PHASE CONTRAST MICRO-IMAGING IN NEUROSCIENCE

An initial perspective toward application in neurology research and clinical diagnostics

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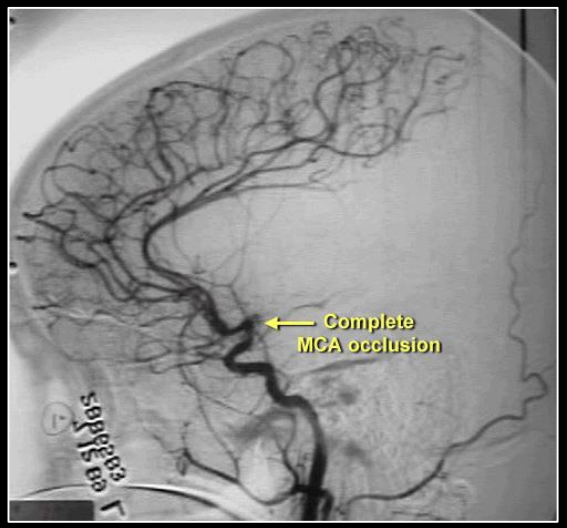
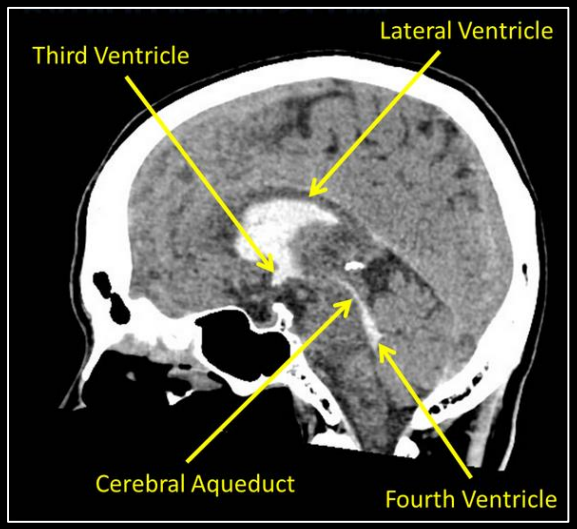
ICTR-PHE 2016 - Geneva

NEUROIMAGING TODAY IN CLINICAL PRACTICE



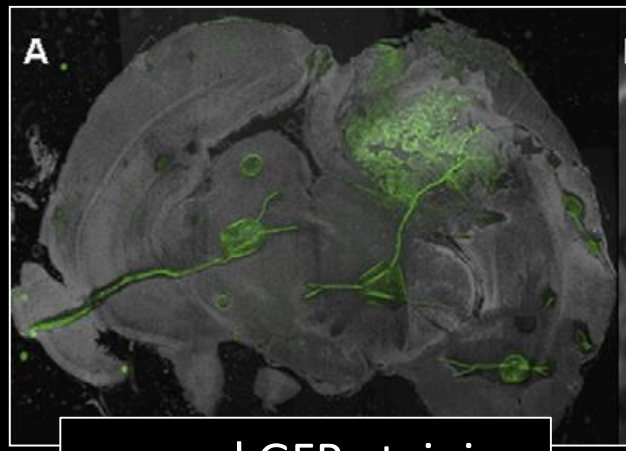
Cerebral angiography

T1, T2 weighted MRI

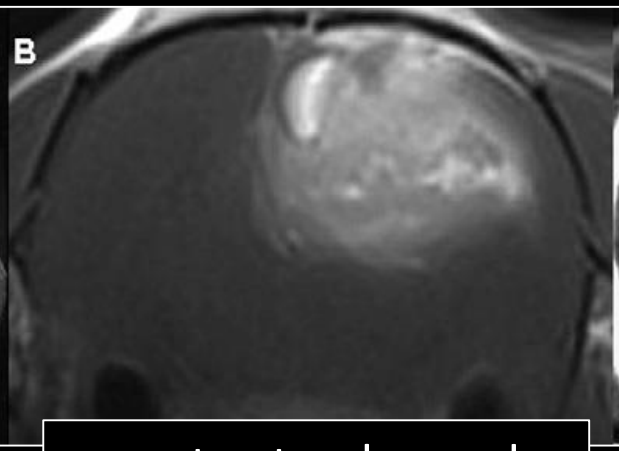


Brain CT

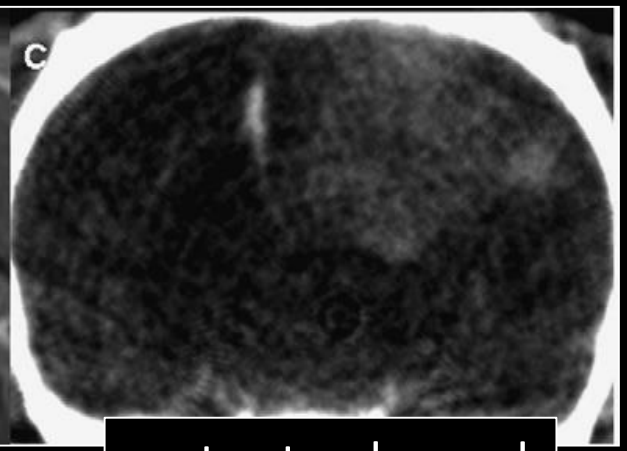
NEUROIMAGING TODAY IN PRECLINICAL RESEARCH



coronal GFP-staining



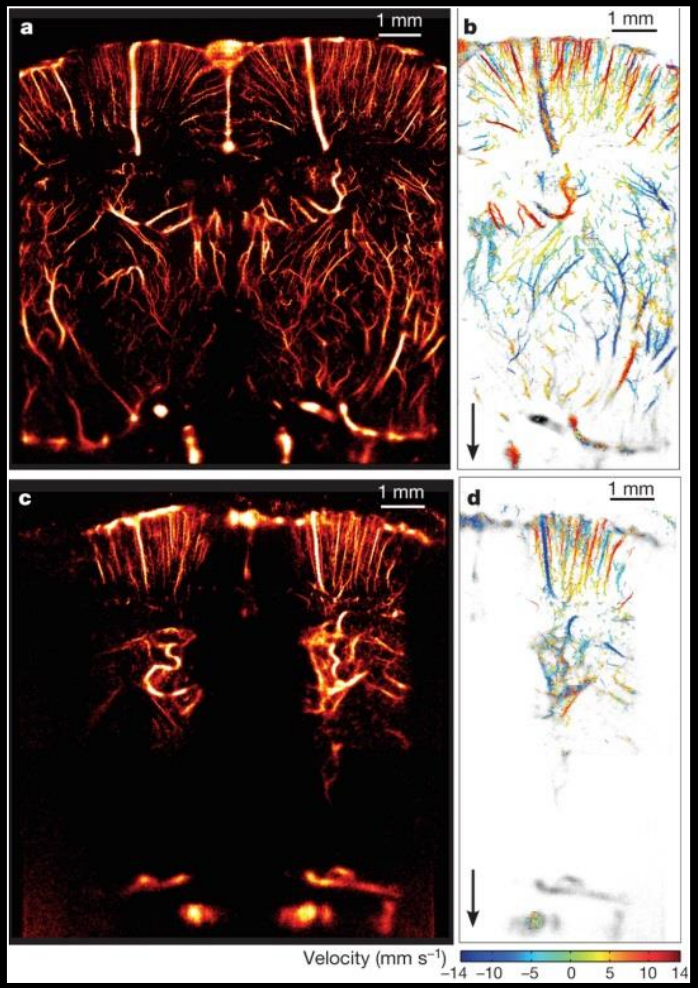
contrast-enhanced (T1,T2) (3-11 T) MRI



contrast-enhanced micro-CT

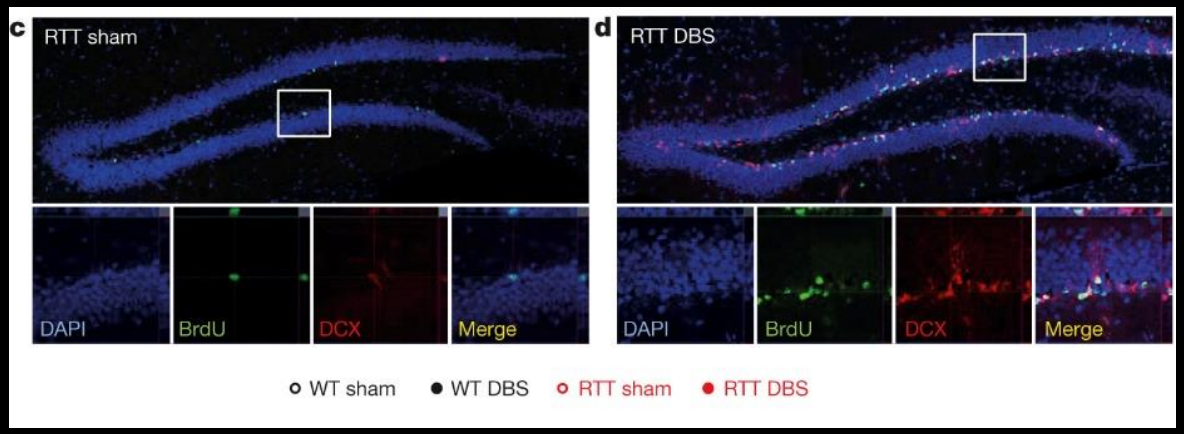
Engelhorna, Neuroscience Letters 2009

CUTTING-EDGE NEUROIMAGING



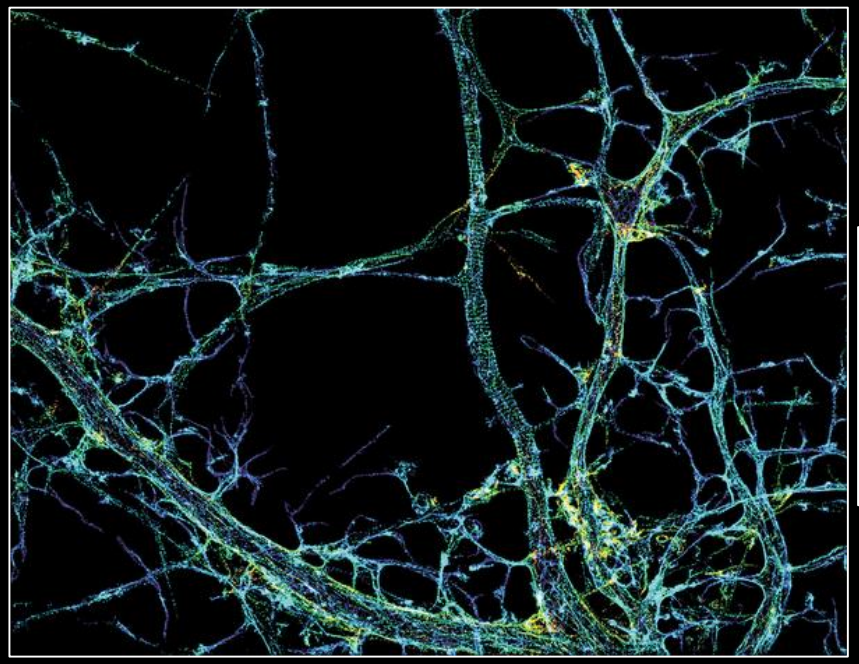
ULTRASOUND – *in vivo*

C Errico et al. Nature **527,** 499-502 (2015) doi:10.1038/nature16066



IMMUNOHISTOLOGY – *functional imaging*

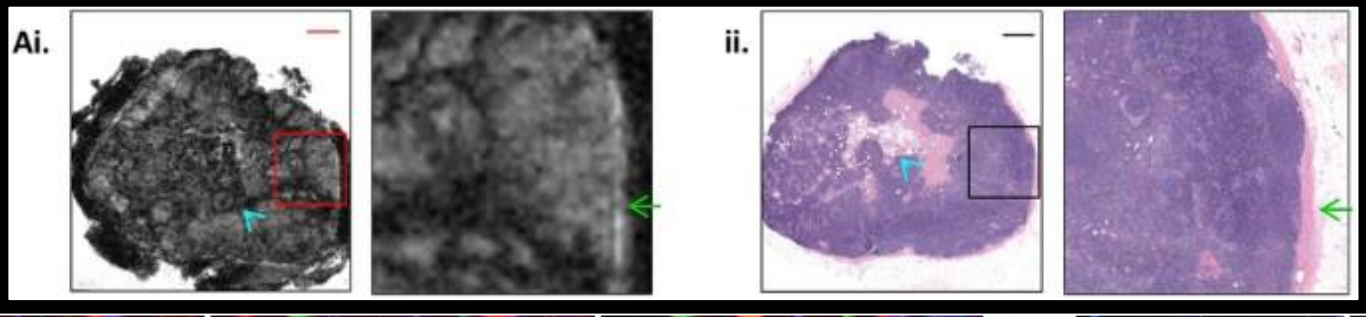
S Hao *et al. Nature* **526,** 430-434 (2015) doi:10.1038/nature15694

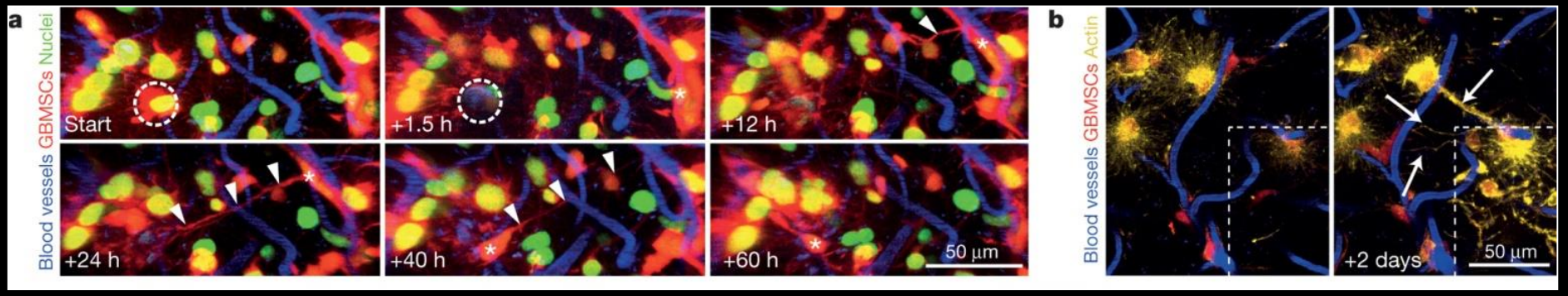


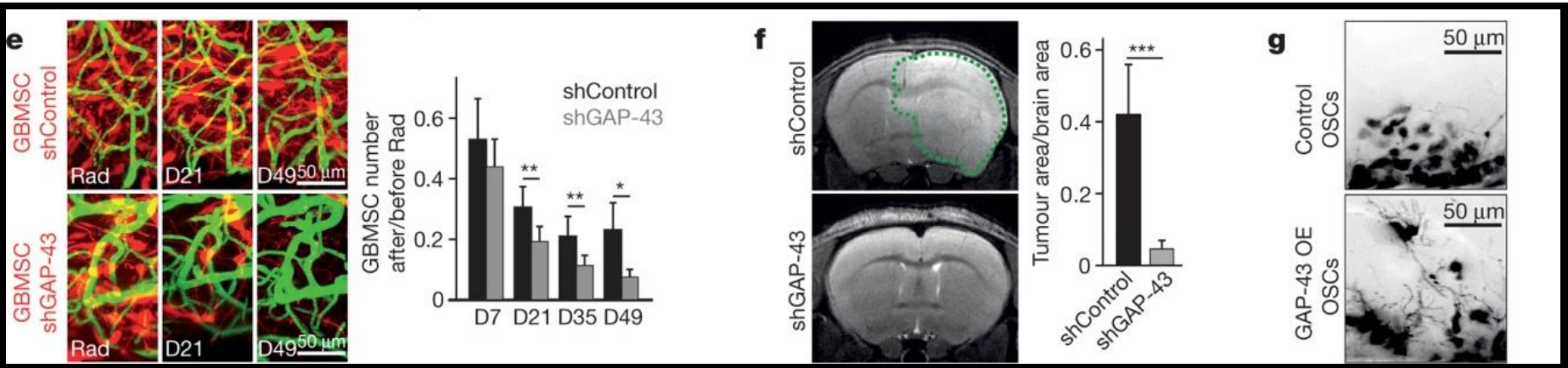
OPTICAL MICROSCOPY - *Cellular resolution*

CUTTING EDGE NEUROIMAGING

MULTISCALE MULTIMODAL IMAGING







M Osswald *et al. Nature* 1-6 (2015) doi:10.1038/nature16071

THE DREAM In CLINICAL Neuroimaging

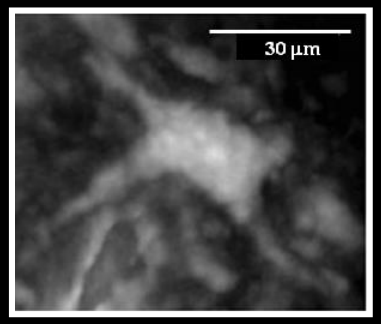
‘SINGLE SHOT’ PROCEDURE:

SENSITIVE

HARD and SOFT TISSUE CONTRAST

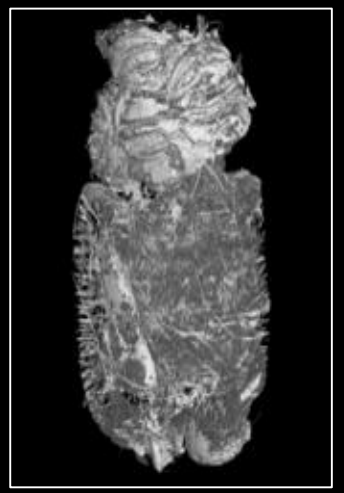
HIGH- RESOLUTION

3D detailed visualization of Neuronal Network + Vascular Network



MULTI- SCALE

Cellular to Full-Organ Imaging ➔ nm to cm



NON-INVASIVE

NO CONTRAST AGENT – LOW DOSE – IN-VIVO

AVAILABLE/LOWCOST

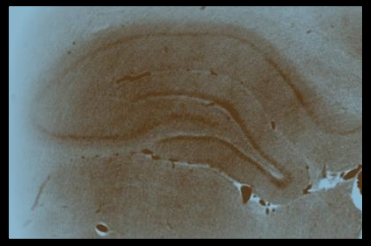

IF YOU CAN DREAM IT,
YOU CAN DO IT.
Walt Disney

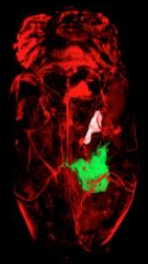
OUR PROJECT

X-RAY PHASE CONTRAST COMPUTED TOMOGRAPHY
for
NEUROIMAGING

high contrast and MICROMETER spatial resolution

visualization of anatomy – pathology – Radiotherapy effects

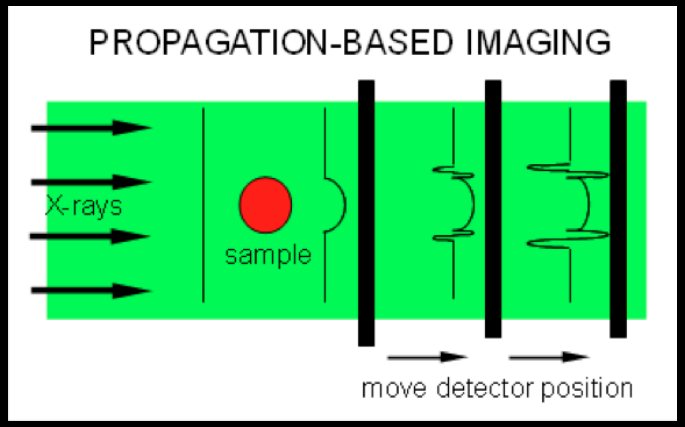




3D NERVOUS SYSTEM "VIRTUAL HISTOLOGY"

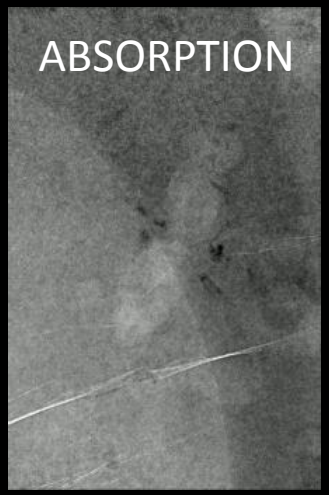
X-RAY PHASE CONTRAST COMPUTED TOMOGRAPHY

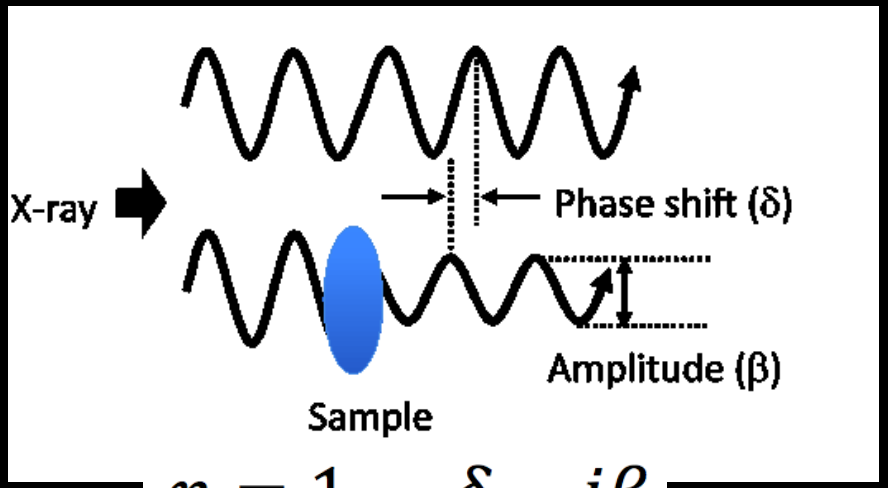
With an appropriate setup and light - source:



ESRF

Phase contrast is up to 3 orders of magnitude higher than absorption contrast!





$$n = 1 - \delta - i\beta$$

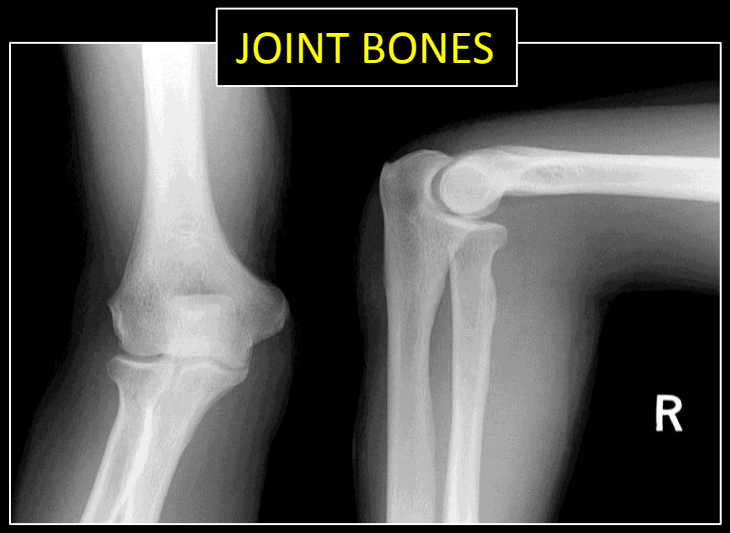
δ >> β

P. Tafforeau, LGBPH (CNRS), ESRF and M. Lak, ESRF

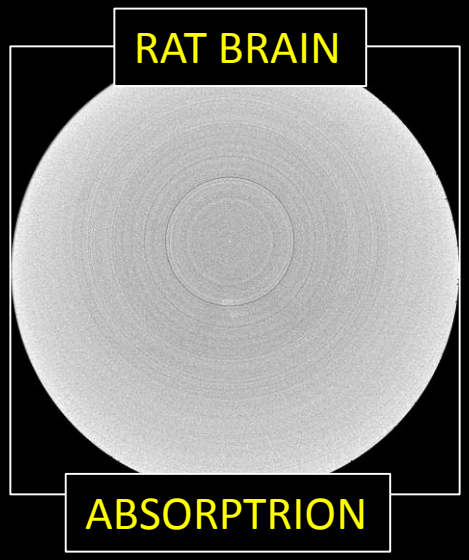
TODAY'S X-ray CLINICAL RADIOGRAPHY and CT:

Uses **absorption contrast,** which depends on the linear attenuation coefficient μ.

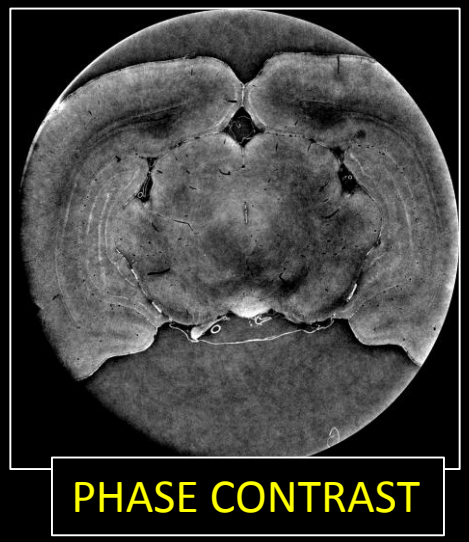
Good for High Absorption Materials



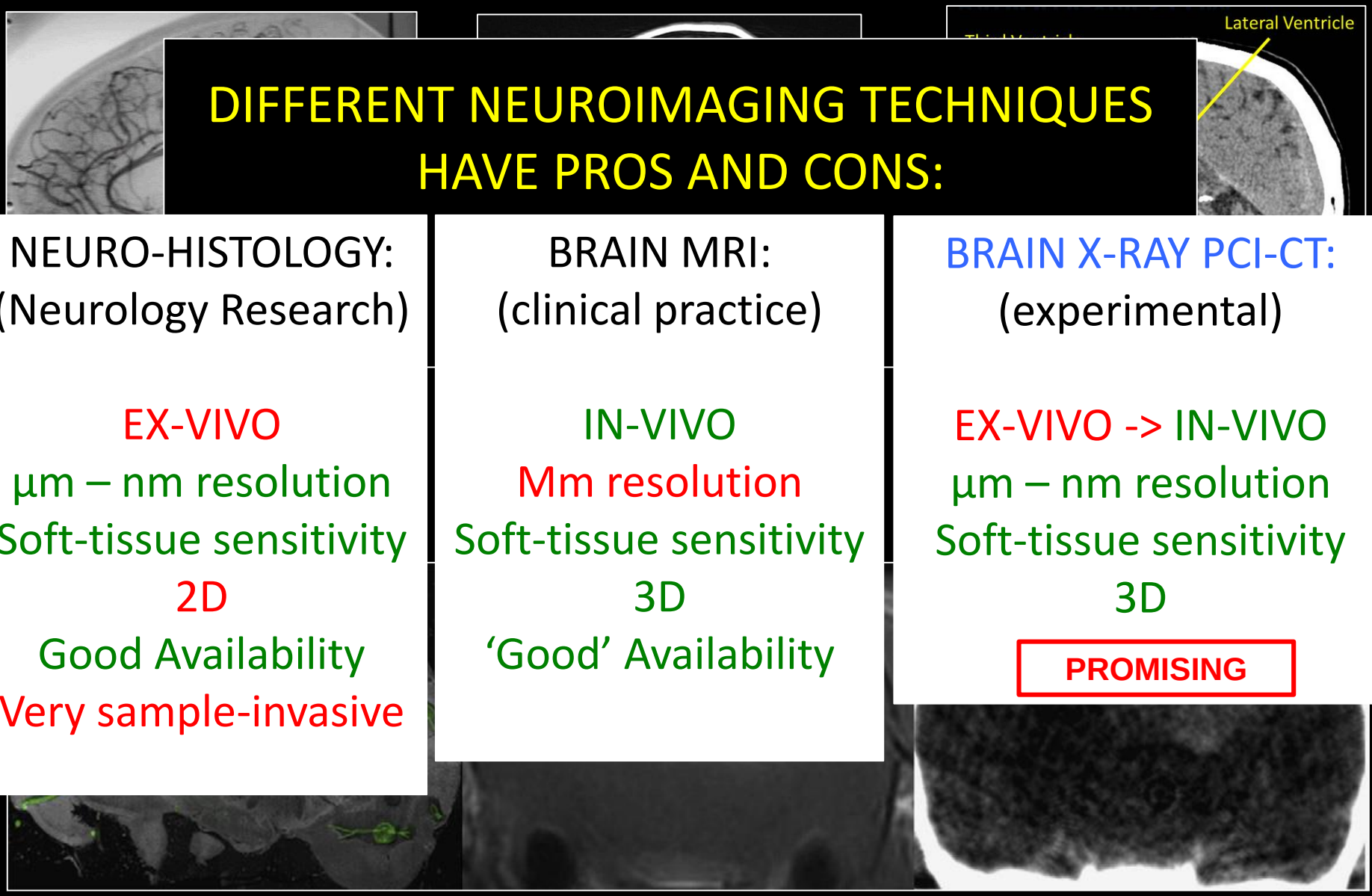
NOT so good for Low-Absorption Materials



Can Phase Contrast Imaging play an important role in NEUROSCIENCE?



DIFFERENT NEUROIMAGING TECHNIQUES HAVE PROS AND CONS:



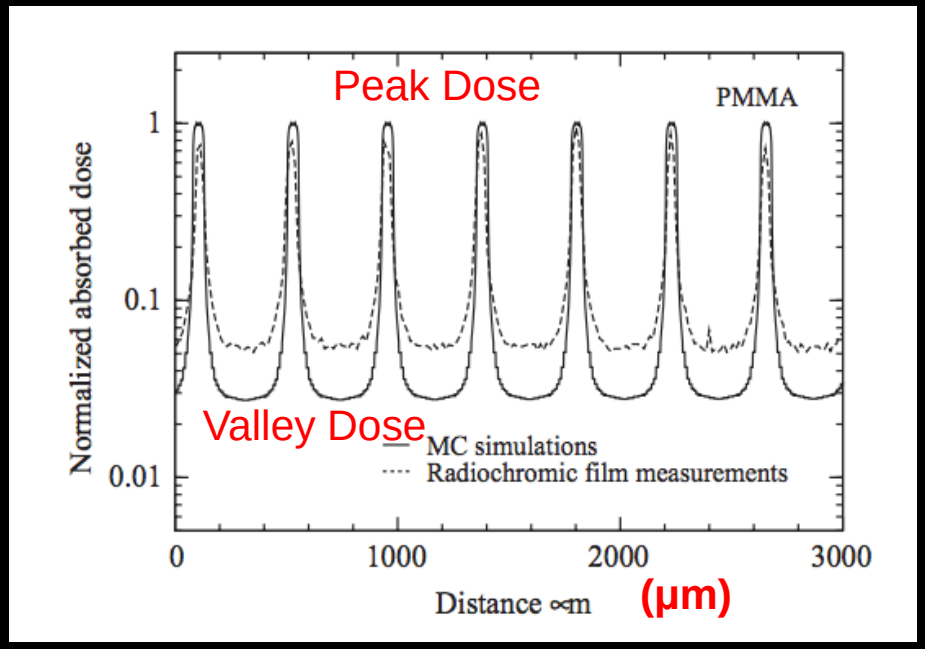
NEURO-HISTOLOGY: (Neurology Research)	BRAIN MRI: (clinical practice)	BRAIN X-RAY PCI-CT: (experimental)
EX-VIVO	IN-VIVO	EX-VIVO -> IN-VIVO
µm – nm resolution	Mm resolution	µm – nm resolution
Soft-tissue sensitivity	Soft-tissue sensitivity	Soft-tissue sensitivity
2D	3D	3D
Good Availability	‘Good’ Availability	**PROMISING**
Very sample-invasive		

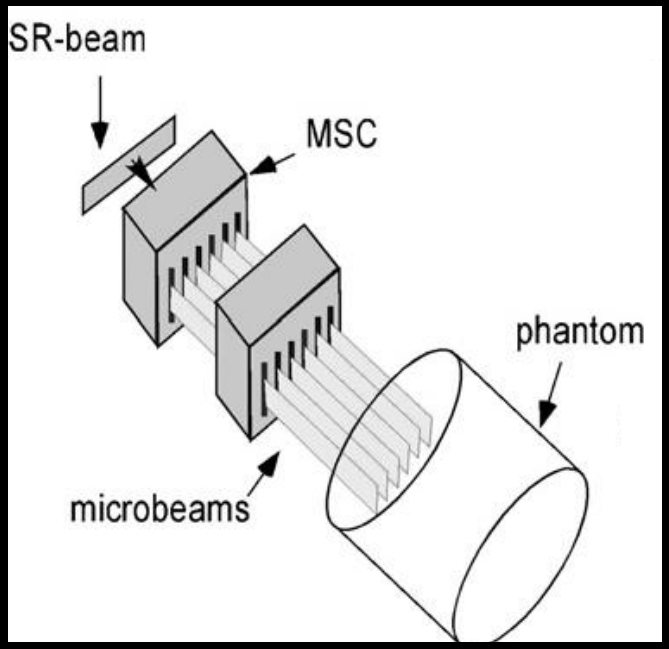
CASE STUDY

MICROBEAM RADIATION THERAPY

An Experimental X-ray radiation therapy technique

1. Arrays of highly collimated quasi-parallel micrometer-thick microbeams
2. Peaks: 25-75 microns; Valleys: 100-400 microns
3. High Peak Doses (>100 Gy); Valley Doses below radiation tissue tolerance levels

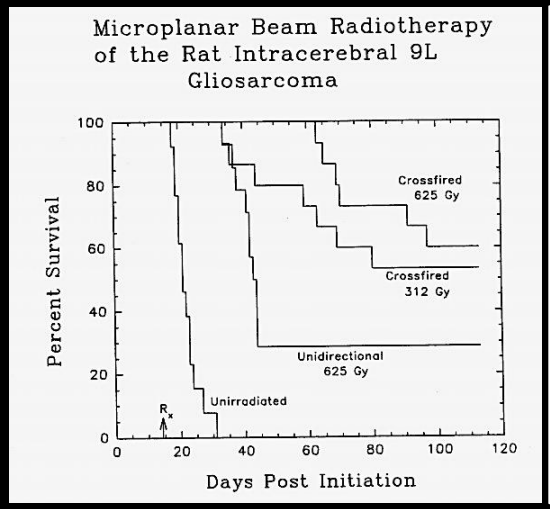


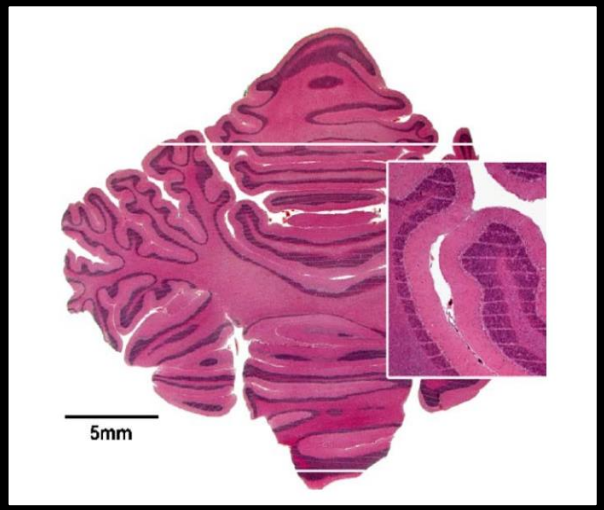


MICROBEAM RADIATION THERAPY (MRT)

1. MOTIVATION BEHIND MRT: the DOSE-VOLUME effect

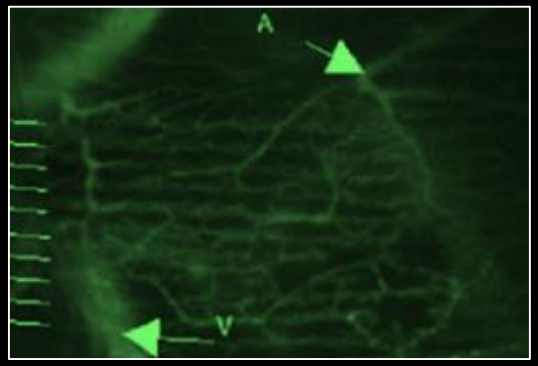
→ **Healthy tissues**: microbeams @ very high doses (> 200 Gy) are very well tolerated
→ **Tumoral tissues**: more fragile and unable to effectively repair the damage

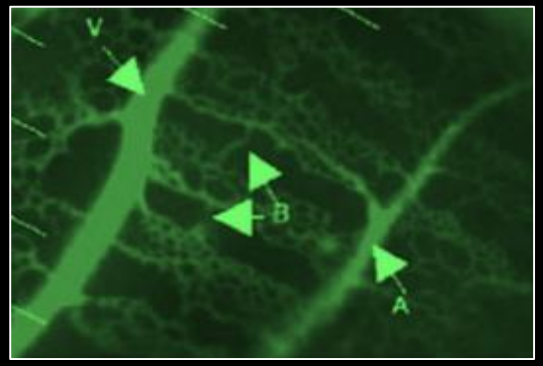




Laissue et al, 2001

2. MRT's success: the difference in the radioresistance of healthy vs. tumoral blood-vessels





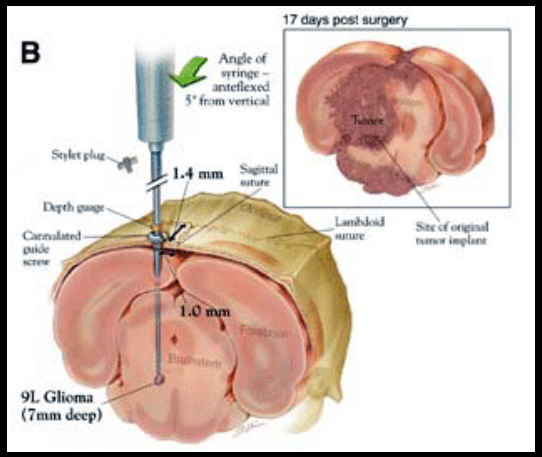
Blattmann et al., 2005

3. MRT is currently undergoing Pet Trials at ID17 as preparation for clinical trials

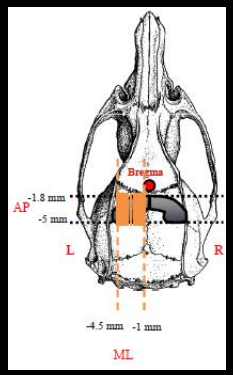
EXPERIMENT DESIGN

Rat-Model Samples:
- with/without TUMOR

1. TUMOR IMPLANTATION + GROWTH



2. MRT TREATMENT



Microbeams parameters:

a. Parallel micro-beams size = 75 μm
b. Center-to-Center distance = 400 μm
c. peak dose = 600 Gy

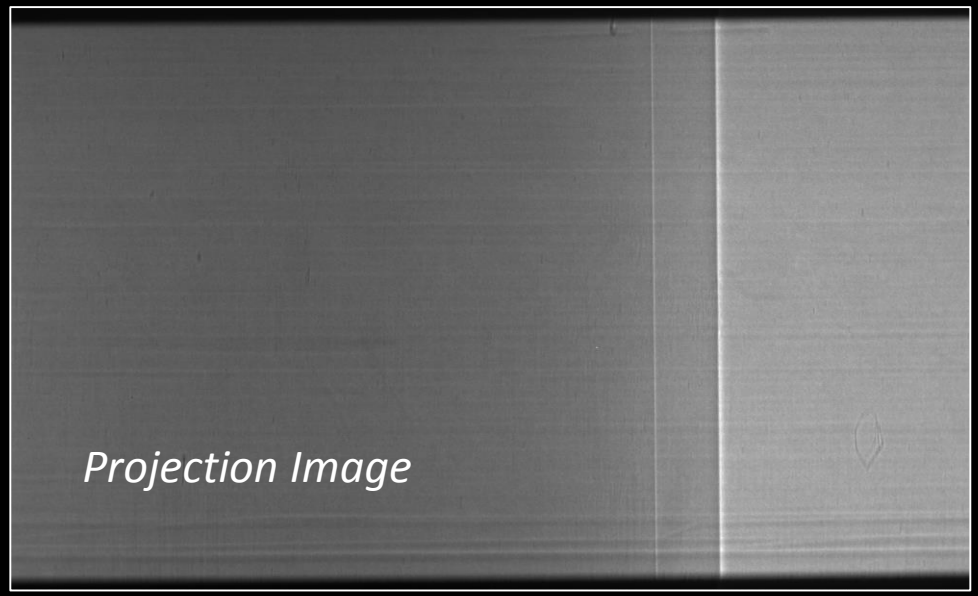
3. BRAIN EXTRACTION

(treatment + 1.5 months)

in formalin

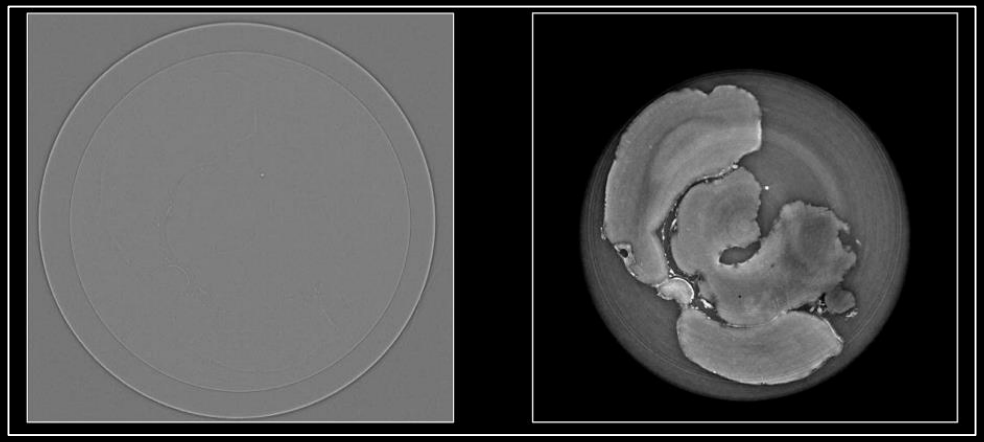
4. PBI IMAGING EXPERIMENT

(30 keV - 8 MICRON RESOLUTION - 11m sample-to-detector distance)



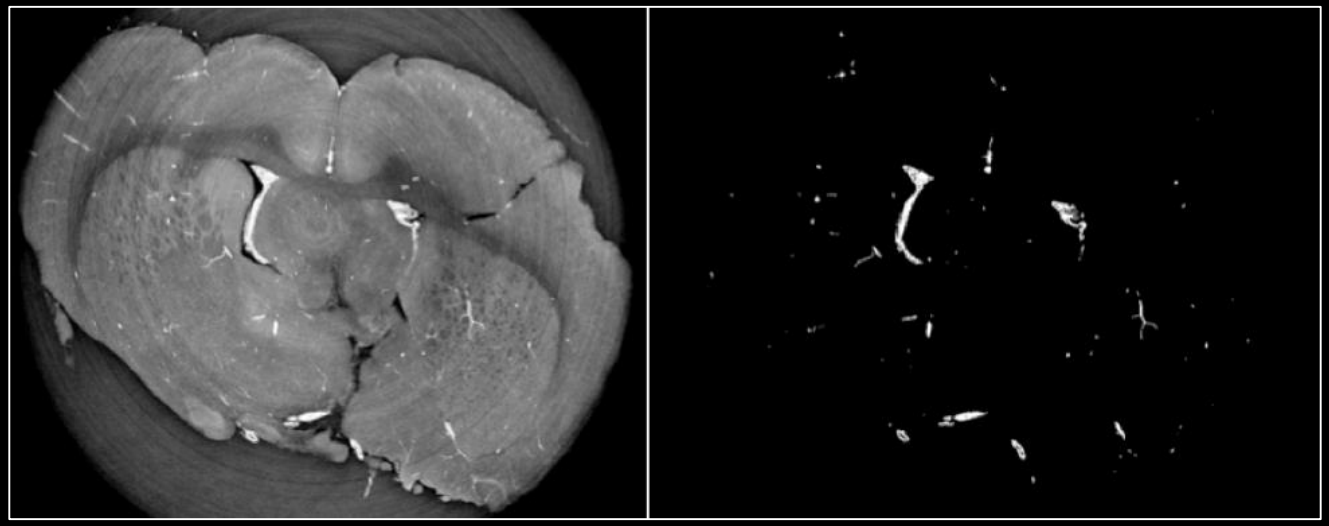
DATA ANALYSIS

1. CT Reconstruction (FBP or iterative) + PAGANIN Phase Retrieval



NO PAGANIN FILTER WITH PAGANIN FILTER

2. Segmentation of features by Region Growing or Thresholding

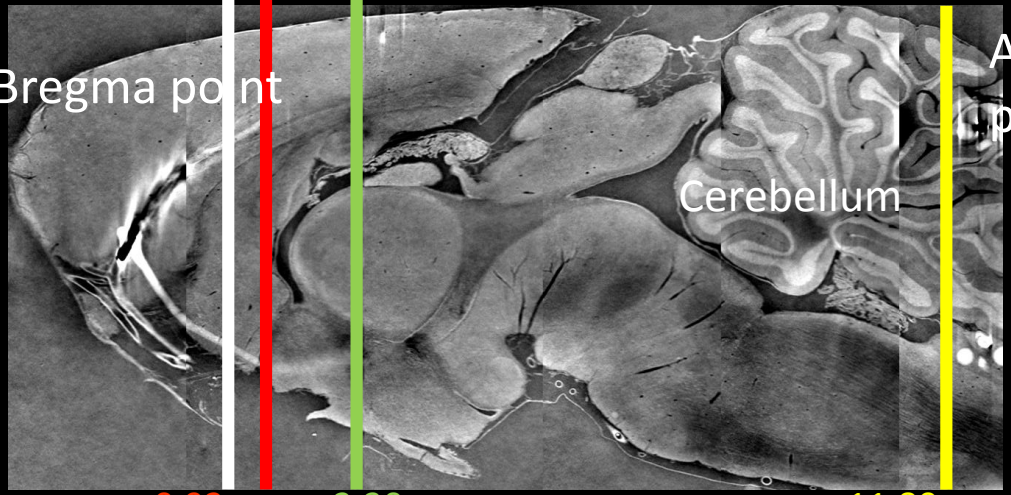


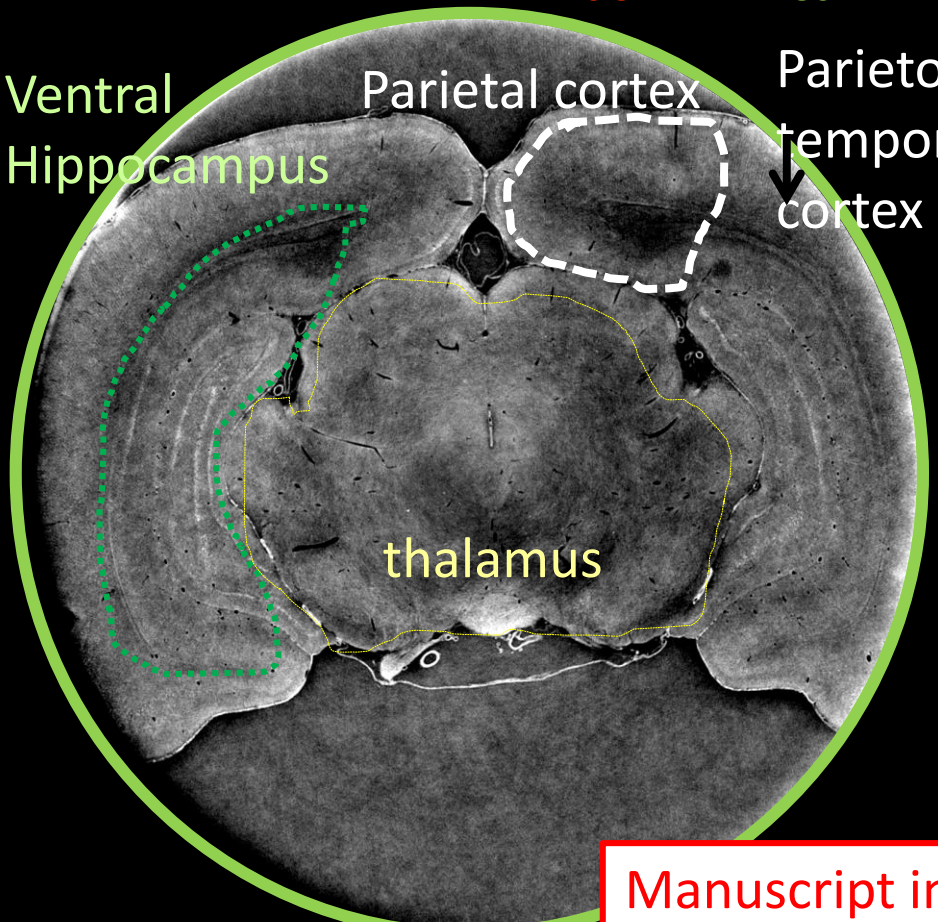
RECONSTRUCTION SEGMENTATION

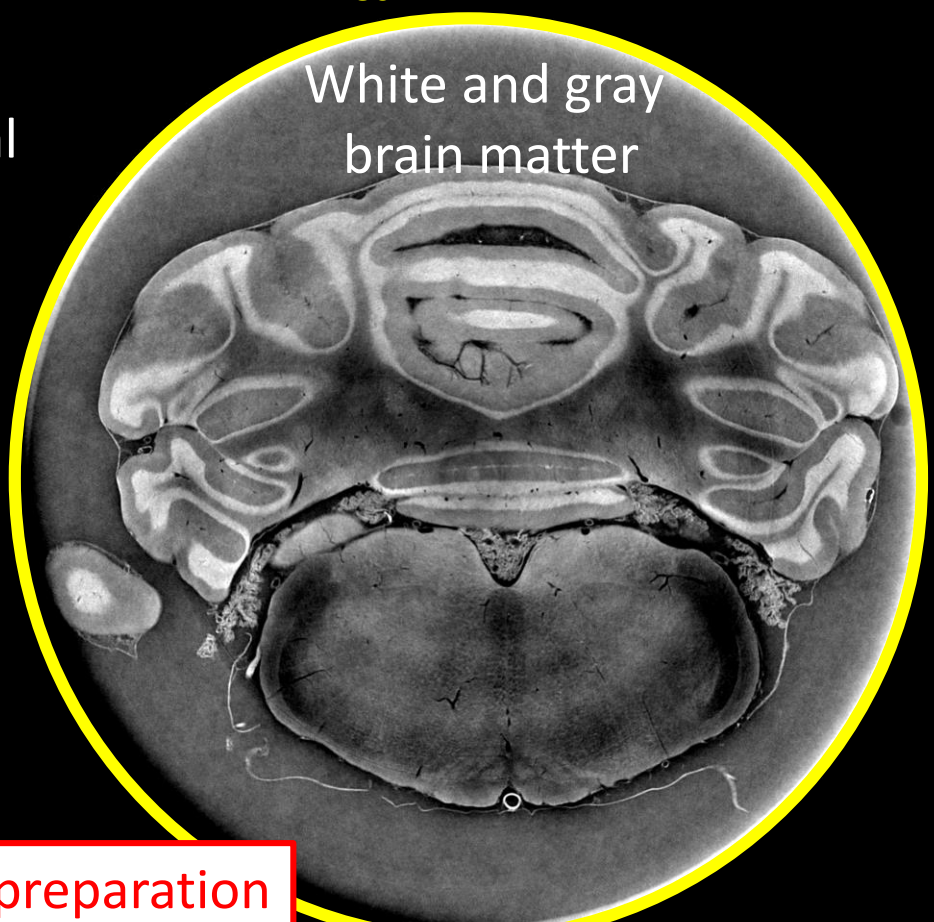
RESULTS:

Anatomy

energy = 30 keV
pxl size = 8 µm





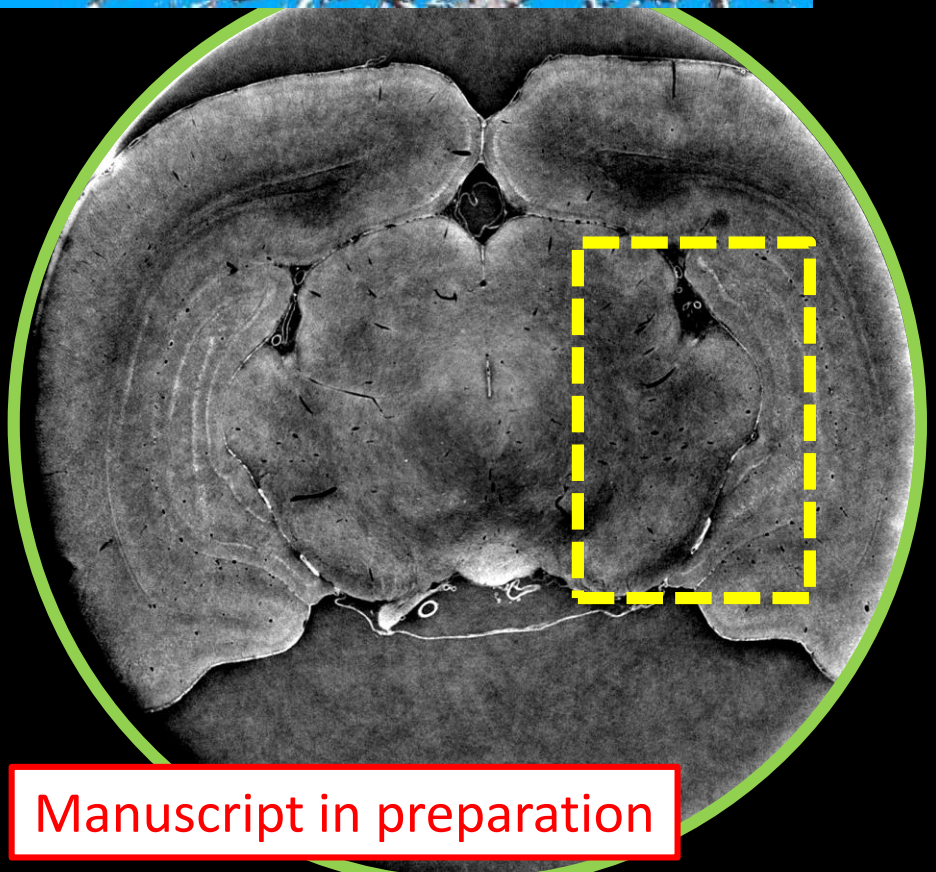


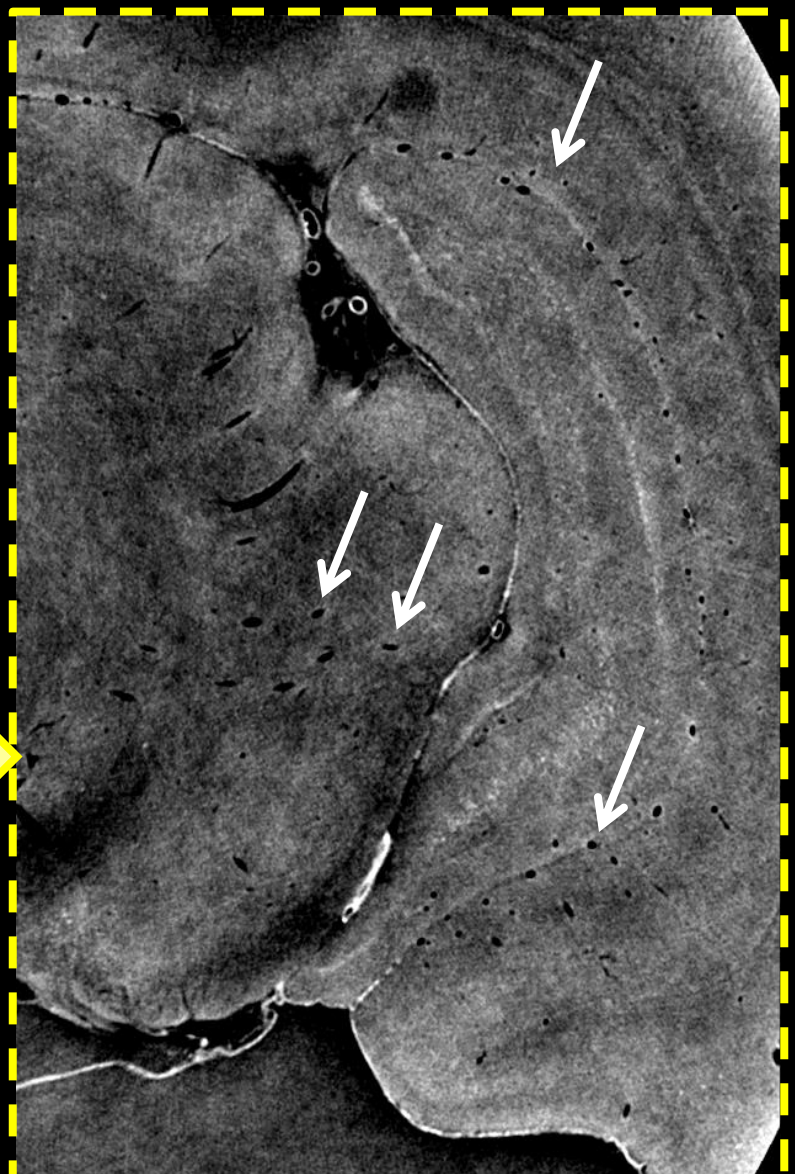
Manuscript in preparation

RESULTS: VESSEL NETWORK SEGMENTATIONS

Segmentation of the vascularization

WITHOUT ANY CONTRAST AGENT





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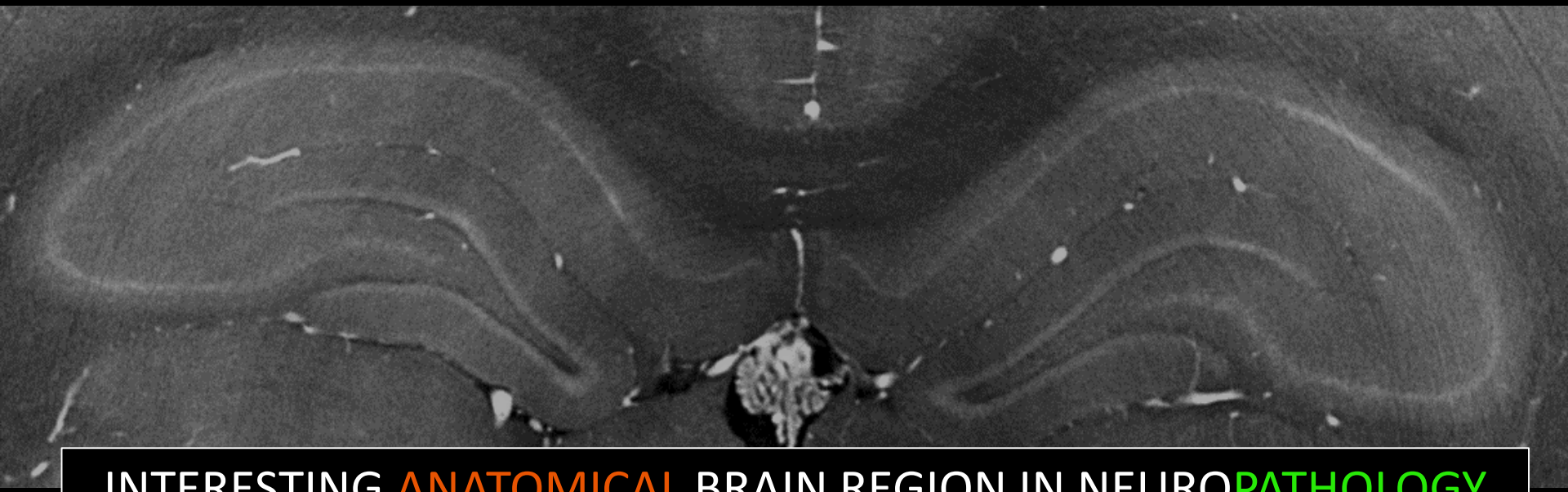
CASE STUDY: THE HIPPOCAMPUS



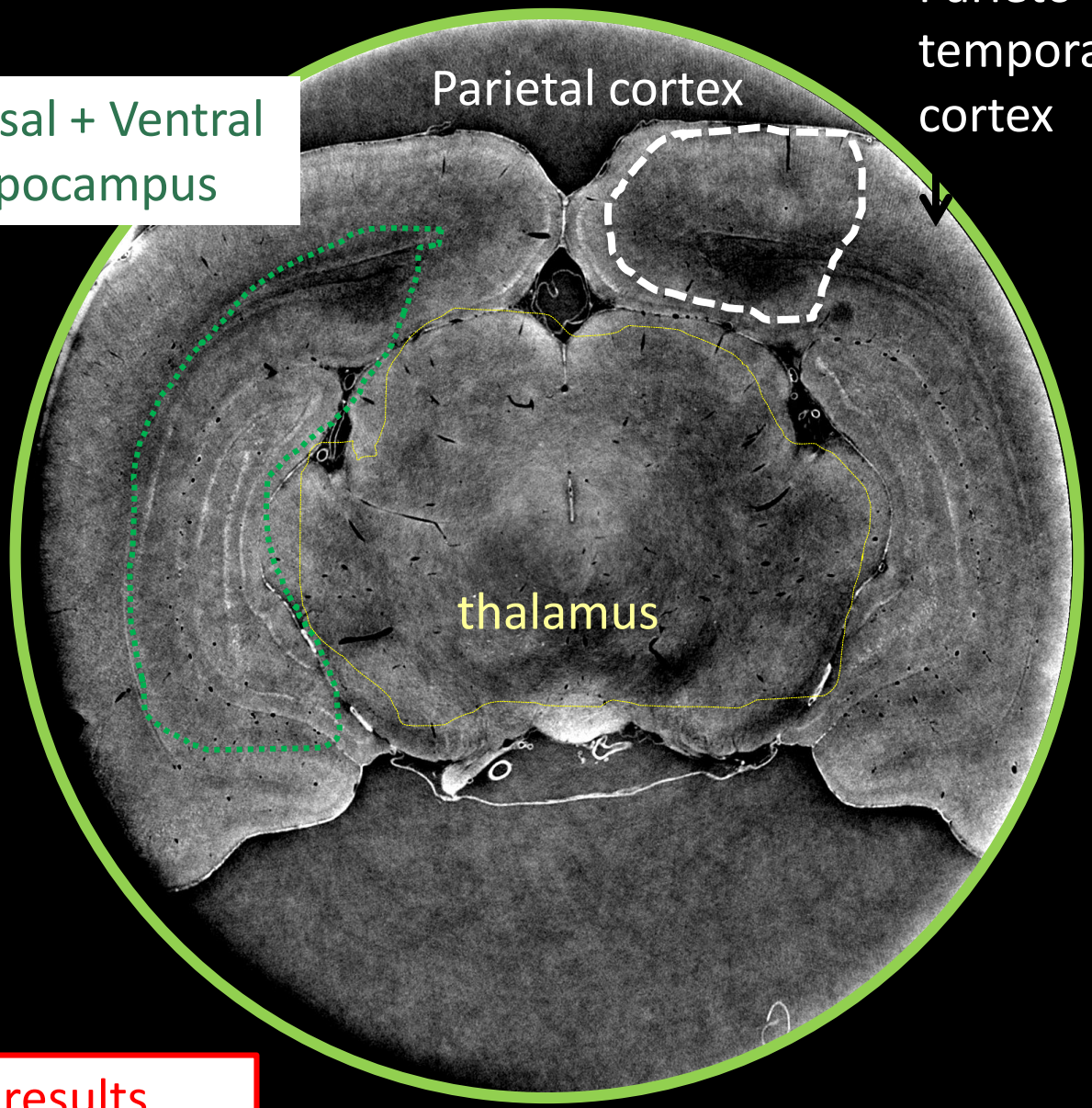
INTERESTING ANATOMICAL BRAIN REGION IN NEUROPATHOLOGY

-> CENTER FOR EMOTIONS, MEMORY and AUTONOMIC NERVOUS SYSTEM

-> MISFUNCTION: one of the primary CAUSES of NEURODEGENERTIVE DISEASES: ALZHEIMER'S, PARKINSON'S DISEASES …

HIGH IMPACT ON PATIENTS AND HEALTH SYSTEMS WORLDWIDE

Hippocampus



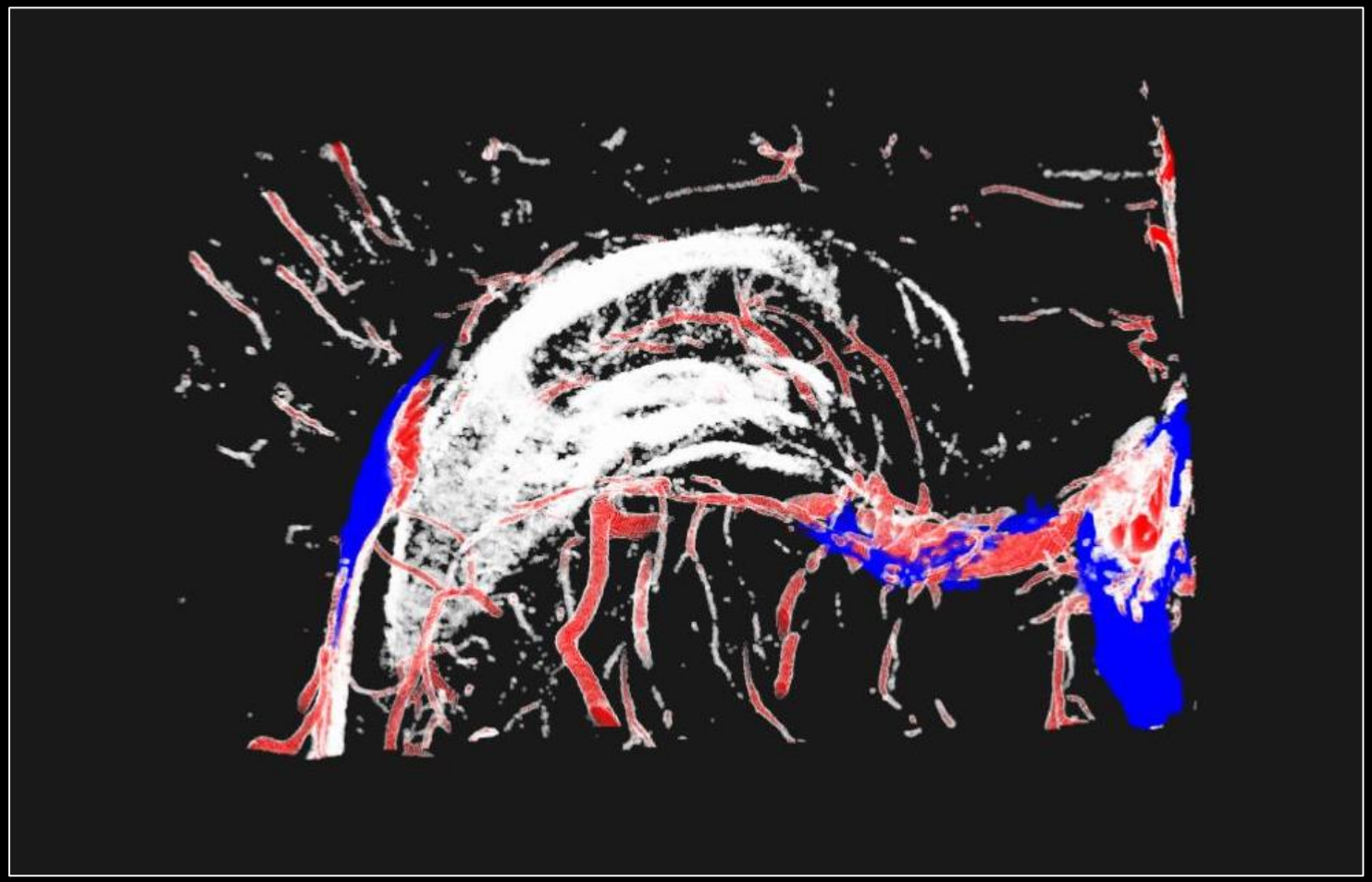
Unpublished results

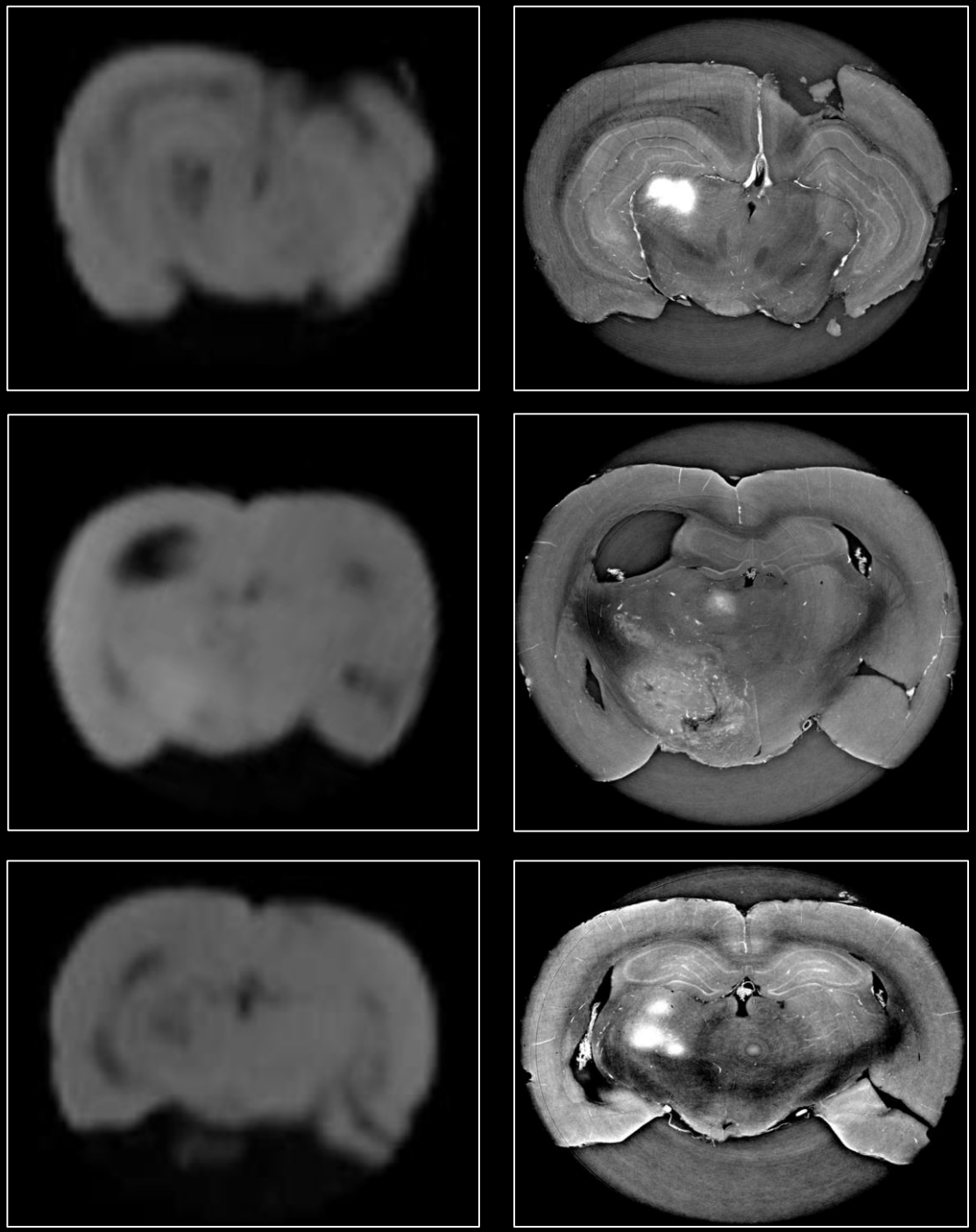
HIPPOCAMPAL VIRTUAL HISTOLOGY

DISCRIMINATE layers of the CORNU AMMONIS:
1. STRATUM ORIENS (Or)
2. STRATUM PYRAMIDALE (Py)
3. STRATUM RADIATUM(Rad)

DISCRIMINATE layers of the DENTATE GYRUS:
1. STRATUM MOLACULARE (Mol)
2. STRATUM GRANULOSUM (Gr)
3. HILUM (Hil)

HIPPOCAMPAL VIRTUAL 3D HISTOLOGY
3D VIEWING





3T Clinical MRI
@ Klinikum
Grosshadern
vs.
Synchrotron PCI

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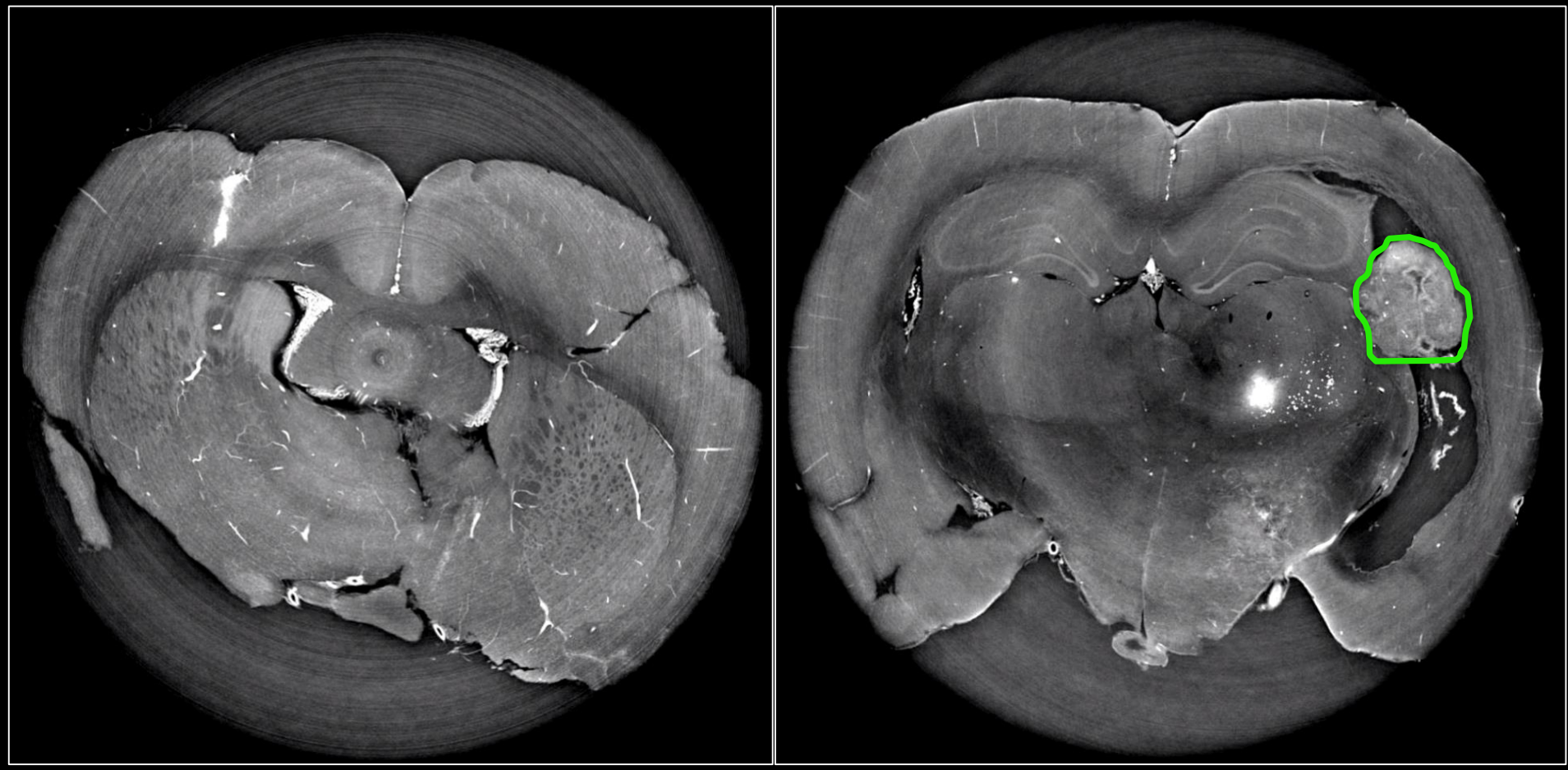
HEALTHY vs. Pathological using PCI-CT IMAGING

HIGH RESOLUTION PCI VISUALIZES A PLETHORA OF MEDICALLY-RELEVANT TISSUE AND SUB-TISSUE SAMPLE DETAILS

HEALTHY BRAIN

TUMOR BEARING BRAIN



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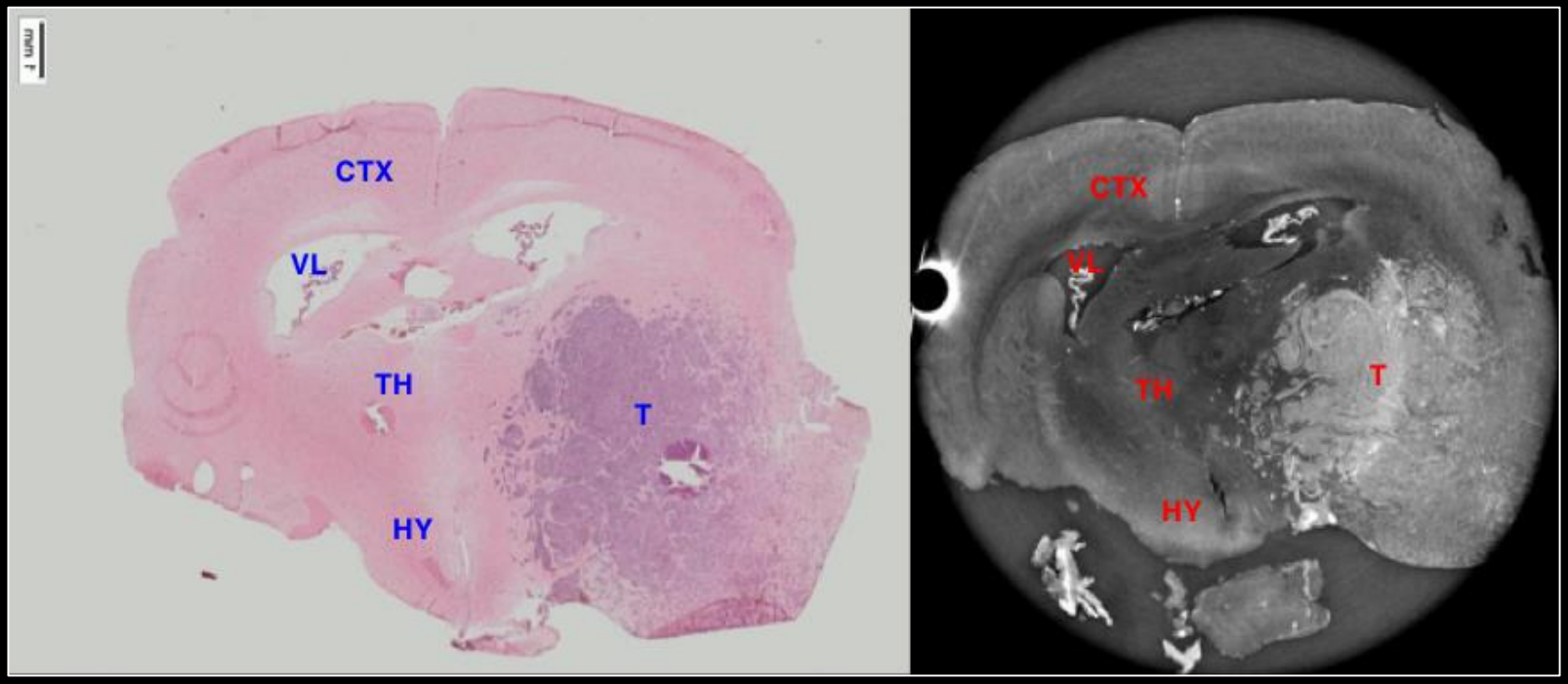
TUMOR RESULTS: COMPARISON TO HISTOLOGY

HISTOLOGY

PCI-CT



- agreement between histology and PCI data
- Support for PCI Imaging as a 3D virtual histology

CTX = cortex, VL = lateral ventricle, TH = thalamus,
HY = hypothalamus, T = tumor

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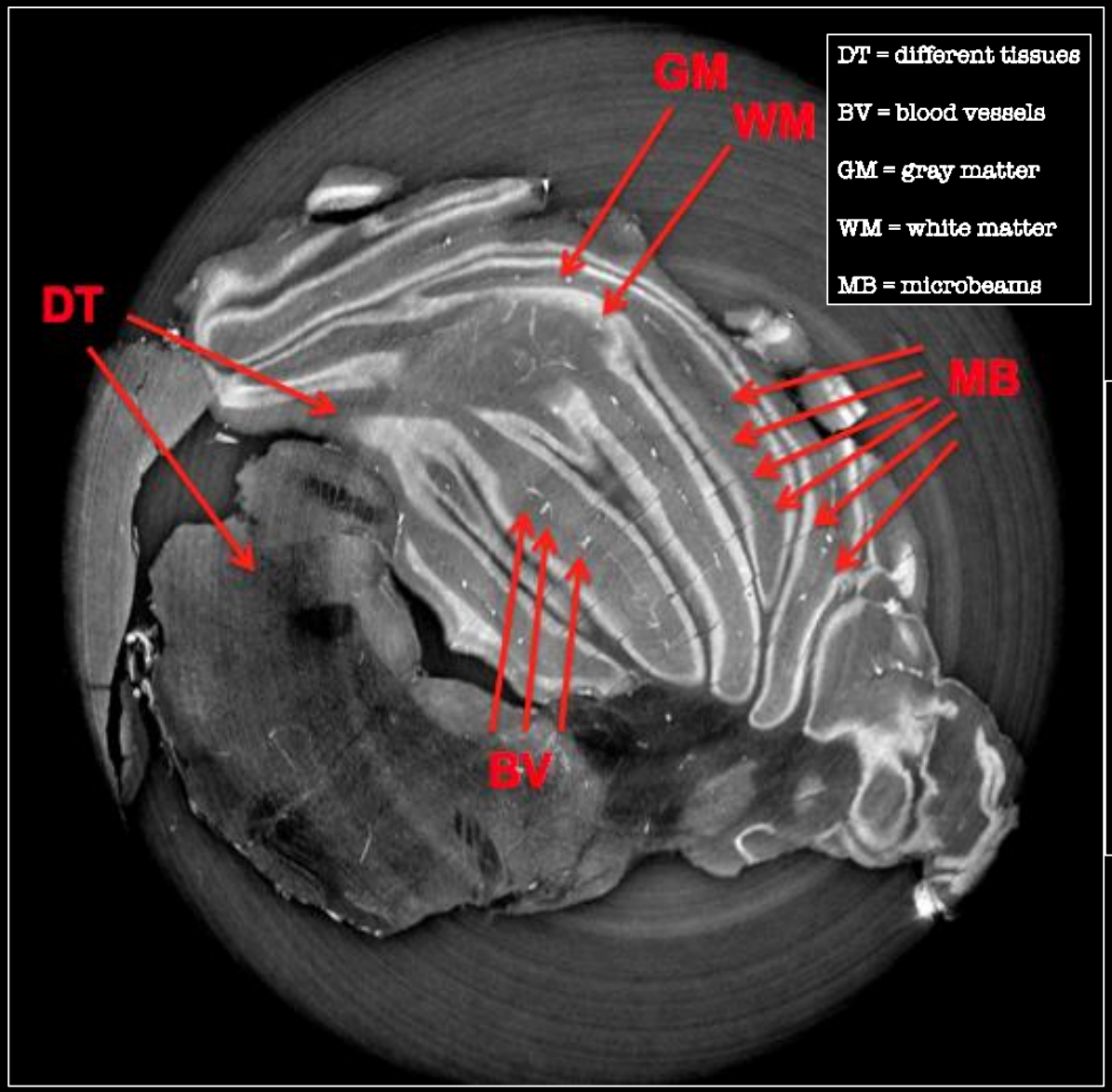
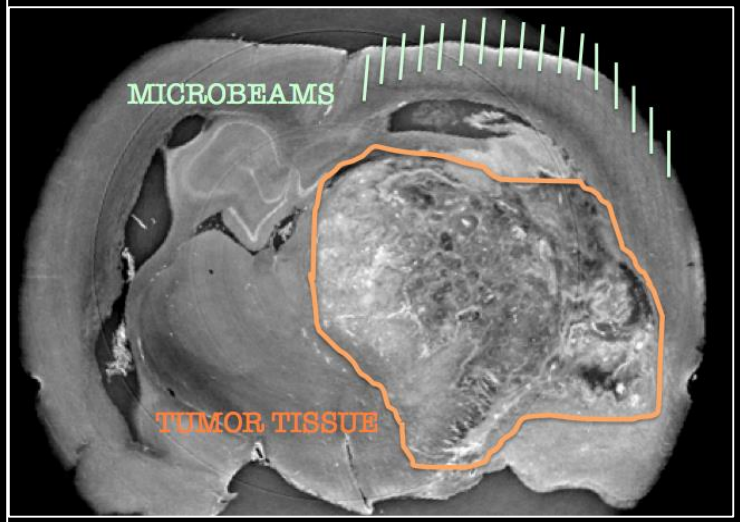
MRT IMAGING using PCI-CT IMAGING:

energy = 30 keV; pixel size = 8 µm; PBI setup at ID17 with 11m s-t-d distance



HIGH RESOLUTION PCI VISUALIZES A PLETHORA OF MEDICALLY-RELEVANT TISSUE AND SUB-TISSUE SAMPLE DETAILS



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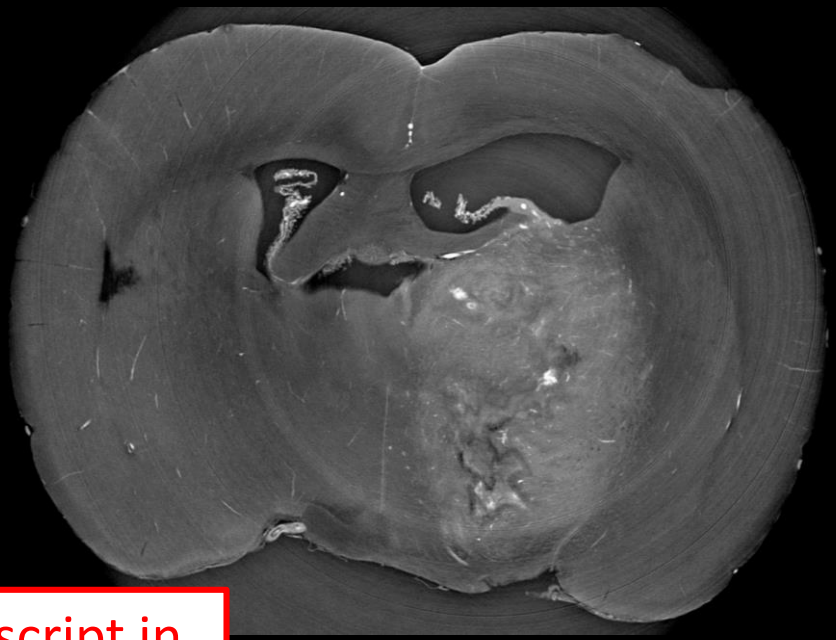
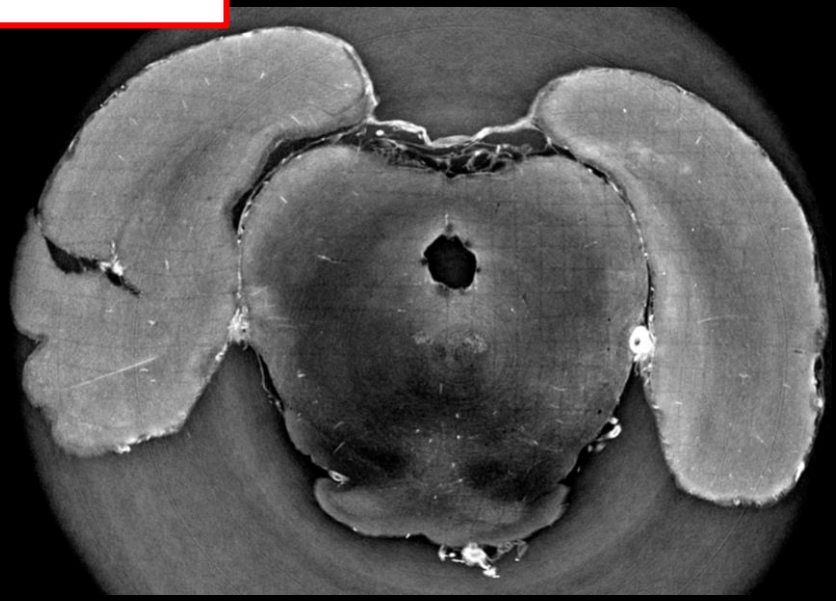
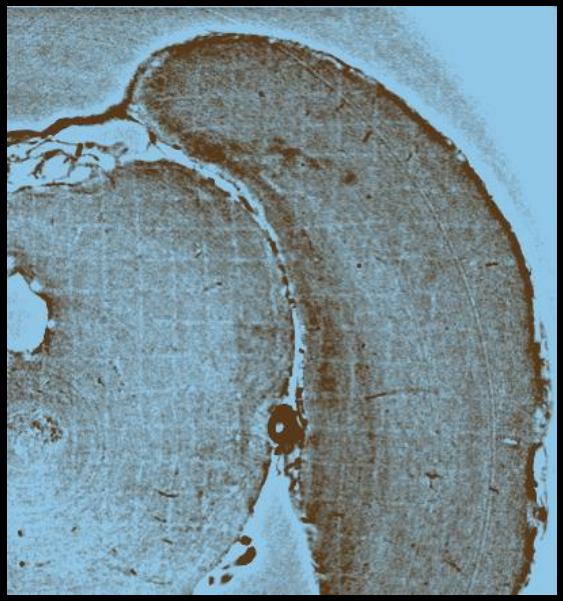
TUMOR TISSUE VIRTUAL HISTOLOGY



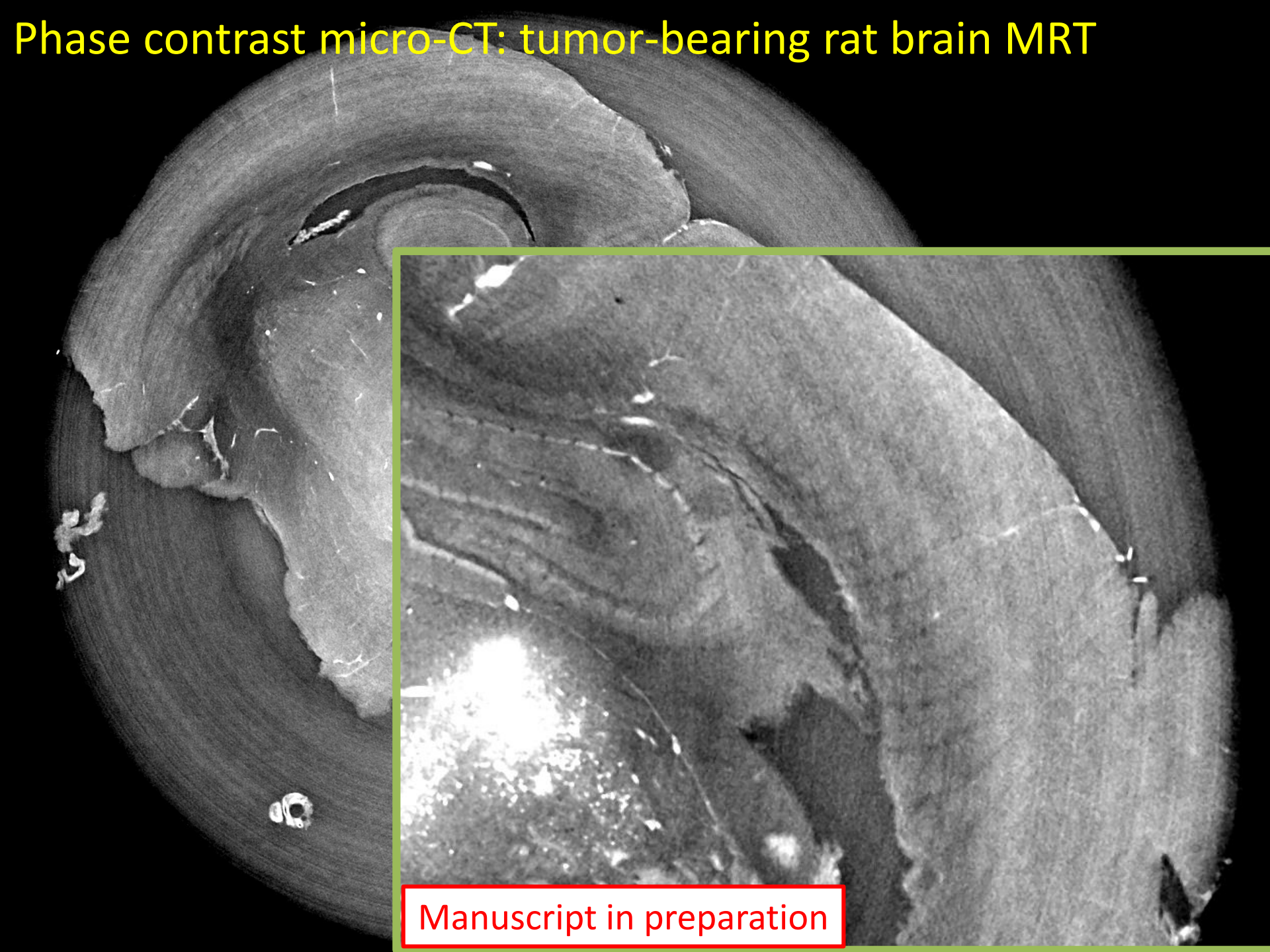
Manuscript in preparation

MRT RADIATION DAMAGE VIRTUAL HISTOLOGY





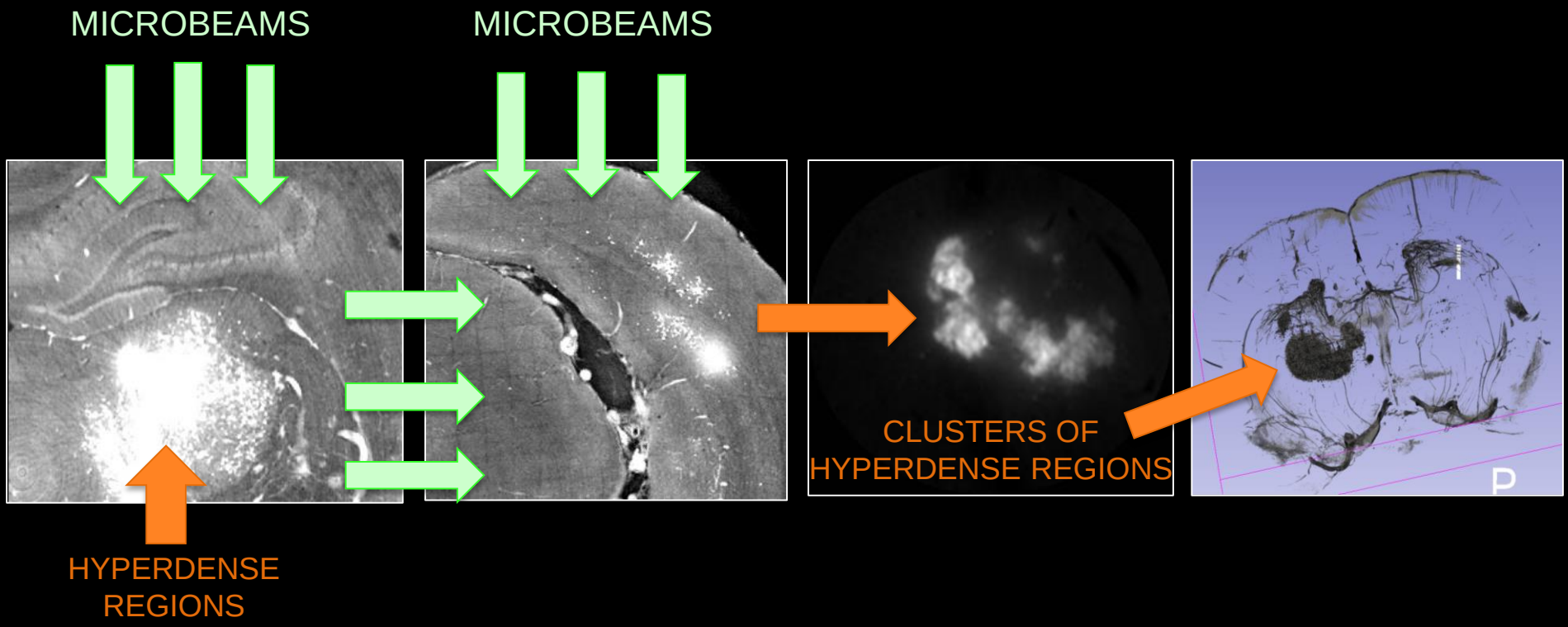
Phase contrast micro-CT: tumor-bearing rat brain MRT



RESULT SUMMARY : VISUALIZATION OF EFFECTS OF MRT

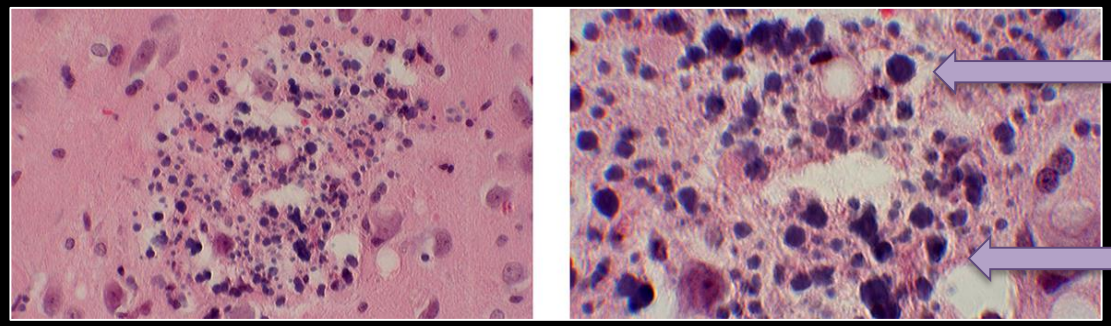
MICRO-BEAM PATHS ARE CLEARLY VISIBLE

HYPERDENSE REGIONS FORM ALONG THE BEAM PATHS



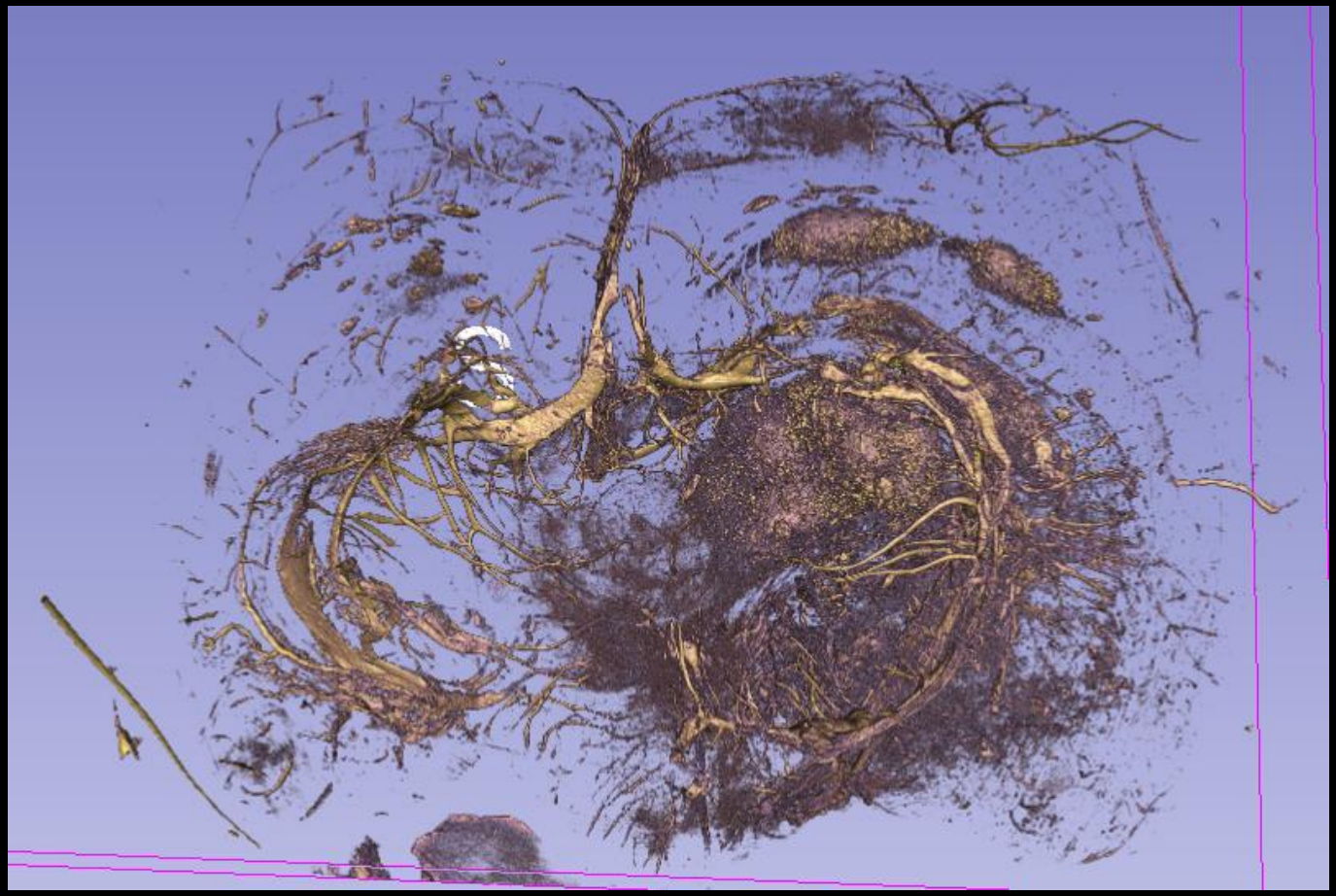
BIOCHEMICAL STUDY CONFIRMS Ca COMPOSITION OF HYPERDENSE REGIONS

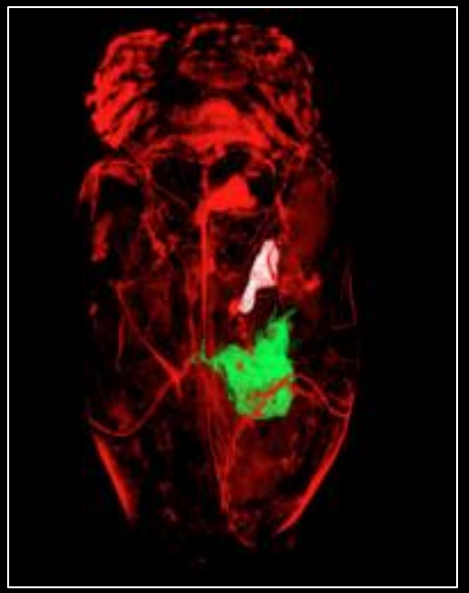
Manuscript in preparation



Phase contrast micro-CT: tumor-bearing rat brain MRT

Segmentation of the tumor, the vascular network and micro-calcifications





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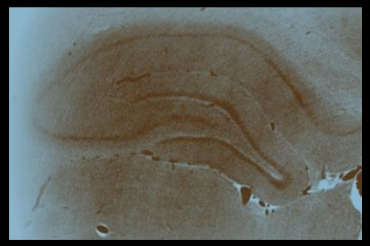
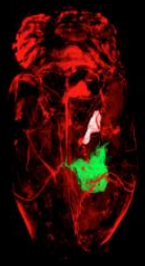
CONCLUSIONS

X-RAY PHASE CONTRAST COMPUTED TOMOGRAPHY
for
NEUROIMAGING

high contrast and MICROMETER spatial resolution visualization of
anatomy – pathology – Radiotherapy treatment effects

SYNCHROTRON RADIATION 3D "VIRTUAL HISTOLOGY"

A BIG THANK YOU to our team + collaborators

LMU (physics)
Coan
Barbone
Mittone (now ESRF)
Brun (now INSERM)

LMU (radiology)
Reiser
Kunz
Auweter
Ertl-Wagner

ESRF
Bravin
Requardt
Le Duc
Bernard
Renier

Neuromed
Battaglia

Centro Diagnostico Italiano
Romanelli

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Cavaletti

Djonov

CNR Segrate
Biella

CNR Roma
Cedola

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and THANK YOU FOR YOUR ATTENTION!!

Giacomo

EXTRA SLIDES

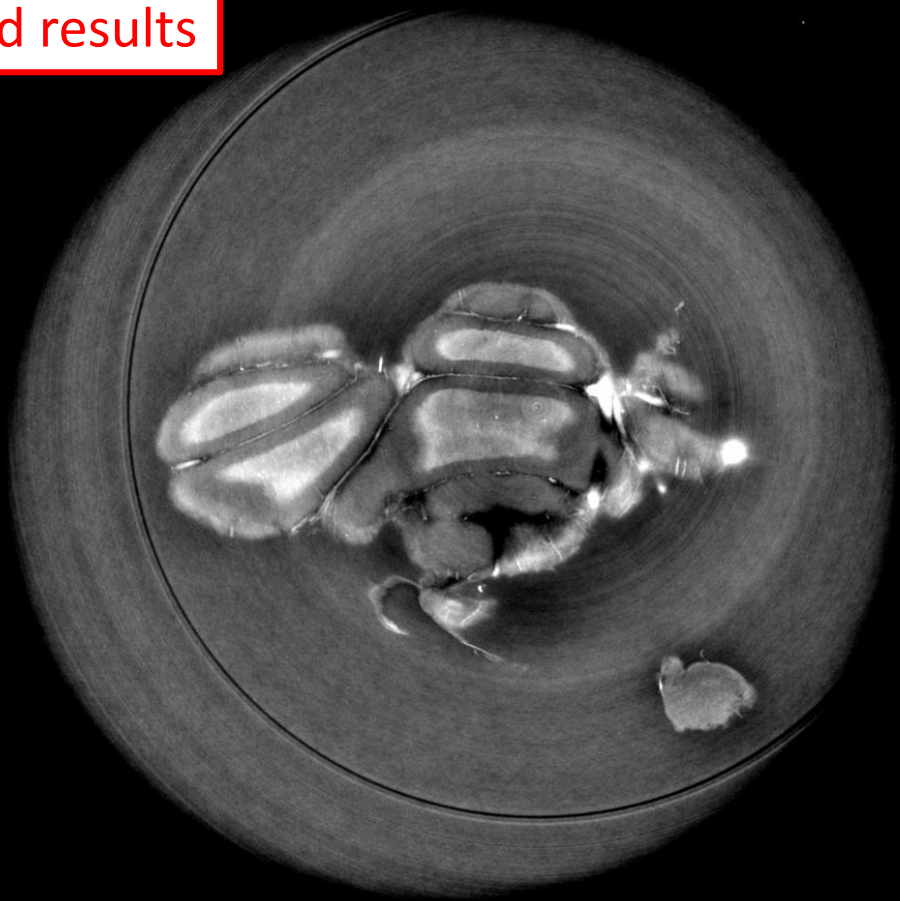
HEALTHY vs. Pathological using PCI-CT IMAGING

HIGH RESOLUTION PCI VISUALIZES A PLETHORA OF MEDICALLY-RELEVANT TISSUE AND SUB-TISSUE SAMPLE DETAILS

HEALTHY BRAIN

TUMOR BEARING BRAIN

Unpublished results



LEFT DORSAL HIPPOCAMPUS VIRTUAL 3D HISTOLOGY

EX-VIVO HUMAN SPINAL CORD PCI

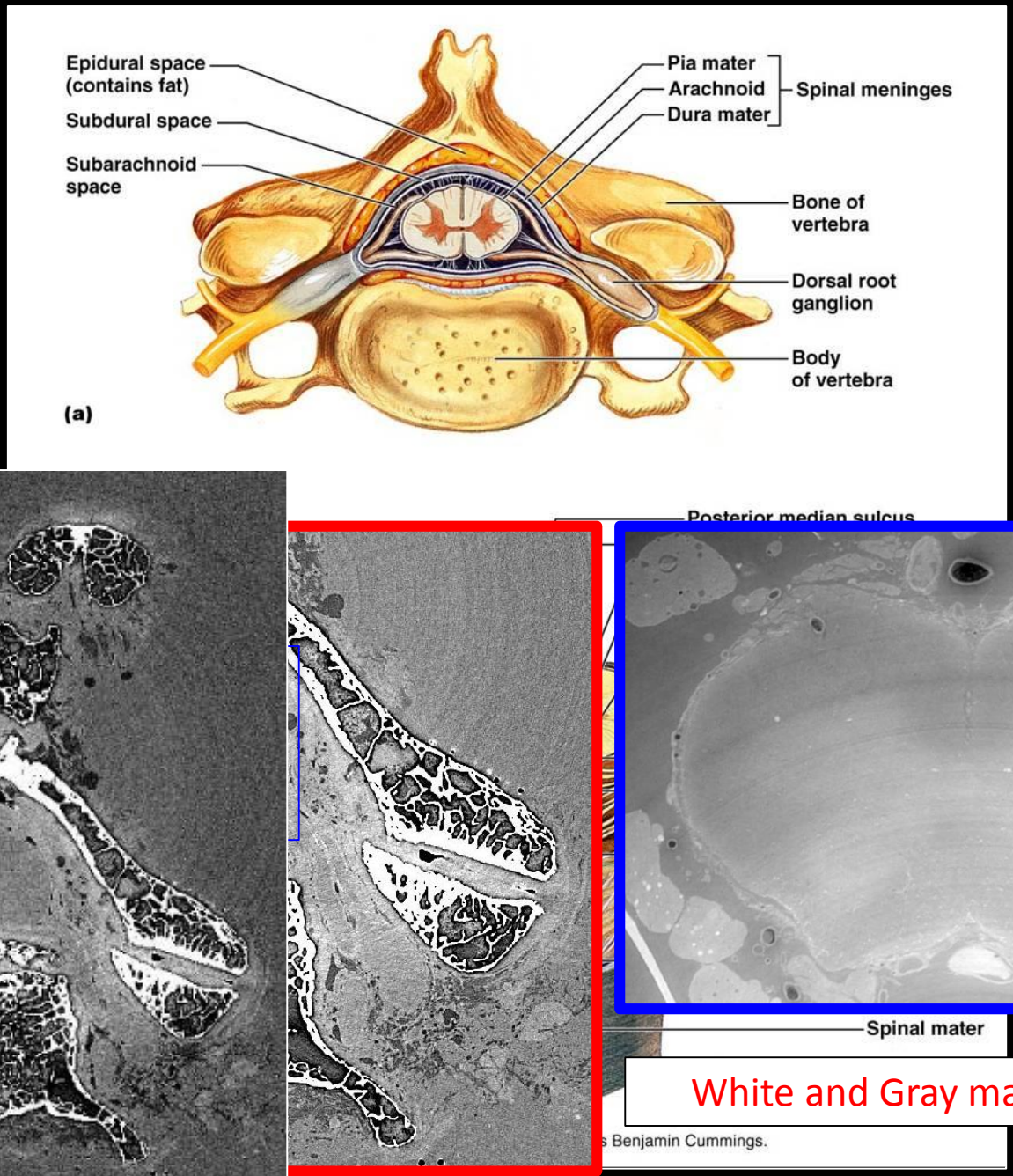
Setup: PBI
Resolution: 46 and 8 micron pixels
Energy: 50 keV
Samples: Ex-vivo Human Vertebral Column

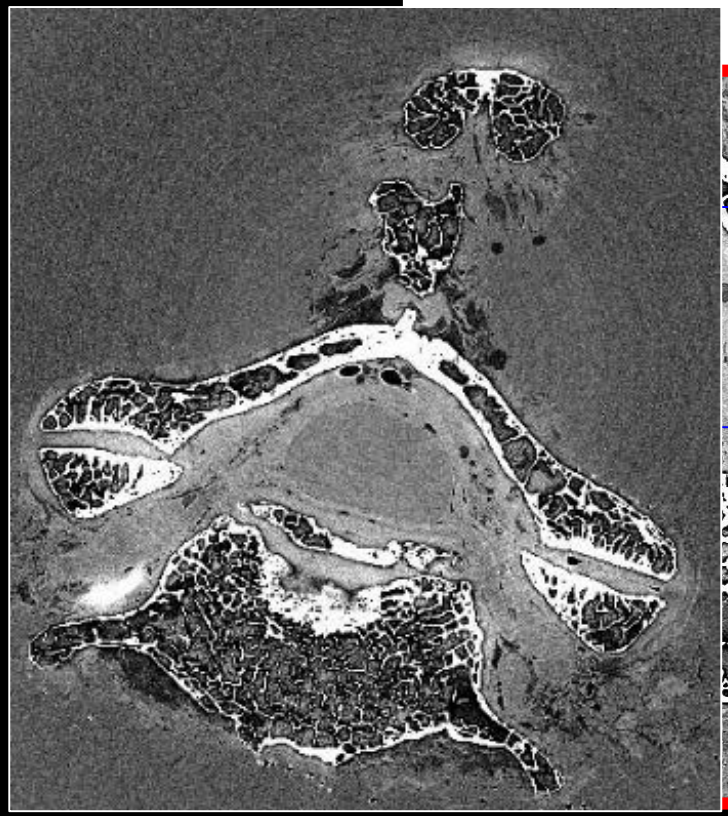
First Results:

Unpublished results

RESULTS: 46/8 MICRON – EX-VIVO HUMAN SPINAL CORD VIRTUAL HISTOLOGY

FIRST IMAGES ON HUMAN SAMPLES



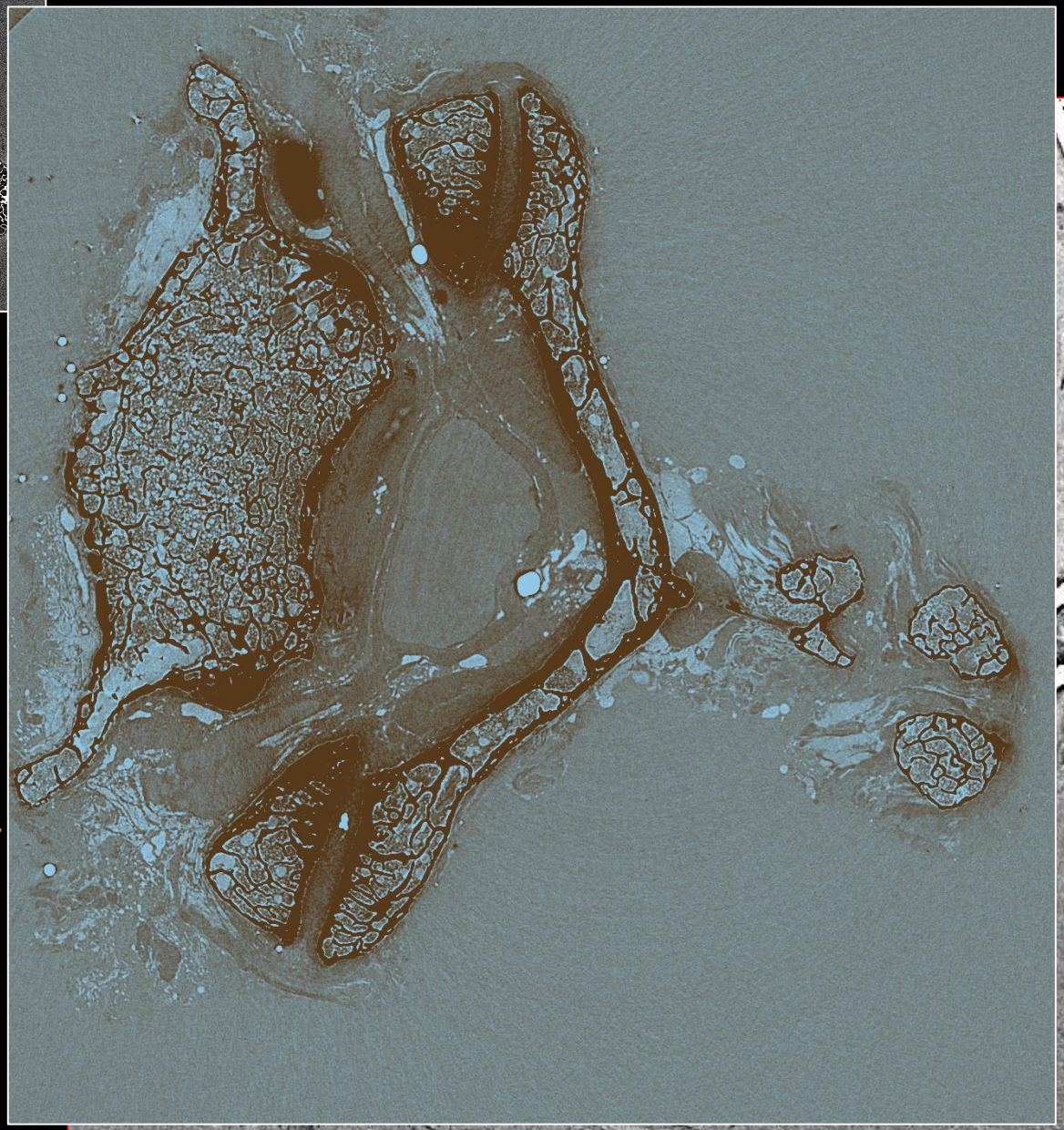


White and Gray matter VISIBLE!!

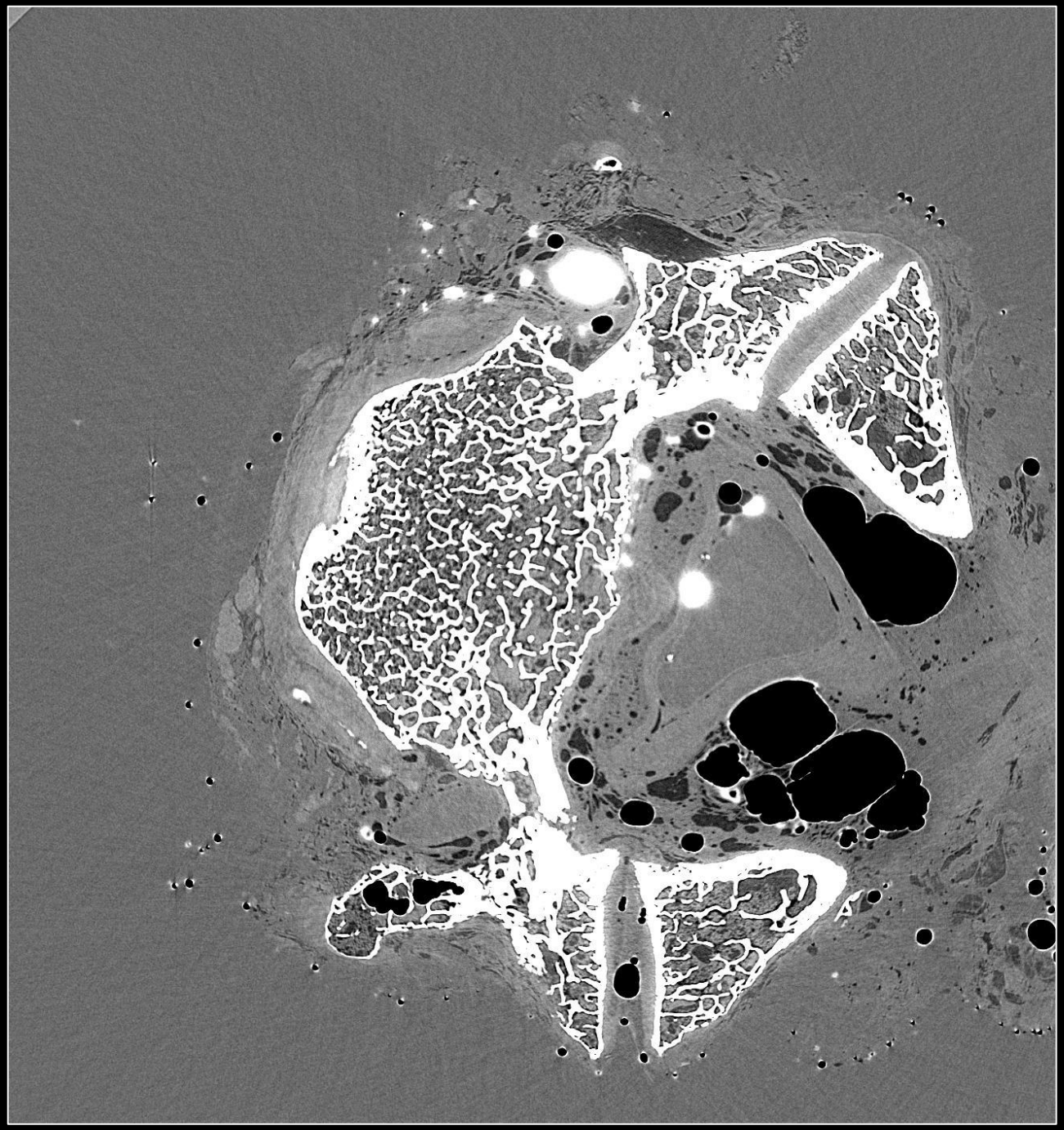
HUMAN SPINAL CORD: EARLY RESULTS

TO SEE:

1. CANCELLOUS BONE OF THE VERTEBRAL BODY
2. VENTRAL AND DORSAL NERVES
3. DORSAL ROOT GANGLION
4. DURA MATER
5. ARACHNOID MATER
6. PIA MATER



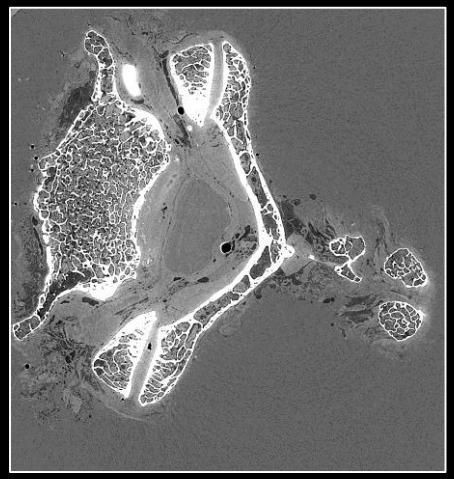
Unpublished results



HUMAN SPINAL CORD: 3D imaging

Unpublished results

HUMAN SPINAL CORD: 3D imaging



“Orthogonal View”

Unpublished results