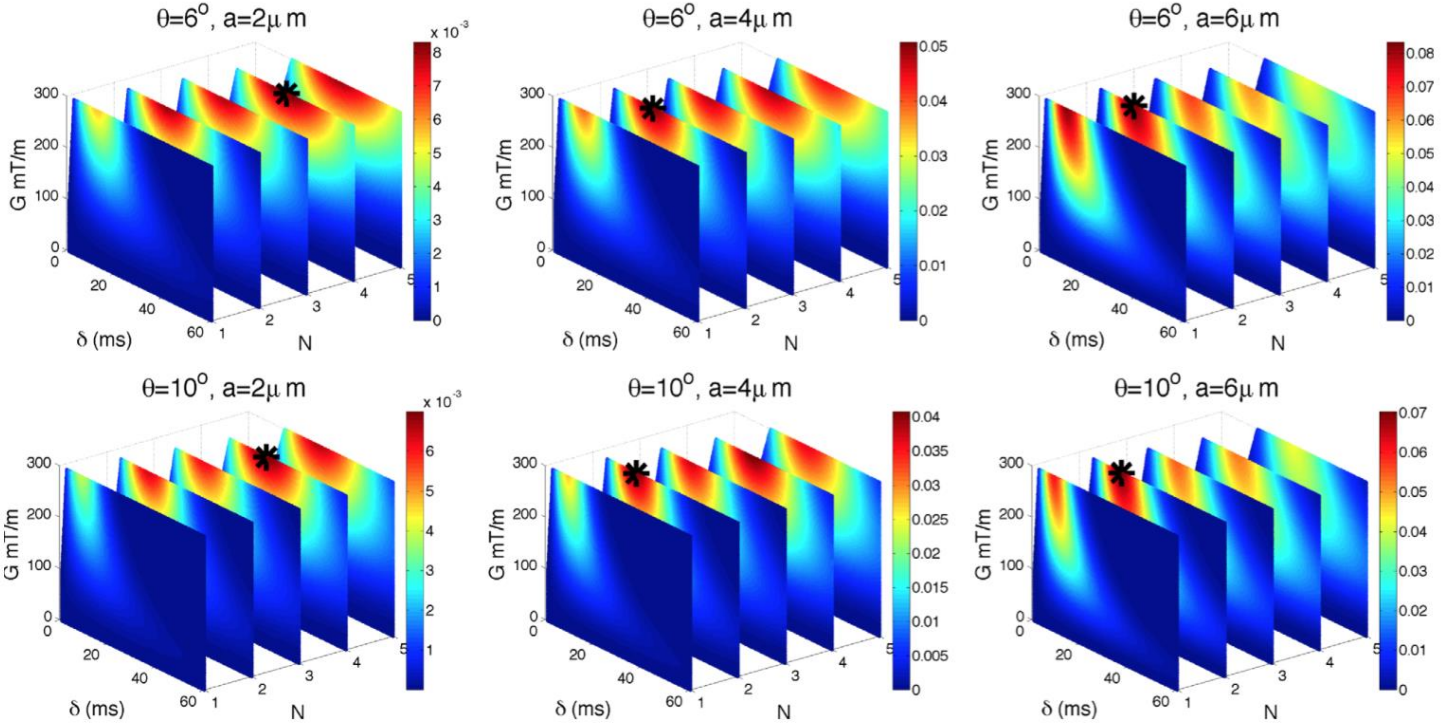
Low frequency OGSE improves signal sensitivity to axon diameter in practical cases



Drobnjak et al (MRM 2015);

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Aim

To experimentally investigate the benefits of OGSEs over PGSEs

to estimate axon diameter index

in a viable rat sciatic nerve

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Active Ax Framework

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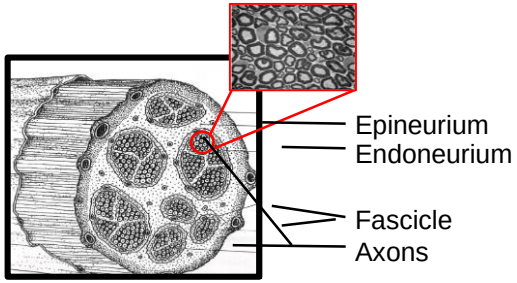
PNS nerve microstructure



Butler et al (2000)

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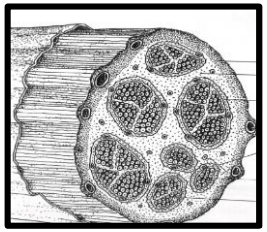
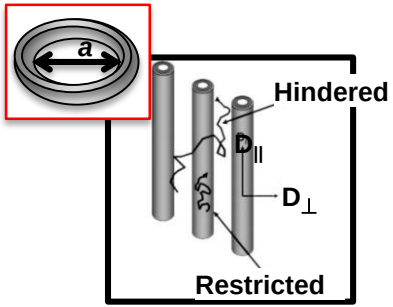
Tissue model





$S = fS_r(D_{||}, a) + (1-f)S_h(D_{||}, D_{\perp})$

Simplified CHARMED tissue model

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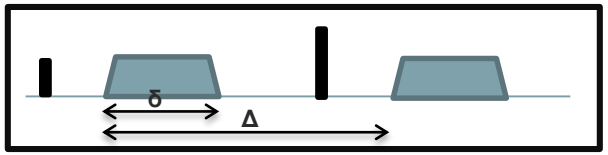
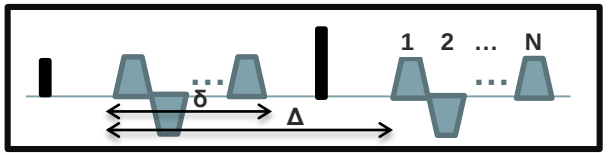
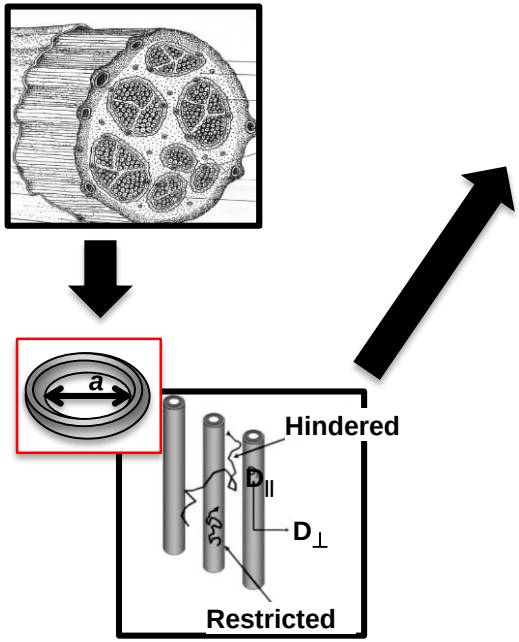
Protocol optimization

Optimized diffusion imaging protocol (**PGSE** and **OGSE**)







$S = fS_r(D_{||}, a) + (1-f)S_h(D_{||}, D_{\perp})$

Scanner parameters:

- G_{max}= 800 mT/m
- SNR = 10 (at TE=30ms)
- # diffusion encoding directions = 32, 16

Model parameter values:

- Volume fraction, ***f*** = 0.6
- Intrinsic diffusivity, $\mathbf{D_{||}}$ = 1.7 μm^2/ms
- Perpendicular diffusivity, $\mathbf{D_{\perp}}$ = 0.7 μm^2/ms
- Axon diameter, ***a*** = 2.3 μm, 4.5 μm, 6.4 μm

Alexander et al (MRM 2008); Alexander et al (NeuroImage 2010); Ikeda & Oka (Brain & Behaviour 2012)

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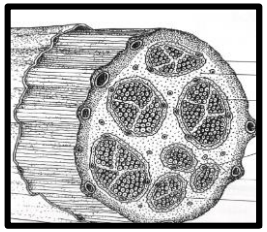
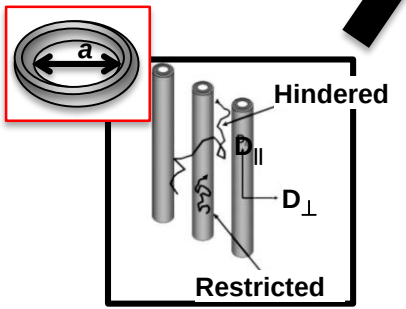
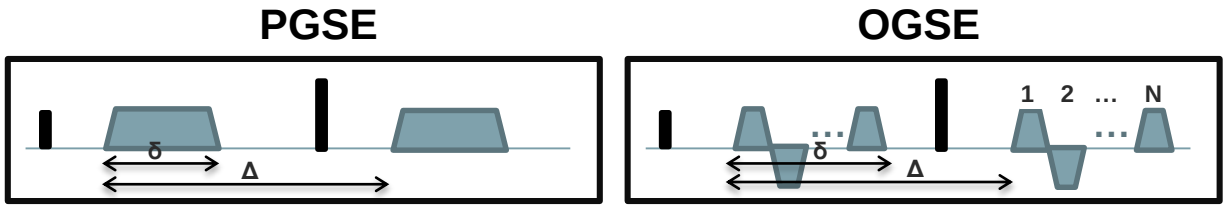
Model fitting





$S = fS_r(D_{||}, a) + (1-f)S_h(D_{||}, D_{\perp})$



Diffusion weighted data

Model fitting accounting for Rician noise

Estimates:

- Diameter index, ***a***
- Intracellular volume fraction, ***f***
- Parallel diffusivity, $\mathbf{D_{||}}$

Alexander et al (MRM 2008); Alexander et al (NeuroImage 2010);

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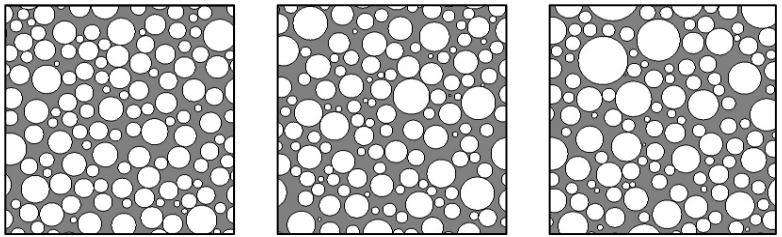
Simulations

- CAMINO Monte Carlo simulator
- Substrates
  - γ distributed diameter cylinders (mean = 2 - 7 μm)
  - *f* = 0.4 - 0.7
- 50 repetitions per substrate (SNR=10)



a = 2.0 μm *a* = 3.9 μm *a* = 6.0 μm

Example γ distributions at *f* = 0.6

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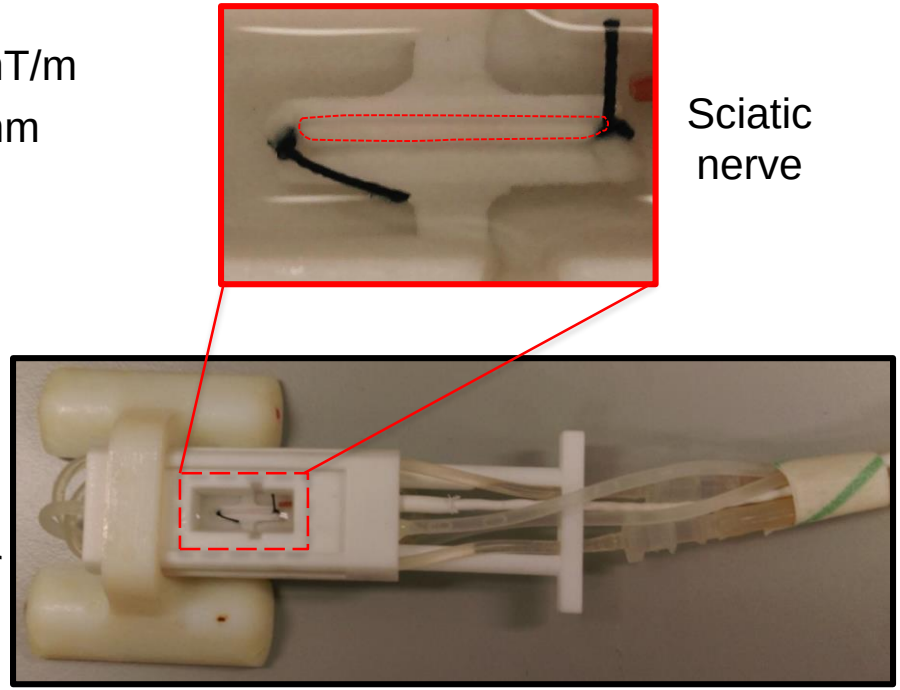
Hall et al (IEEE 2009); Cook et al (ISMRM 2006)

Sciatic nerve experiments

- Scanner
  - 9.4 T Agilent Technolgies; G = 800mT/m
  - Resolution = 94 µm × 94 µm × 2 mm
  - NSA = 8
- Sciatic nerve
  - Male Sprague Dawley rat
- Viability
  - Ligation + Excision
  - MRI compatible incubation chamber
  - Oxygenated aCSF @ 37°C
  - Fixation



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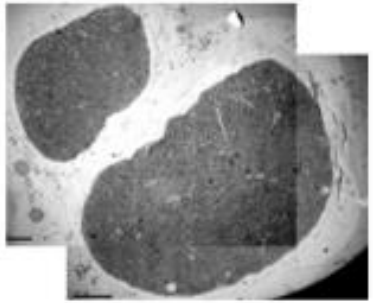
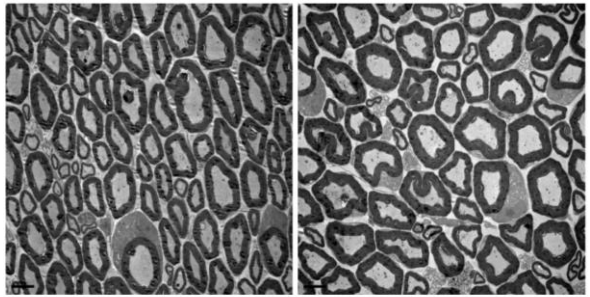
Richardson et al (MRM 2014)

Ground truth estimates from histology

- Transmission electron microscopy (TEM)
  - Central slice
  - Resolution = 64 μm × 64 μm × 5 μm
  - 28 TEM images
  - Matlab based image processing algorithm



TEM of whole sciatic nerve



Samples of magnified TEM of sciatic nerve

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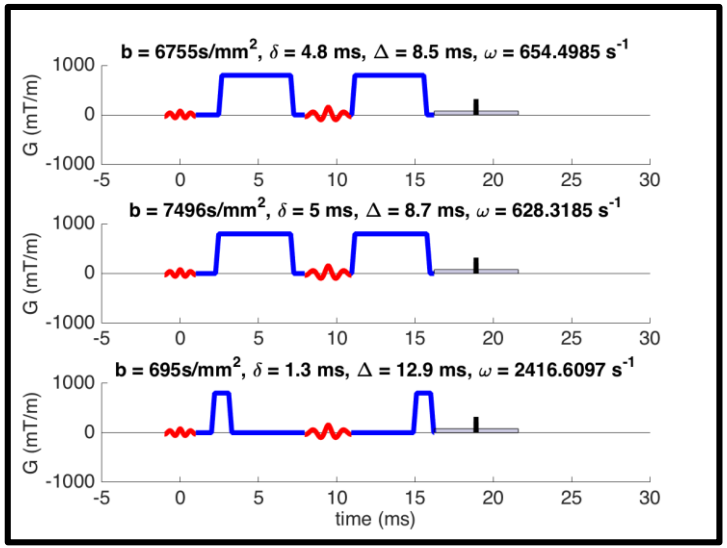
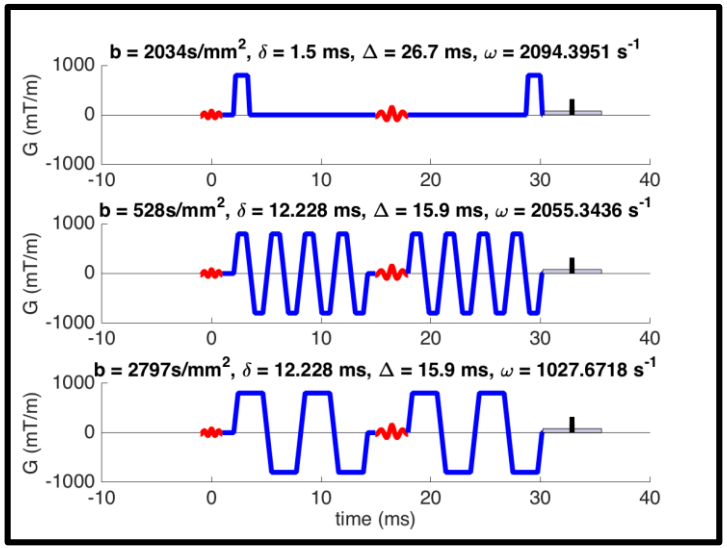
Optimized protocols

PGSE



OGSE



32 gradient directions

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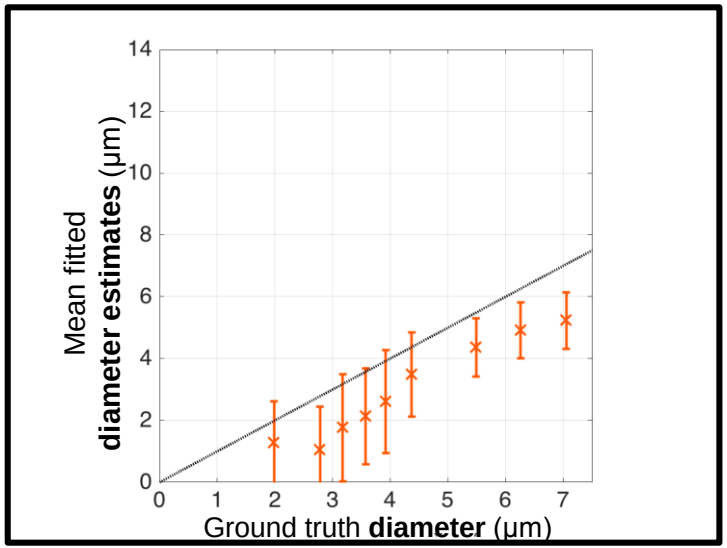
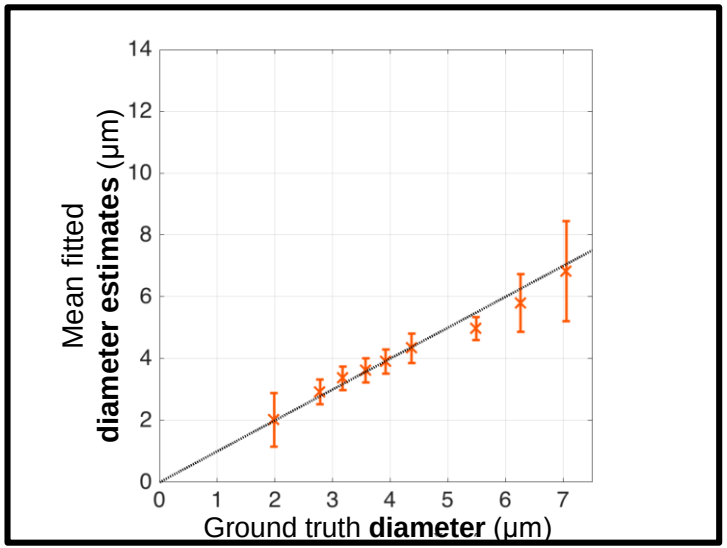
Simulations: Accuracy of diameter index

PGSE



f = 0.7

OGSE



OGSE protocol estimates are more **accurate** than PGSE protocol estimates

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Simulations: Accuracy of diameter index

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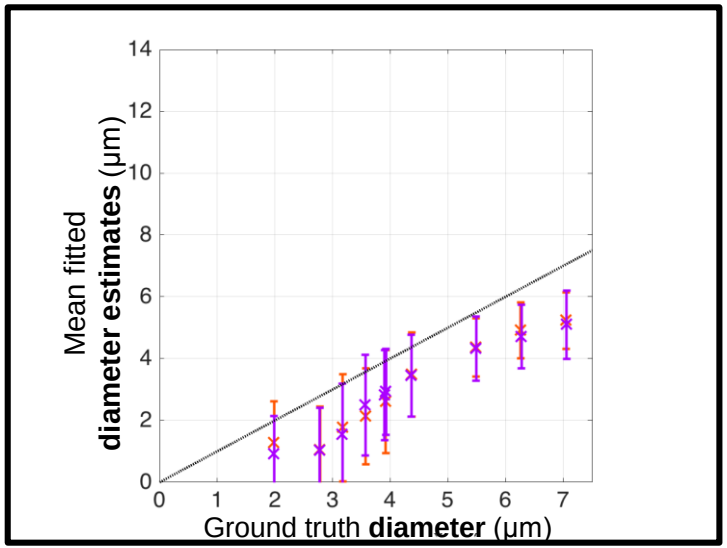
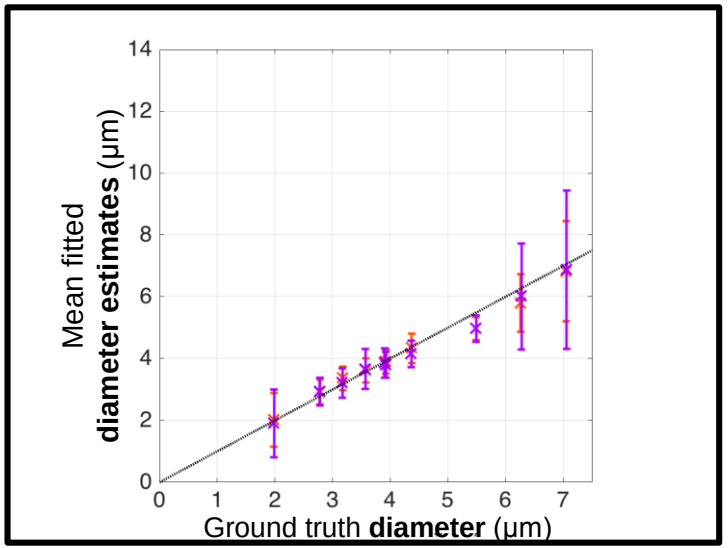


OGSE



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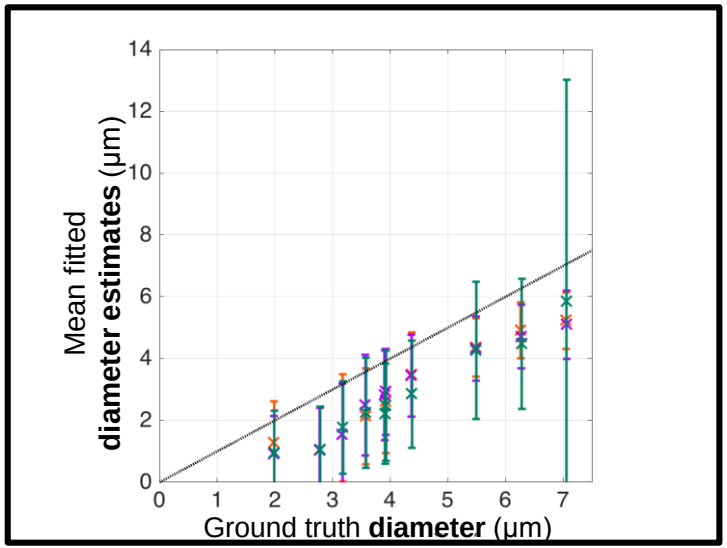
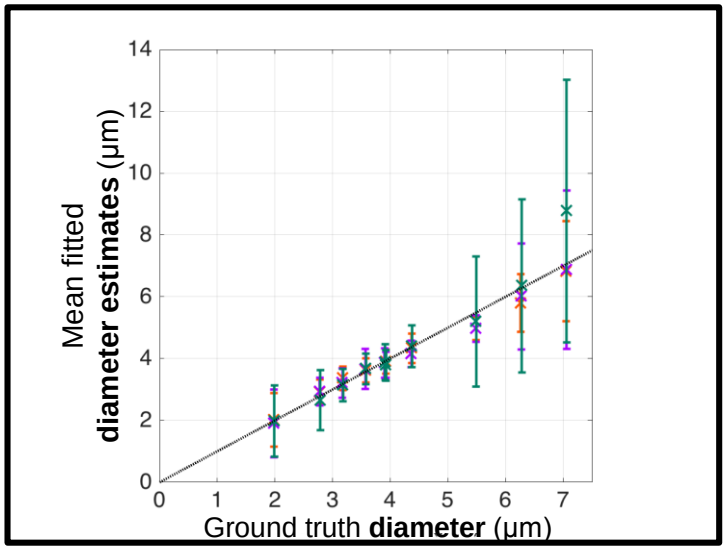


f = 0.7
f = 0.6
f = 0.5

OGSE



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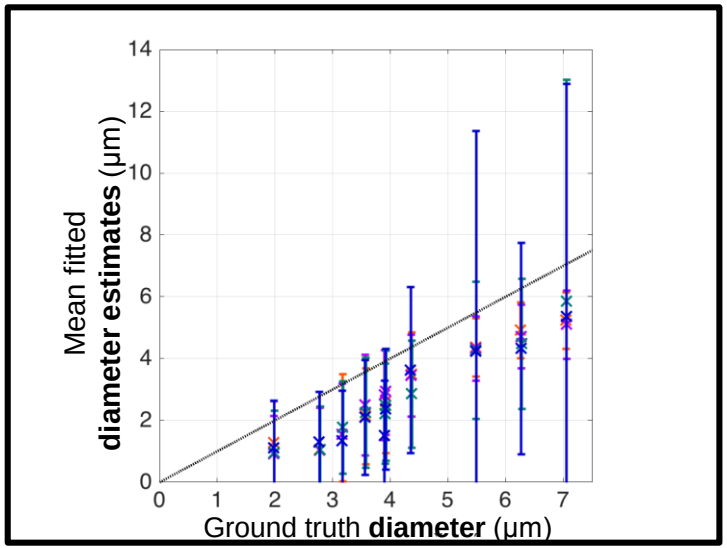
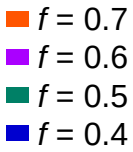
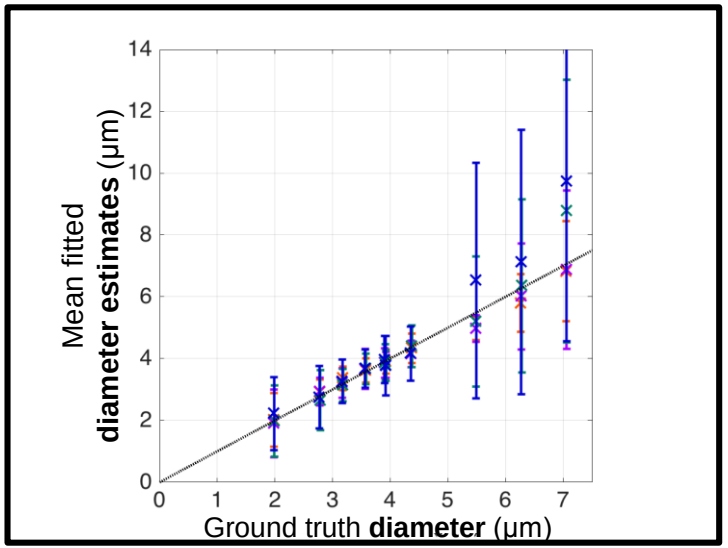




OGSE



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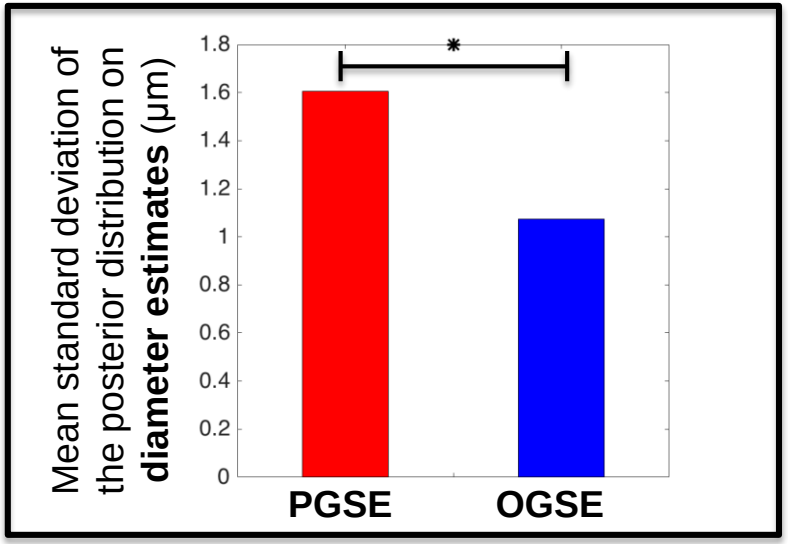
Simulations: Precision of diameter index



* Represents $p < 0.05$

OGSE protocol estimates are more **precise** than PGSE protocol estimates

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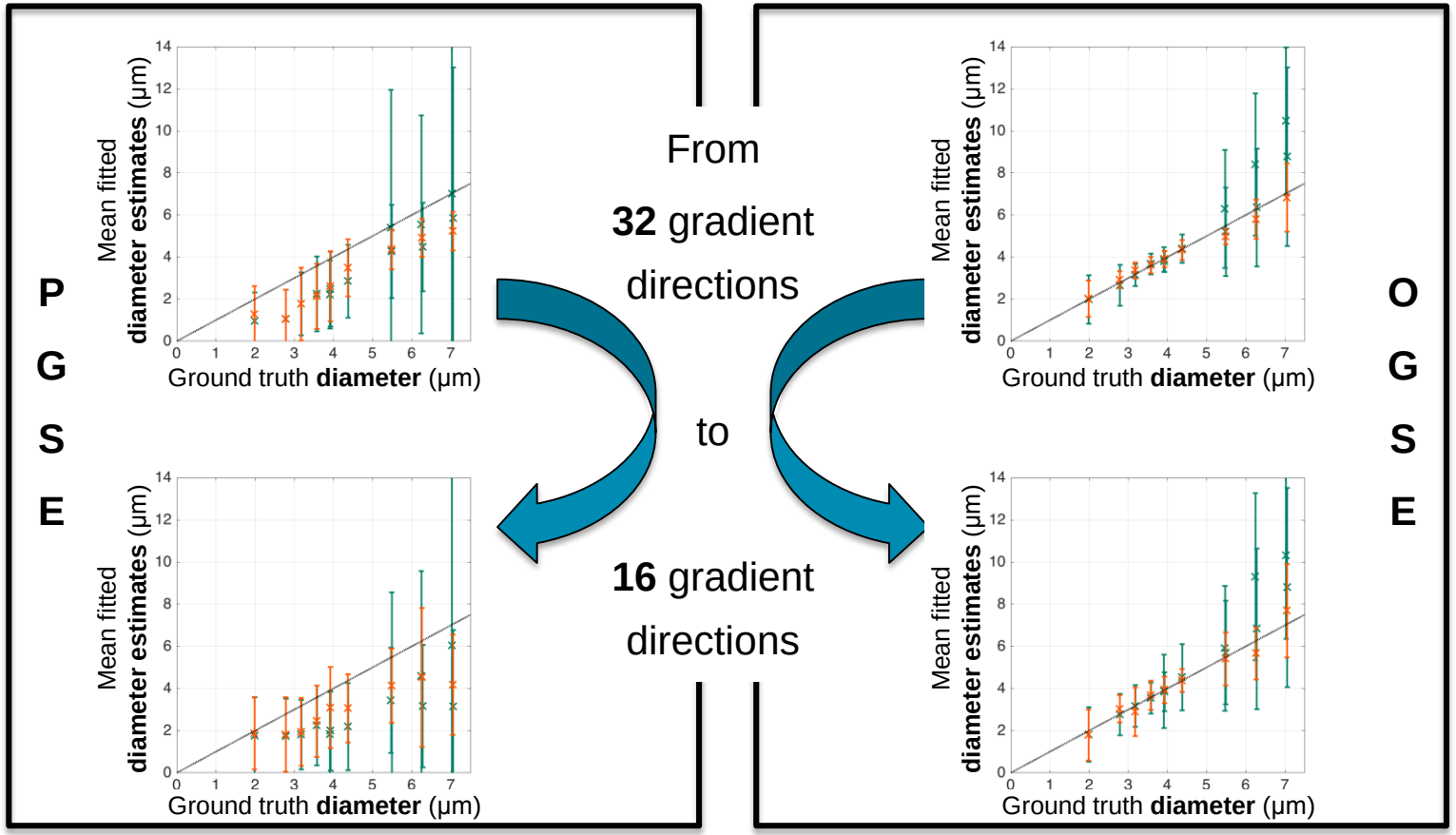
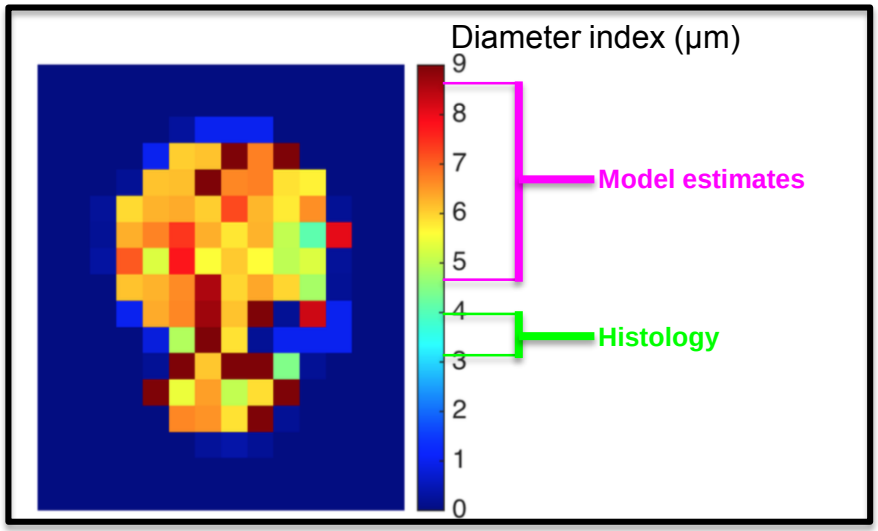
Simulations: Robustness

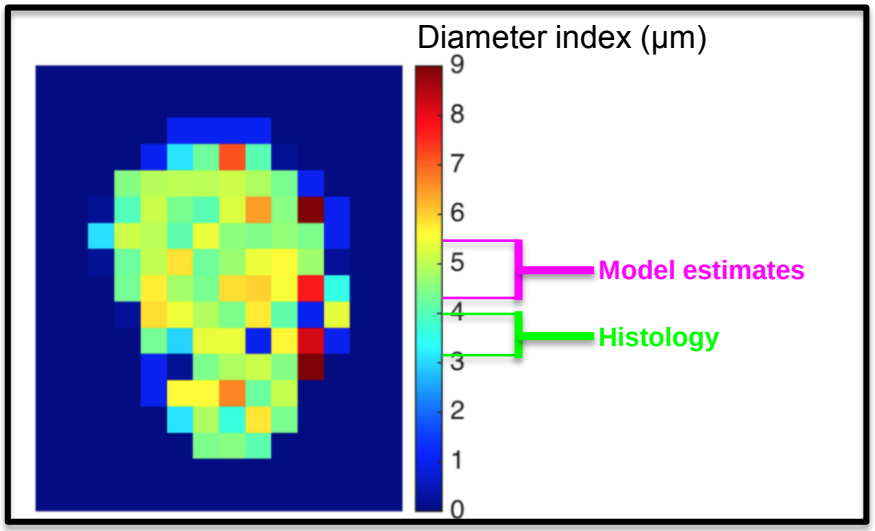


Nerve: Accuracy of diameter index

PGSE



OGSE



OGSE protocol estimates are more **accurate** than PGSE protocol estimates

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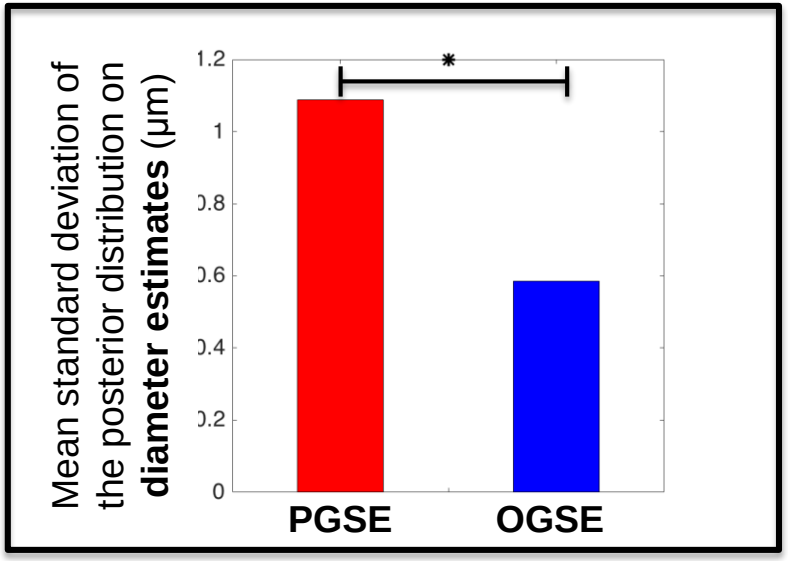

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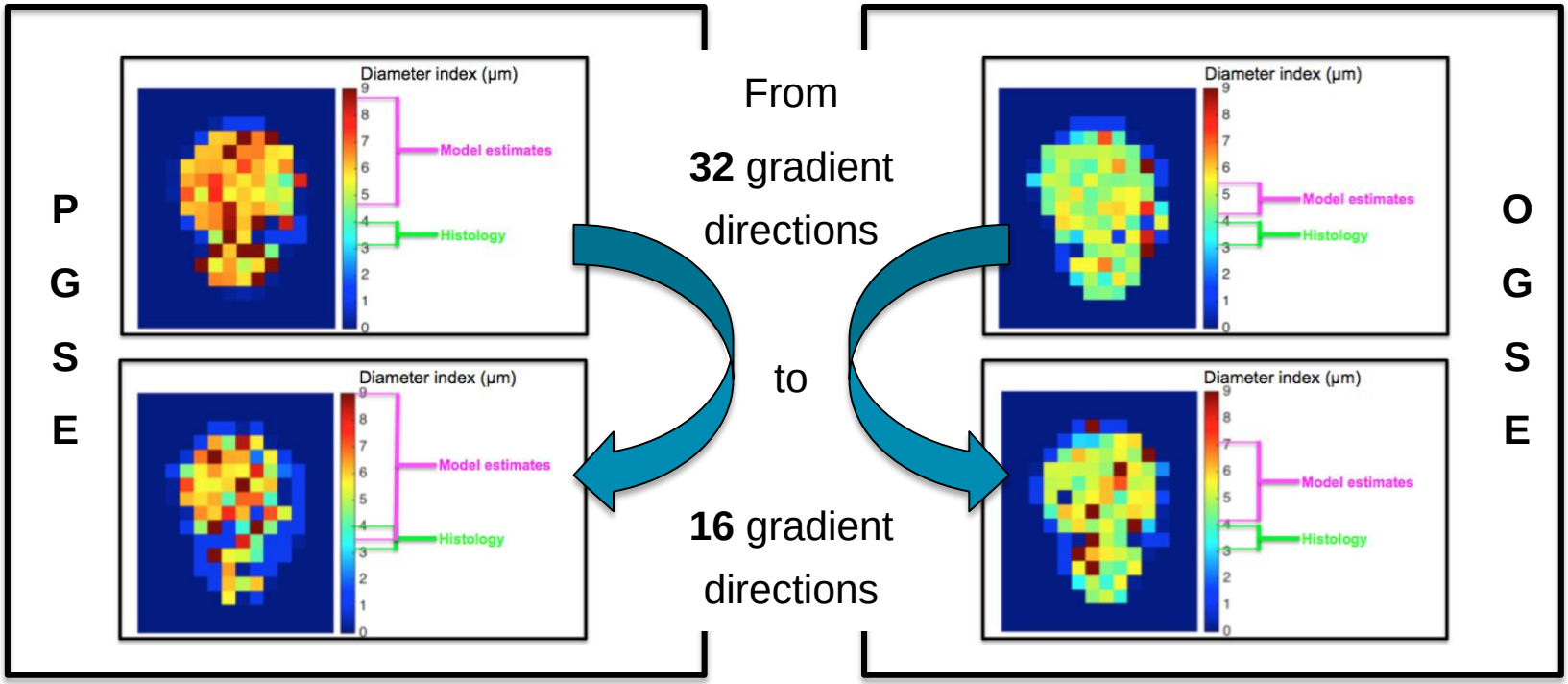

OGSE diameter estimates are **more robust**

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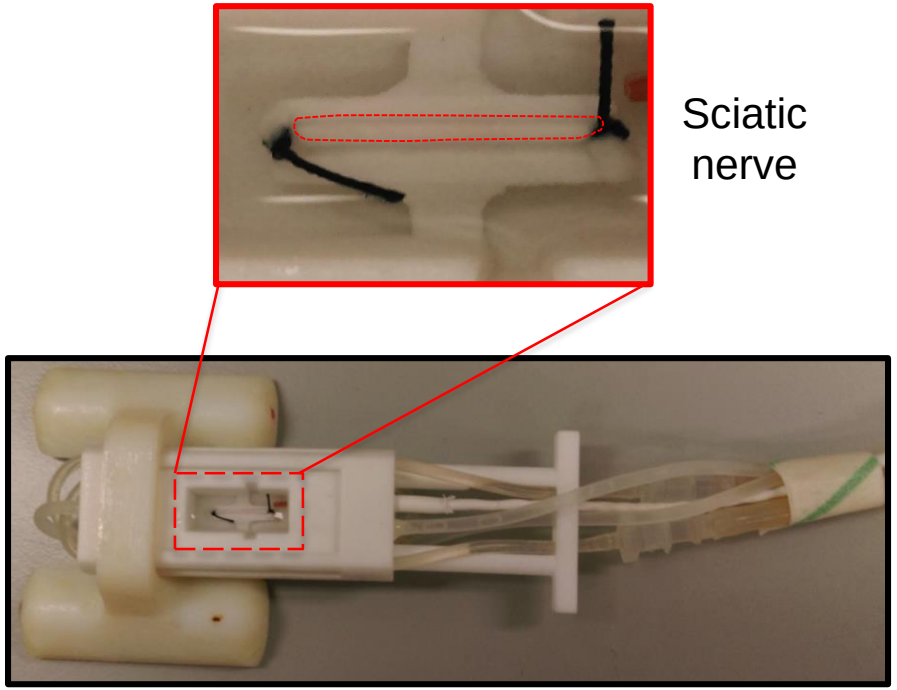
Conclusion

- Viable tissue
  - Avoid fixation effects
  - Realistic diffusion coefficient



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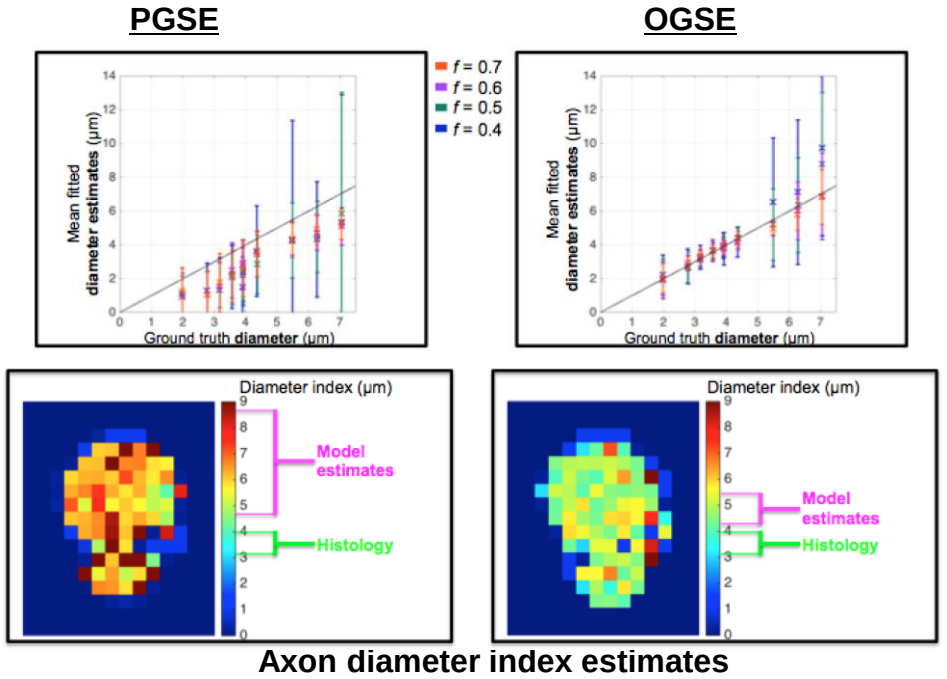

Axon diameter index estimates

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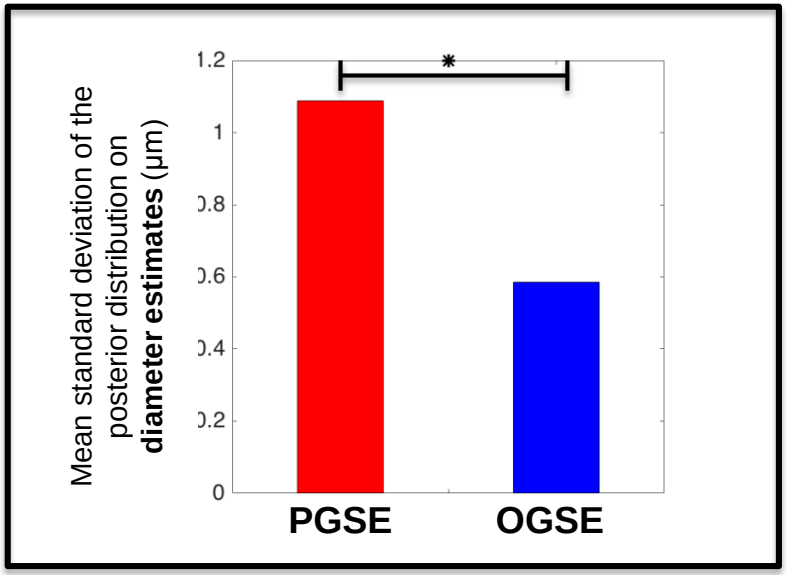

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Conclusion

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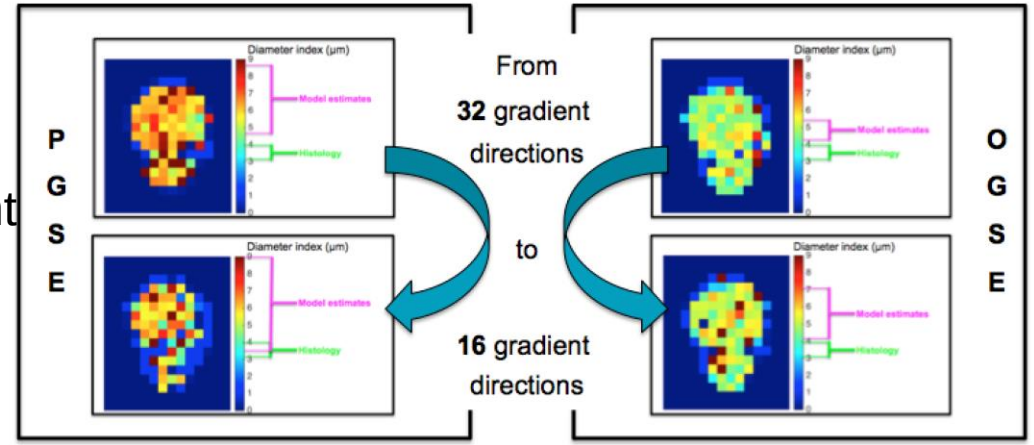
  - More **precise** diameter index
  - More **robust** diameter index



Axon diameter index estimates

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