



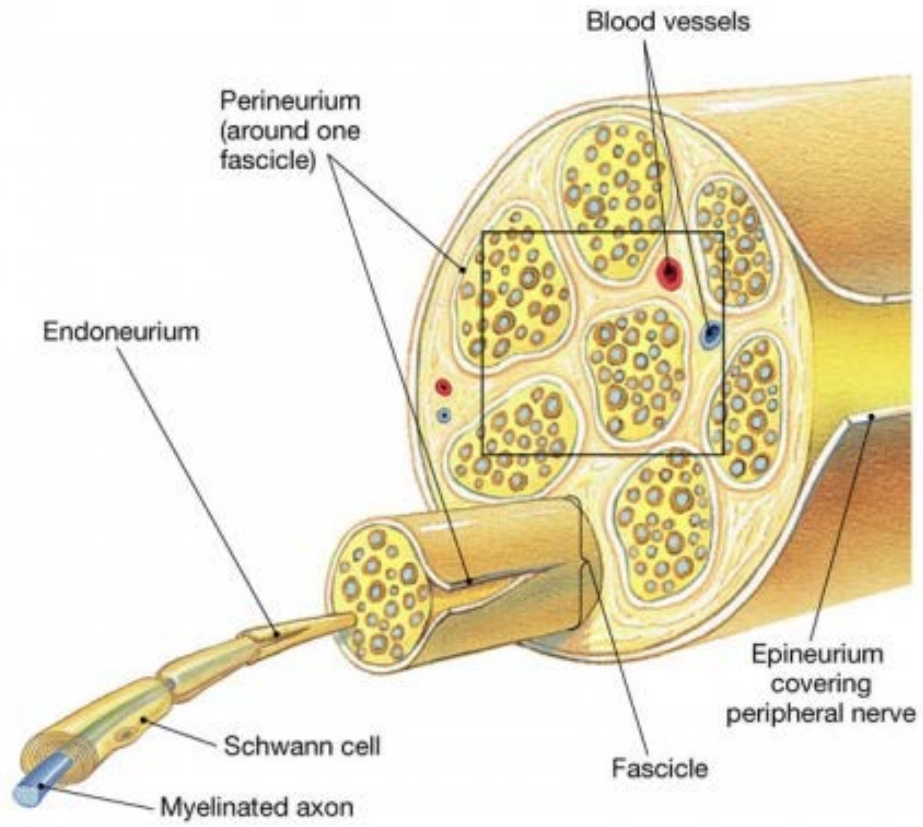
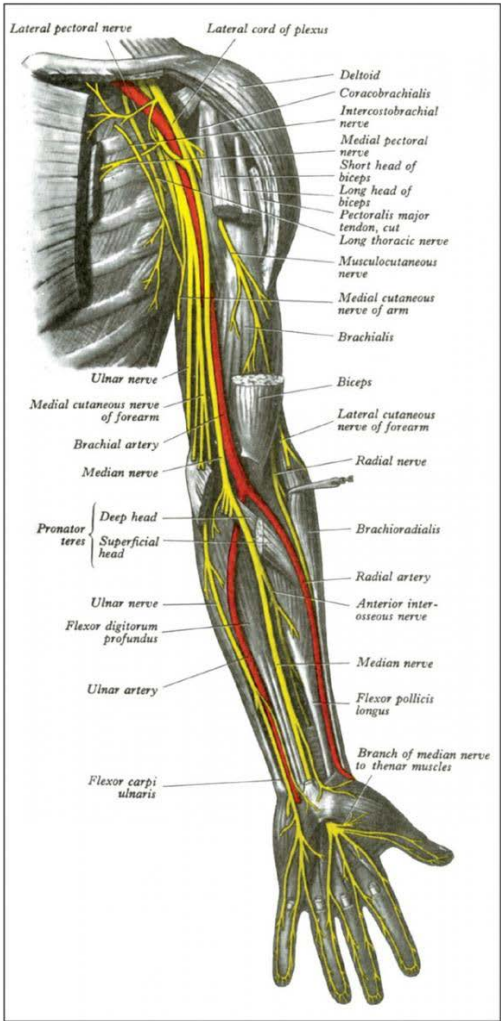
X-ray phase contrast zoom tomography as a tool to visualize human healthy and diabetic peripheral nerves

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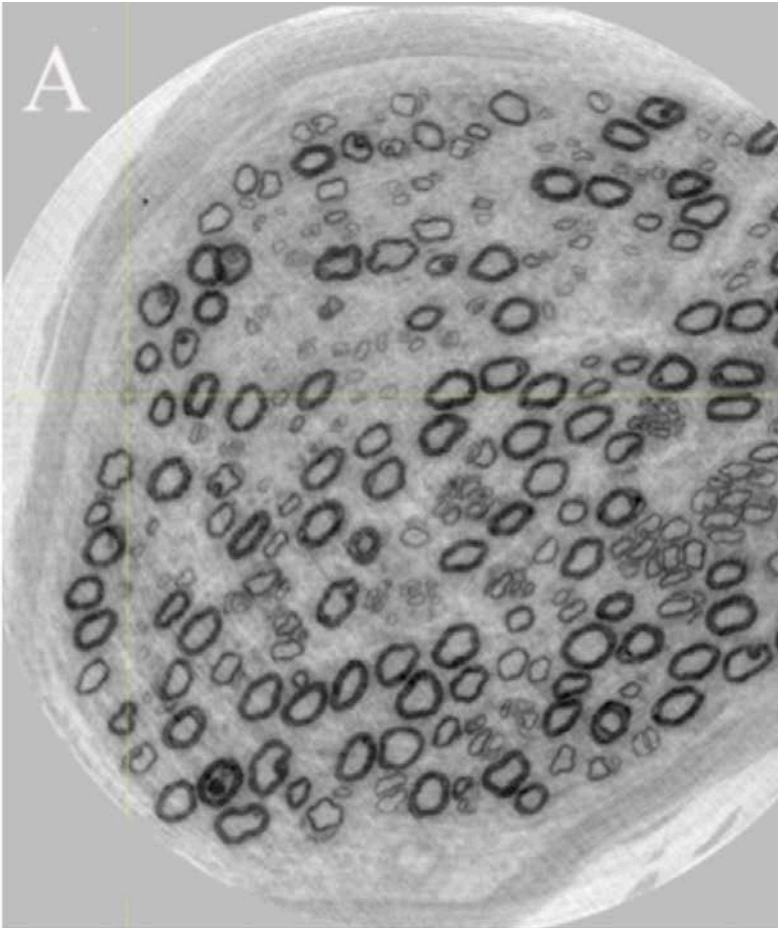
Zoom tomography of biopsies from human peripheral nerves



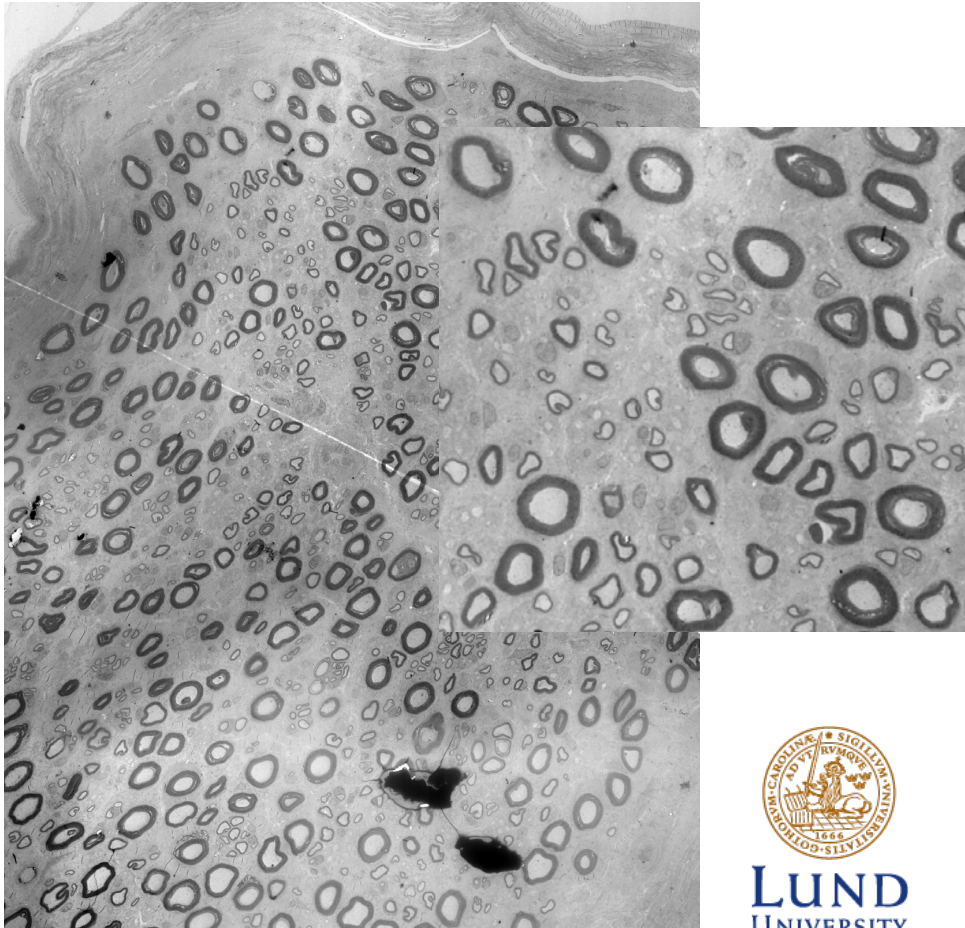
Human nerve fibers

Myelin stained black with osmium

X-ray phase contrast



Histology

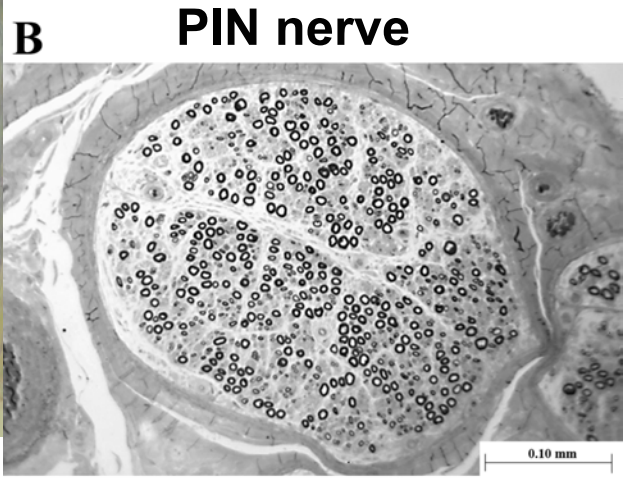
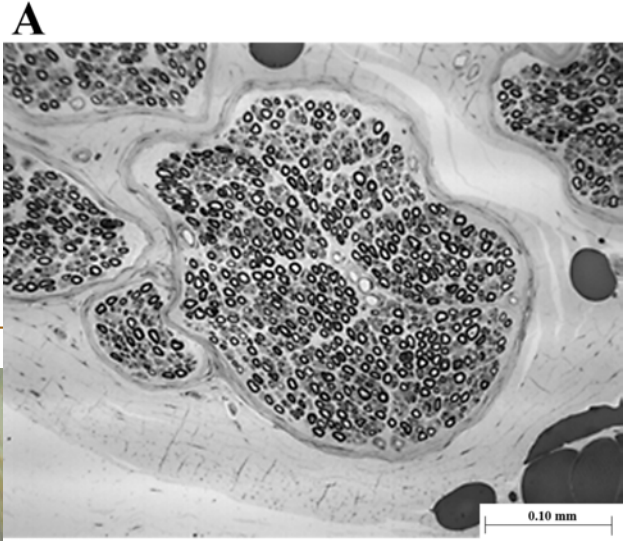


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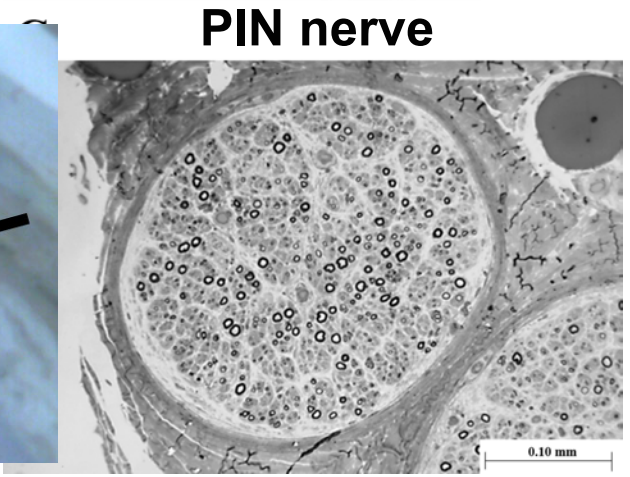
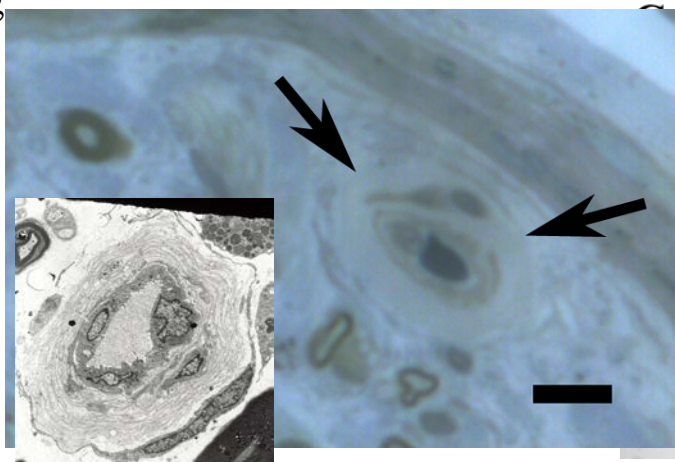
Diabetes and peripheral nerve

- the sural nerve and PIN

- » Myelinated nerve
 - Axonal loss
 - Demyelination
 - Degeneration
 - Regeneration

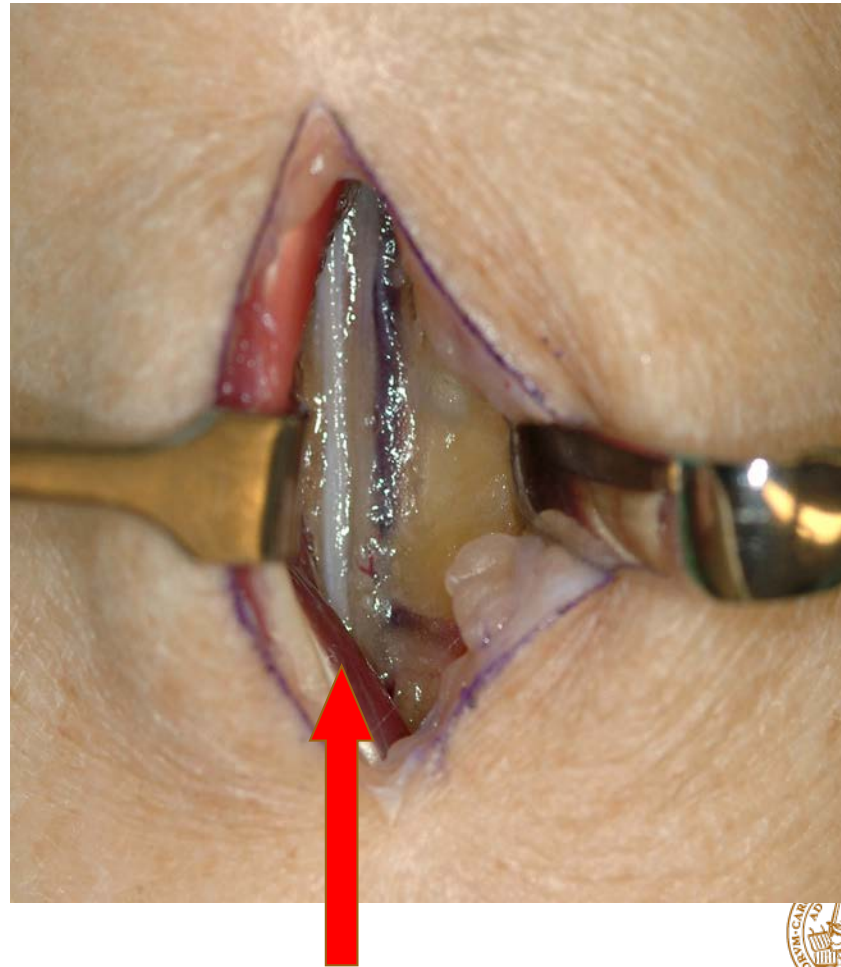
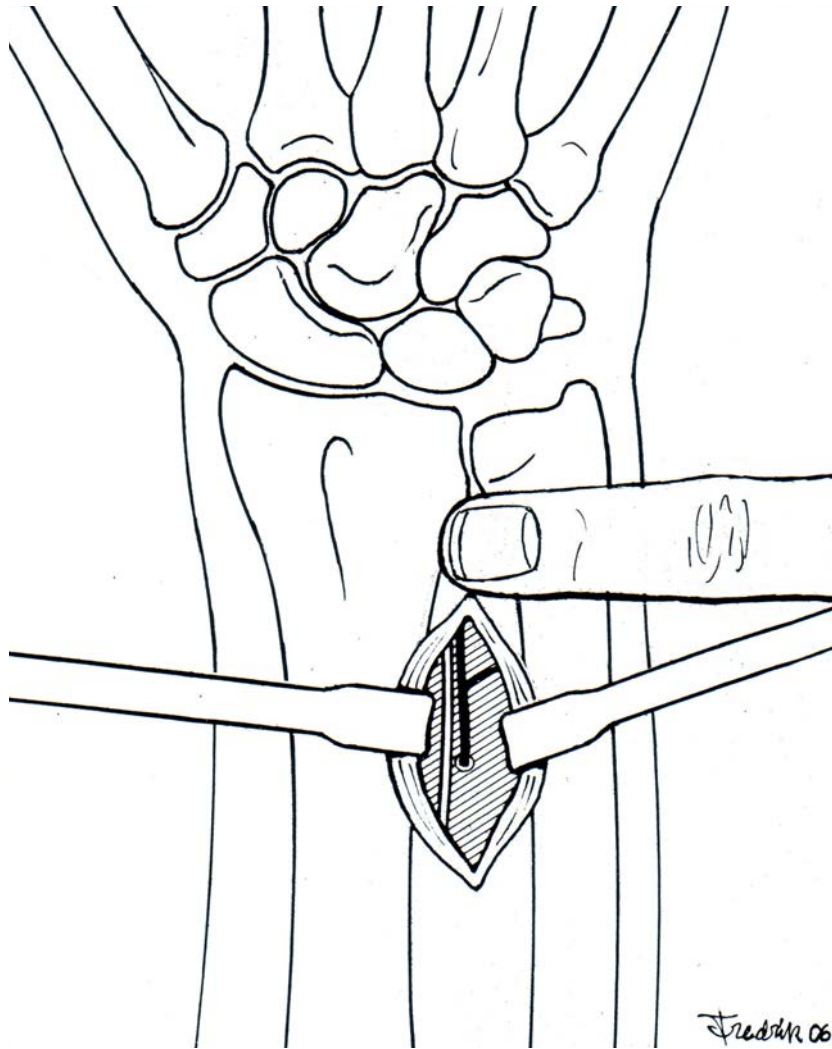


- Basement membrane thickening
- Endothelial cell proliferation
- Reduction in luminal area



Collaboration Rayaz Malik
 Slide courtesy, Lars Dahlin

PIN biopsy method



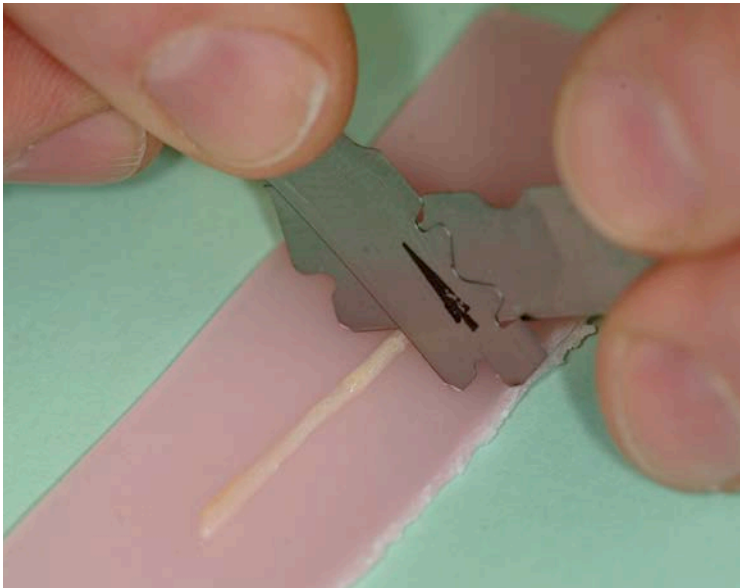
Posterior interosseus nerve

Collaboration Niels Thomsen and Rayaz Malik



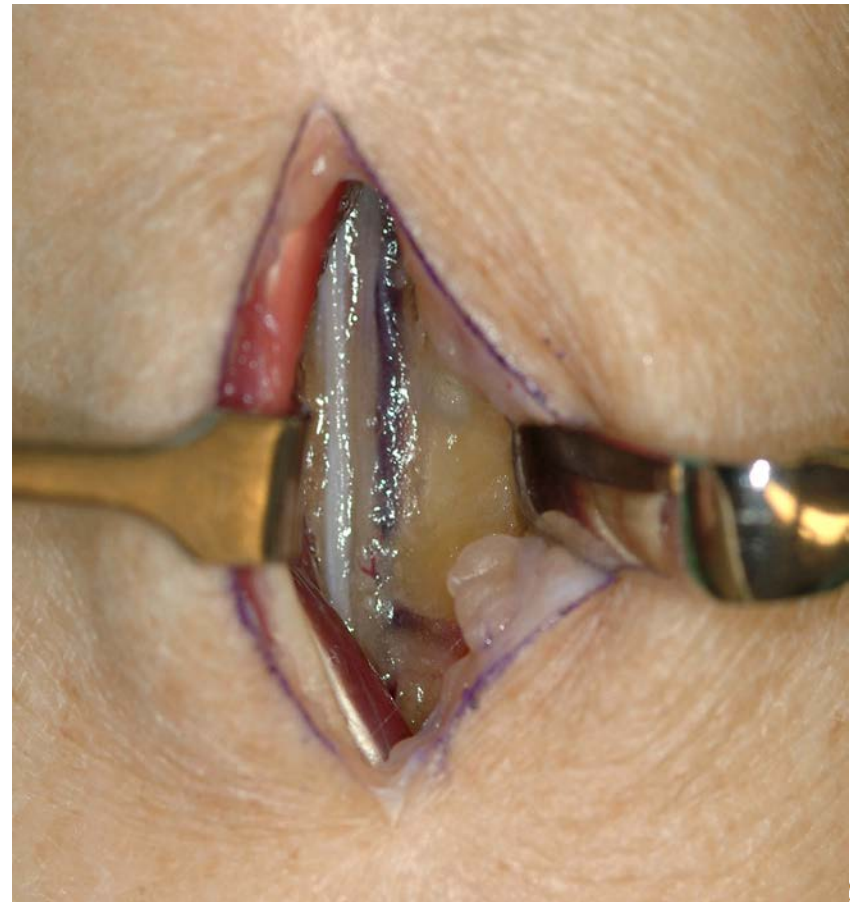
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PIN biopsy

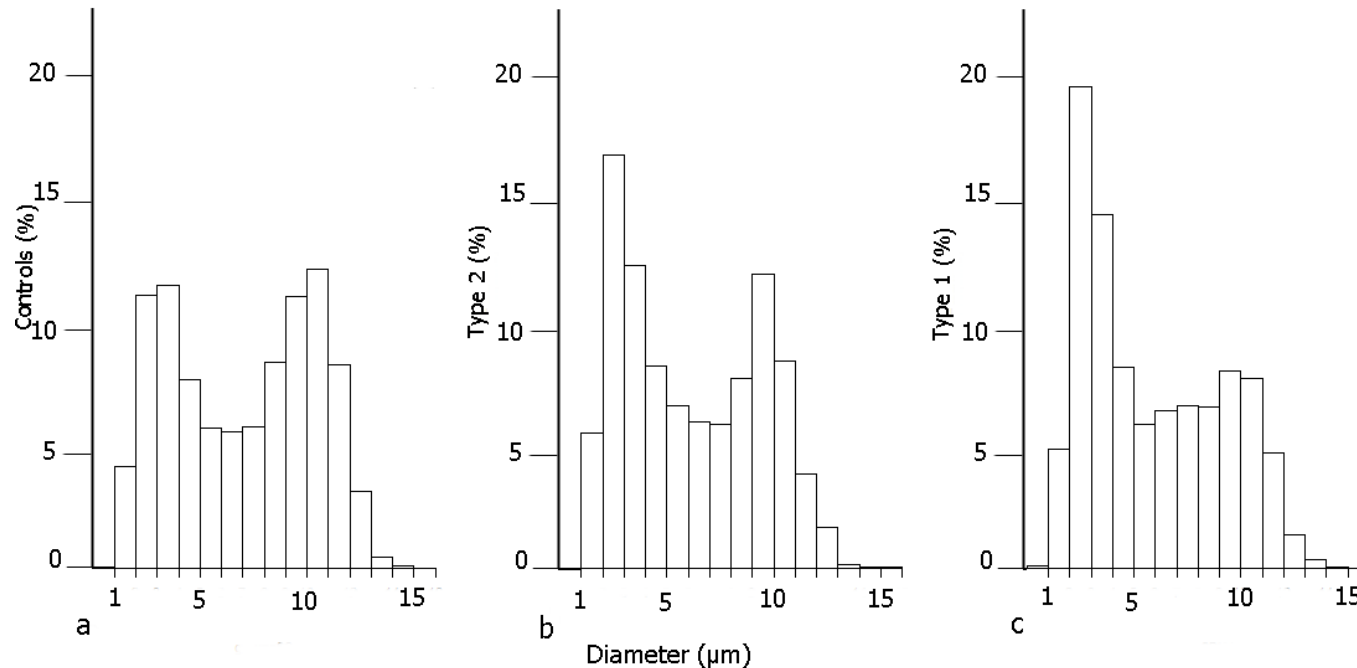
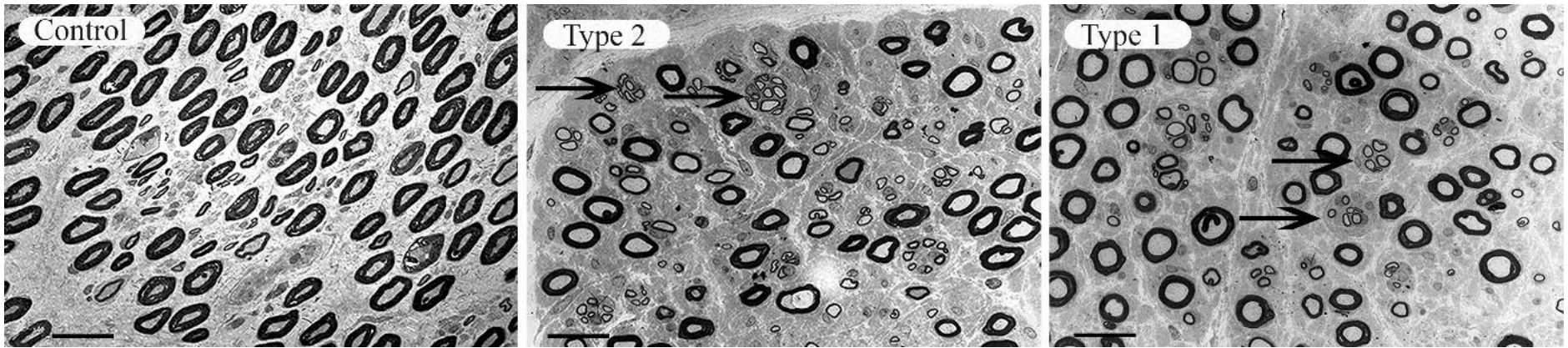


» 3-4 cm nerve biopsy

» 1-3 fascicles



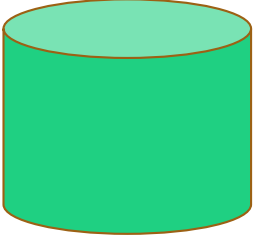


Diabetic Neuropathy – nerve fiber distribution



Posterior interosseous nerve – upper extremity



Synchrotron Nano CT versus 3D Electron microscopy

Technique	Resolution	Field of View	Acquisition Time	Other
Synchrotron Imaging	75 nm	~150 μm 	Hours	Non destructive
3D Electron microscopy	In plane: ~ 5-20 nm Slice-wise: ~ 50+ nm	 Abdollahzadeh et al. 2019 ~15 x 15 x 15 μm^3  Lee et al. 2019 48 x 36 x 20 μm^3	Days	Destructive Artifacts in different slices Need for alignment of 2D images

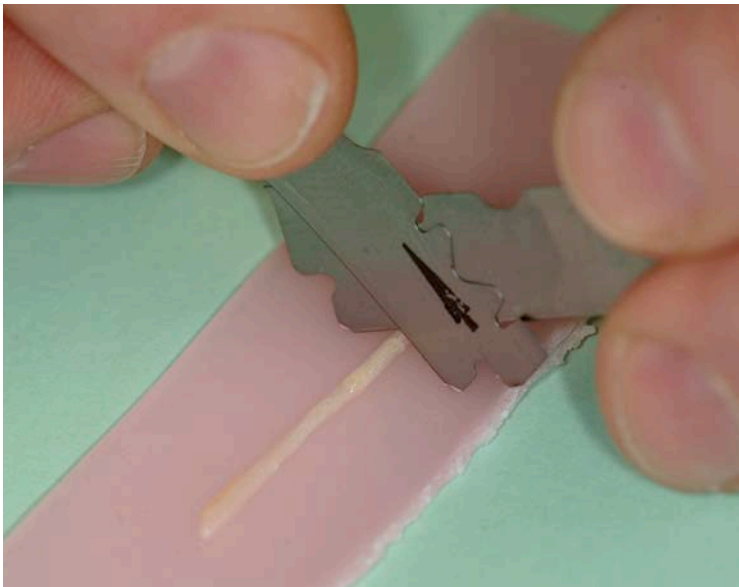


Micro Tomography



Human nerves in health and disease

PIN biopsy and samples



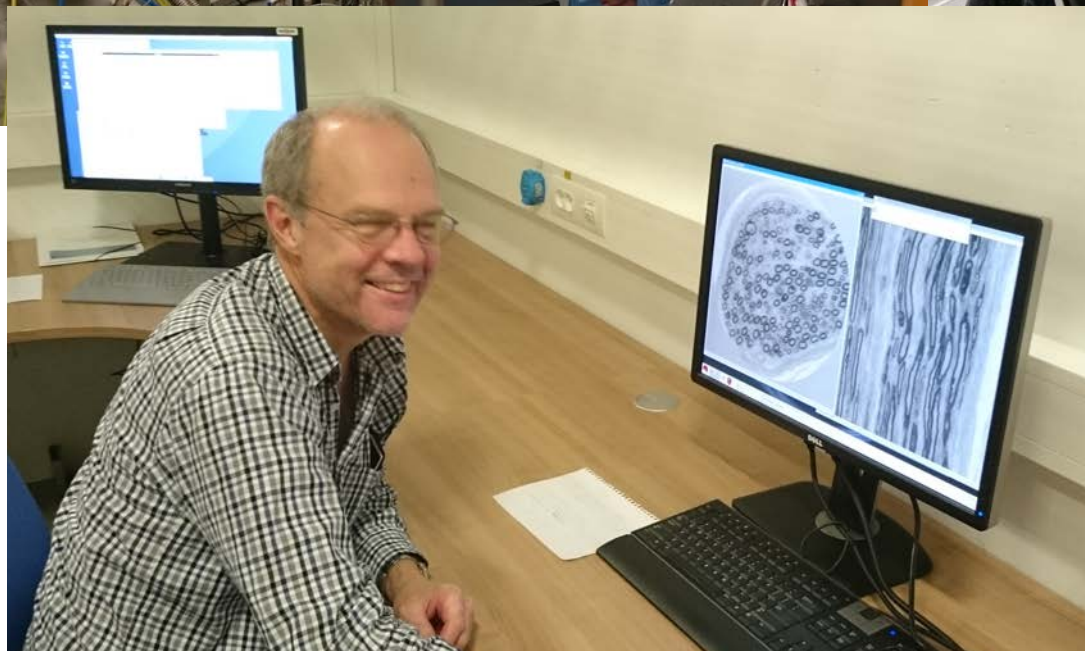
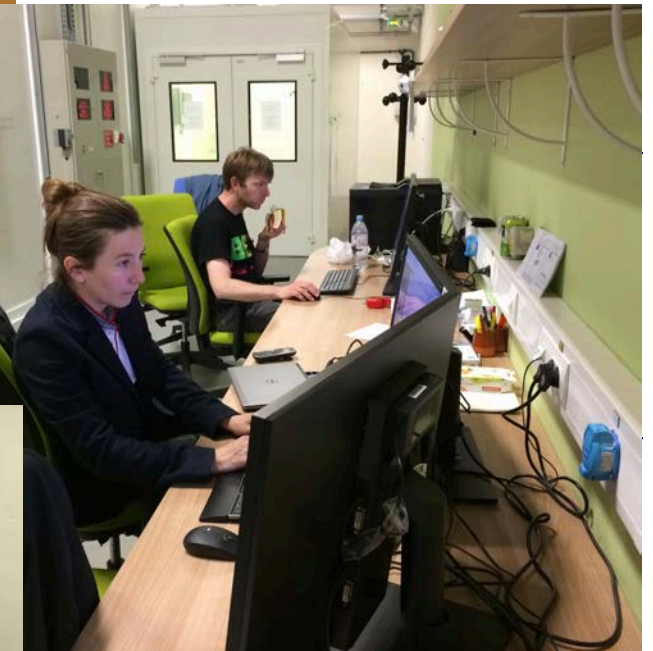
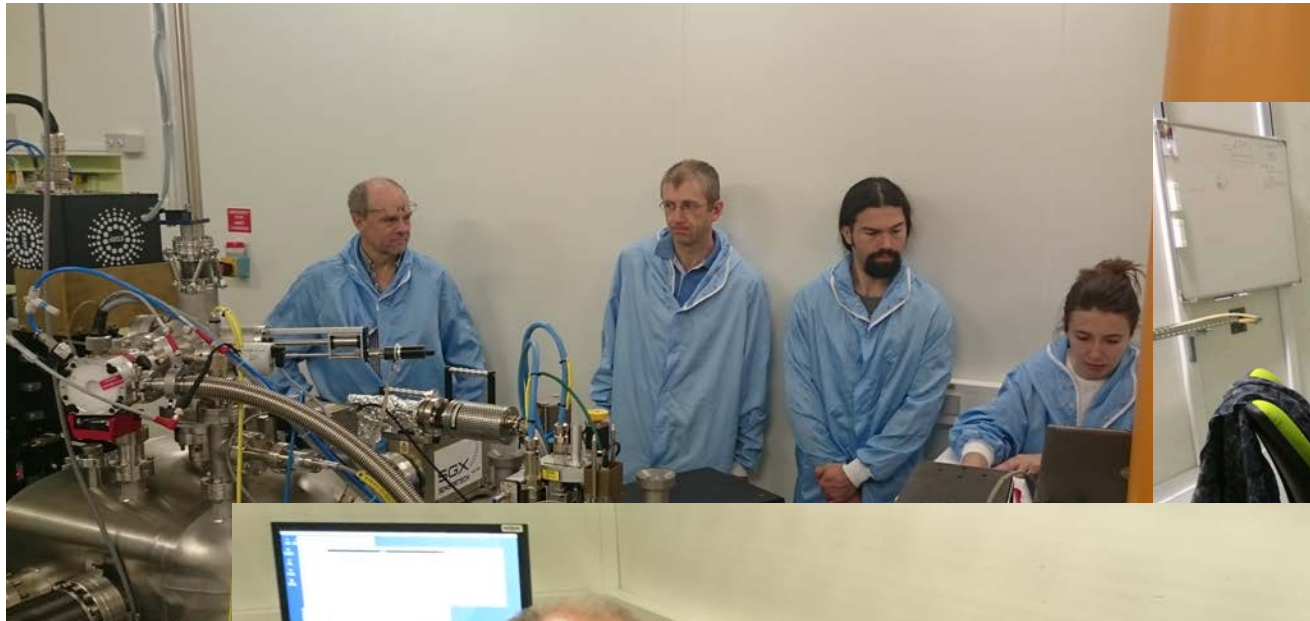
Sample holder: sample size: ~ 1 mm x 3 mm

**Specimens fixed in glutaraldehyde, dehydrated,
post-fixed in osmium and embedded in Epon**



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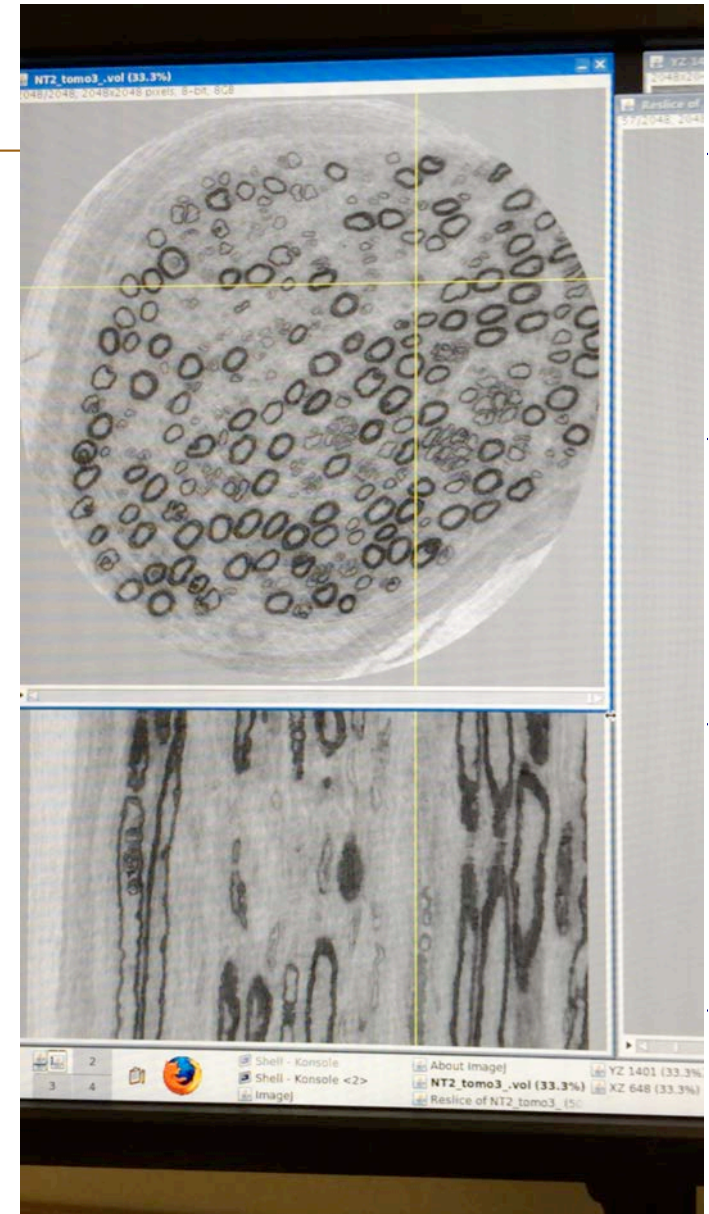
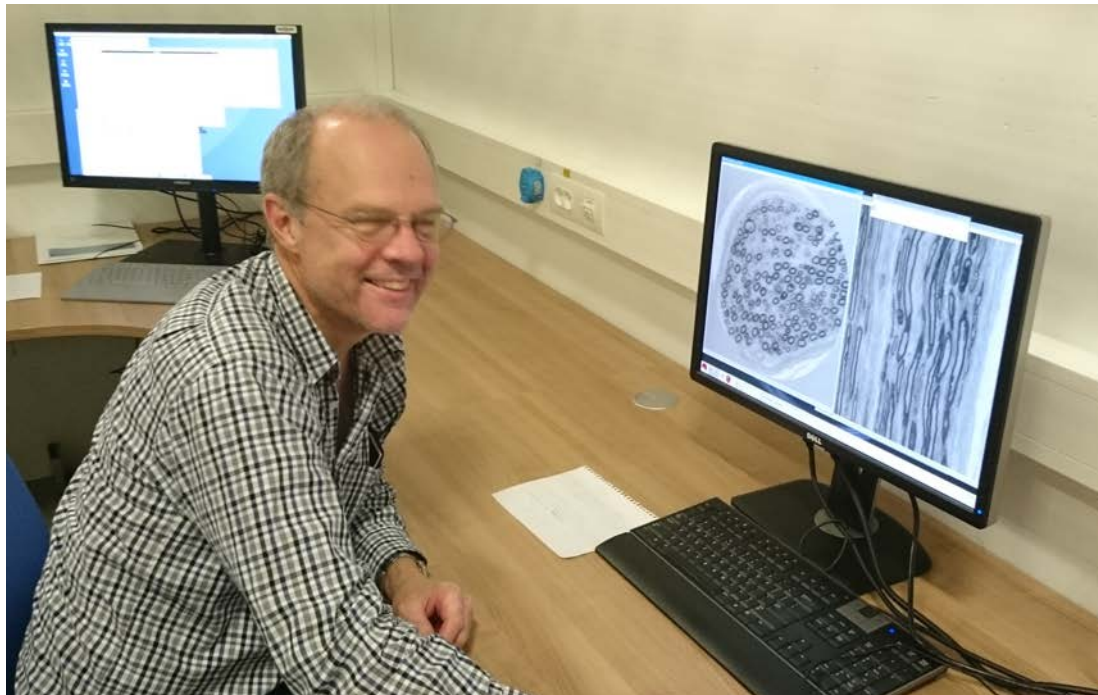
Experiment



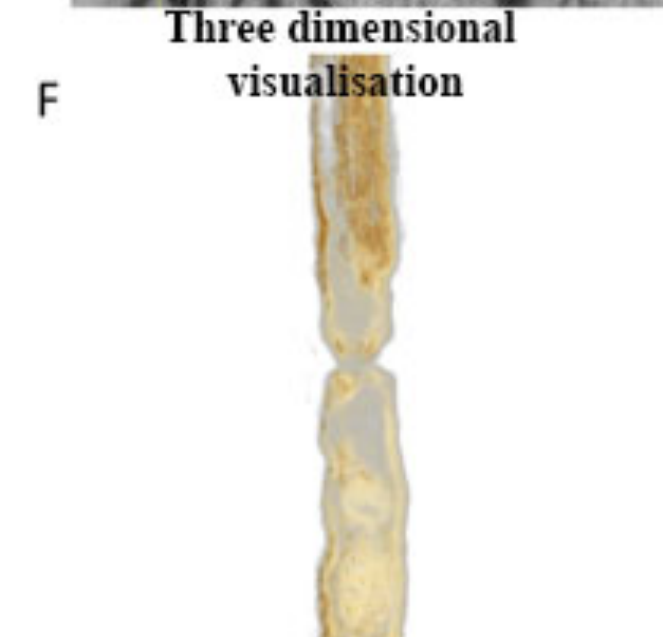
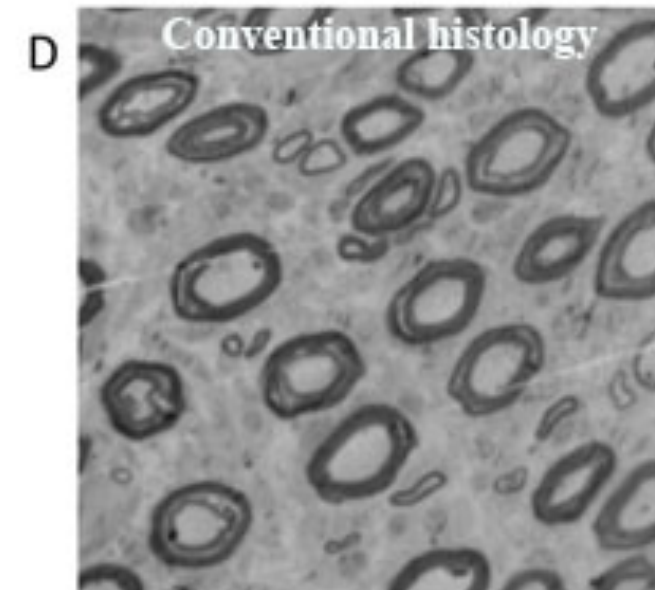
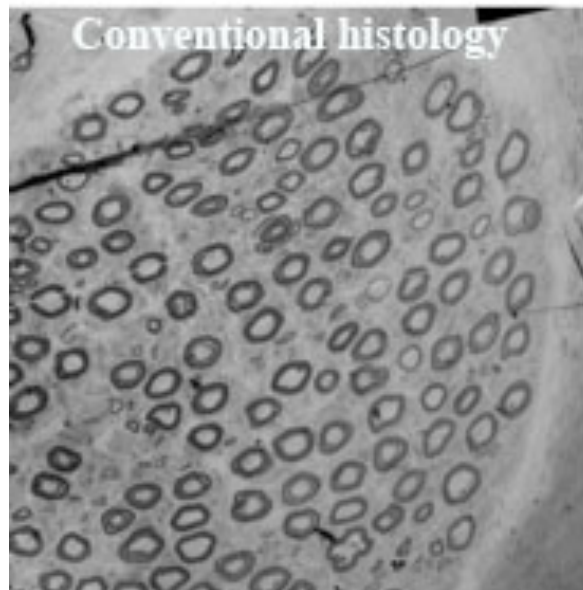
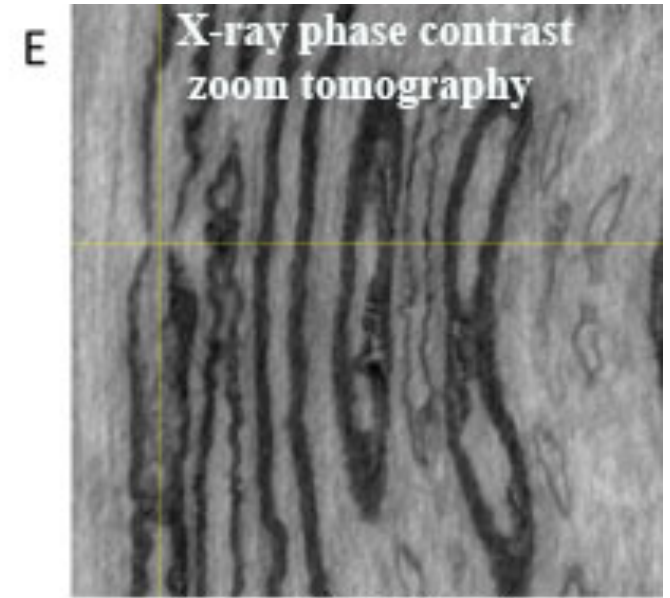
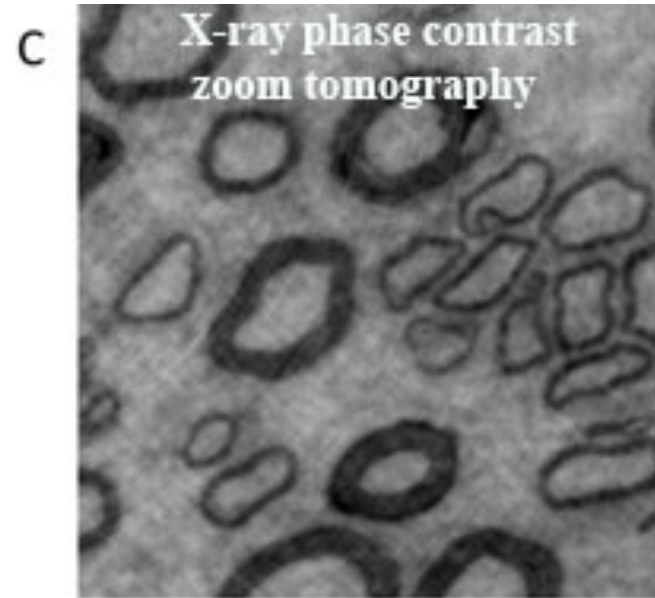
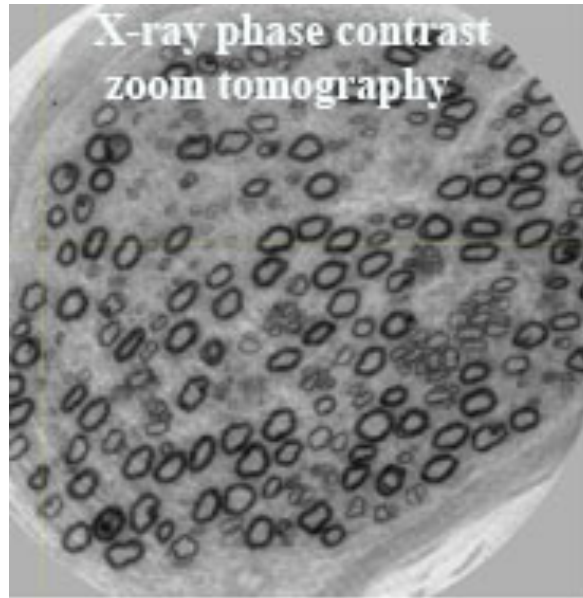
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X-ray phase contrast zoom tomography

First look at reconstruction

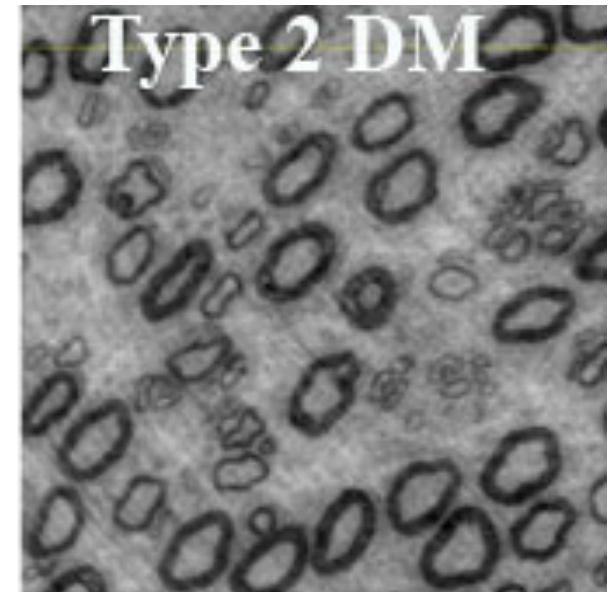
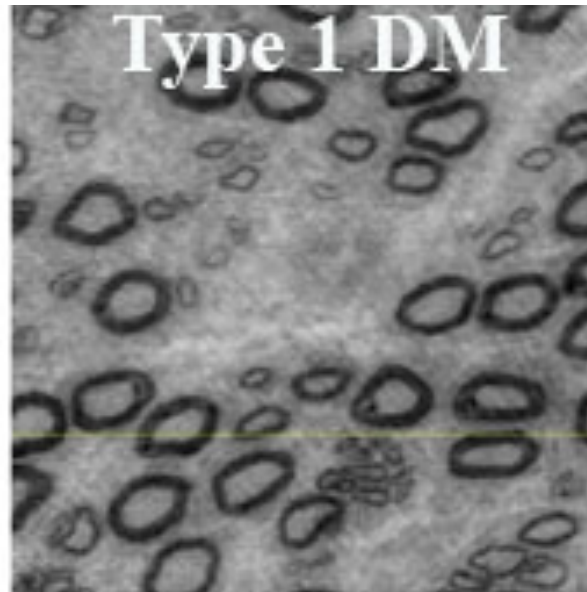
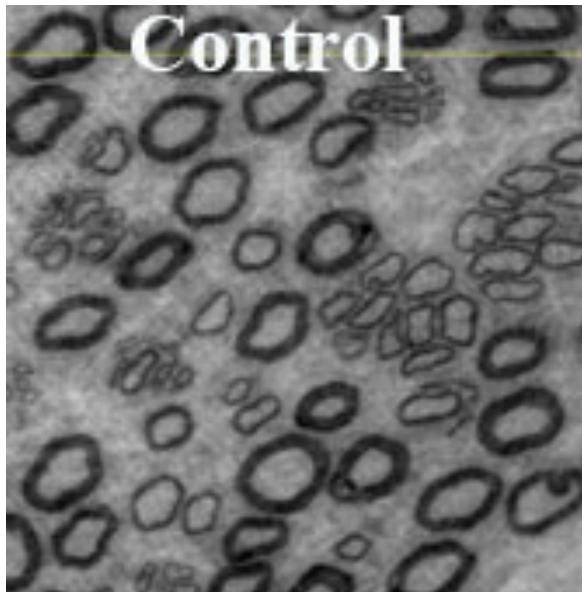


X-ray phase contrast zoom tomography



Human nerve fibers from PIN

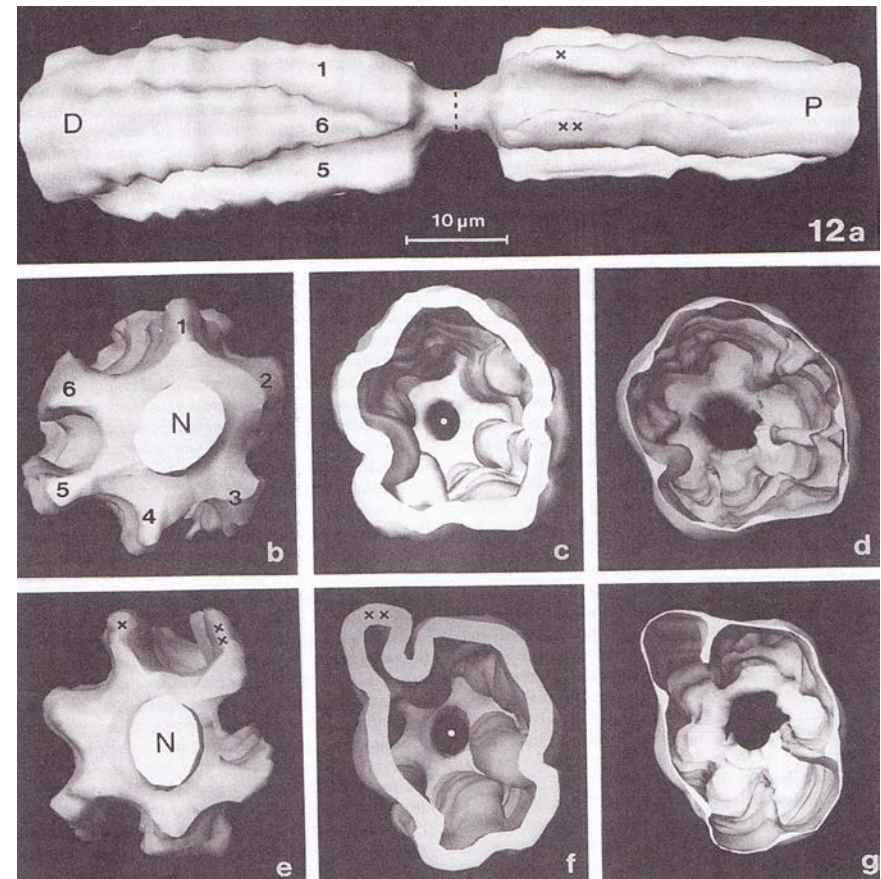
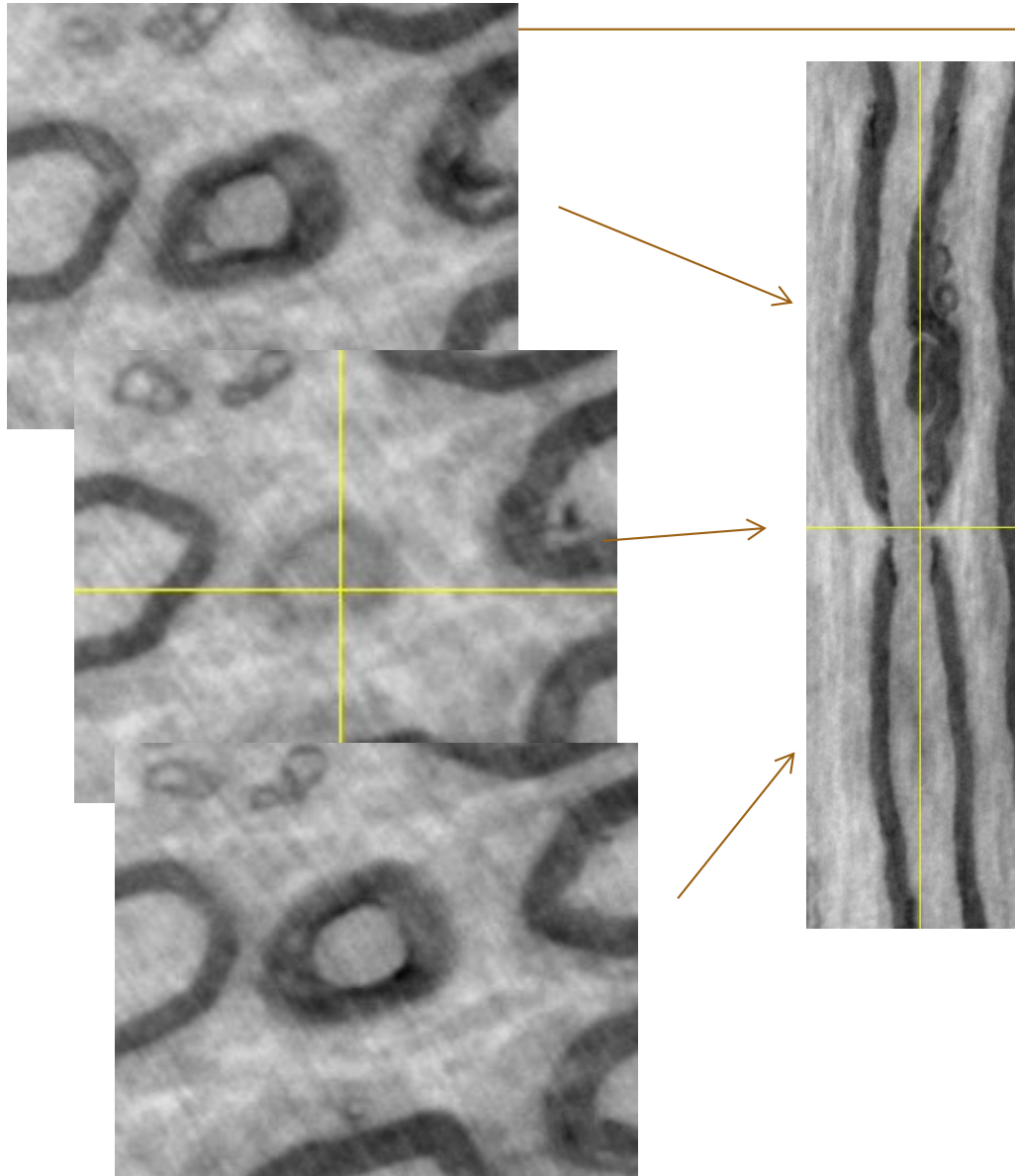
X-ray phase contrast zoom tomography



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Node of Ranvier

Node of Ranvier – myelinated nerve fiber with myelin deleted

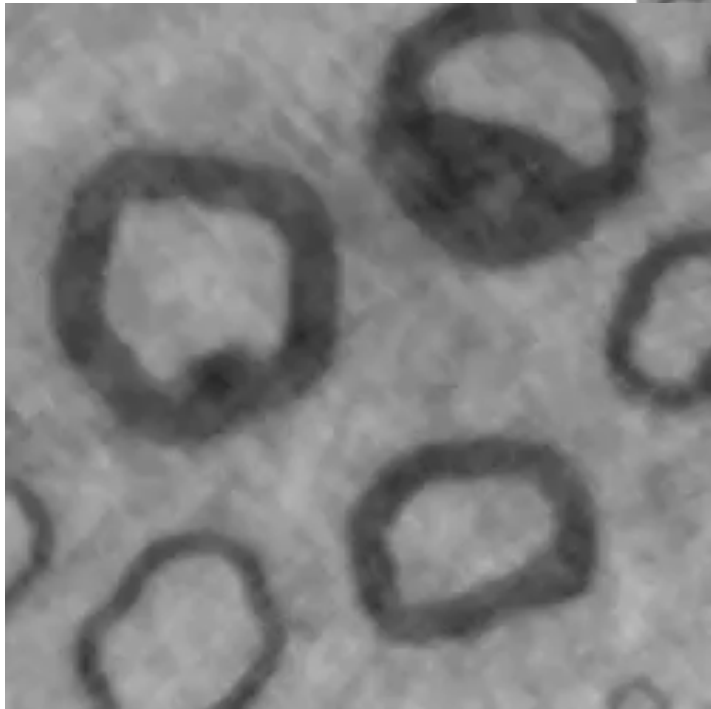
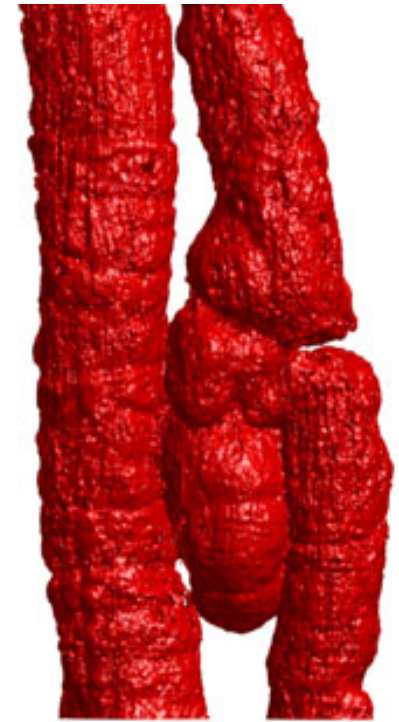
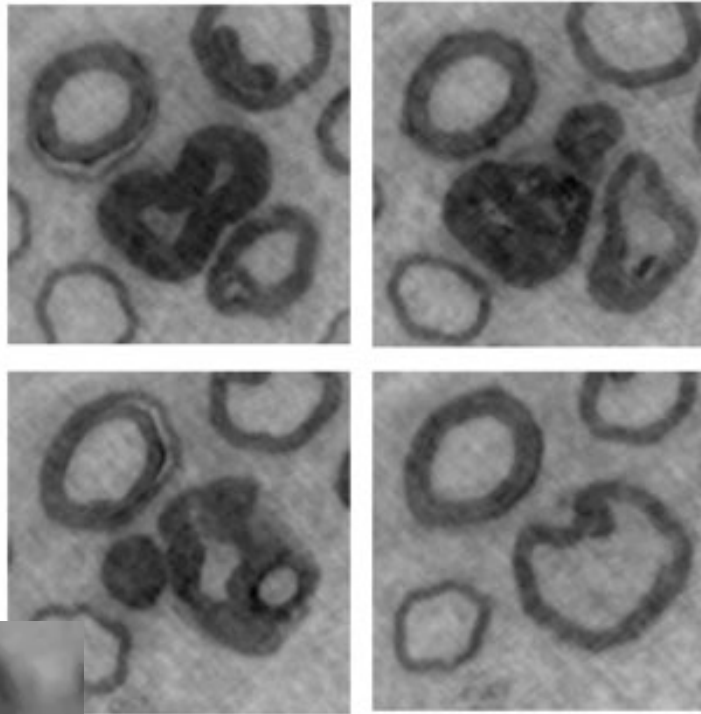


Berthold et al 1990

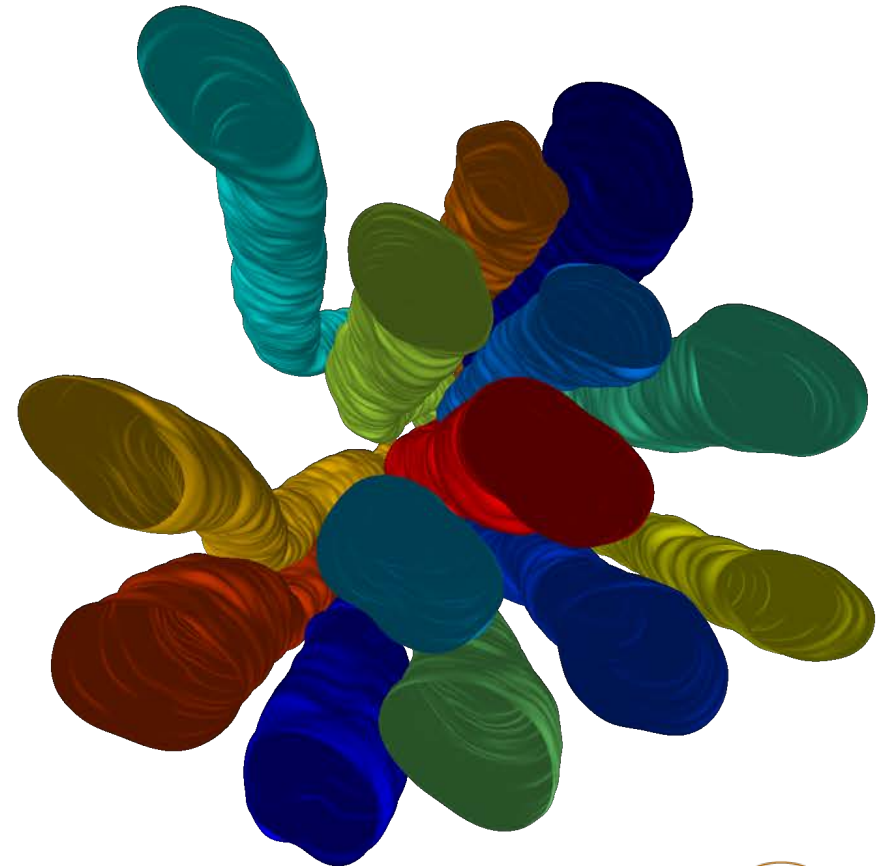
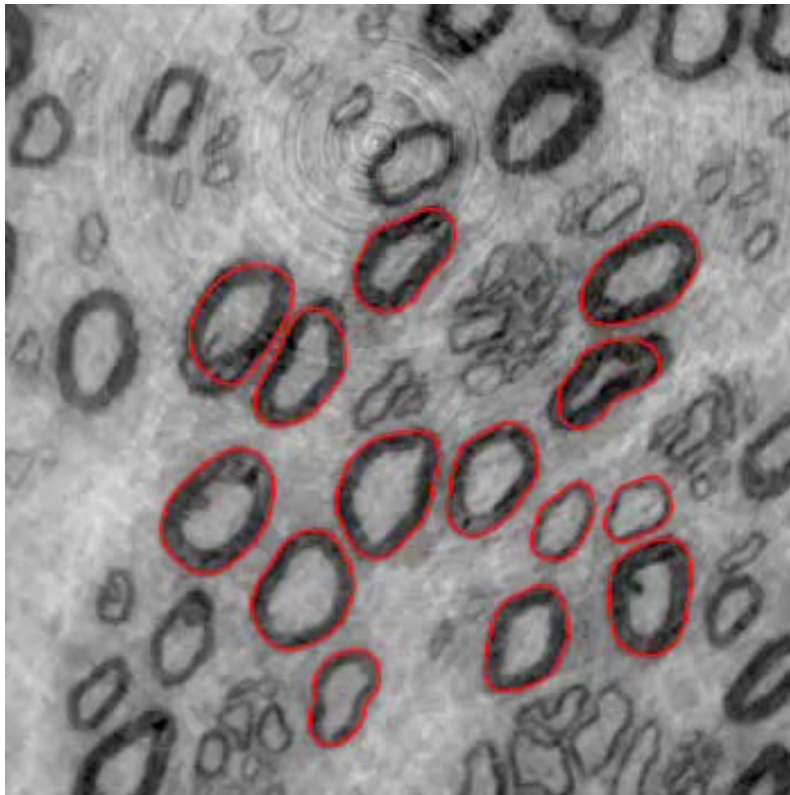


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“Strange knob” – “birth of an axon”



Segmentation at DTU imaging center

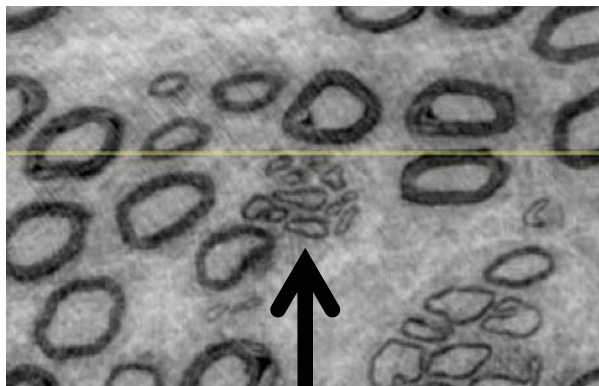
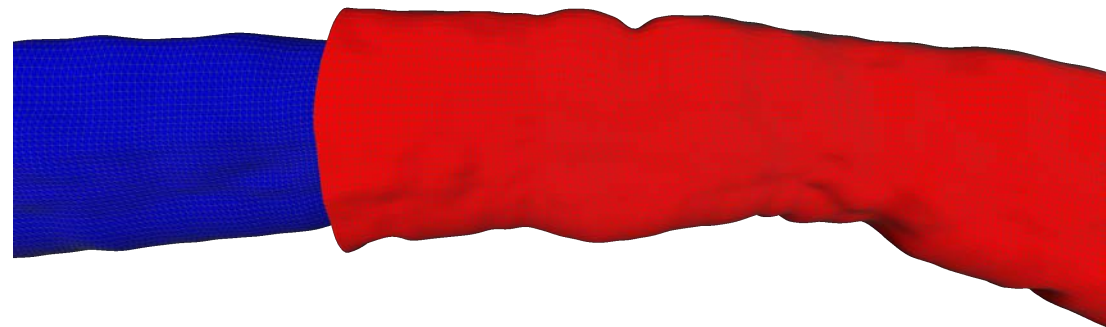
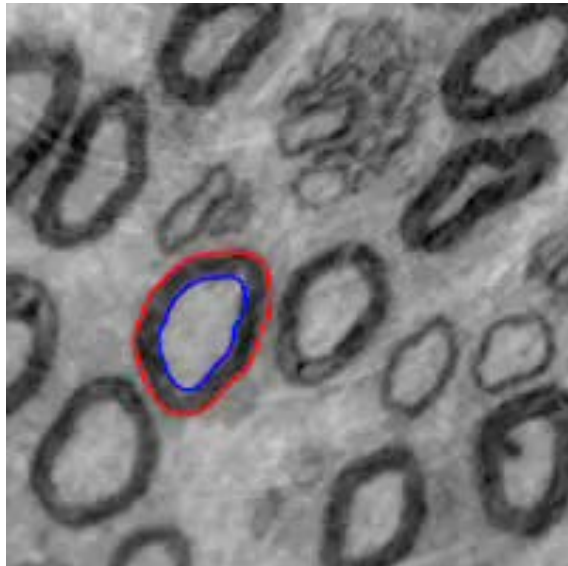


Contour – myelinated axons
Outer surface

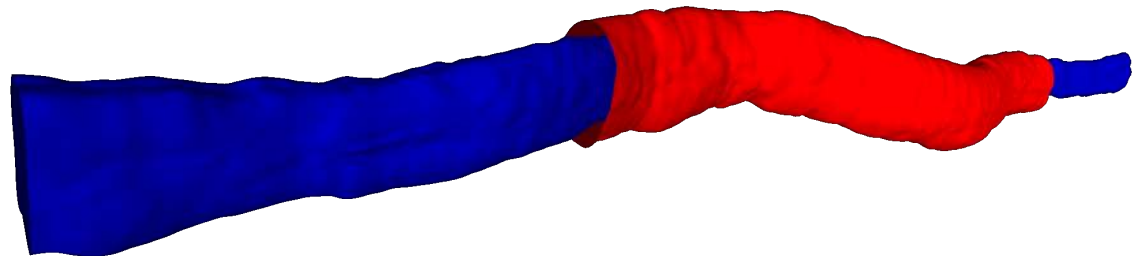


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Segmentation at DTU imaging center



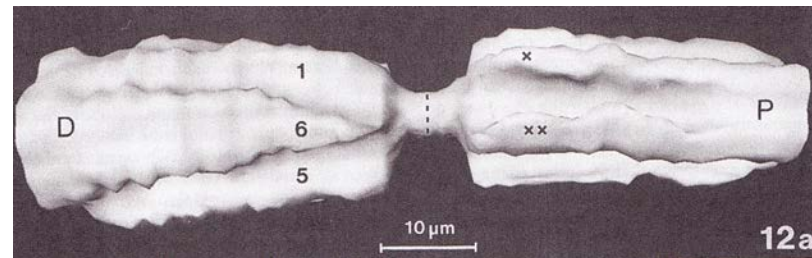
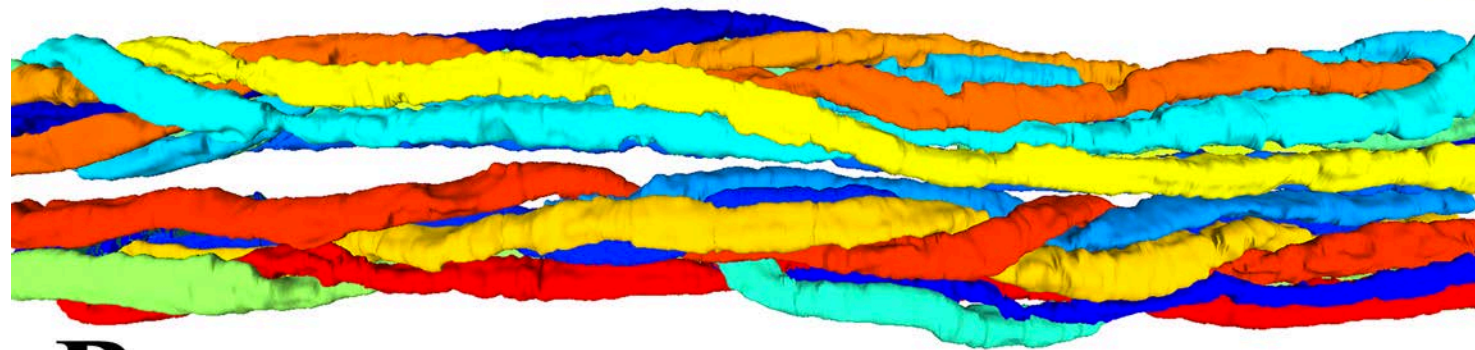
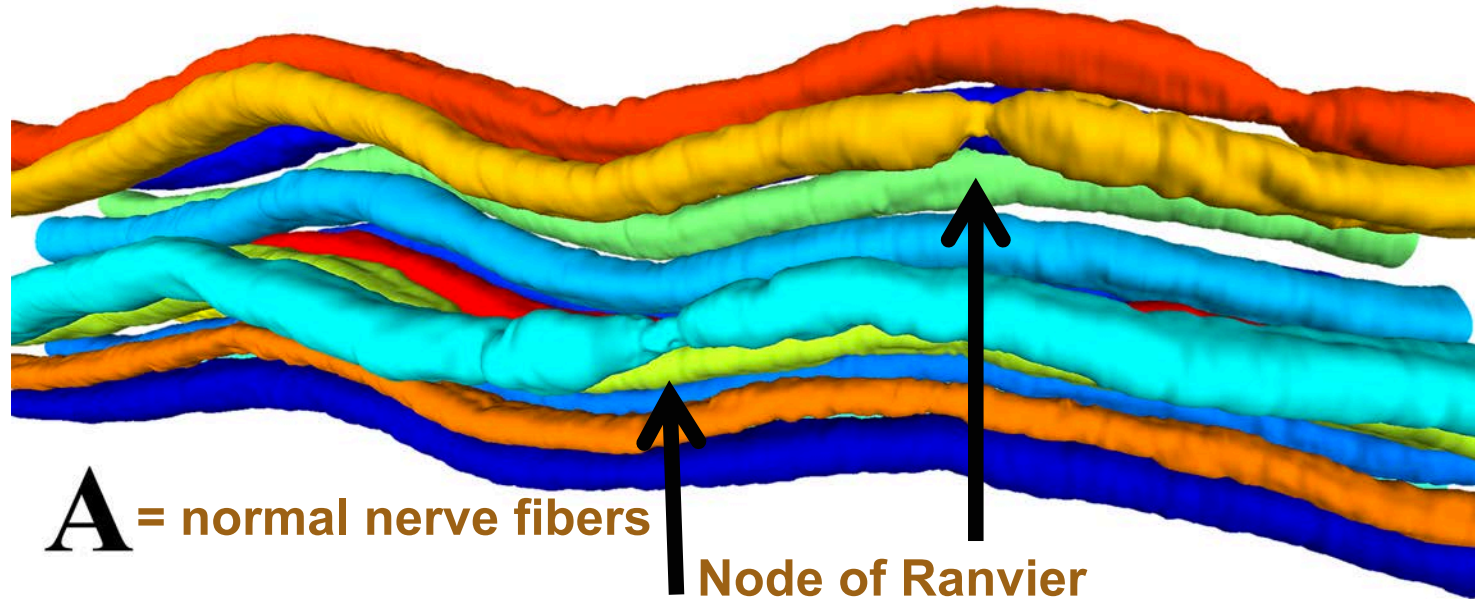
Regenerative clusters



Contour – myelinated axons
Outer and inner surfaces



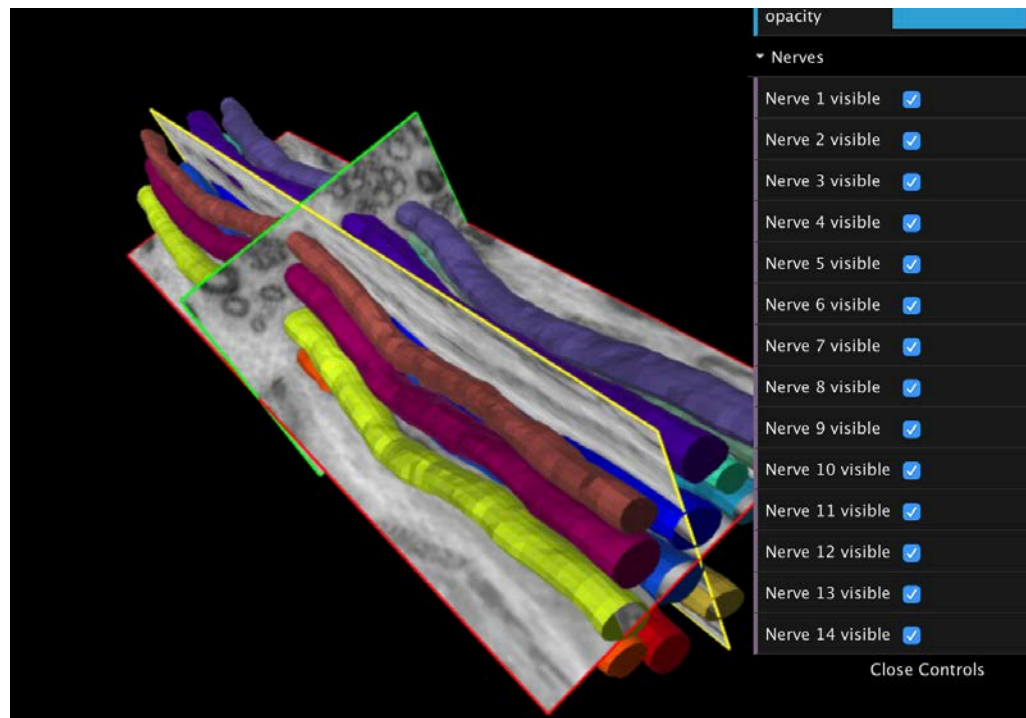
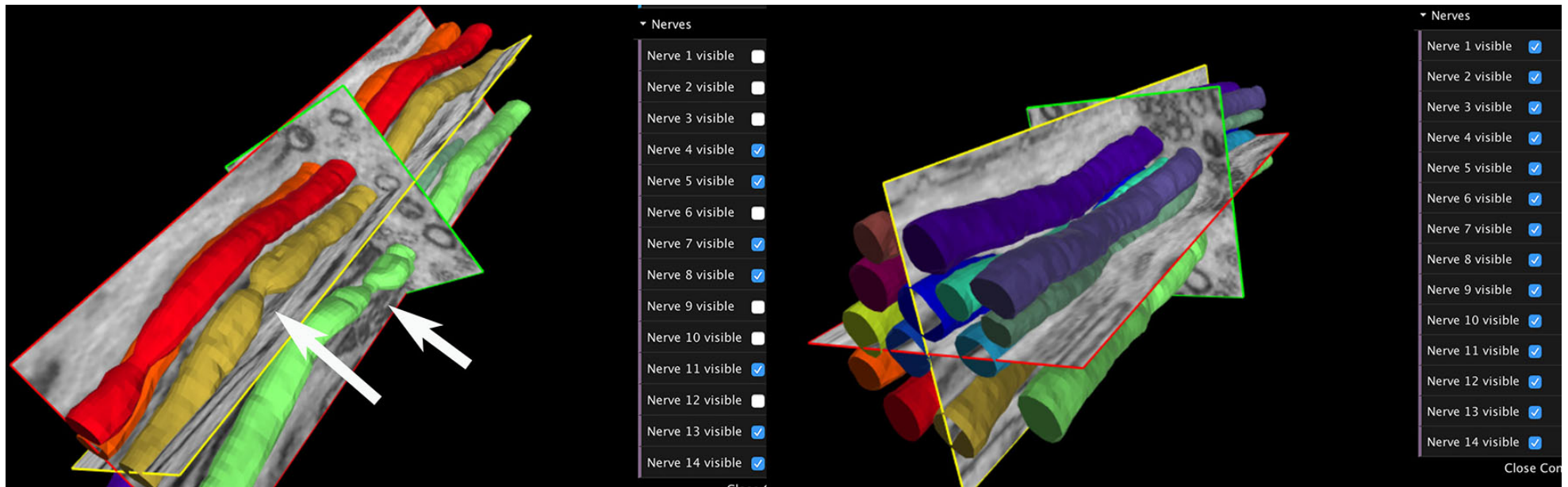
Segmentation at DTU imaging center



Berhold et al 1990



Segmentation at DTU imaging center

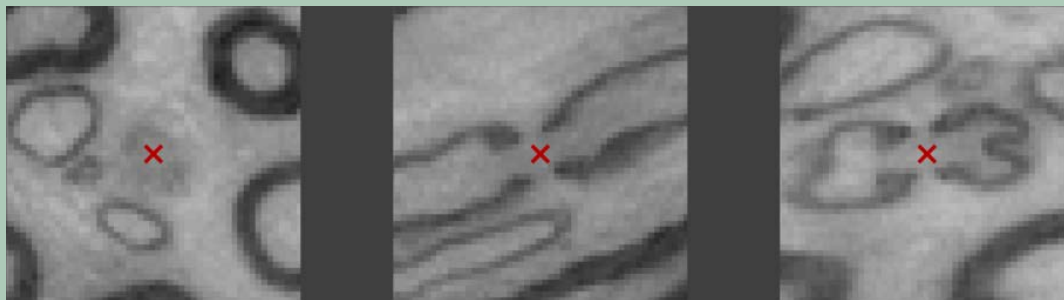


Data summary

- Hand nerve biopsies (N = 16)
- Diabetic (type I & II) vs. healthy
- Fixated and osmium stained (**myelin**)
- Scanned at ID16: 130 nm isotropic voxels

» **Observables to quantify:**

- Nodes of Ranvier
- Myelination
- Morphology



Data analysis

» Overarching clinical goals:

- Qualitative and quantitative comparison of diseased (diabetic neuropathy) vs. healthy tissue

» Sub-goal (data analysis):

- Nerve fiber characterization (explorative):
 - » Distributions of fiber shapes, sizes etc.
 - » Organizational characteristics

» Tasks:

- 1: Segmentation of myelinated tissue (axons + myelin)
- 2: Extraction of various characterization metrics and statistics

Healthy (idealized) features



- Big
- Fat
- Densely packed
- Straight
- Parallel
- Regular shape

Pathologic features?

- Smaller?
- Less myelin?
- Less dense?
- Disorganized?
- Irregular shaped?



Work by
Hans Martin Kjer, DTU

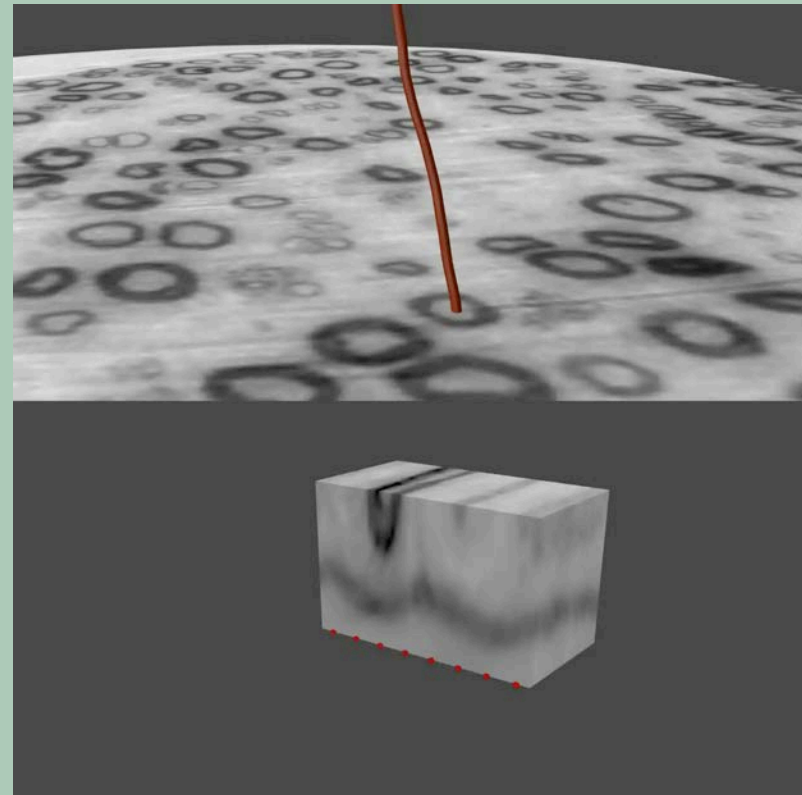


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Data segmentation

- » Extraction of subvolume by circular resampling from centerline

Dahl, V. A., Trinderup, C. H., Emerson, M. J., & Dahl, A. B. (2018) Content-based Propagation of User Markings for Interactive Segmentation of Patterned Images. IEEE Transactions on Image Processing. 2018



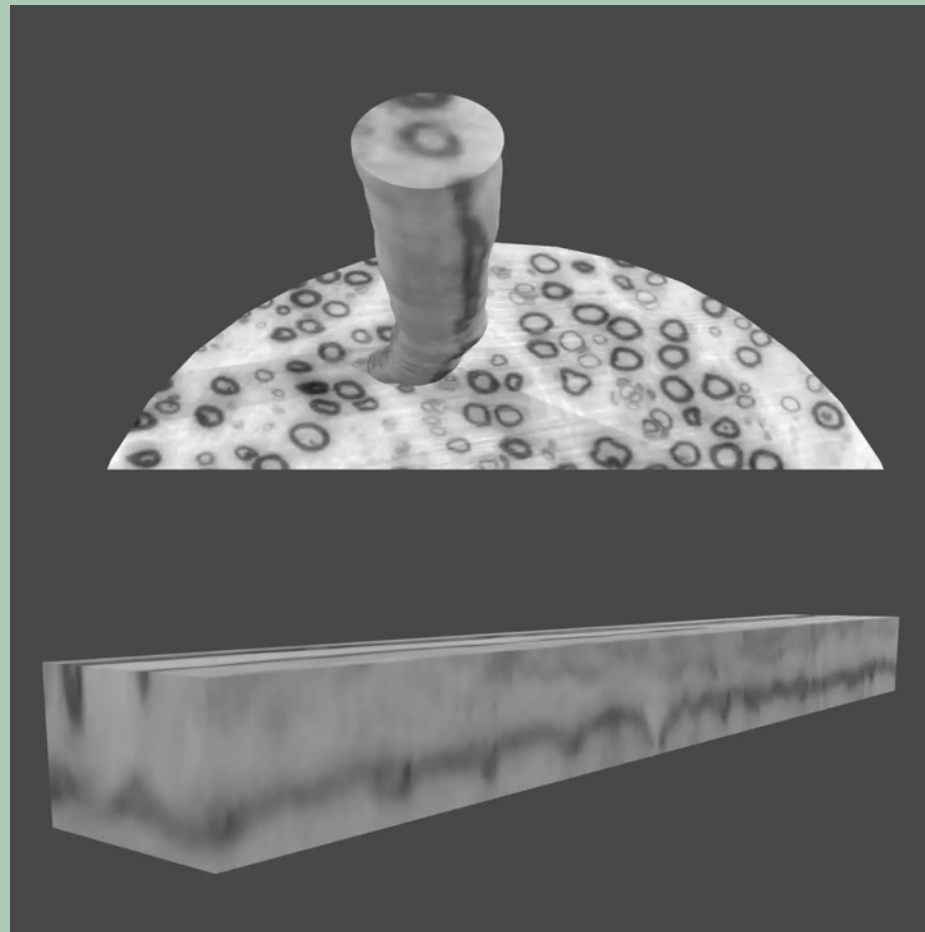
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Data segmentation

» Extraction of both inner and outer surface

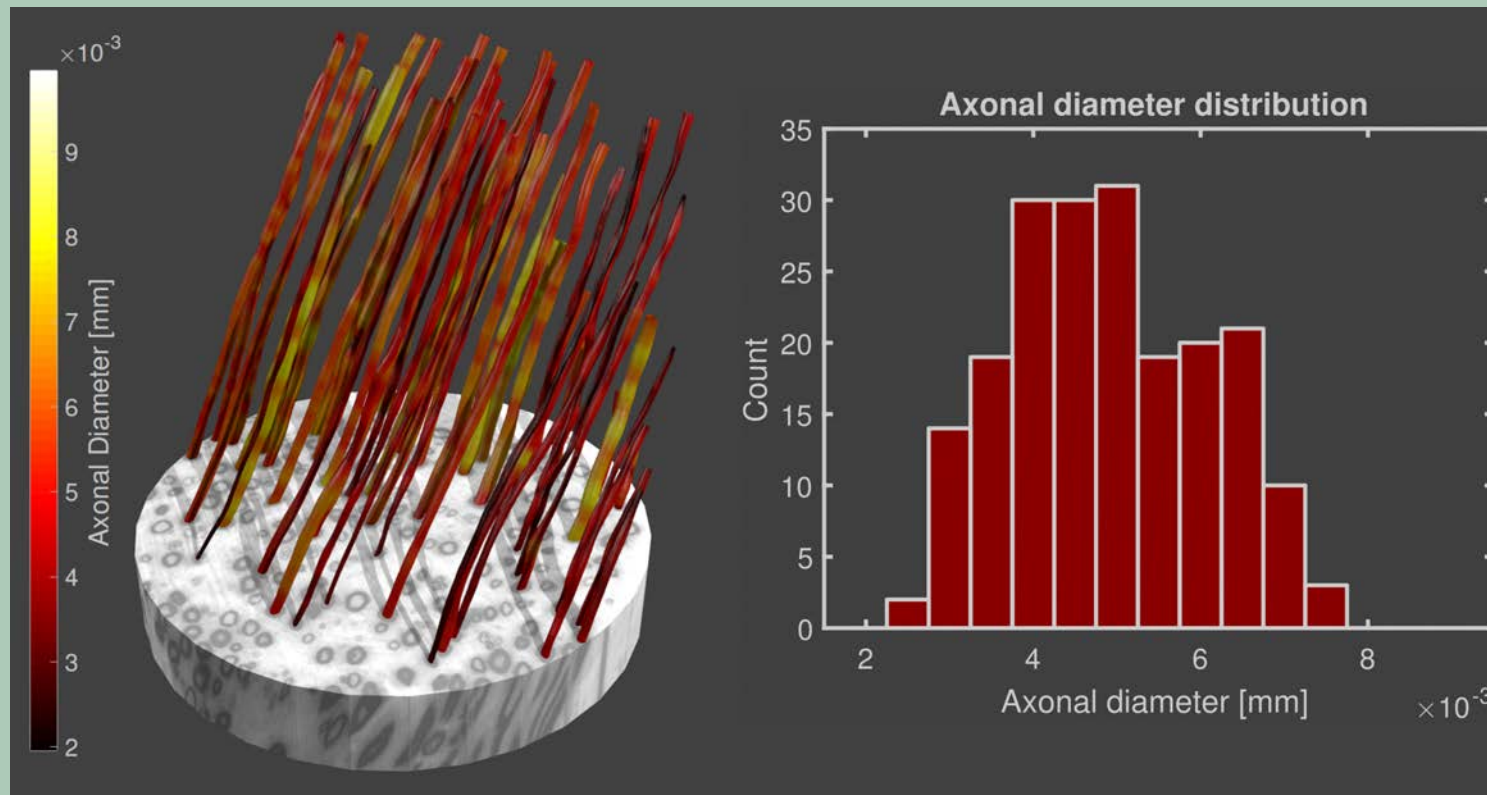


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Morphology: Axonal diameter



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