Multimodal approach for the study of mouse CNS.

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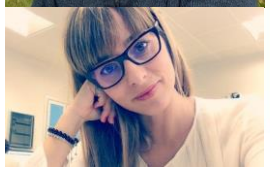

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OUTLINE

- **Scientific problem**: necessity to find a more comprehensive approach to characterize tissue, neuronal and vascular network damage in pathological conditions (injury, neurological disease).
- **Proposed strategy** combination of many techniques as well as ad hoc analysis correlating and integrating information arising from different techniques in particular X-ray phase contrast micro tomography (XPCT), histology, Diffusion Tensor Imaging, (DTI).
- **Conclusion** and future research

SCIENTIFIC PROBLEM

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Neurodegenerative diseases affect hundreds of millions of humans in the world

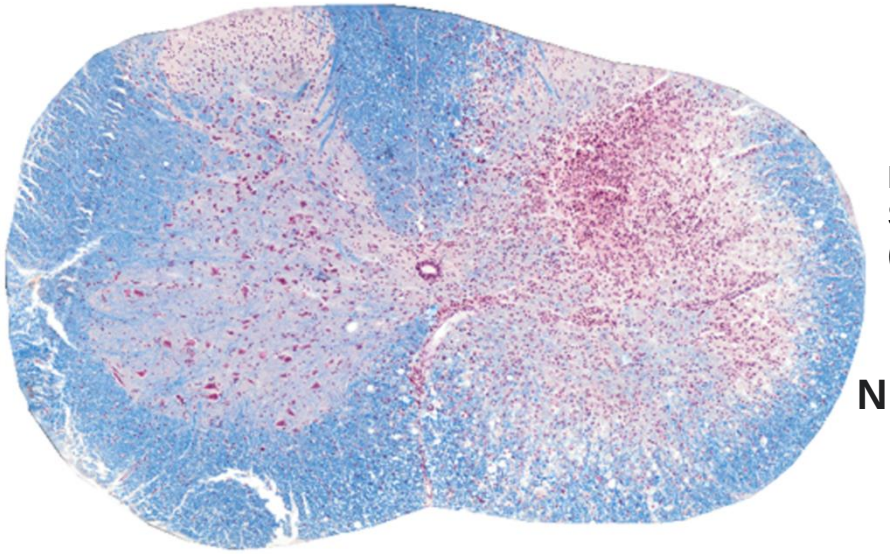
The pathophysiology of many of these diseases is poorly understood and we still lack of effective therapies

It appears essential to define morphological and topological quantitative parameters characterizing a healthy neuronal network architecture to understand changes of these features in any part of the CNS in disease samples

Development of a multimodal approach based on **3D high resolution image techniques, histology and theoretical tools to discriminate the smallest capillaries and the neuron morphology in ex-vivo healthy animal model, *is crucial***

Histology vs XPCT

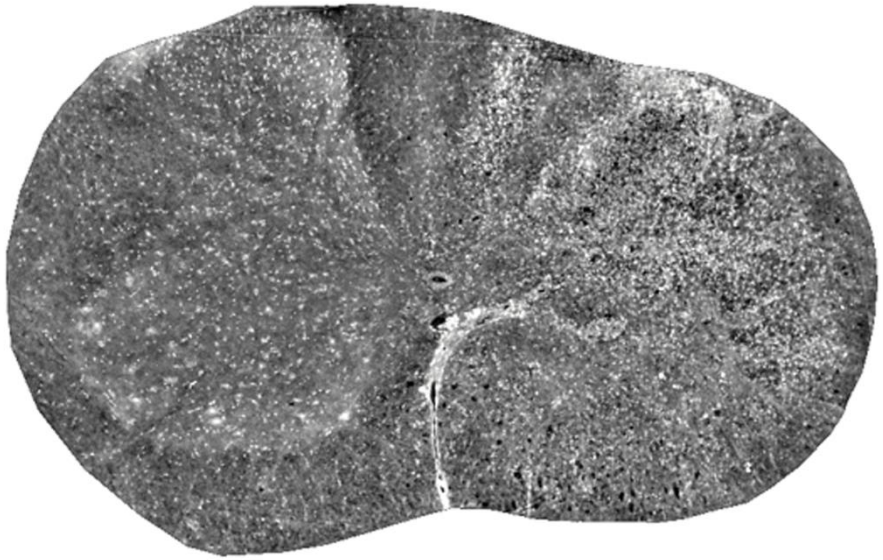
- Histology is highly sensitive to different cell type but requires sectioning of the sample and is a 2D technique.
- XPCT is less sensitive to specificity of cell but is a 3D, hight resolution and non invasive (it doesn’t require staining or sectioning) technique for ex situ studies.
- However, the combination of the two techniques allows to reach a more high level of specificity (as in the case of a mouse CNS injury).



MOUSE MODEL OF SPINAL CORD INJURY (SCI) 7 DAYS

Nissl staining

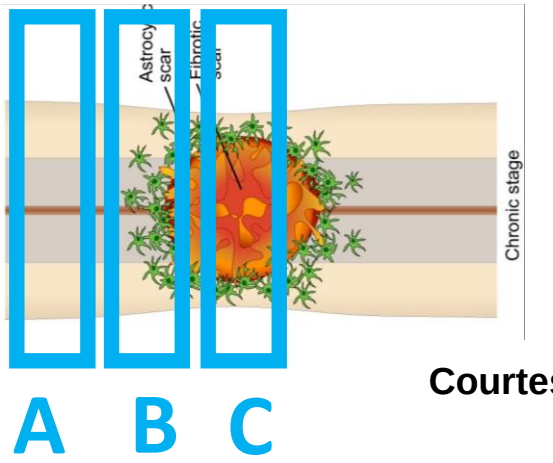
Courtesy of Charles Nicaise

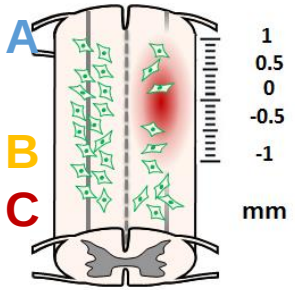


XPCT, TOMCAT beamline (PSI)

Pixel size 0.65 µm, Slab of 15 µm thickness

The case of the spinal cord injury (SCI)





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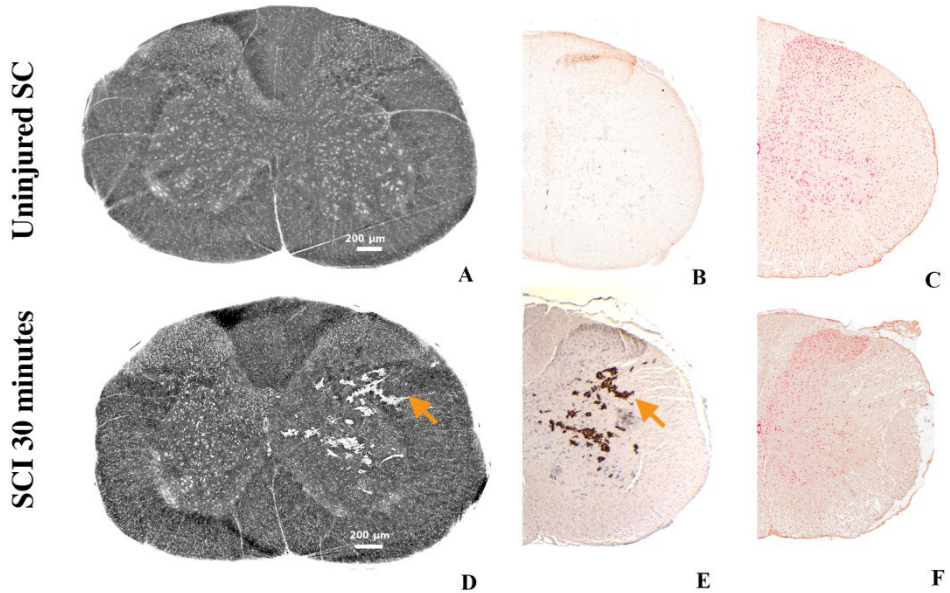

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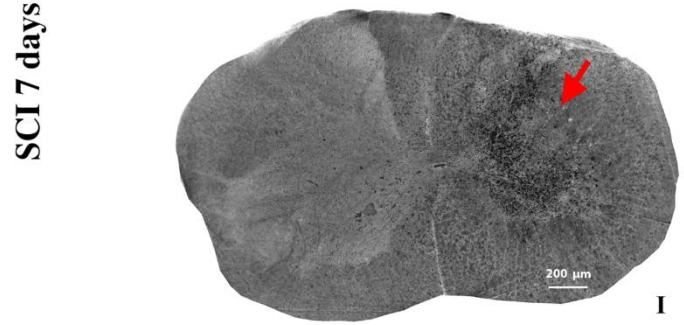
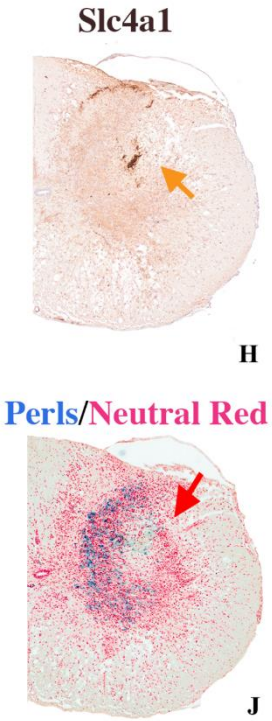




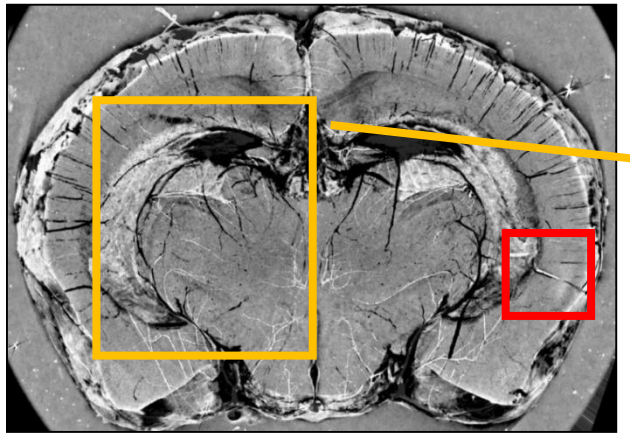
Courtesy of Charles Nicaise

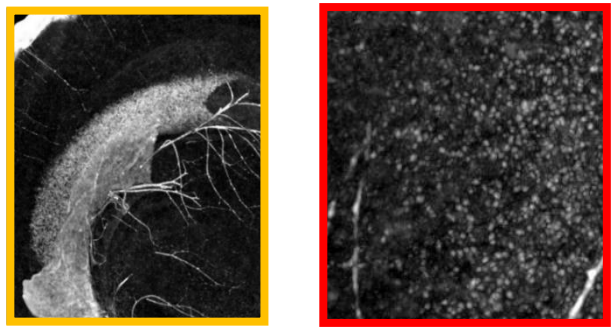
XPCT,
TOMCAT beamline (PSI)

Pixel size 0.65 µm, Slab of 30 µm thickness

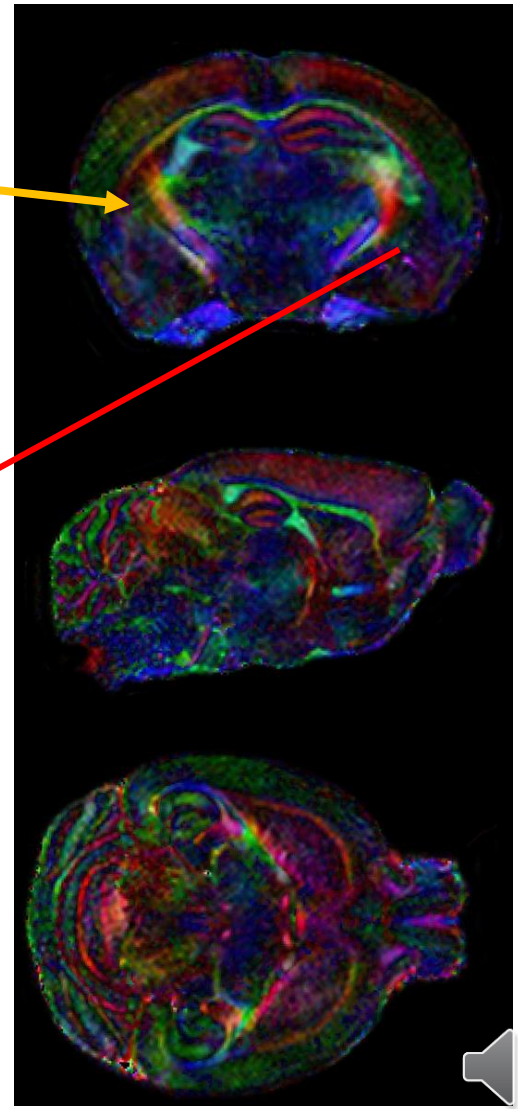
MRI and XPCT

- MRI provides information about anatomy, microstructure and function of the brain and spinal cord, *in vivo, non invasively* but is limited by its low direct spatial resolution and signal specificity
- 3D High resolution information of the CNS arising from other imaging techniques can be used to improve the interpretation of MRI measurements.
- In our study we propose two example from mouse brain and spinal cord





DTI and XPCT combination



DTI combined with XPCT

frontiers in Neuroscience

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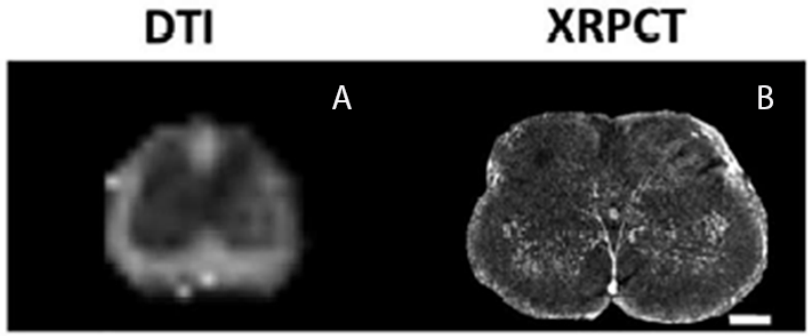
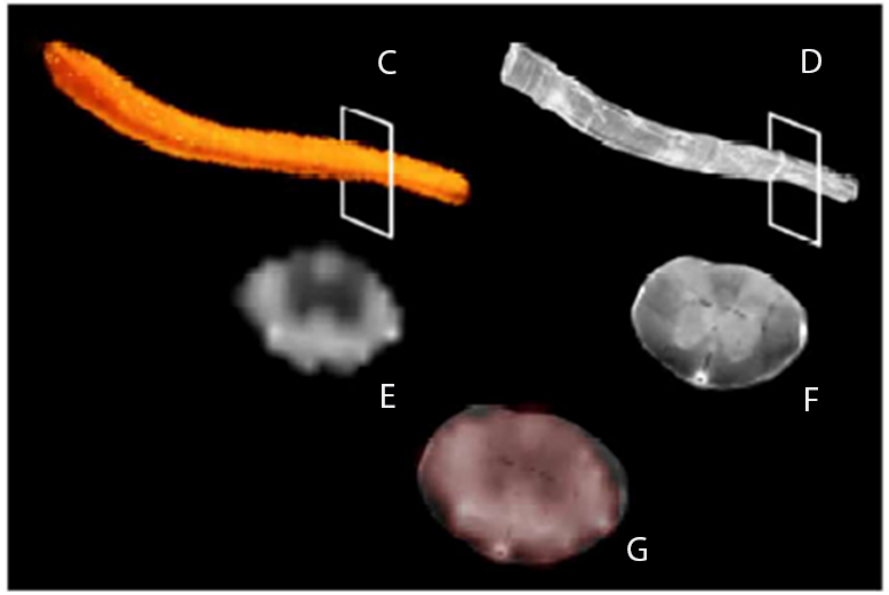
PMID: 32116518

Multiscale Imaging Approach for Studying the Central Nervous System: Methodology and Perspective

Michela Fratini,[1,2,*] Ali Abdollahzadeh,[3] Mauro DiNuzzo,[1] Raimo A. Salo,[3] Laura Maugeri,[1] Alessia Cedola,[2] Federico Giove,[1,4] Olli Gröhn,[3] Jussi Tohka,[3] and Alejandra Sierra[3]

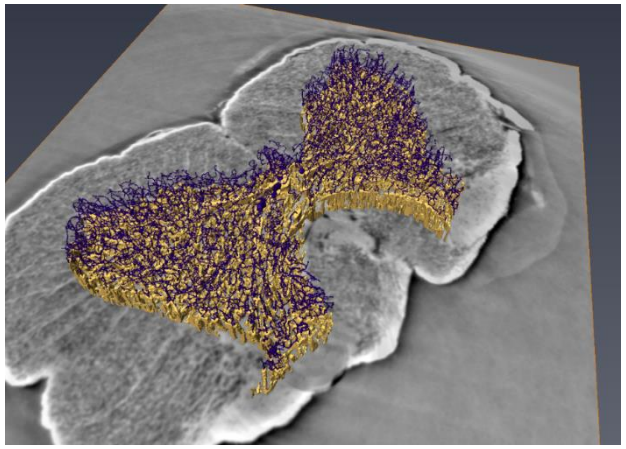
1. Native resolution images





2. Masking and downsampling

3. Segmentation processes to improve information



MRI combined with XPCT for the study of mouse/rat brain

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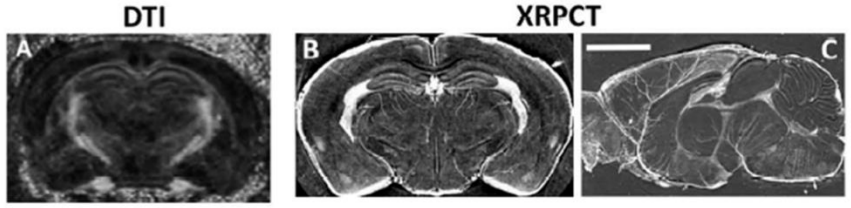
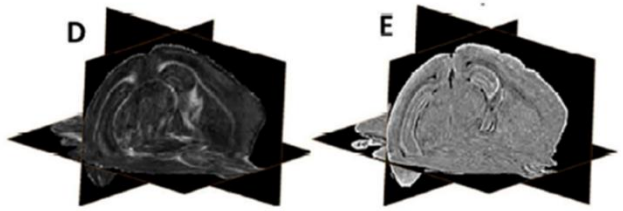
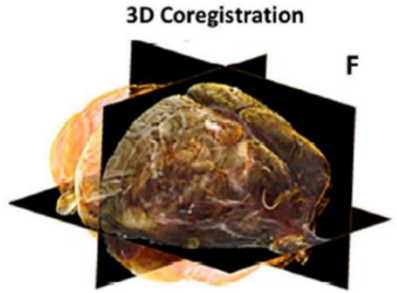
C57BL/6J healthy mouse brain







1. Native resolution images

2. Downsampling of XPCT images (for better comparison with dMRI)
Masking of DTI and XPCT images (using FSL and Matlab routine).

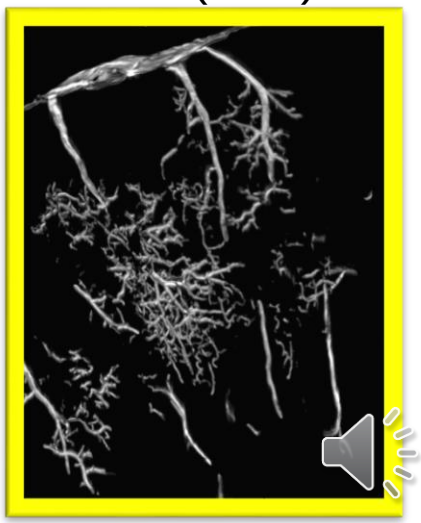
3. 3D Co-registration
XRPCT images masked and dilated have been finally co-registered to Fractional Anisotropy map (obtained from DTI) by means of ANT's software. More fine co-registration has been obtained by means of a non linear registration (SYn)

Traumatic brain injury rat brain

- Highest size
- Model for neuropathologies (i.e. epilepsy)

XPCT

More care for segmentation.
Application of ad hoc filters for vasculature (S3D)



Conclusion

- **Possibility to obtain more specificity especially useful when we are interested in vascular and neuronal damage (occurring in CNS neuropathologies)**
- **Improving co-registration methods allows to increase the resolution of standard imaging techniques (MRI) and to increase the information level of standard 2D techniques**

Acknowledgments

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