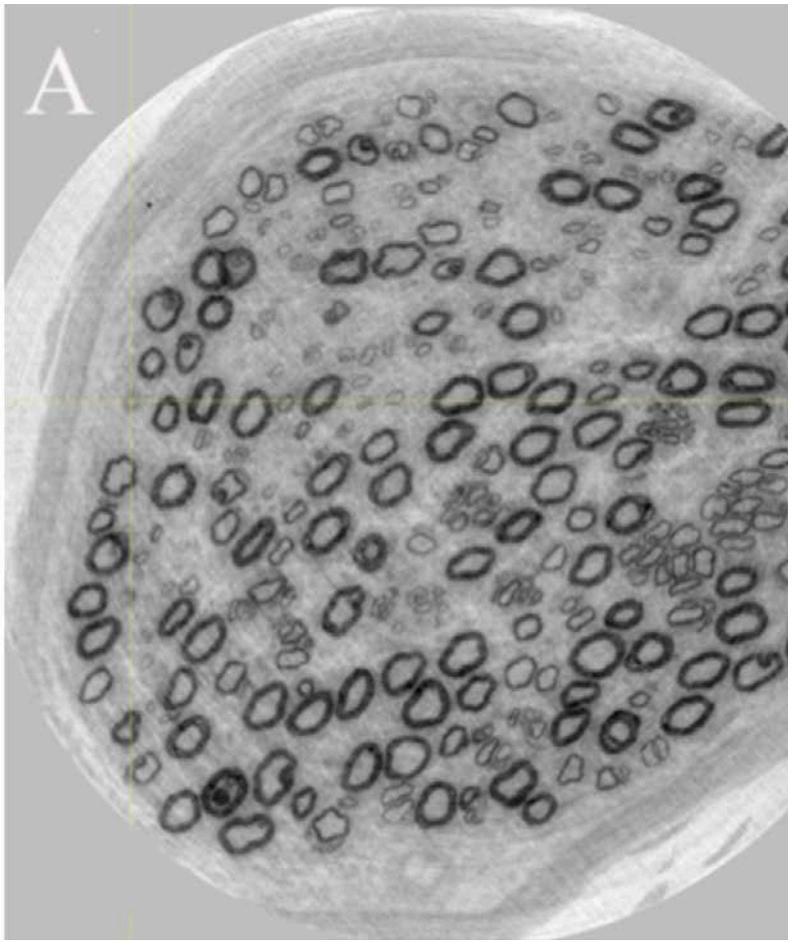
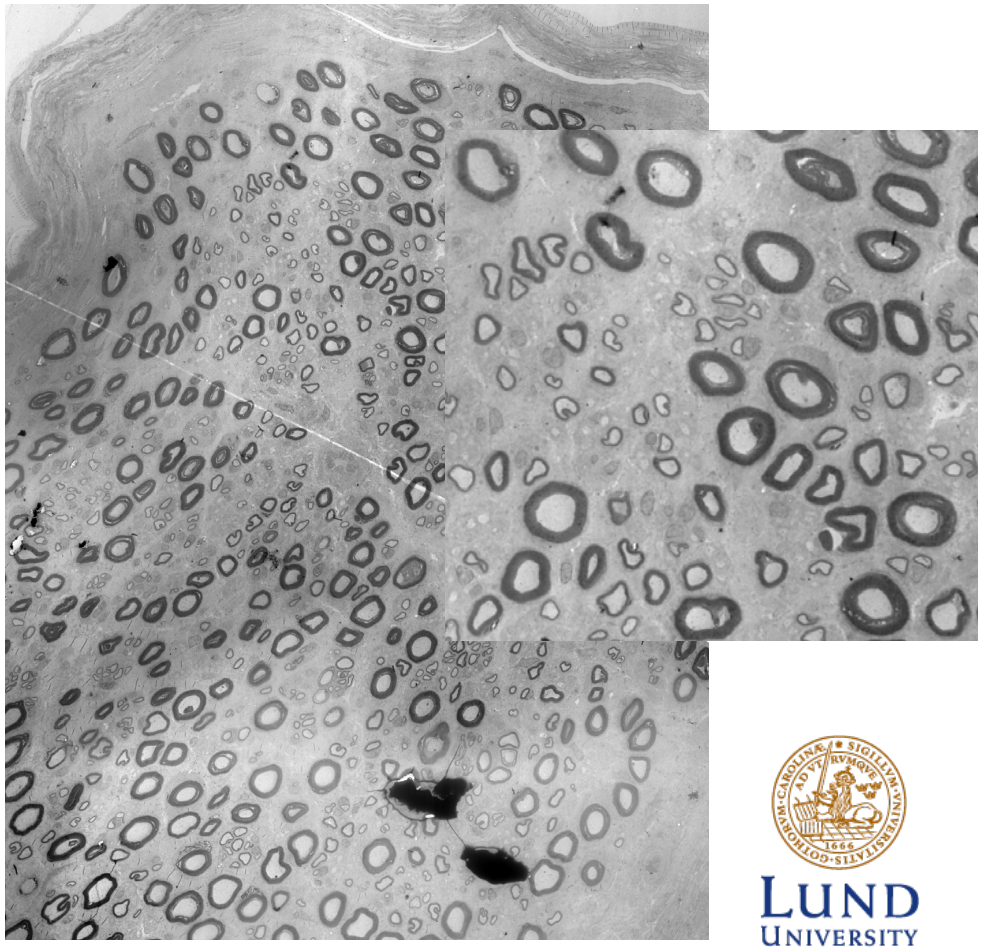
Human nerve fibers

Myelin stained black with osmium

X-ray phase contrast



Histology



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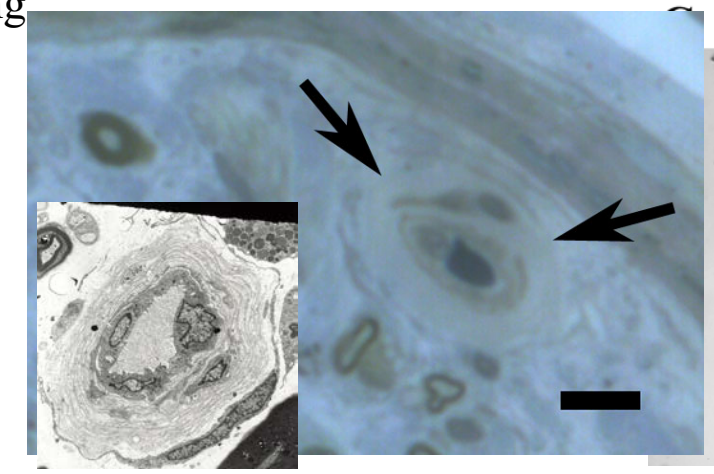
Diabetes and peripheral nerve

- the sural nerve and PIN

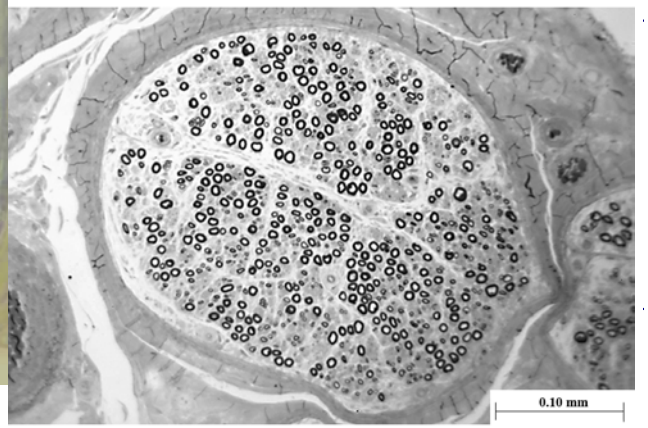
- Myelinated nerve
  - Axonal loss
  - Demyelination
  - Degeneration
  - Regeneration
- Basement membrane thickening
- Endothelial cell proliferation
- Reduction in luminal area

Collaboration Rayaz Malik

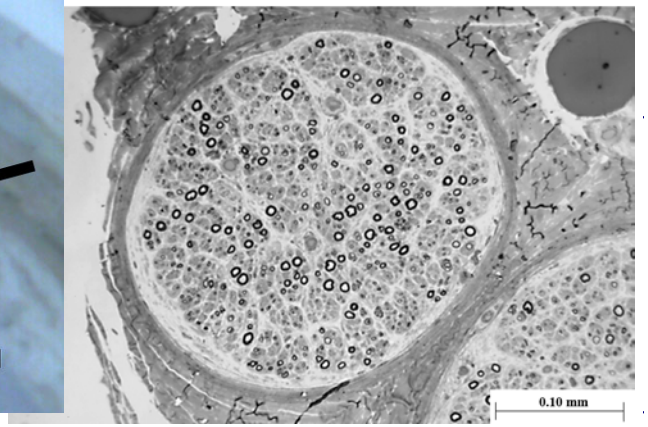
Slide courtesy, Lars Dahlin



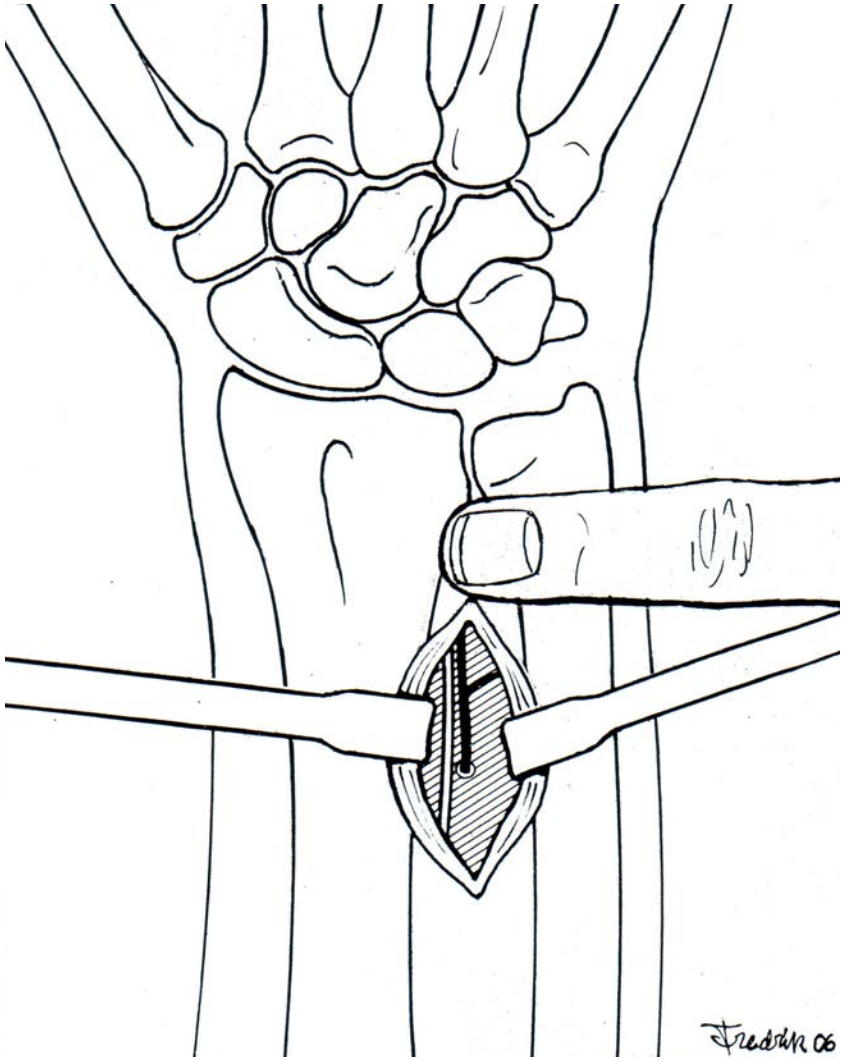
PIN nerve

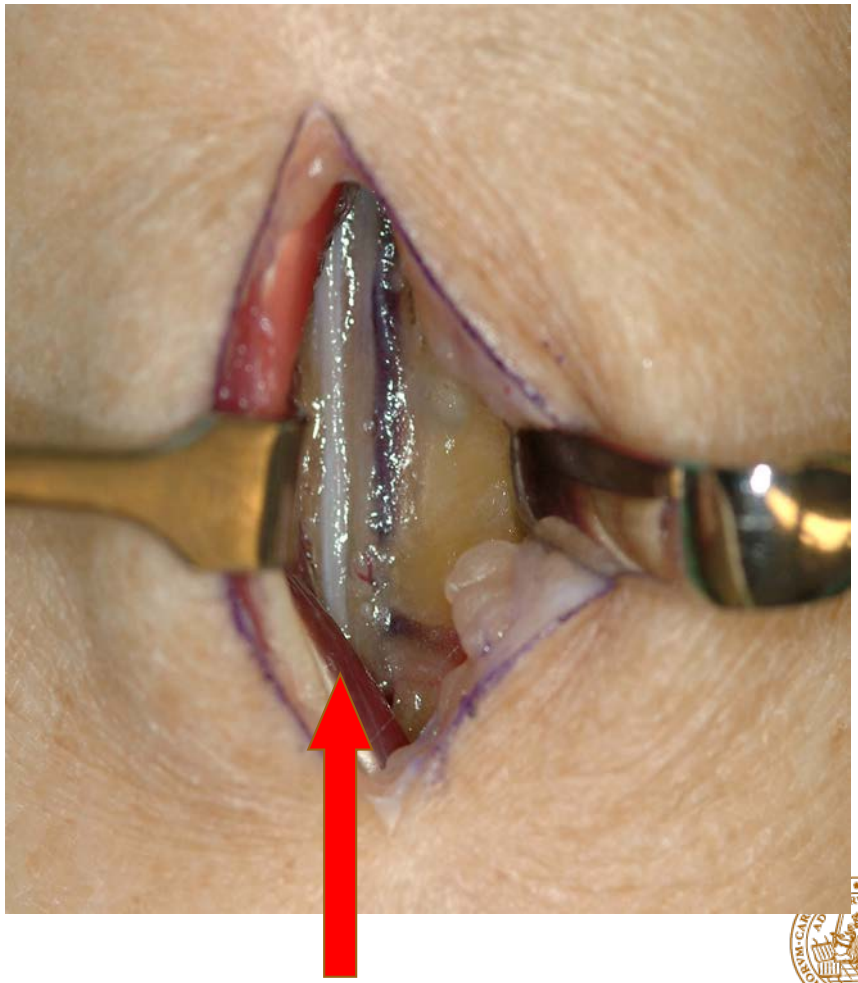


PIN nerve



PIN biopsy method





Posterior interosseus nerve

Collaboration Niels Thomsen and Rayaz Malik

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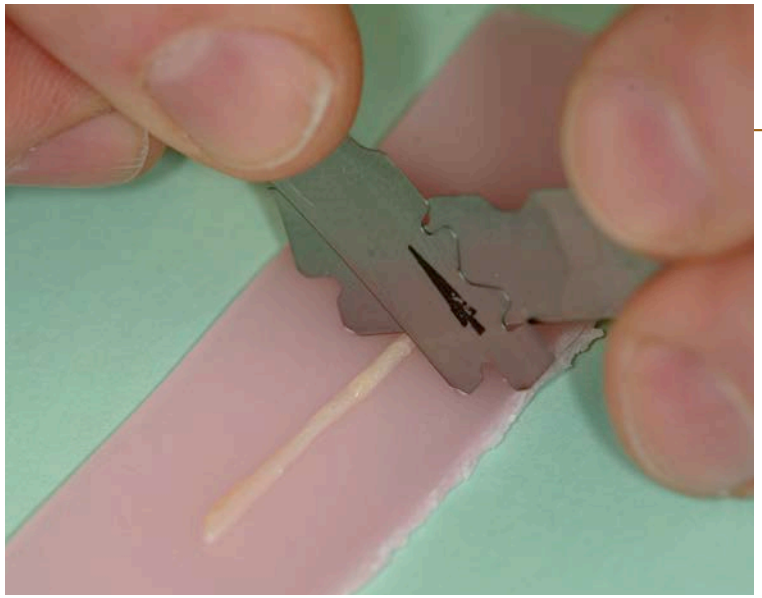
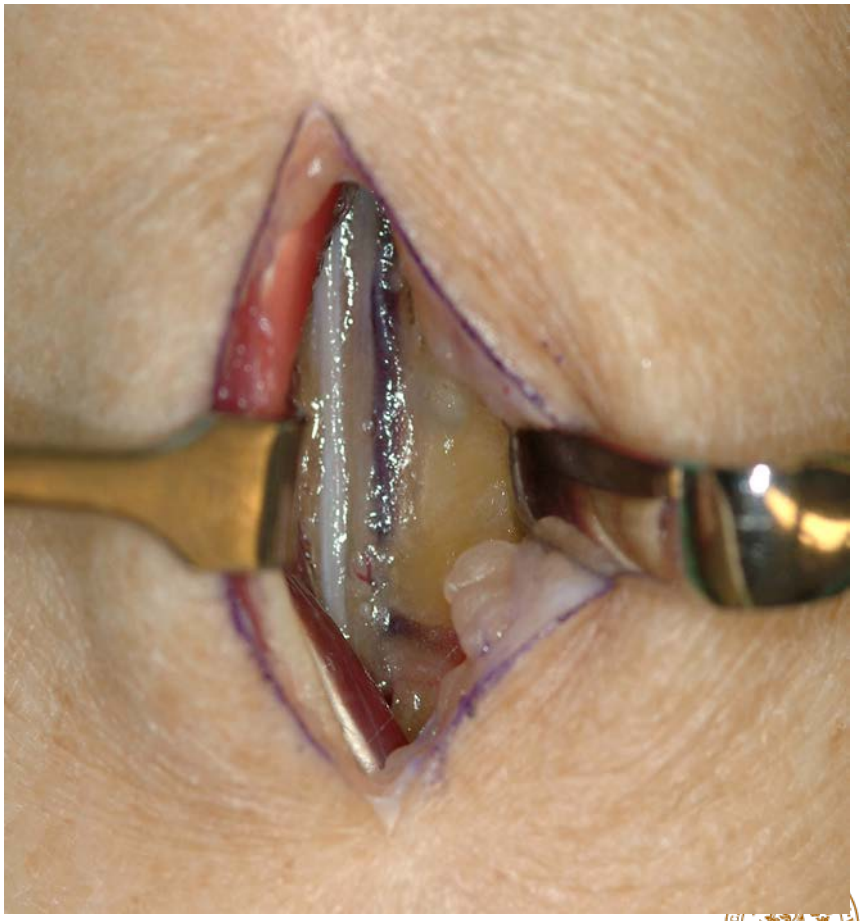
PIN biopsy





- 3-4 cm nerve biopsy
- 1-3 fascicles

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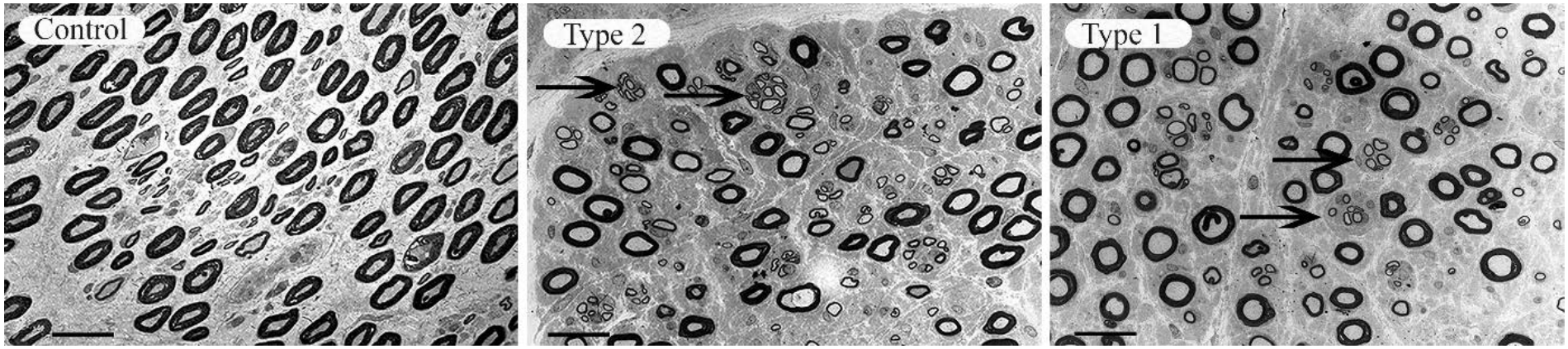
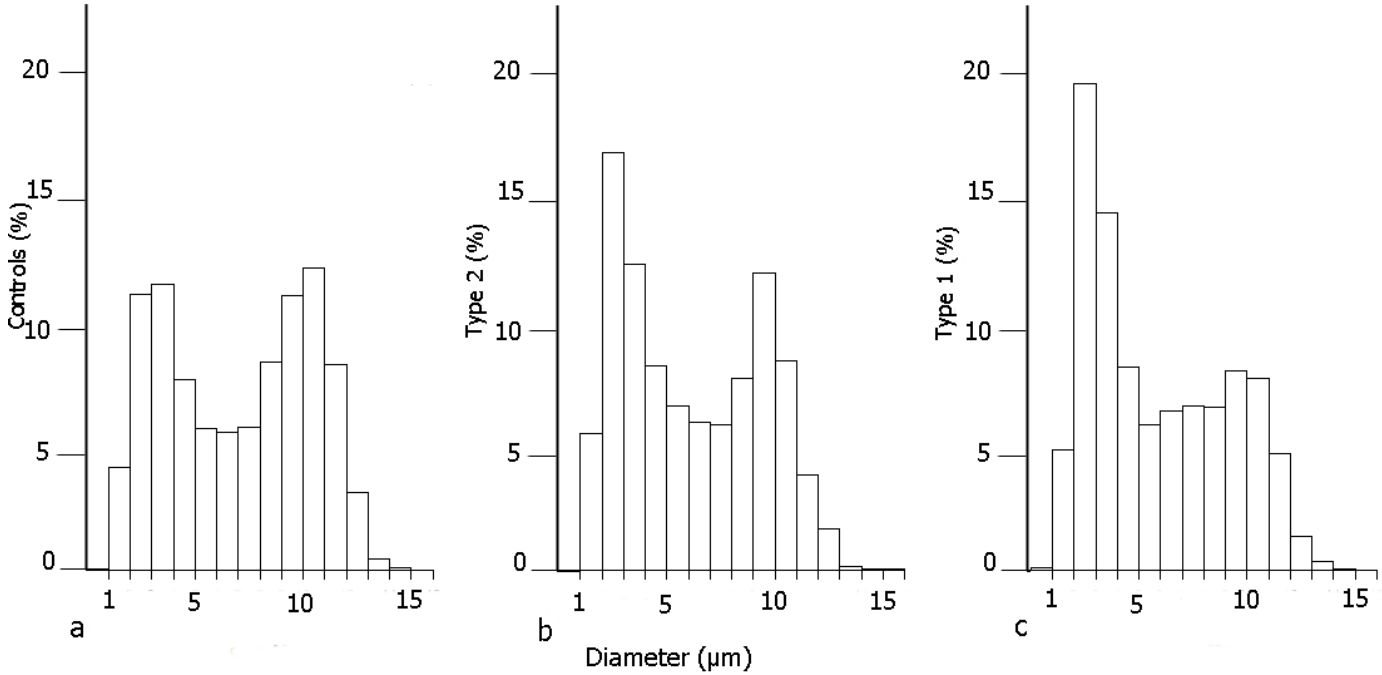
Diabetic Neuropathy – nerve fiber distribution





Posterior interosseous nerve – upper extremity

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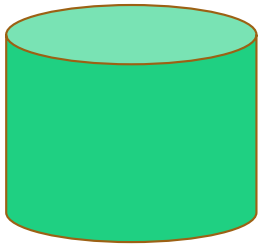
Synchrotron Nano CT versus 3D Electron microscopy

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

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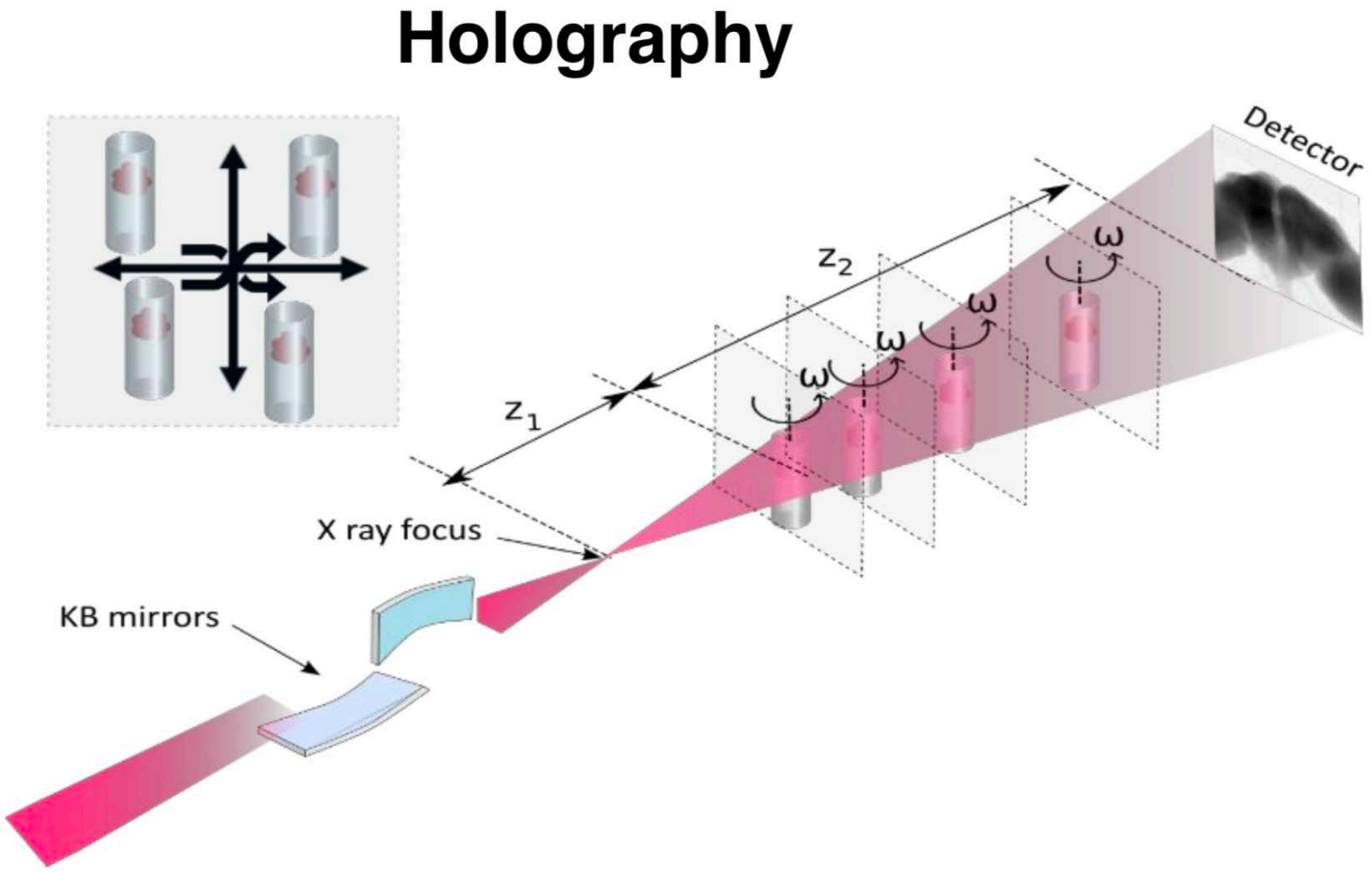
Micro Tomography

ESRF ID-16 Nano-Imaging



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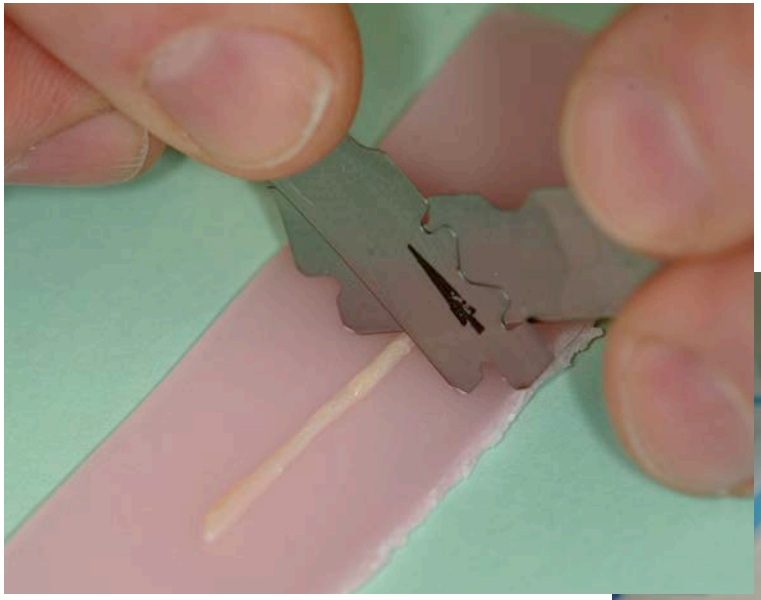
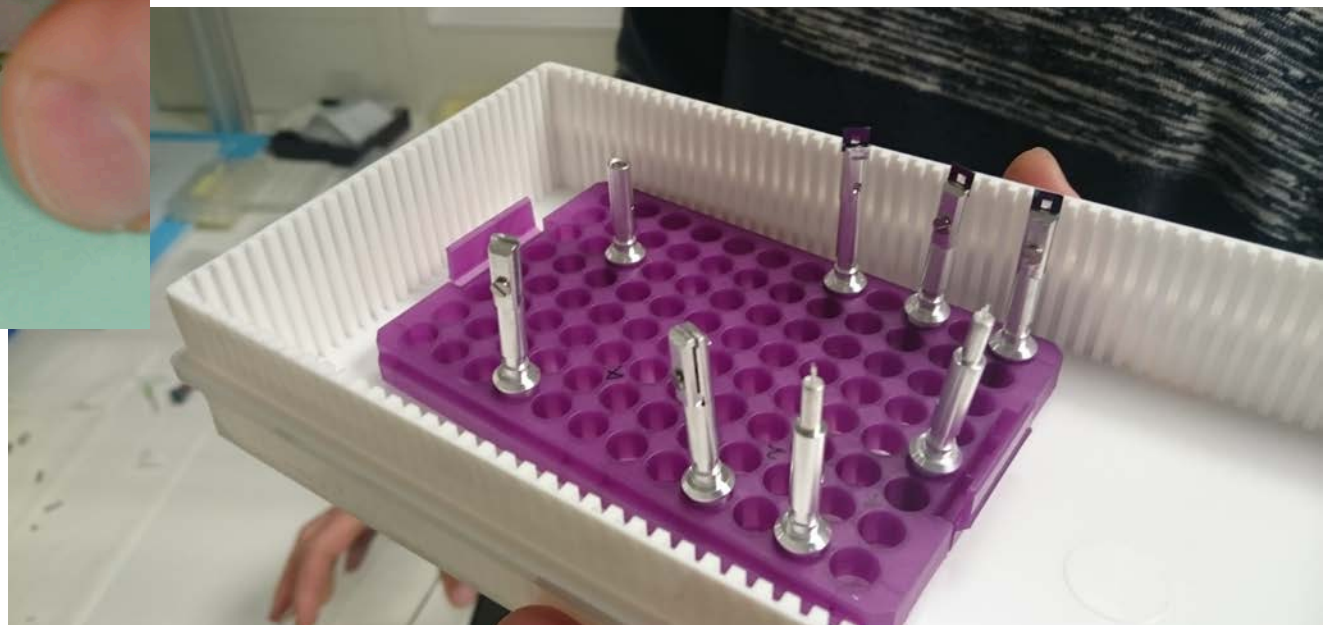
Human nerves in health and disease
PIN biopsy and samples





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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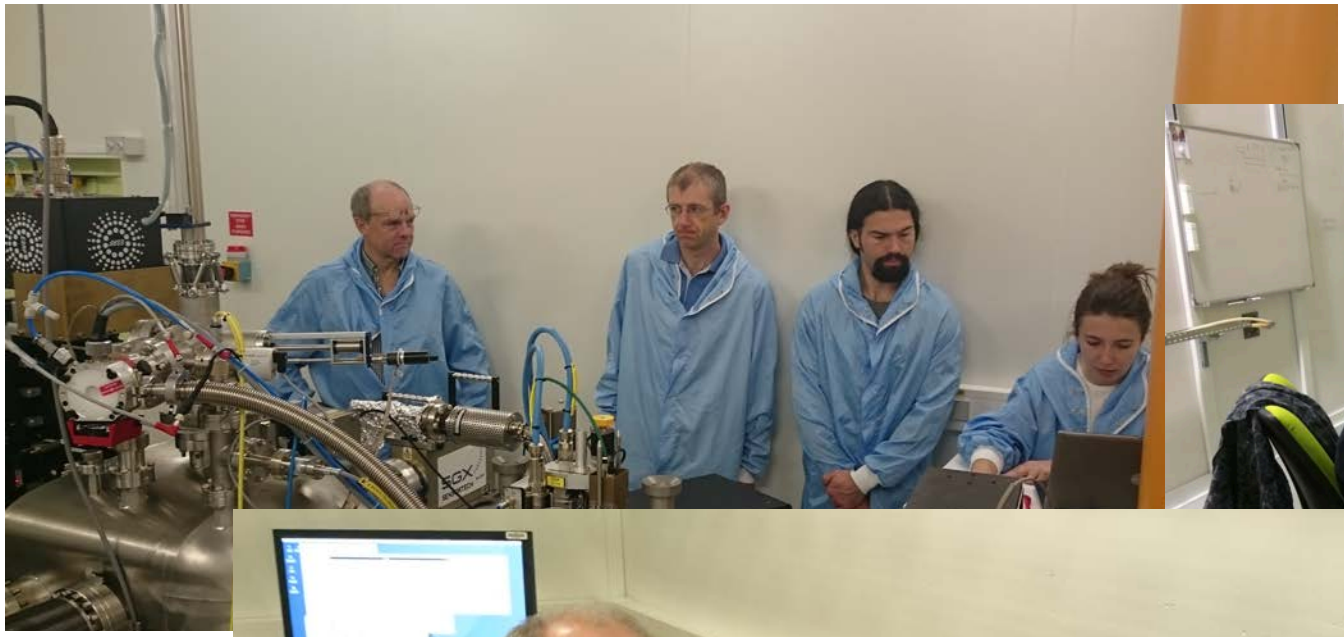
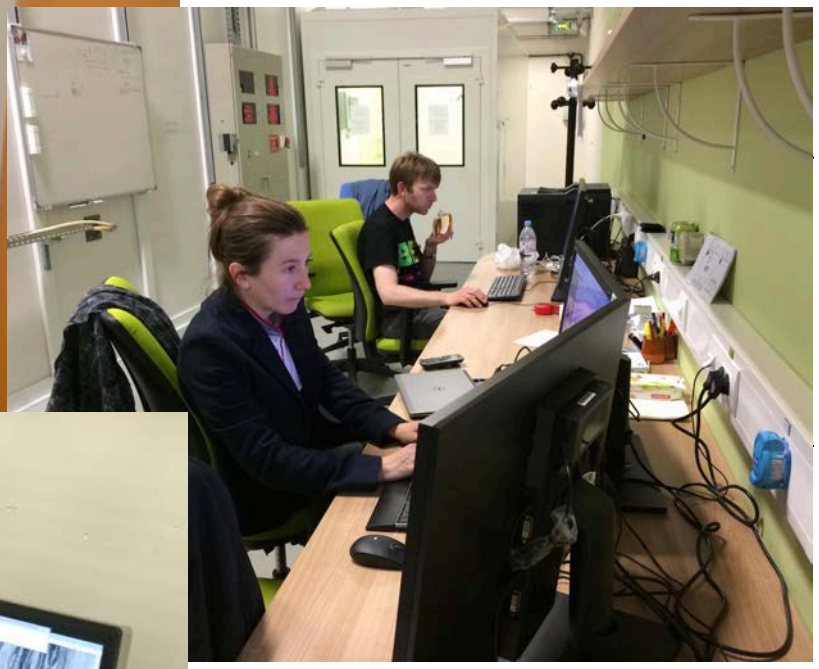
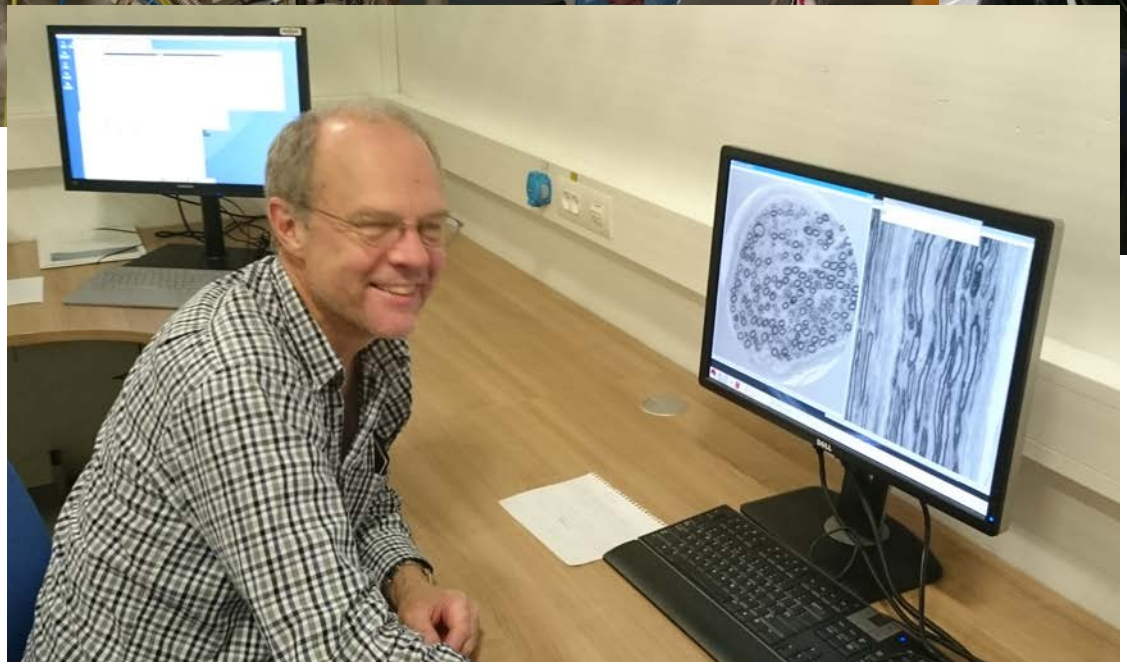
Experiment







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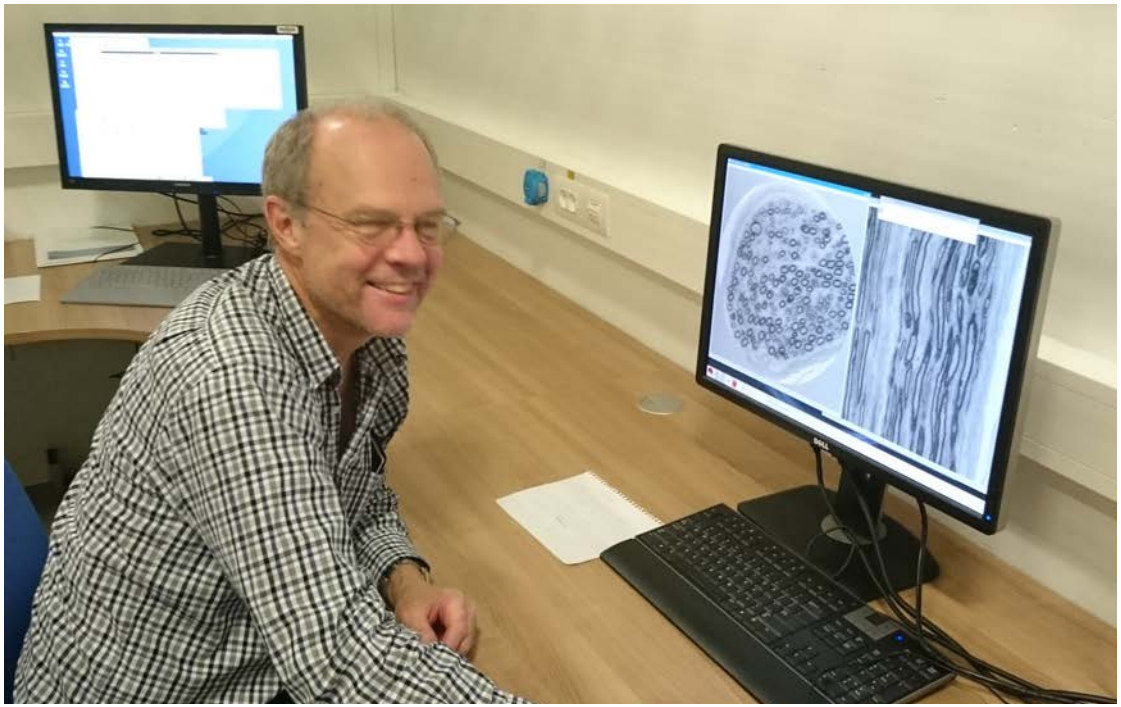
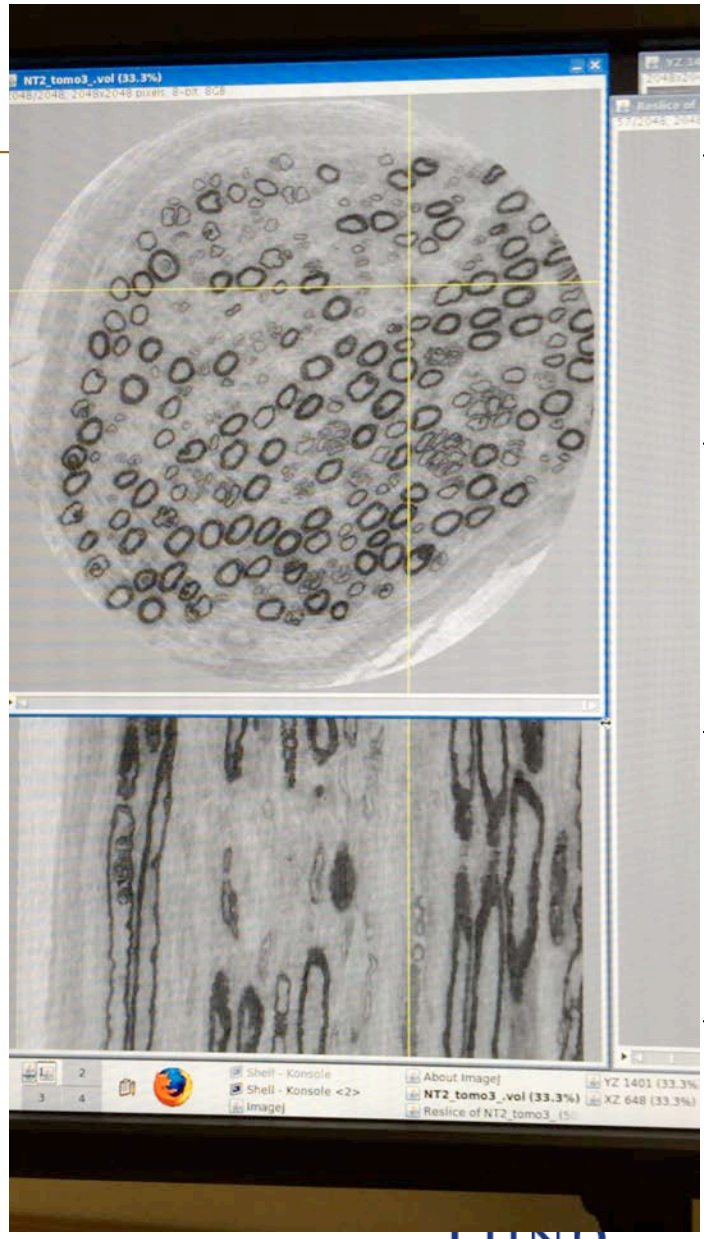
X-ray phase contrast zoom tomography
First look at reconstruction





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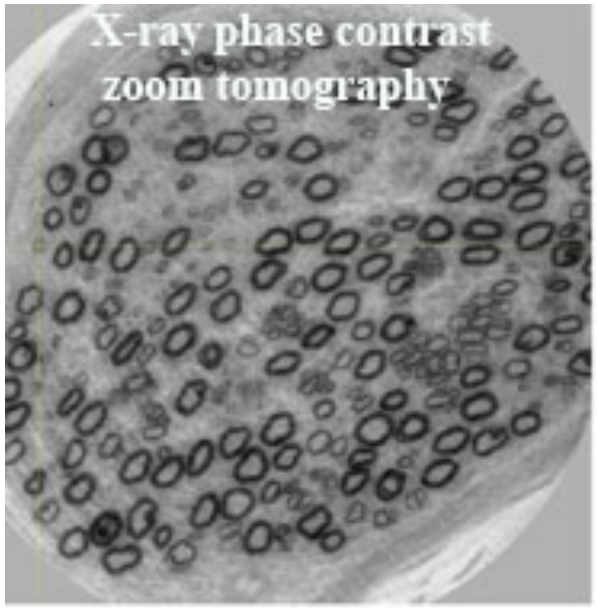
X-ray phase contrast zoom tomography



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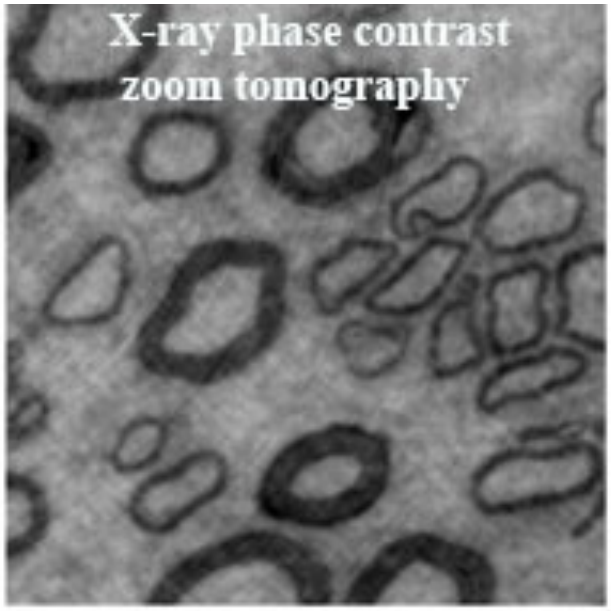

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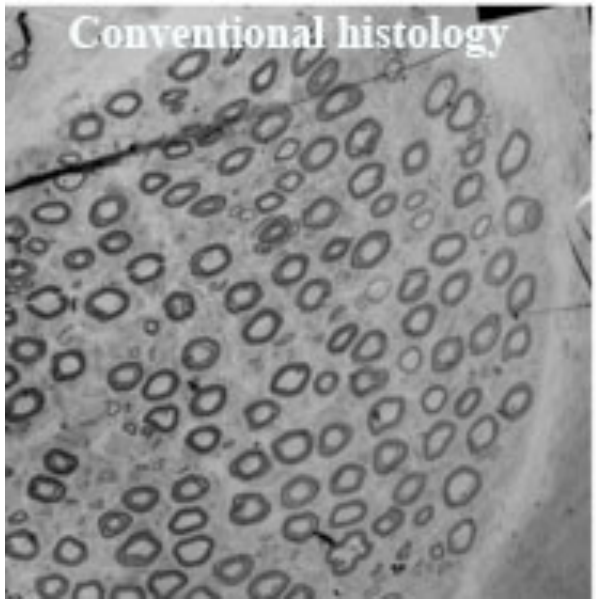

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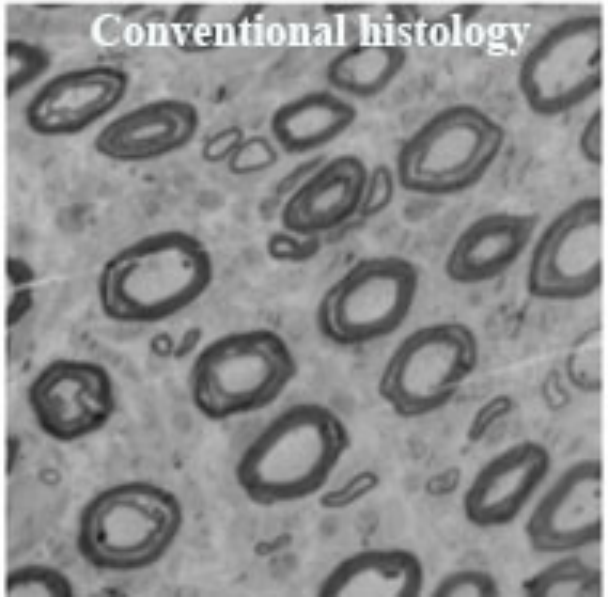
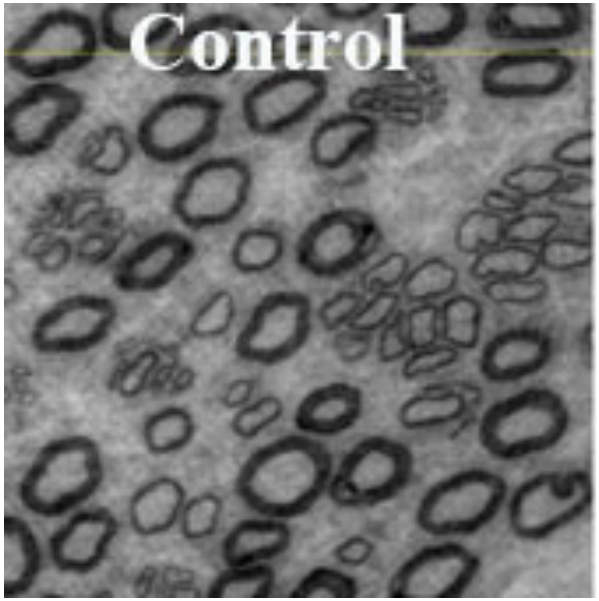


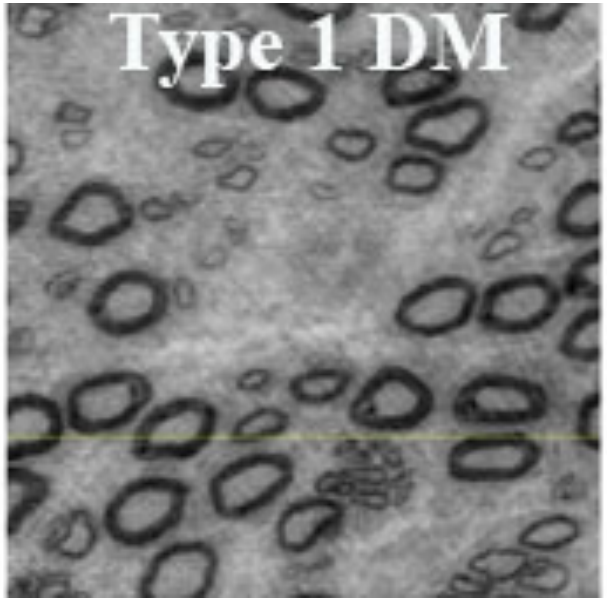
F

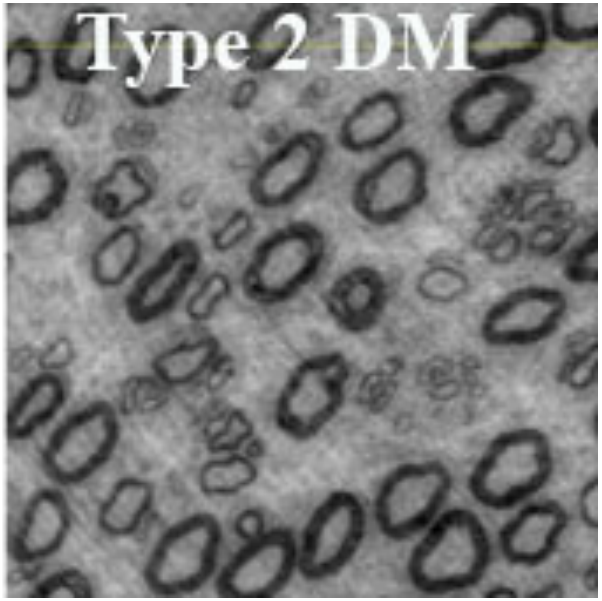
Three dimensional
visualisation

Human nerve fibers from PIN

X-ray phase contrast zoom tomography







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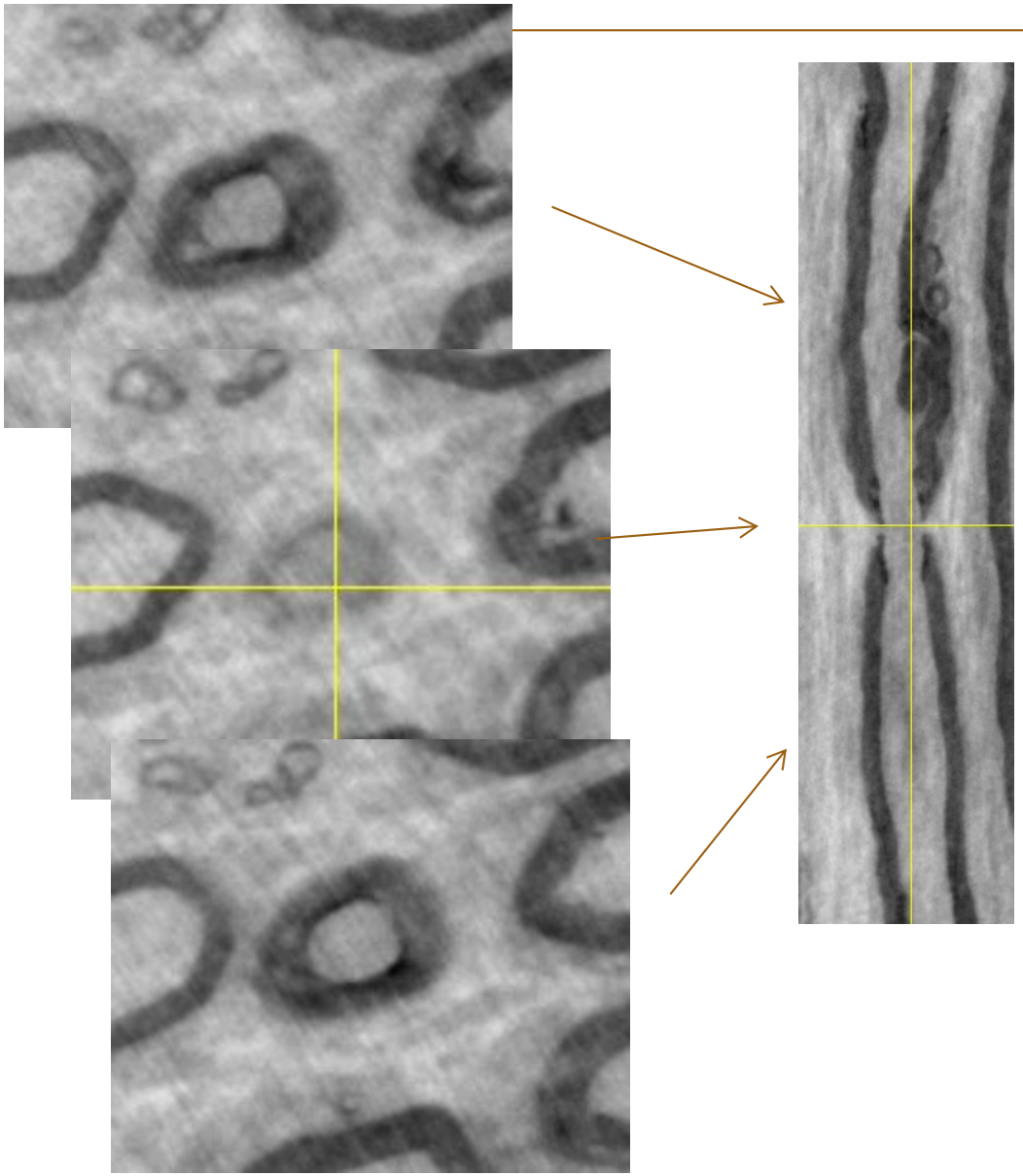
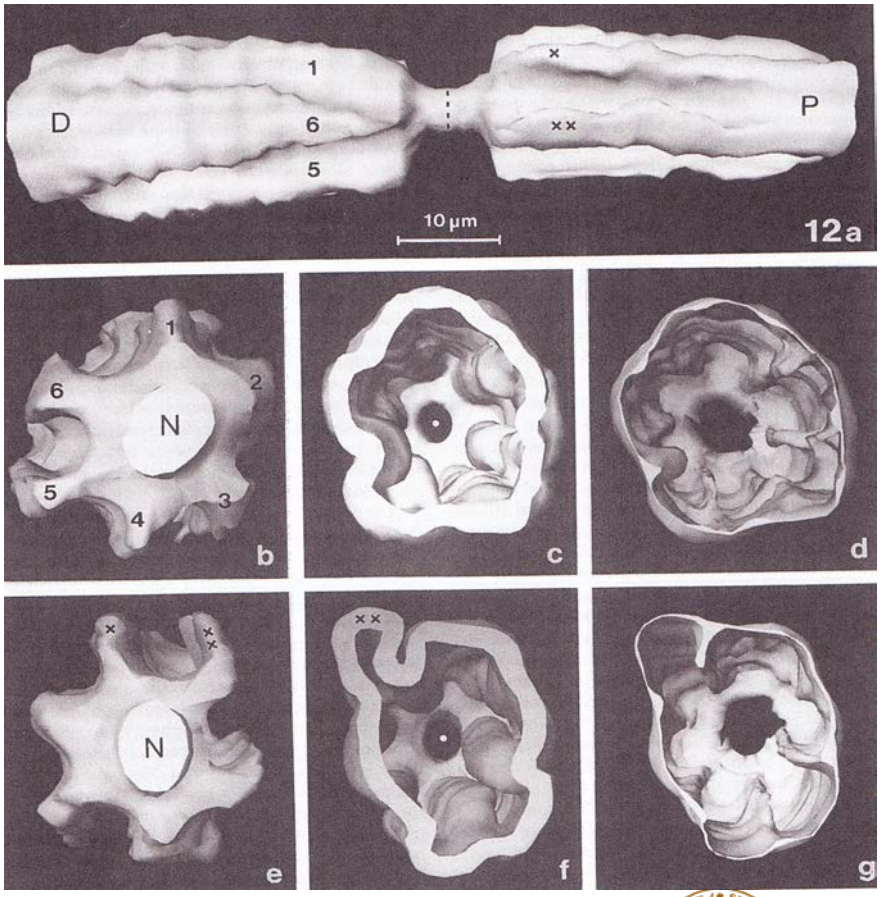
Node of Ranvier

Node of Ranvier – myelinated nerve fiber with myelin deleted





Berthold et al 1990

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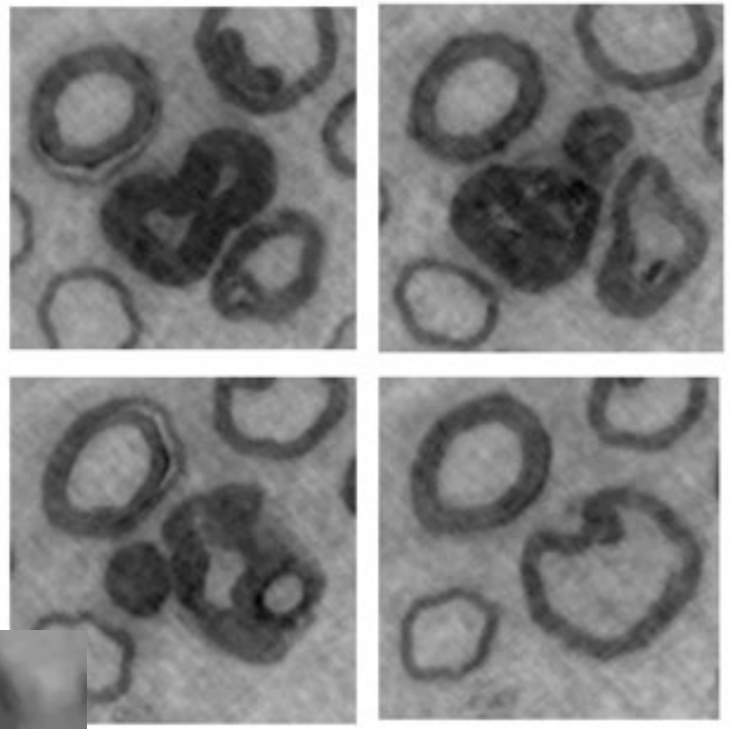
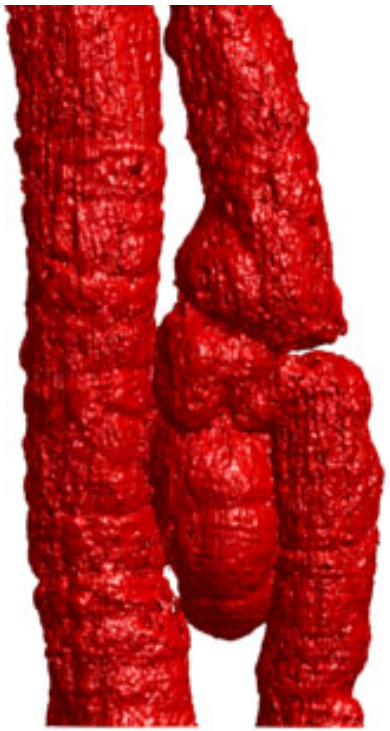
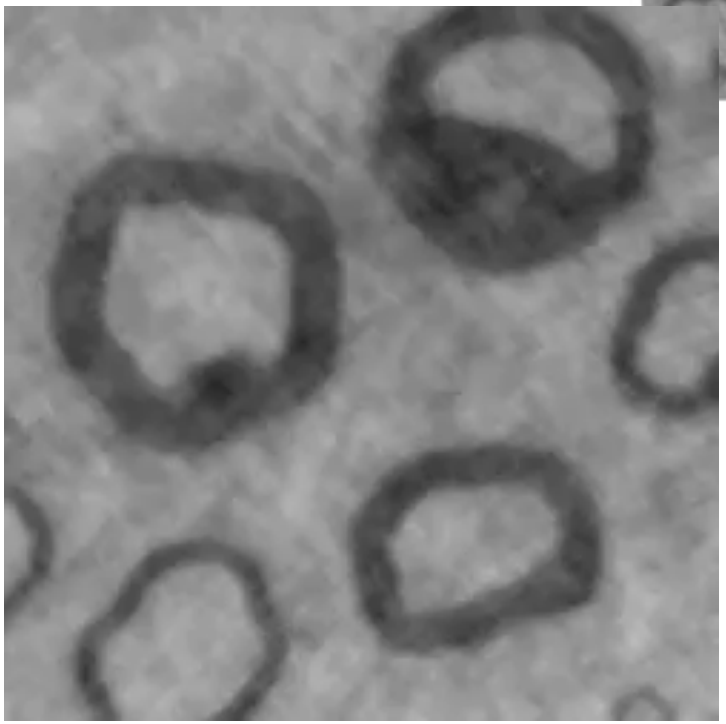
“Strange knob” – “birth of an axon”







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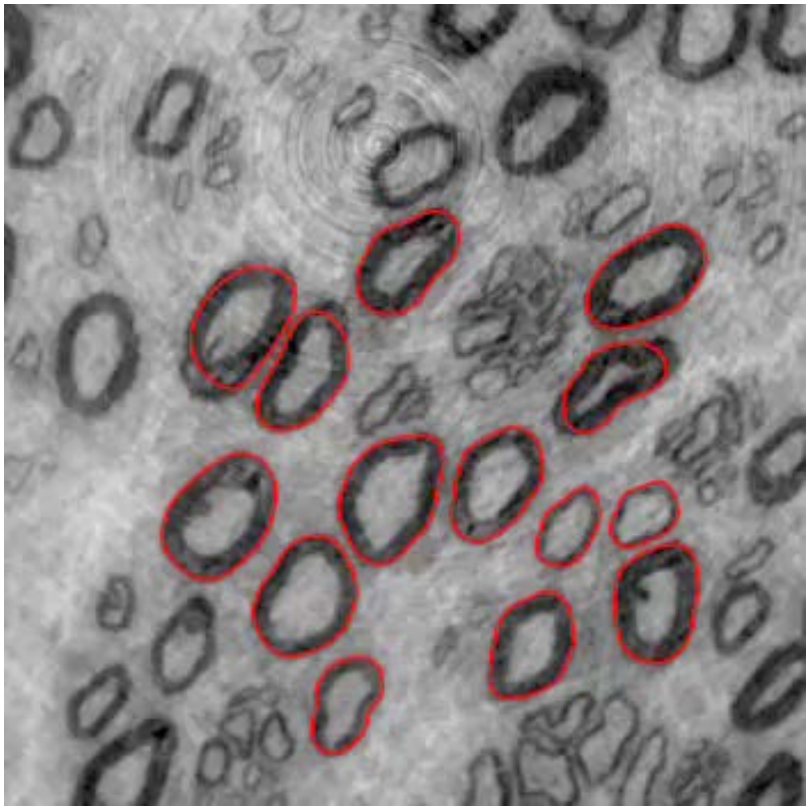
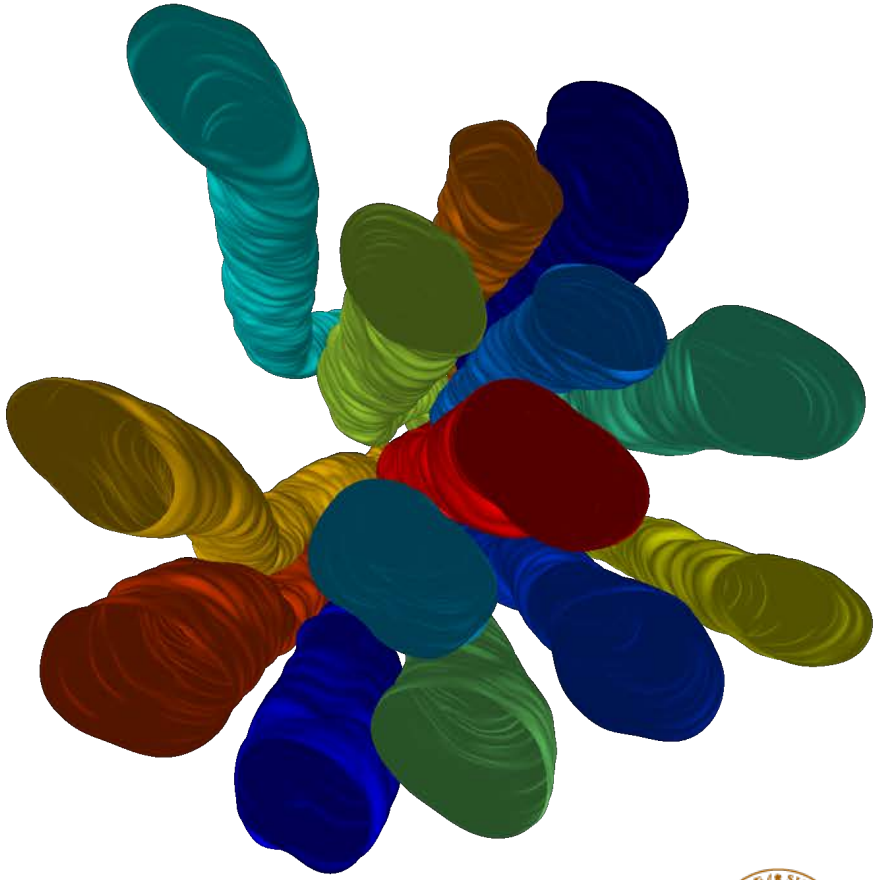
Segmentation at DTU imaging center





Contour – myelinated axons
Outer surface

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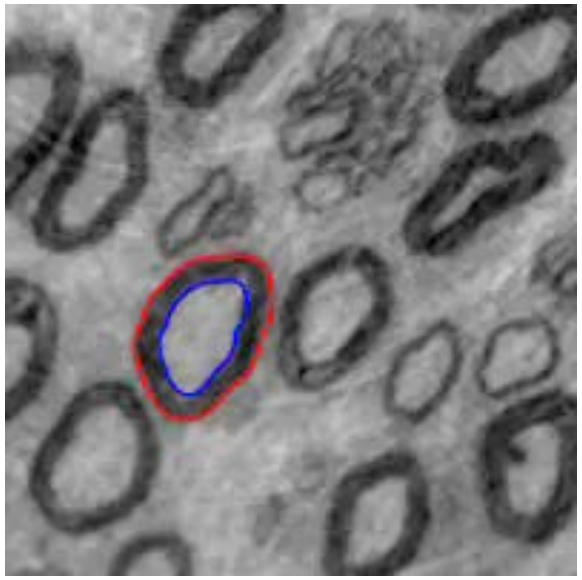
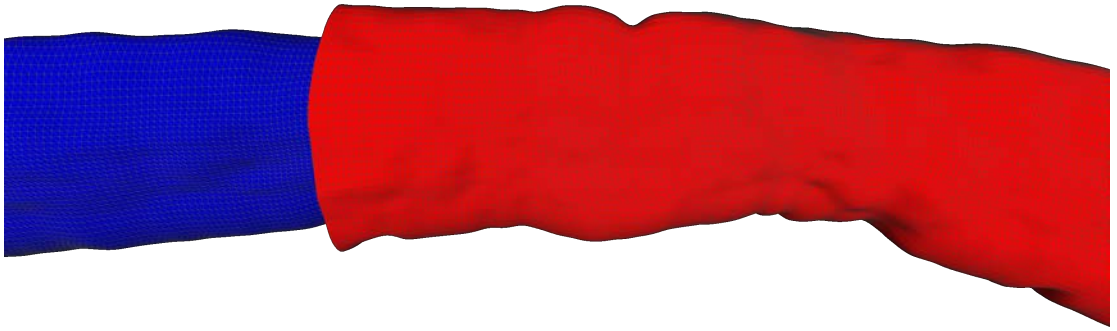
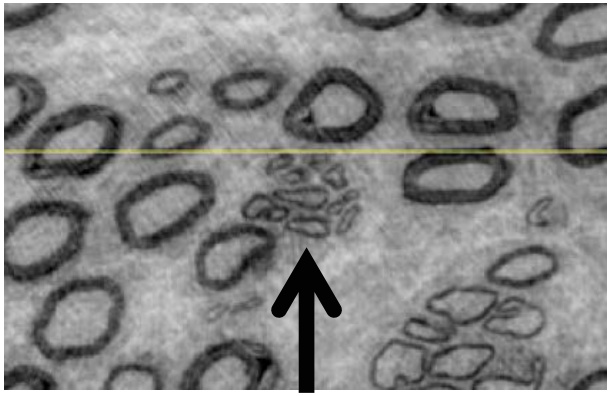
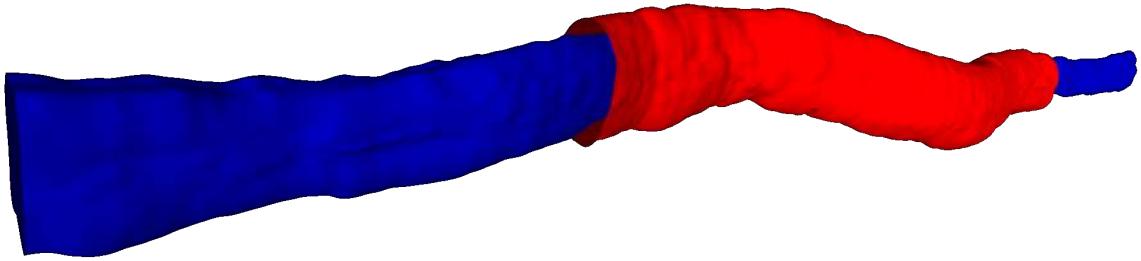
Segmentation at DTU imaging center









Contour – myelinated axons
Outer and inner surfaces

Regenerative clusters

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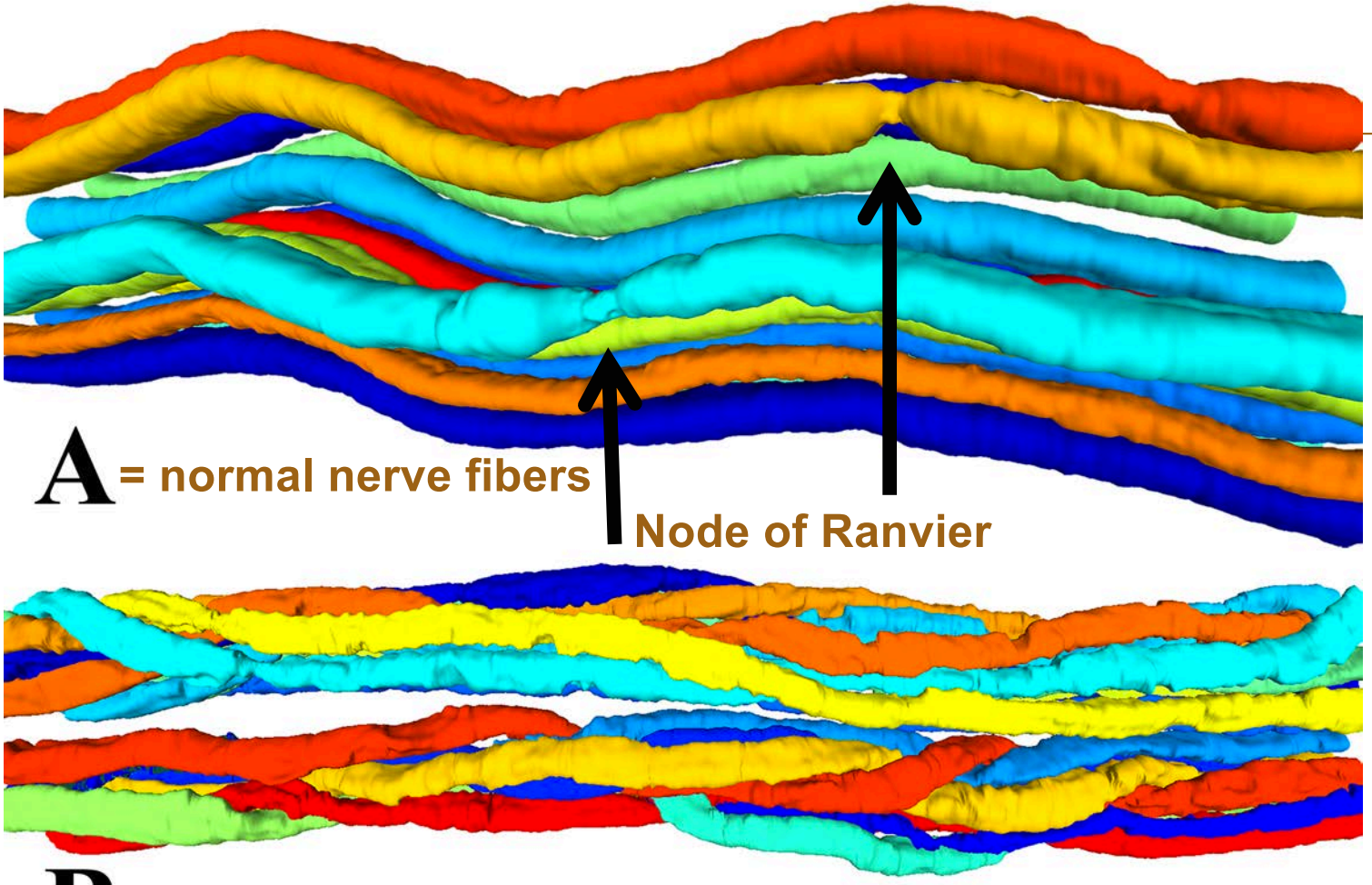
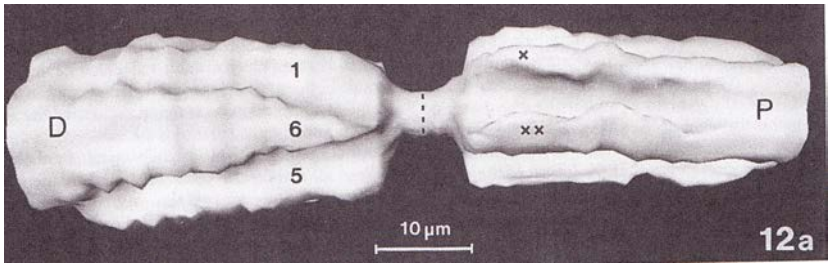
Segmentation at DTU imaging center



= regenerative clusters



Berhold et al 1990

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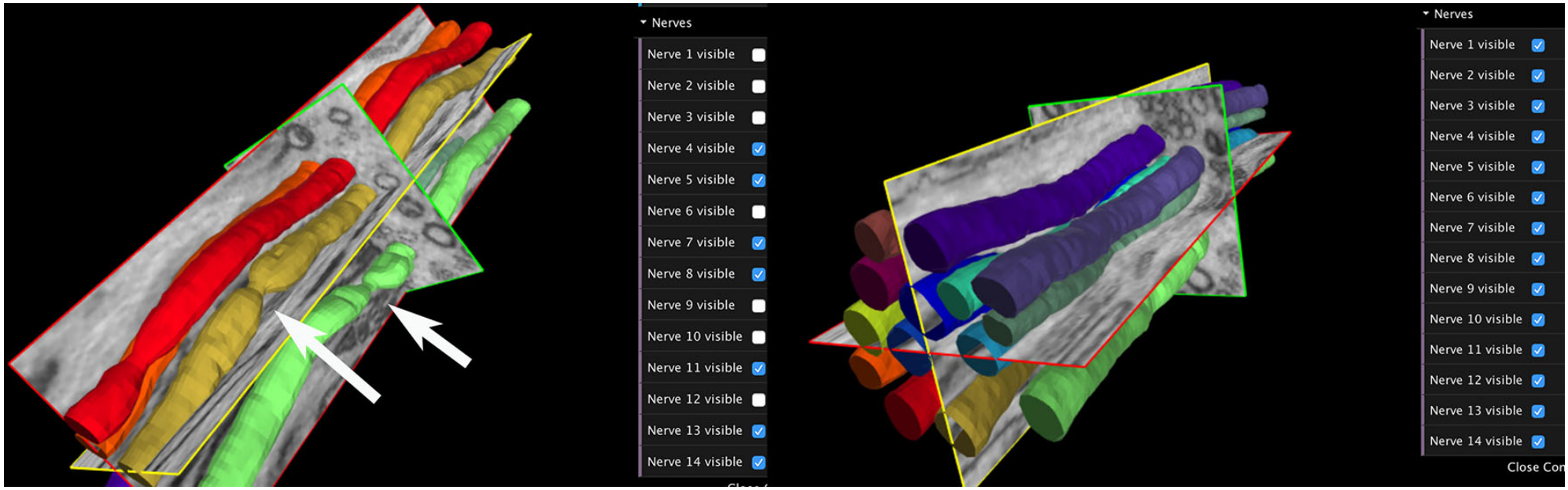
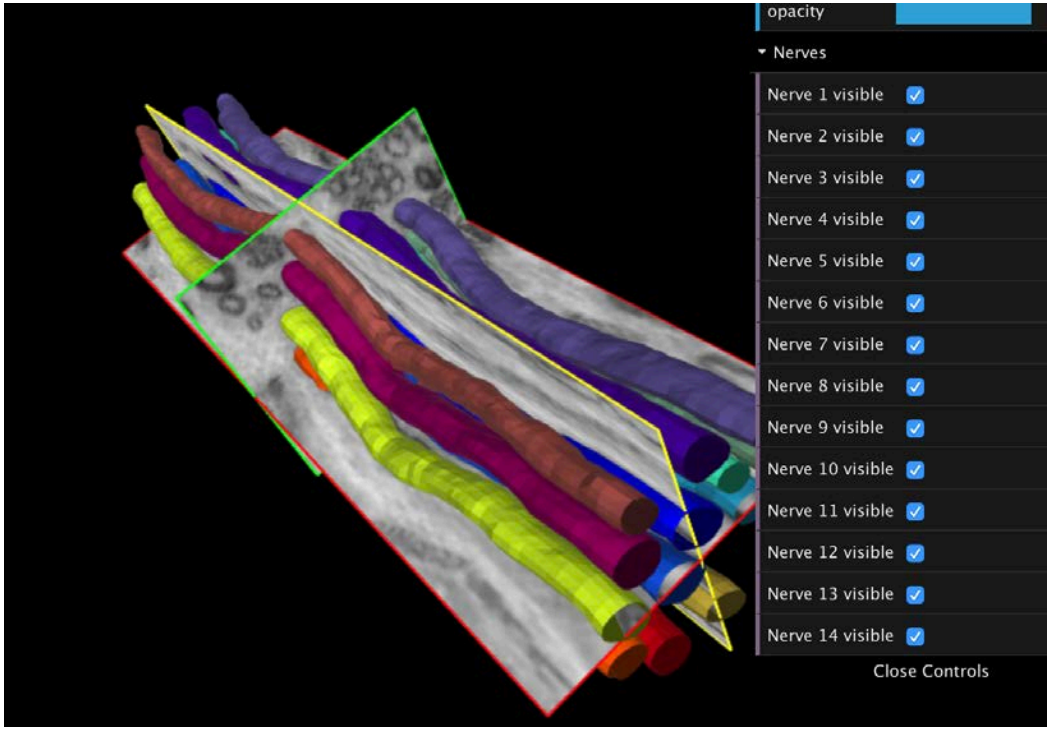
Segmentation at DTU imaging center





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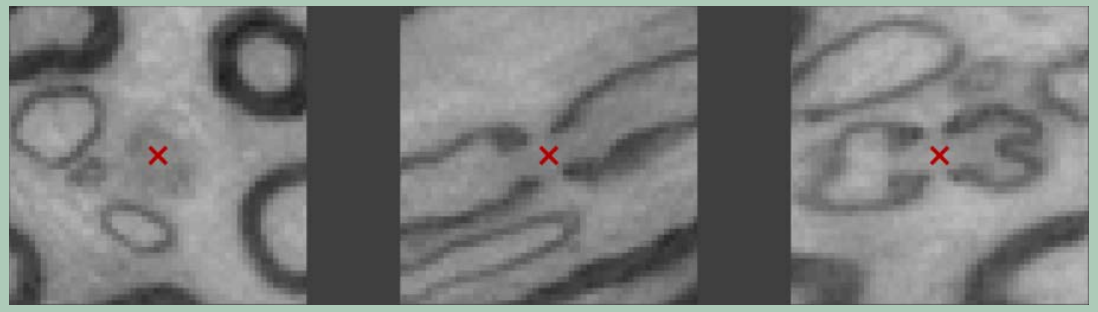
Data summary

– 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



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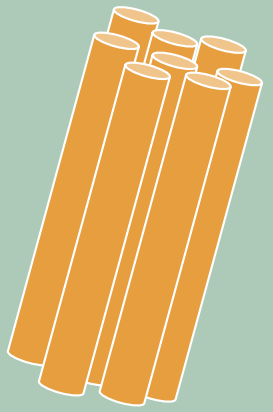
Data analysis

- **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?

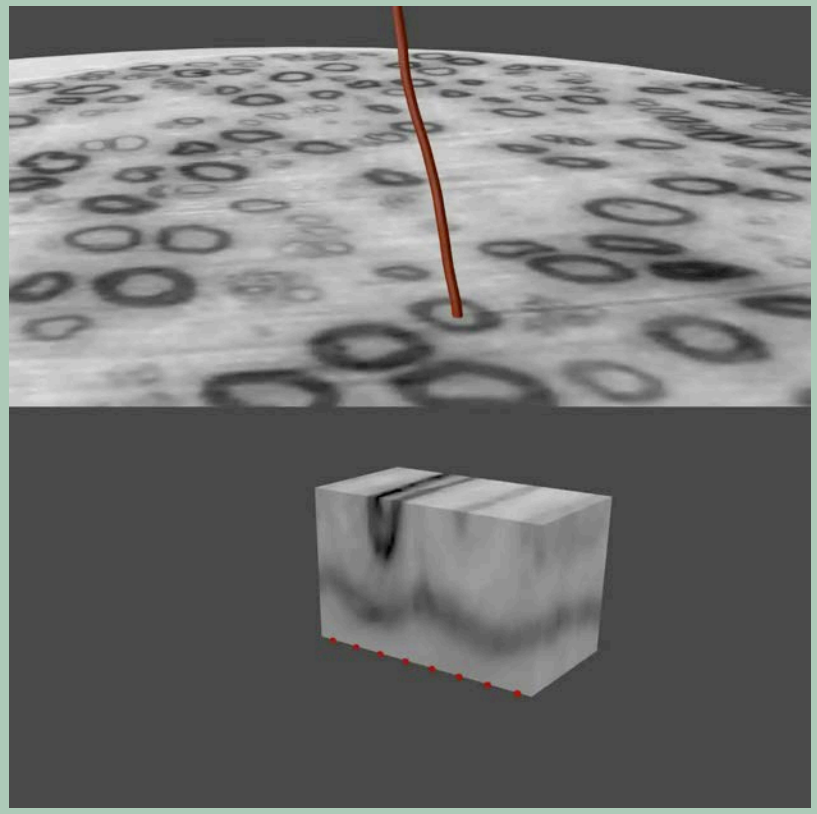
- **Smaller?**
- **Less myelin?**
- **Less dense?**
- **Disorganized?**
- **Irregular shaped?**

Work by
Hans Martin Kjer, DTU

LUND UNIVERSITY

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

Work by Hans Martin Kjer

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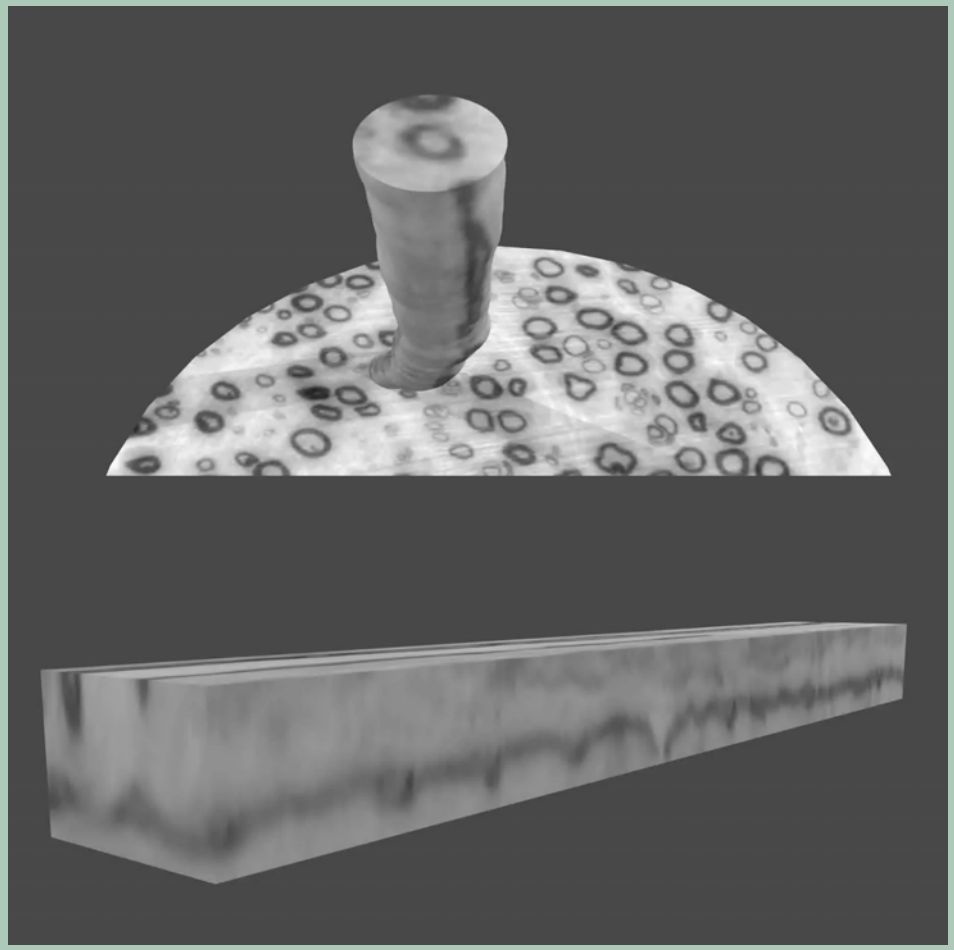
Data segmentation

» Extraction of both inner and outer surface



Work by
Hans Martin Kjer

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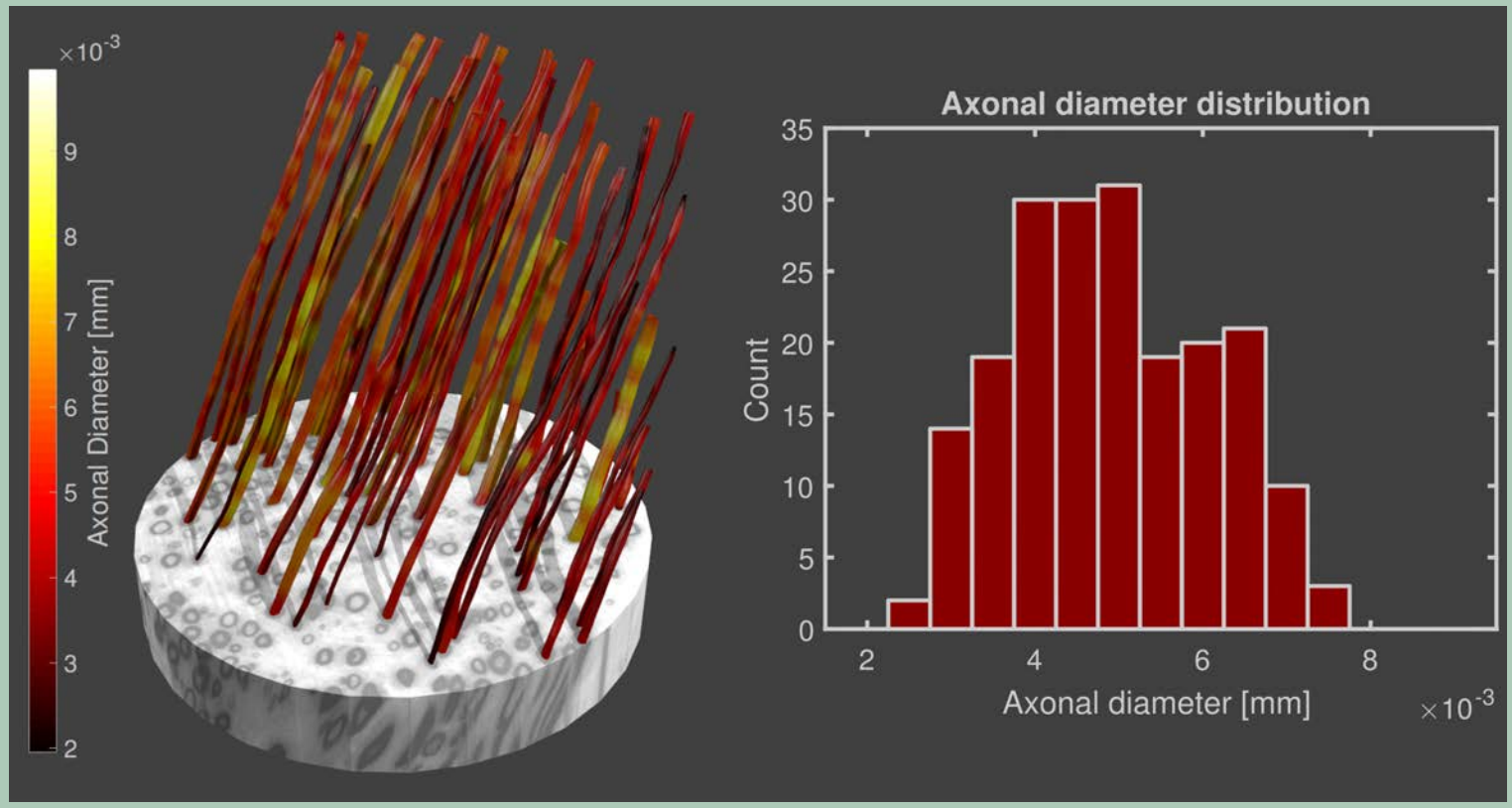
Morphology: Axonal diameter



Work by Hans Martin Kjer

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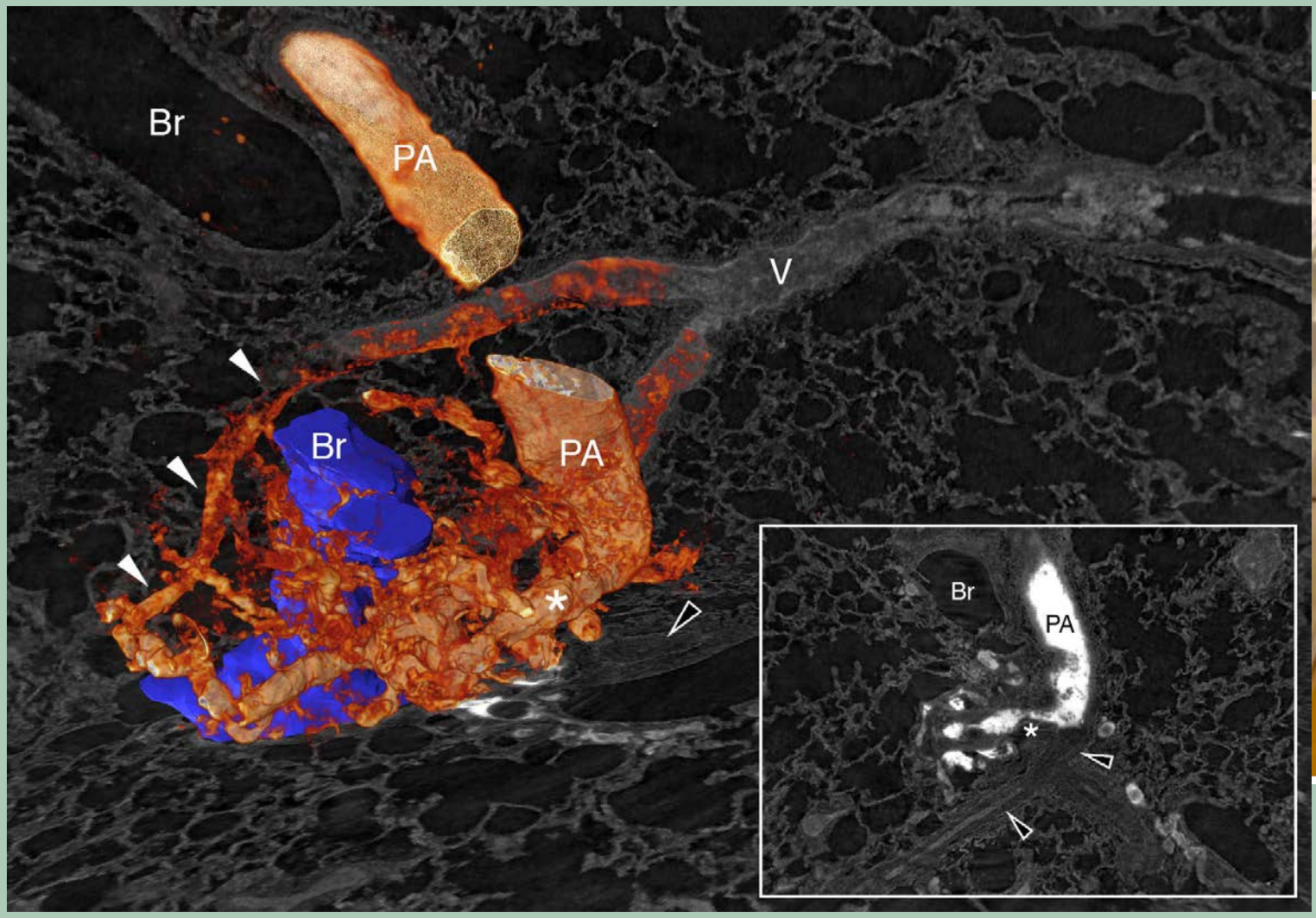
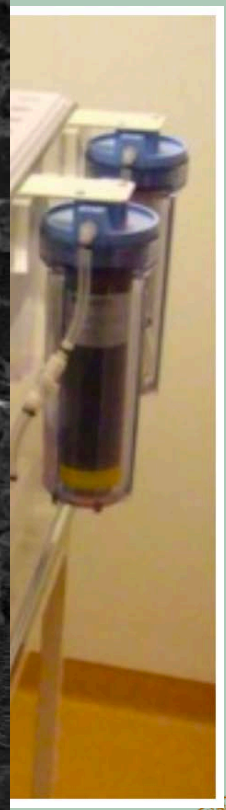
Other examples

Pulmonary hypertension

Pulmonary hypertension





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THANK YOU!

Diabetes Project

Lars Dahlin, LU
Vedrana Dahl, DTU
Anders Dahl, DTU
Peter Cloetens, ESRF
Alexandra Pacureanu, ESRF
Kristian Rix, DTU
Simin Mohseni, LiU
Johan Malmström, LU
Niels Thomsen, SUS
Erik Ising, SUS

Brain Project

Mariam Andresson, DTU
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H. Martin Kjer, DTU/DRCMR
Jonathan Rafael Patino, EPFL
Jean-Philippe Thiran, EPFL
Anders Dahl, DTU Compute
Vedrana Dahl, DTU Compute
Susanne Sørensen, Region H

Lung Project

Christian Norvik, LU
Christian Westö, LU
Karin Tran-Lundmark, LU
Niccolo Peruzzi, LU
Rajmund Mokso, Max IV
Goran Lovric, PSI

MEDICON VILLAGE

REGION SKÅNE

ESRF
The European Synchrotron

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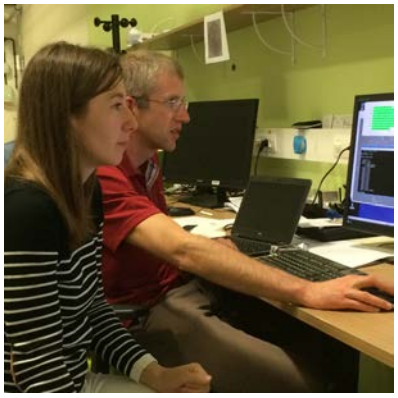
THANK YOU!

Lars Dahlin, LU

Vedrana Dahl, DTU

Anders Dahl, DTU

Simin Mohseni, LiU



Peter Cloetens, ESRF
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Erik Ising, SUS

Johan Malmström, LU

MEDICON VILLAGE

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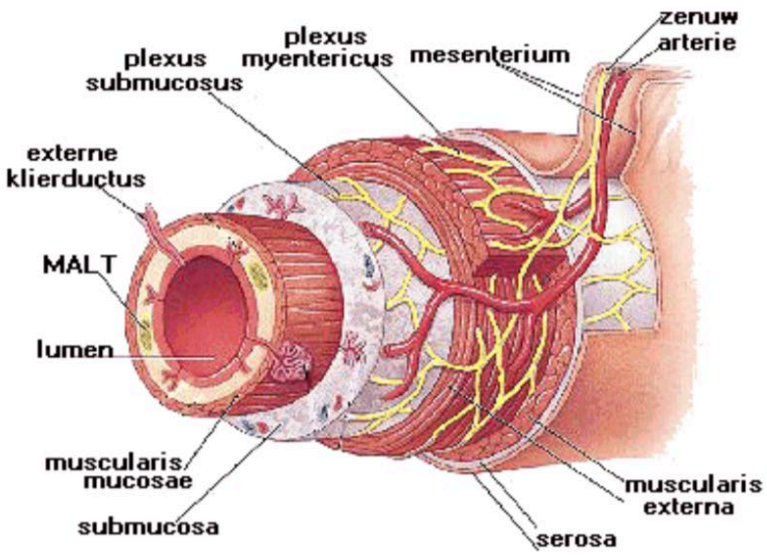
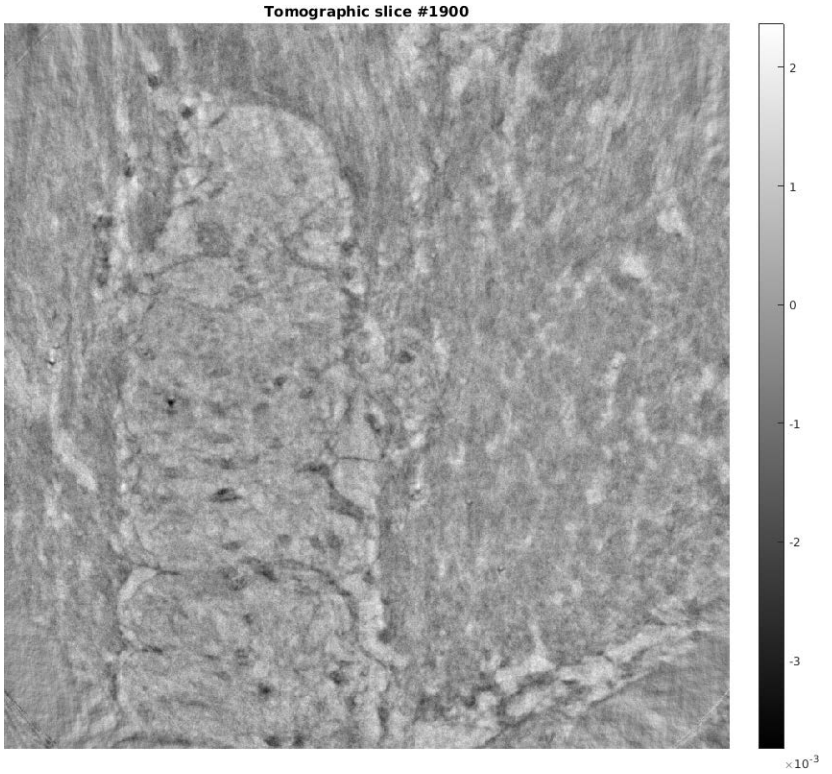
Examples of Clinical research projects Irritable Bowels Syndrome (IBS)





Control, Myenteric plexus

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