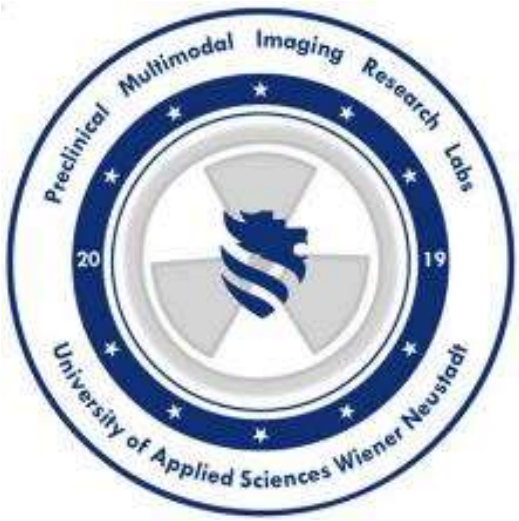


FACHHOCHSCHULE
WIENER NEUSTADT
Austrian Network for Higher Education

Competence Center for Preclinical Imaging and Biomedical Engineering

Faculty of Health, University of Applied Sciences Wiener Neustadt, Austria

Univ.-Lektor Ing. Dr. Markus Zeilinger, BSc MSc MBA
Head of Competence Center for Preclinical Imaging and Biomedical Engineering
Head of Bachelor study programme „Radiological Technology“
Head of Master study programme „MedTech – Functional Imaging, Conventional and Ion Radiotherapy“
Head of Mast study programme „Sonography“
University of Applied Sciences Wiener Neustadt, Austria

Forschungsteam

FACHHOCHSCHULE
WIENER NEUSTADT
Austrian Network for Higher Education

Head of research institute

Univ.-Lektor Ing. Dr. Markus ZEILINGER, BSc MSc MBA

+43 50421 1263
markus.zeilinger@fhwn.ac.at

Study services

Birgit PRUDIC

+43 50421 1208
birgit.prudic@fhwn.ac.at

Academic staff member

Vanessa FRÖHLICH, BSc MSc

+43 50421 1266
vanessa.froehlich@fhwn.ac.at

Academic staff member

Petra GRÖGER, MSc

+43 50421 1265
petra.groeger@fhwn.ac.at

Animal Care Taker

Tina Pfeiffer

+43 50421 1265
tina.pfeiffer@meduniwien.ac.at

Academic staff member

Sabine LEITNER, MSc

+43 50421 1264
sabine.leitner@fhwn.ac.at

Academic staff member

DI Michael RAUTER

+43 50421 1242
michael.rauter@fhwn.ac.at

PhD Student

Silvia STOCCHIERO, BSc MSc

+43 50421 1265
silvia.stocchiero@fhwn.ac.at

Academic staff member

DI Esaú POBLADOR RODRÍGUEZ, MSc PhD

+43 50421 1268
esau.pobladorrodriguez@fhwn.ac.at

Veterinarian

Mag. Katharina HILL

+43 50421 1267
katharina.hill@fhwn.ac.at

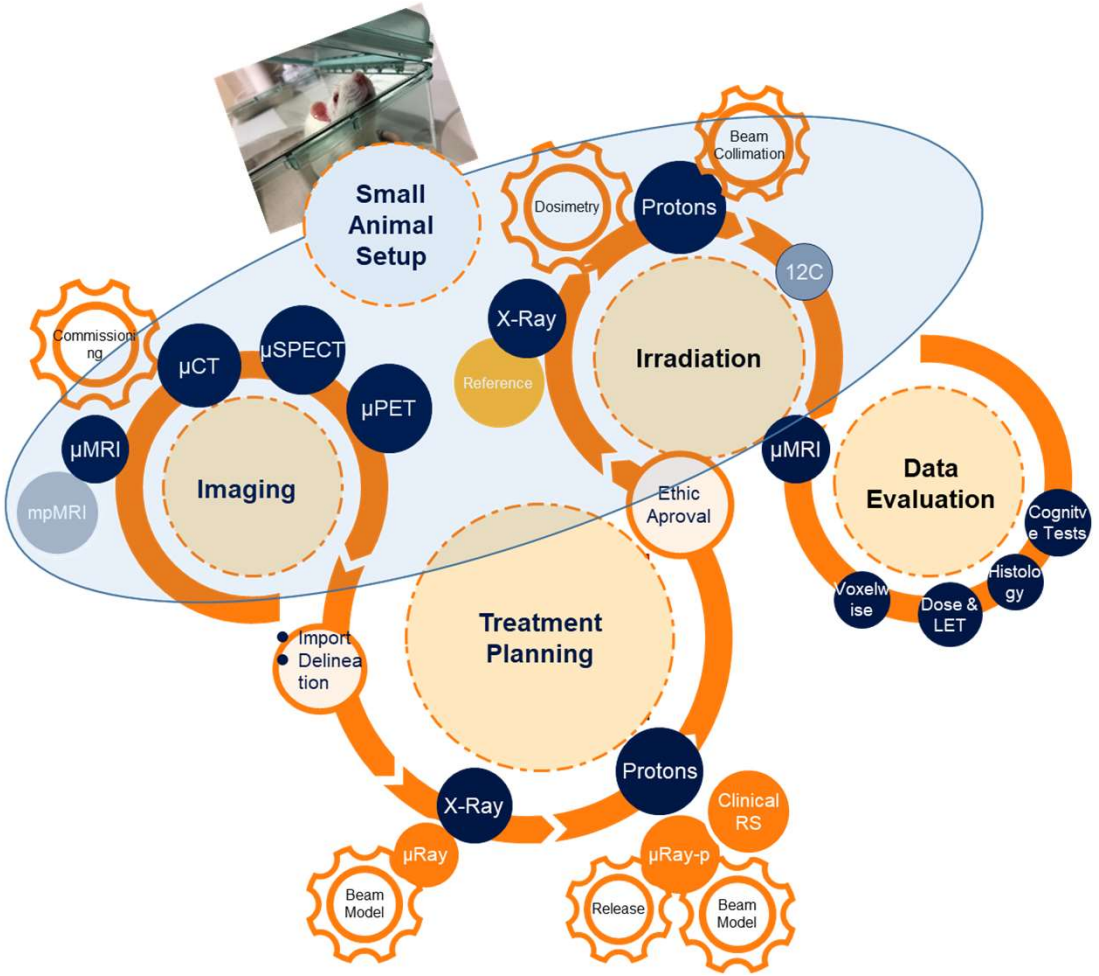
PhD Student

Isselmou Abdarahmane, BSc MSc

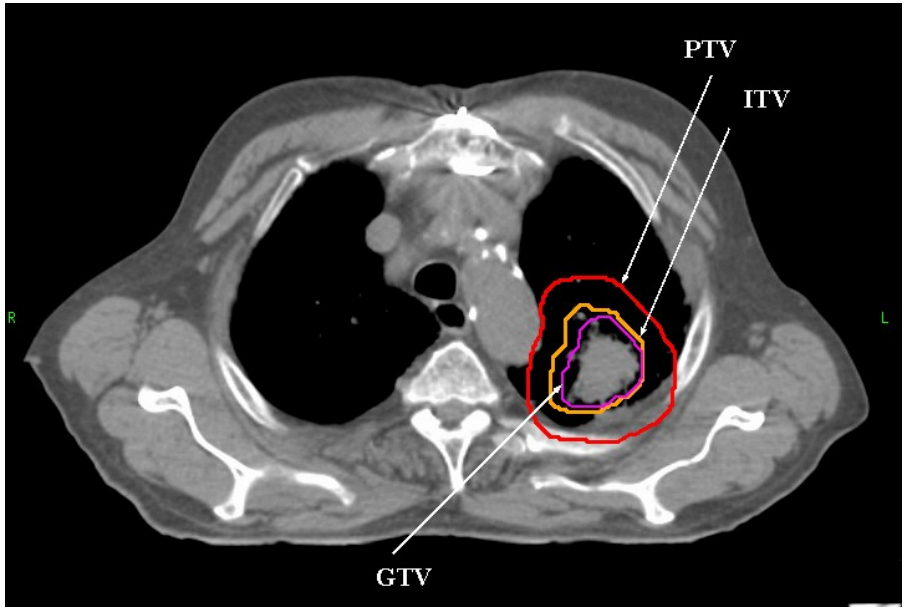
+43 50421 1265
i.mohamedabdarahmane@fhwn.ac.at

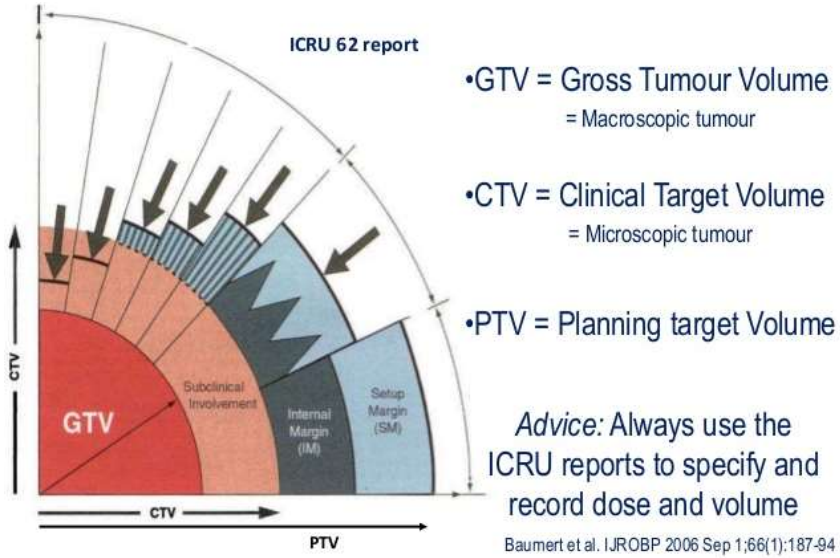
Kompetenzzentrum für Präklinische Bildgebung und Medizintechnik

FACHHOCHSCHULE
WIENER NEUSTADT
Austrian Network for Higher Education



Aspekte bei der Zielvolumendefinition



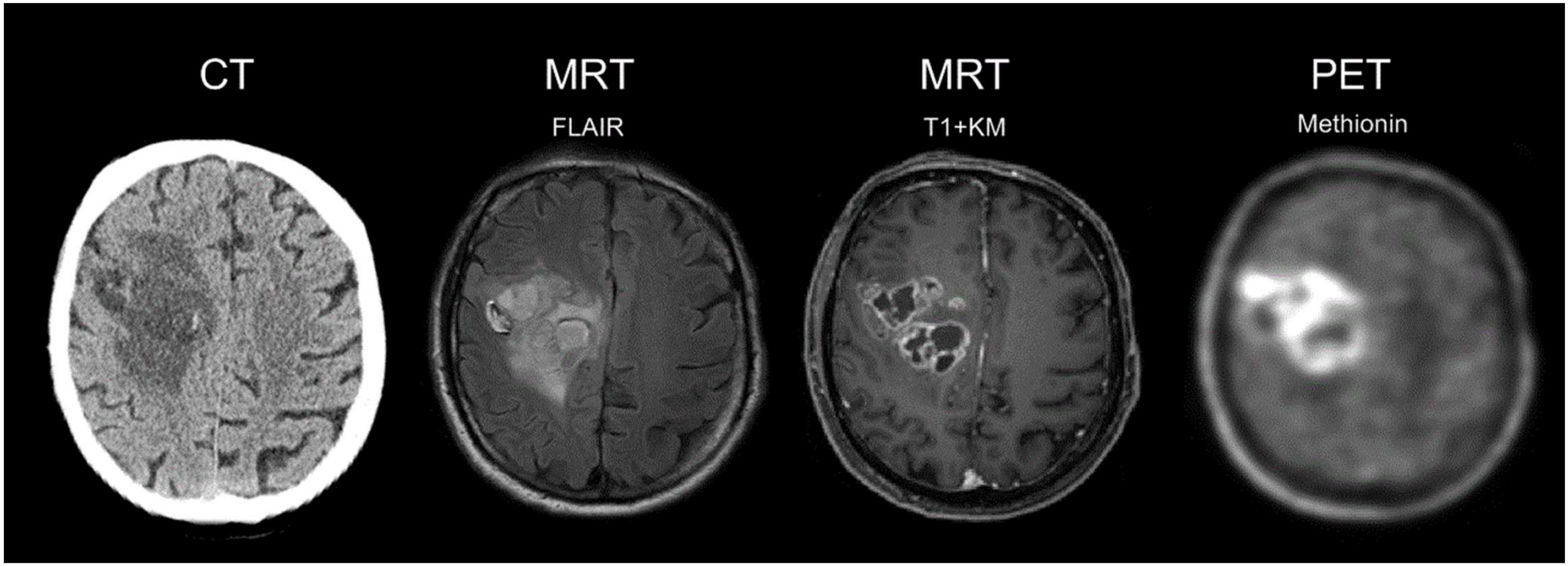


Bildquellen:
ICRU 62 report
Baumert et al. 2006

Aspekte bei der Zielvolumendefinition

FACHHOCHSCHULE
WIENER NEUSTADT
Austrian Network for Higher Education

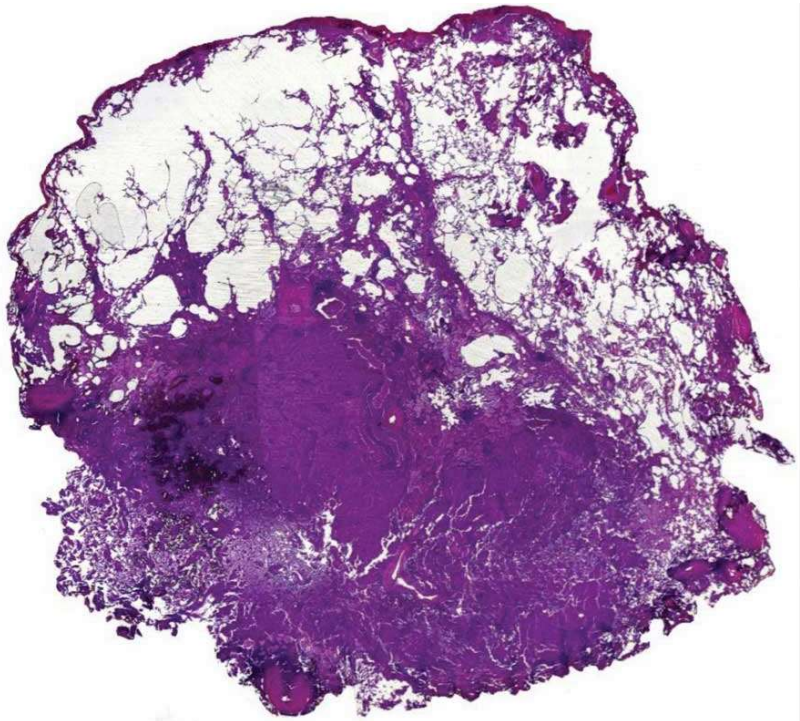
Ein Tumor hat viele Gesichter !!!

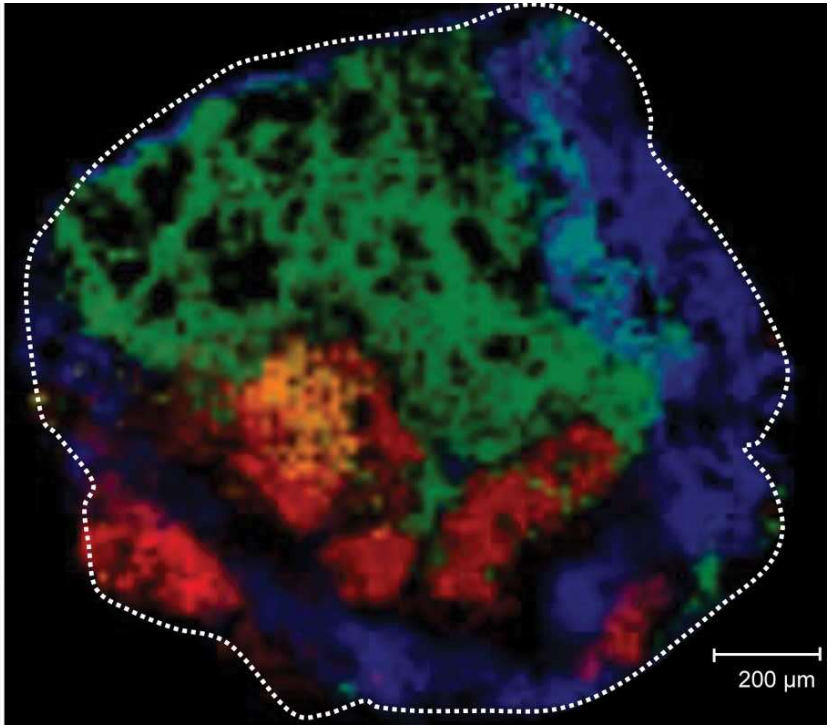


Aspekte bei der Zielvolumendefinition

FACHHOCHSCHULE
WIENER NEUSTADT
Austrian Network for Higher Education

Ein Tumor hat viele Gesichter !!!





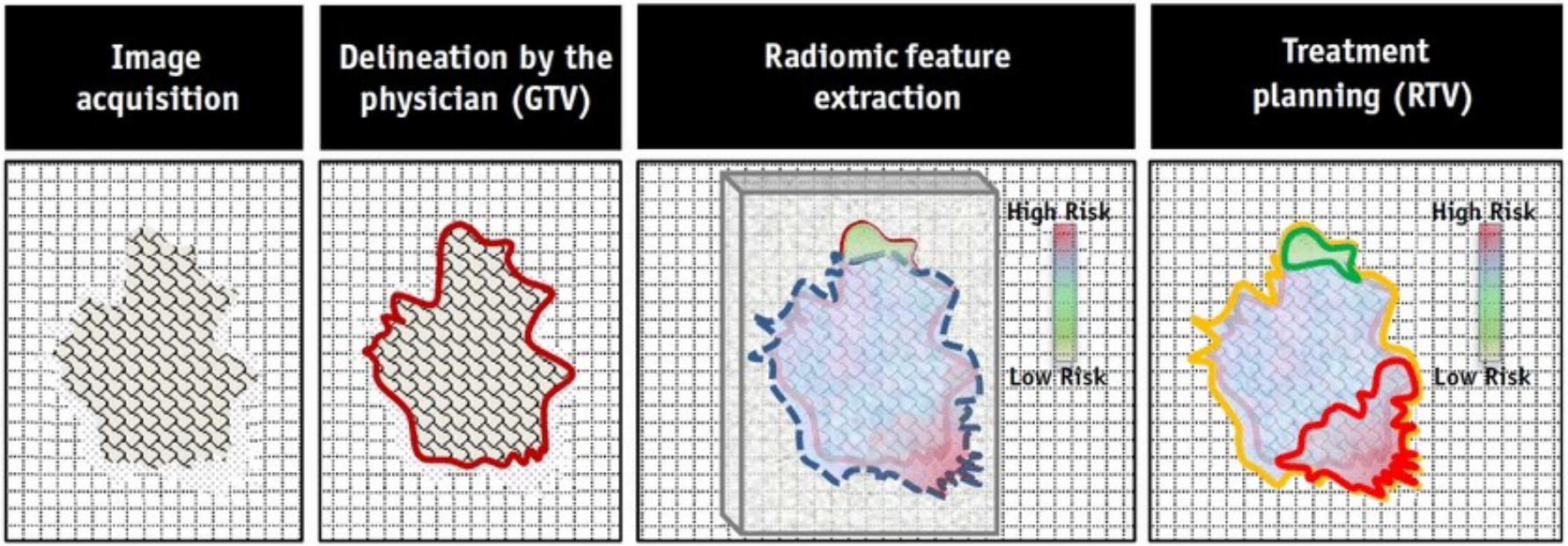
Bildquellen:
Zeilinger et al. 2015

Aspekte bei der Zielvolumendefinition

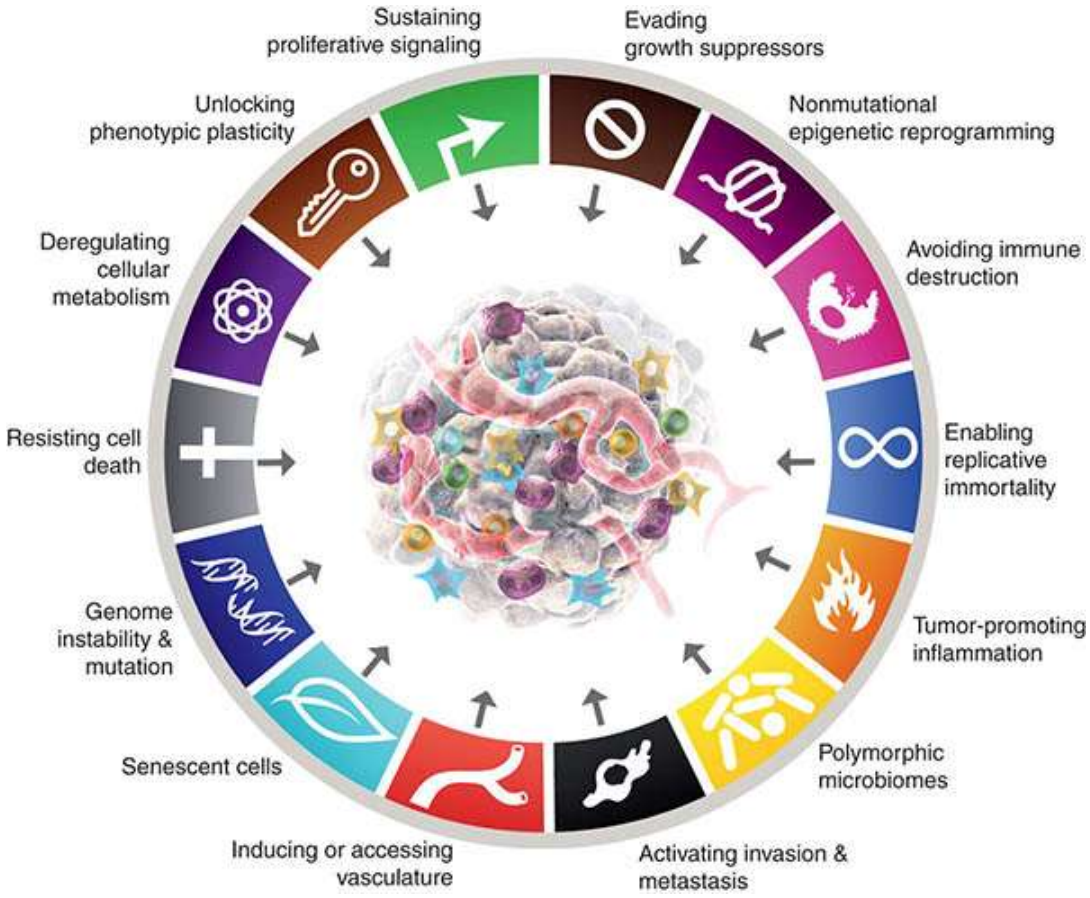
FACHHOCHSCHULE
WIENER NEUSTADT
Austrian Network for Higher Education

Aspekte für die Zielvolumendefinition

Morphologische und molekulare Information ➔ komplementär



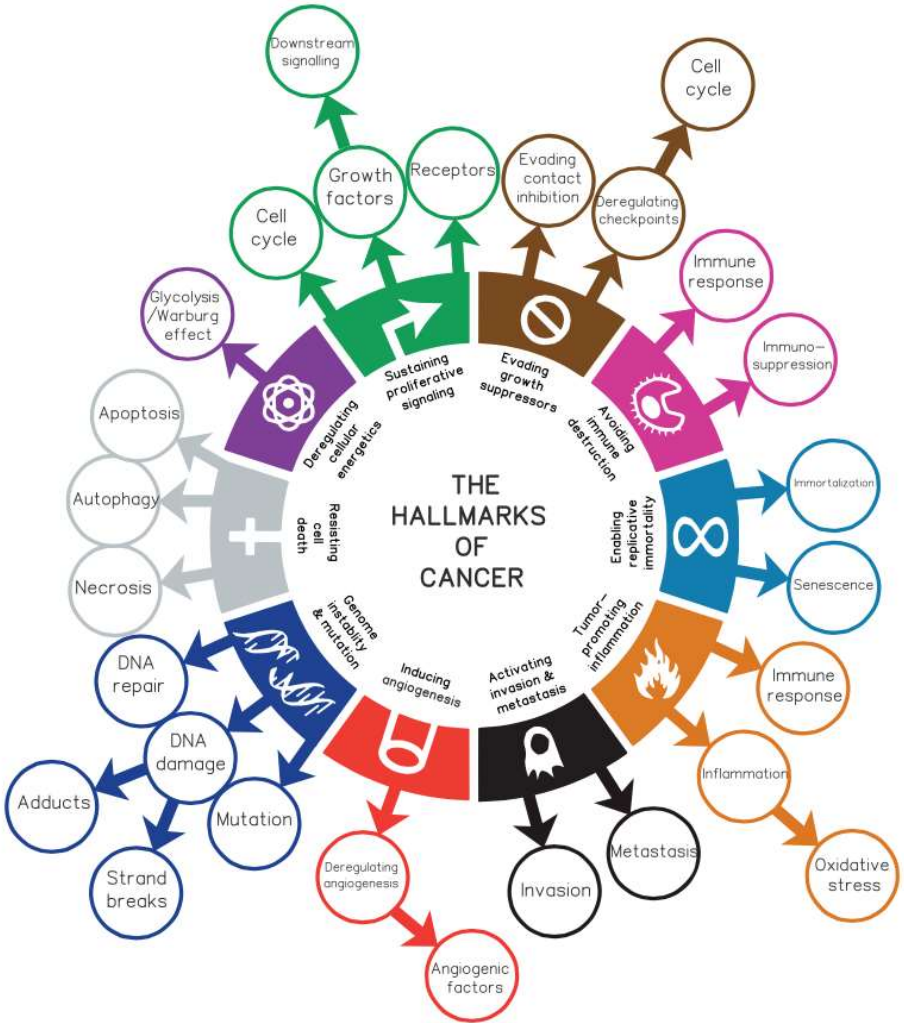
Molecular imaging of specific tumor(patho)physiological processes



Mod. Hanahan und Weinberg, 2022

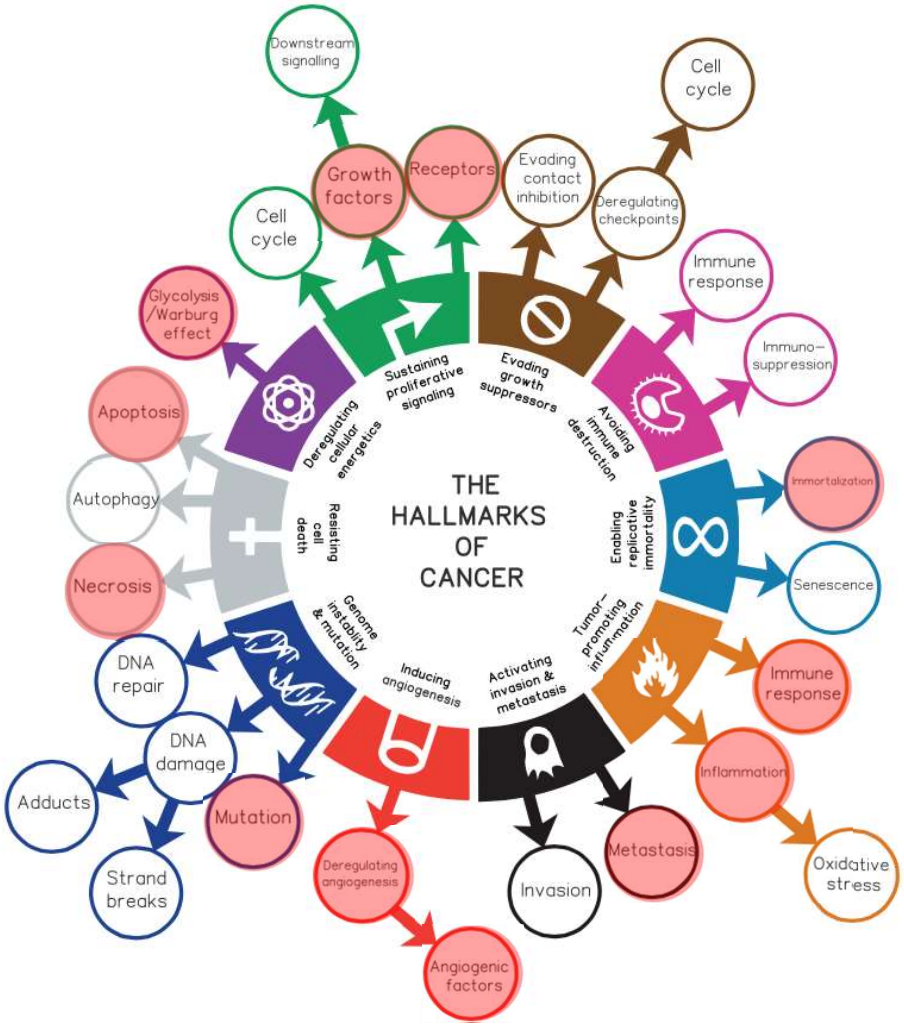
Molecular imaging of specific tumor(patho)physiological processes

FACHHOCHSCHULE
WIENER NEUSTADT
Austrian Network for Higher Education



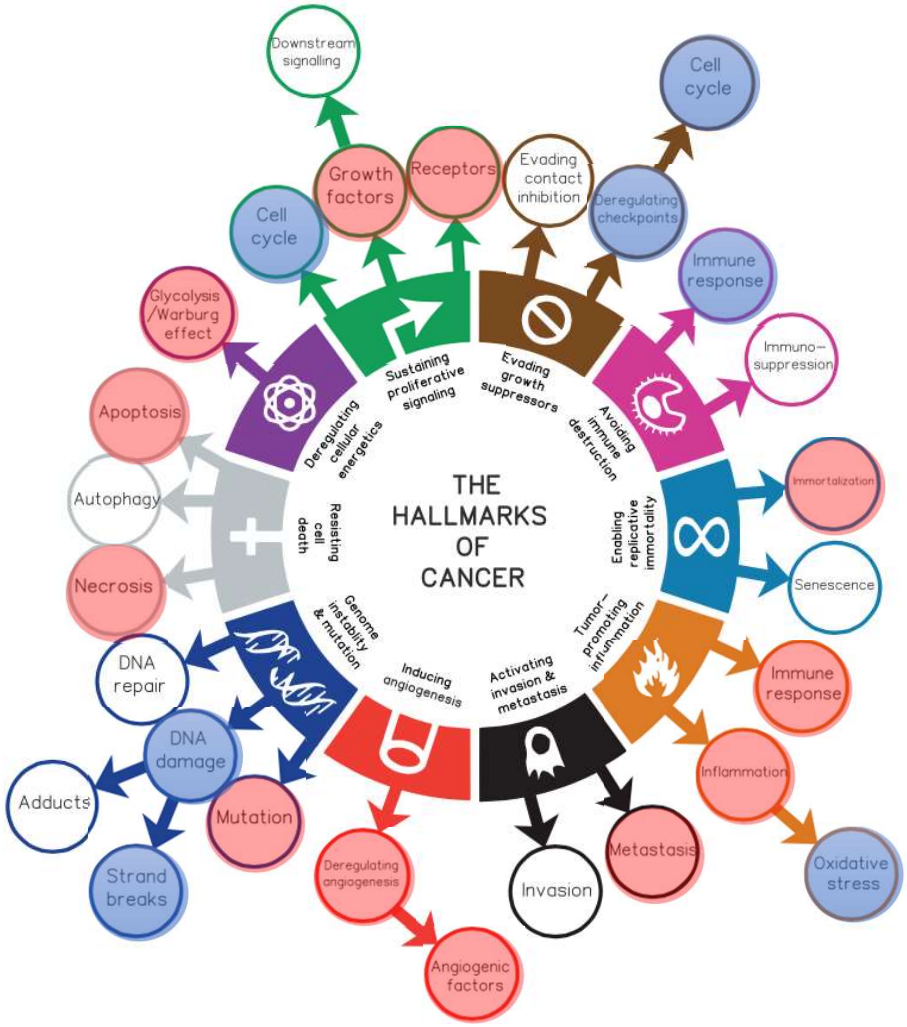
Mod. Hanahan und Weinberg, 2011

Molecular imaging of specific tumor(patho)physiological processes



Mod. Hanahan und Weinberg, 2011

Molecular imaging of specific tumor(patho)physiological processes



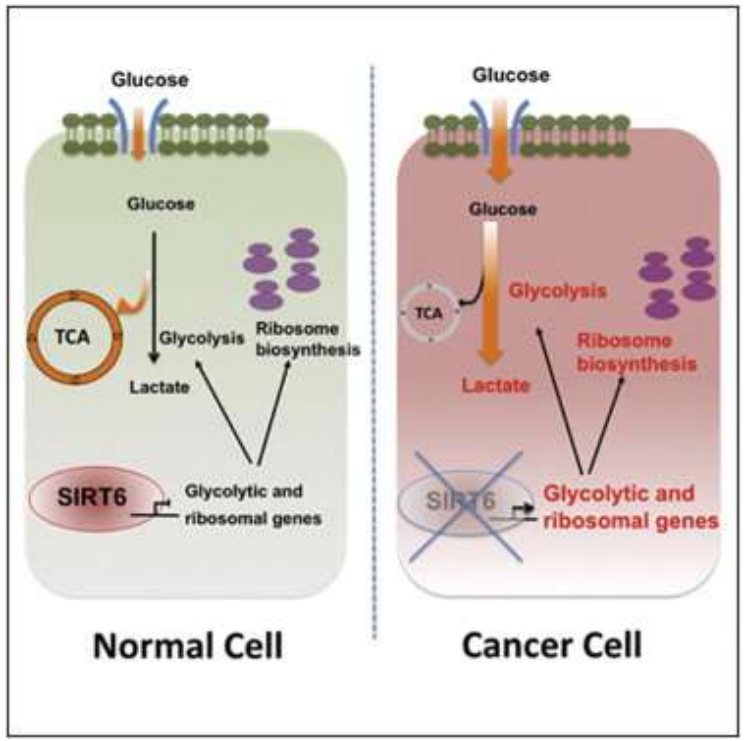
Mod. Hanahan und Weinberg, 2011

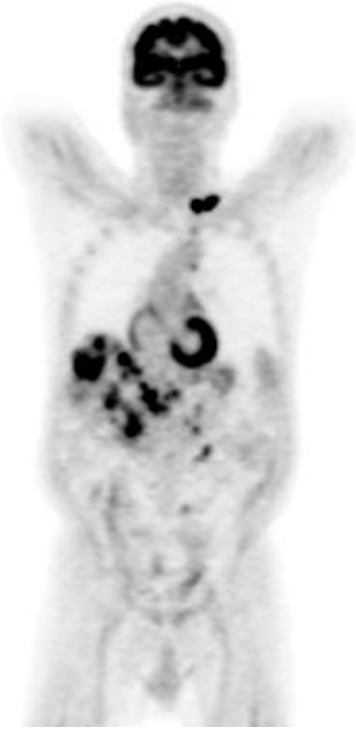
Molecular imaging with PET in radiotherapy

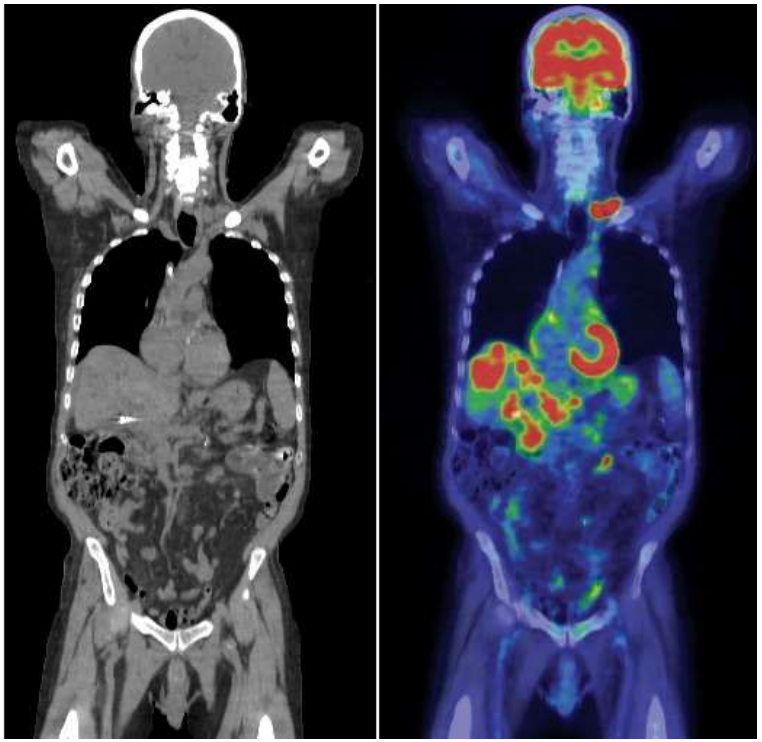
FACHHOCHSCHULE
WIENER NEUSTADT
Austrian Network for Higher Education

Change of energy metabolism

[^{18}F]FDG ➔ glucose utilization







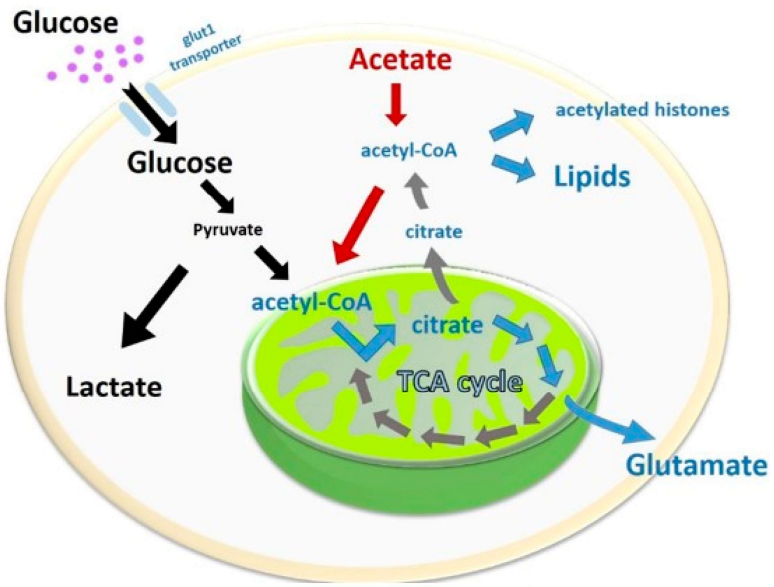
http://www.cell.com/abstract/S0092-8674(12)01351-7
https://usa.healthcare.siemens.com

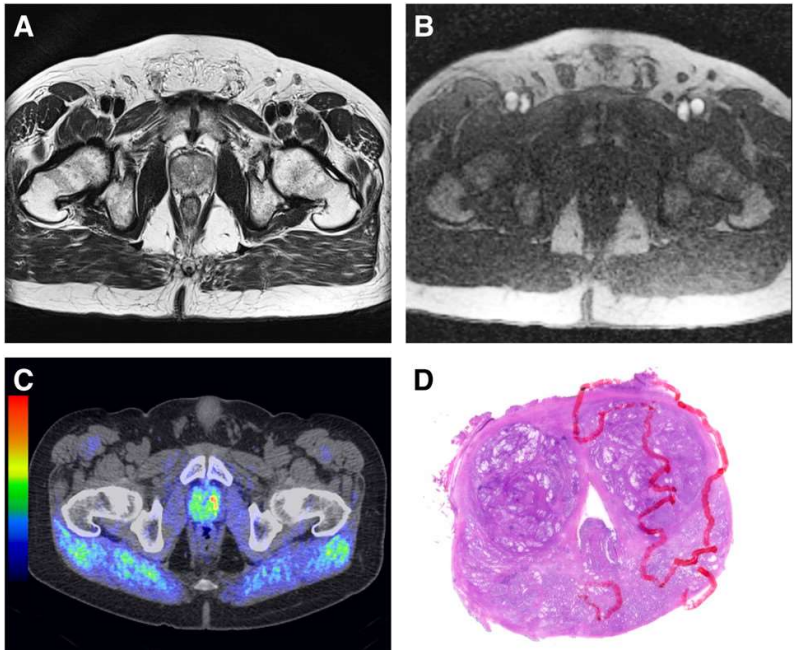
Molecular imaging with PET in radiotherapy

FACHHOCHSCHULE
WIENER NEUSTADT
Austrian Network for Higher Education

Changes of lipid homeostasis

[^{11}C]Acetat ➔ lipid homeostasis



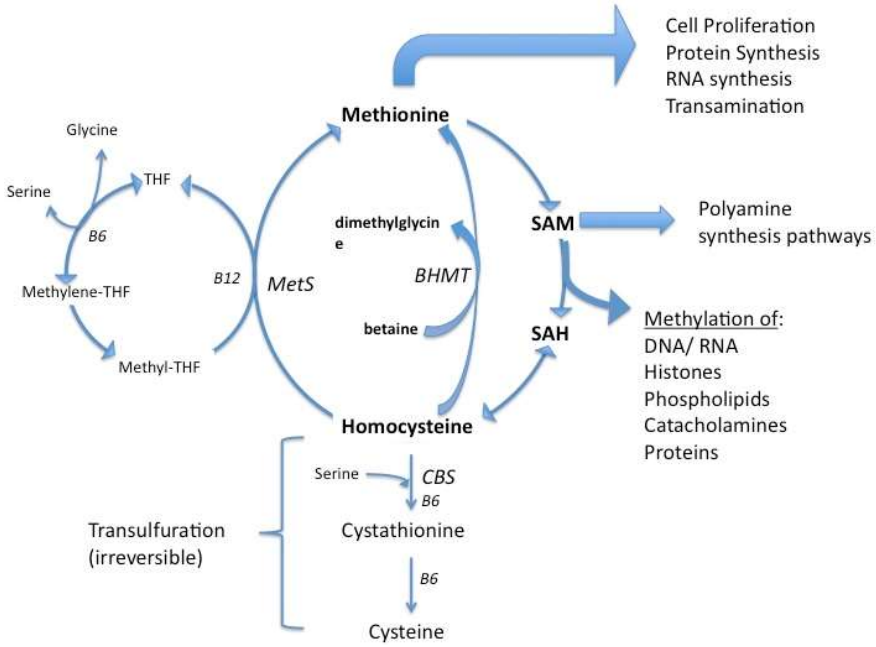


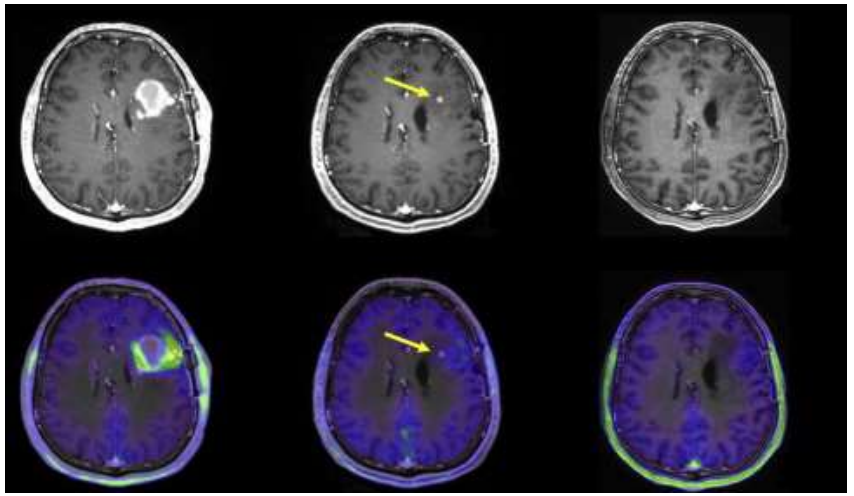
Molecular imaging with PET in radiotherapy

FACHHOCHSCHULE
WIENER NEUSTADT
Austrian Network for Higher Education

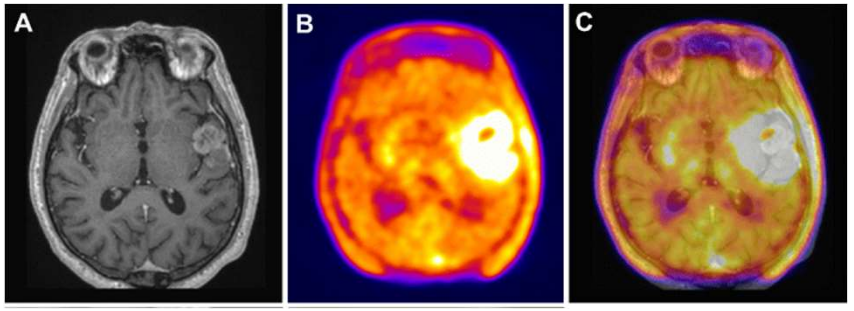
Change of protein and amino acid metabolism

[^{18}F]FET ➔ amino acid metabolism
[^{11}C]Methionin ➔ amino acid metabolism
[^{18}F]FABCB ➔ amino acid transport





[^{11}C]MET



[^{18}F]FET

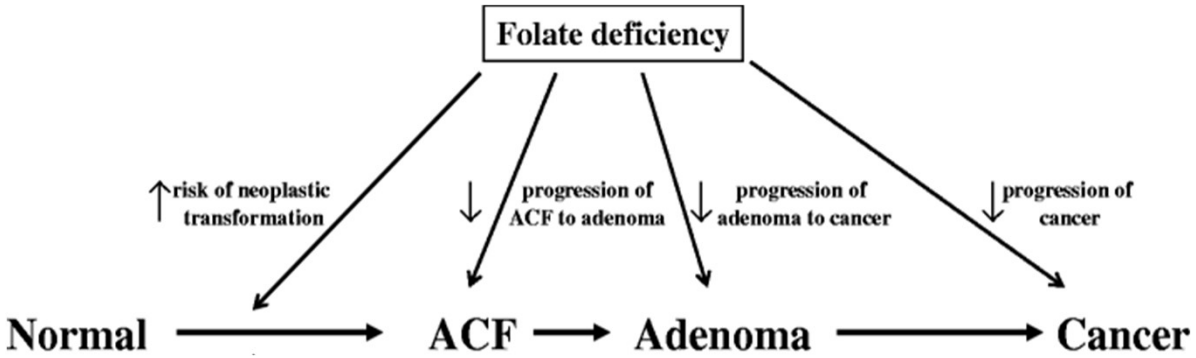
https://upload.wikimedia.org
http://jnm.snmjournals.org/content/49/5/694

Molecular imaging with PET in radiotherapy

FACHHOCHSCHULE
WIENER NEUSTADT
Austrian Network for Higher Education

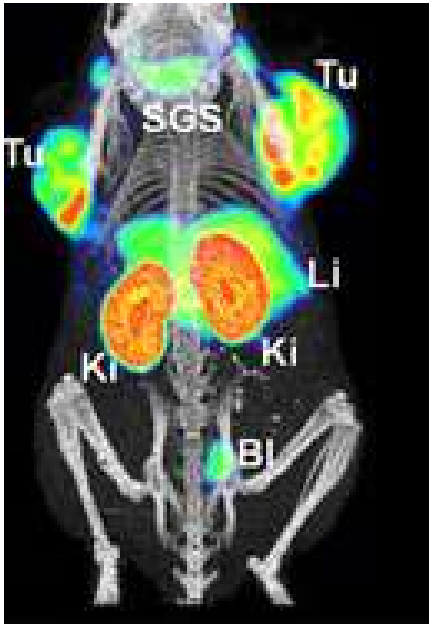
Change of protein and amino acid metabolism

[^{18}F]MTHF ➔ folic acid metabolism



[^{111}In]-DTPA-folate

[^{18}F]MTHF



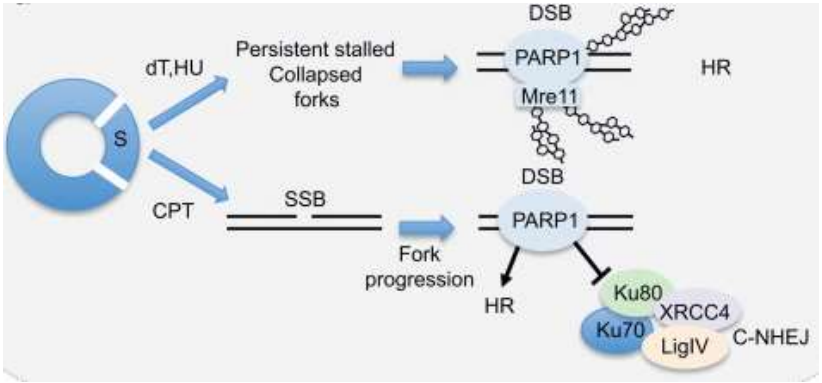
Boss et al. 2011

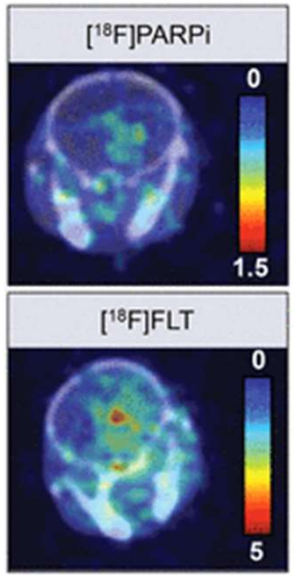
Molecular imaging with PET in radiotherapy

FACHHOCHSCHULE
WIENER NEUSTADT
Austrian Network for Higher Education

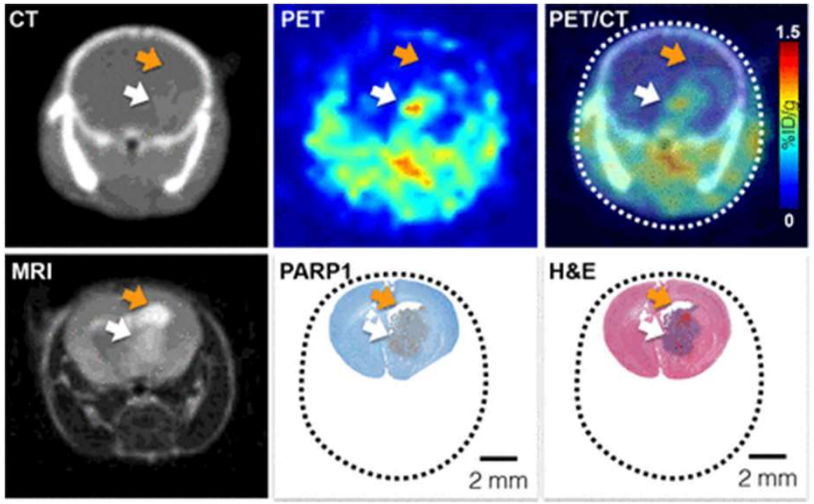
DNA modifications and adoptions

[^{18}F]FLT ➔ DNA synthesis
[^{18}F]PARPi ➔ Poly ADP Ribose Polymerase PARP1





[^{18}F]PARPi



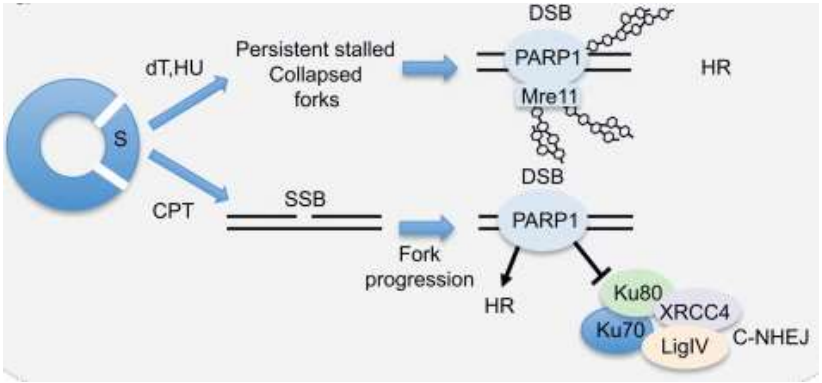
Beck et al. 2014

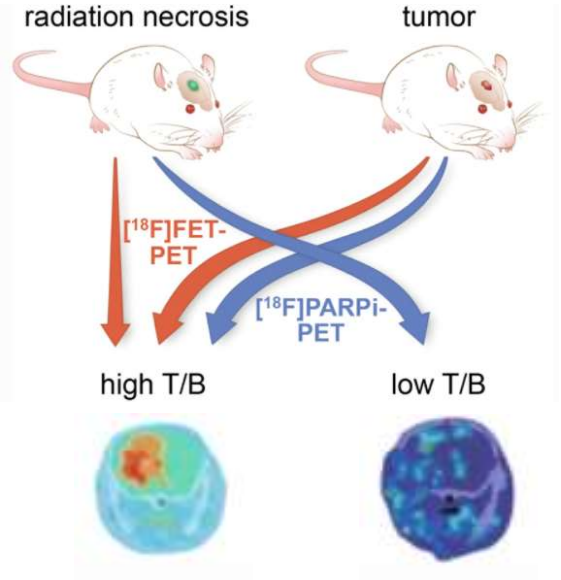
Molecular imaging with PET in radiotherapy

FACHHOCHSCHULE
WIENER NEUSTADT
Austrian Network for Higher Education

DNA modifications and adoptions

[^{18}F]FLT ➔ DNA synthesis
[^{18}F]PARPi ➔ Poly ADP Ribose Polymerase PARP1





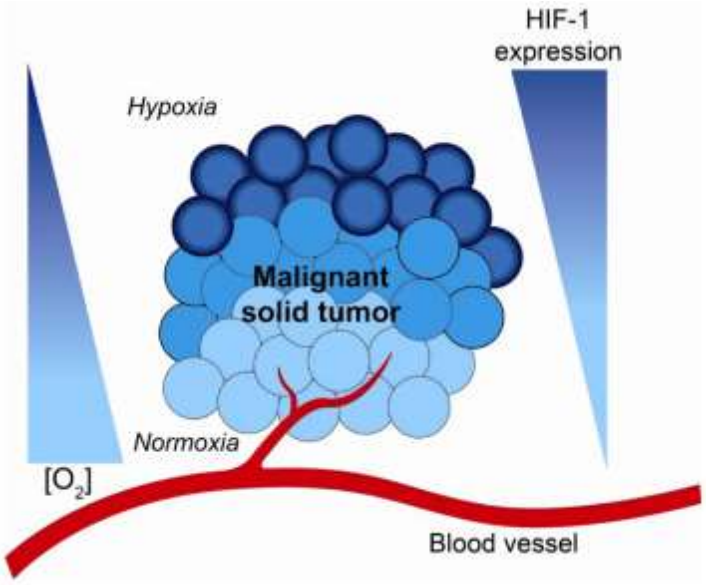
Beck et al. 2014
Kossatz et al. 2018

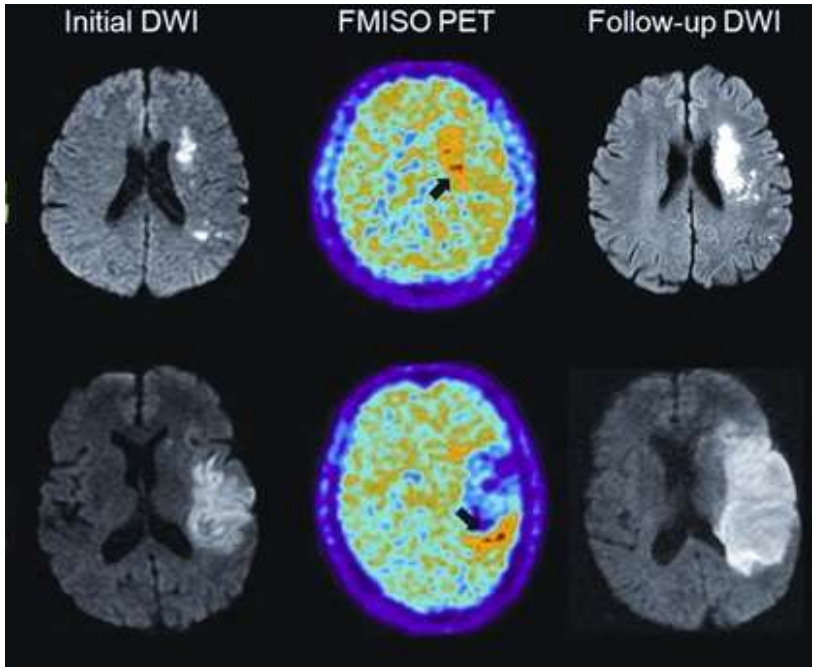
Molecular imaging with PET in radiotherapy

FACHHOCHSCHULE
WIENER NEUSTADT
Austrian Network for Higher Education

Change of oxygen partial pressure and apoptosis

[^{18}F]FMISO	➔ hypoxia
[^{18}F]FAZA	➔ hypoxia
[^{89}Zr]ranibizumab	➔ neoangiogenesis
[^{18}F]Annexin V	➔ Caspase 9
[^{18}F]ML-10	➔ apoptosis





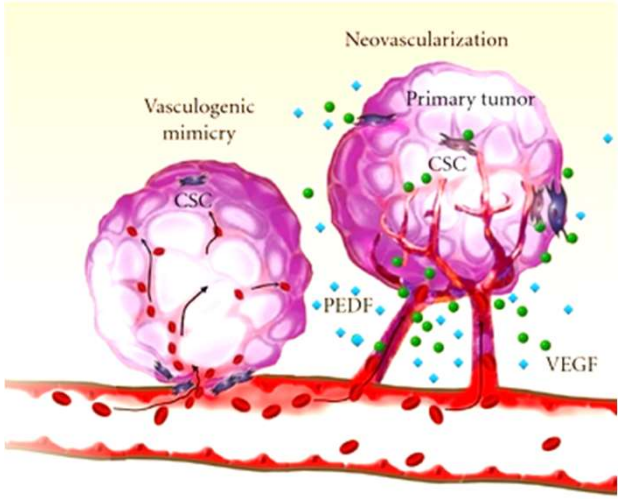
http://pharma.bayer.com
http://www.auntminnie.com

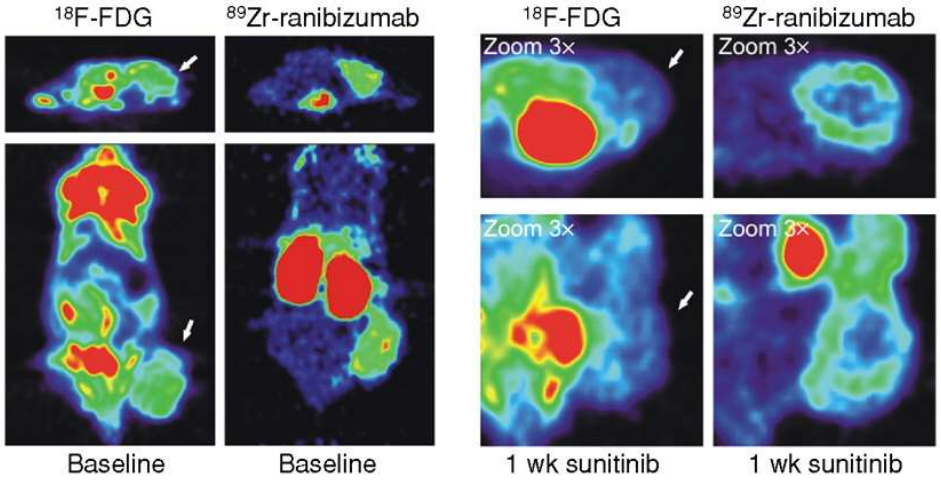
Molecular imaging with PET in radiotherapy

FACHHOCHSCHULE
WIENER NEUSTADT
Austrian Network for Higher Education

Change of oxygen partial pressure and apoptosis

[^{18}F]FMISO	➔ hypoxia
[^{18}F]FAZA	➔ hypoxia
[^{89}Zr]ranibizumab	➔ neoangiogenesis
[^{18}F]Annexin V	➔ Caspase 9
[^{18}F]ML-10	➔ apoptosis





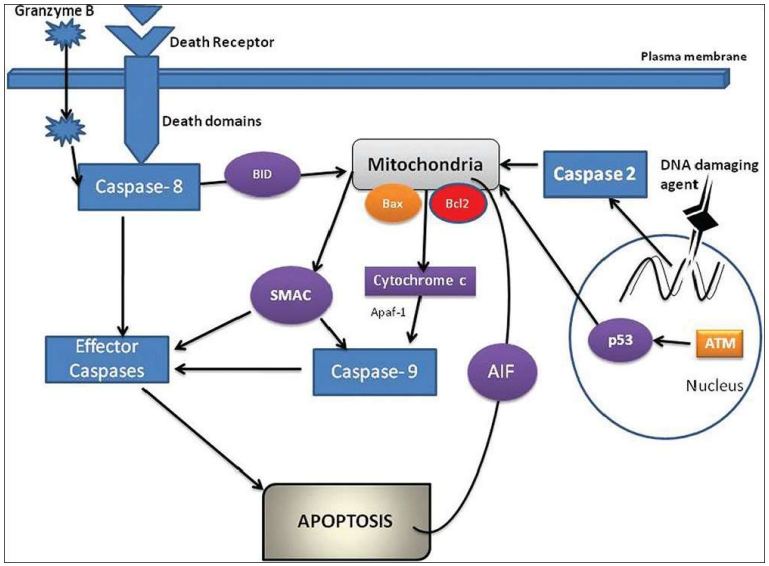
Jung-Tung Liu et al. 2012
http://www.auntminnie.com

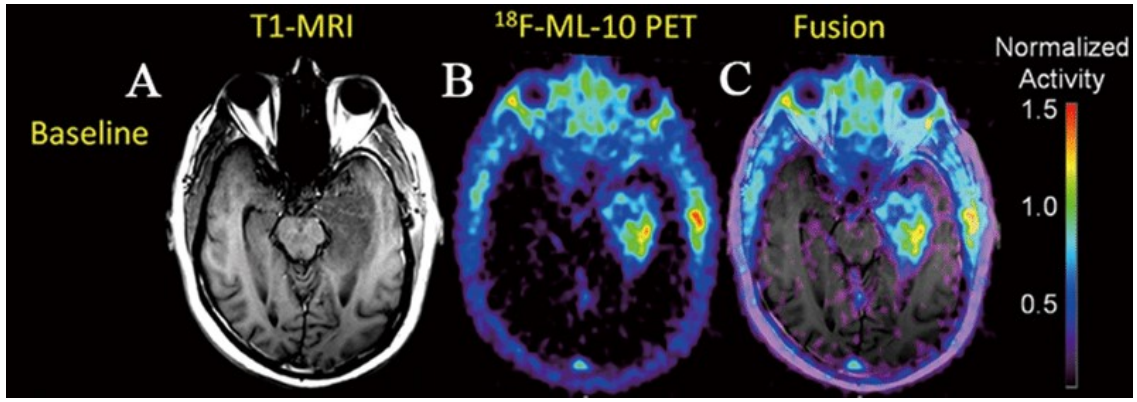
Molecular imaging with PET in radiotherapy

FACHHOCHSCHULE
WIENER NEUSTADT
Austrian Network for Higher Education

Change of oxygen partial pressure and apoptosis

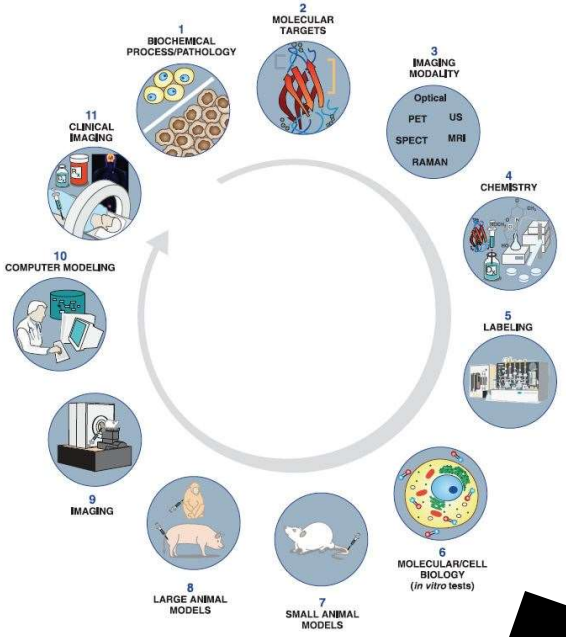
[^{18}F]FMISO	➔ hypoxia
[^{18}F]FAZA	➔ hypoxia
[^{89}Zr]ranibizumab	➔ neoangiogenesis
[^{18}F]Annexin V	➔ Caspase 9
[^{18}F]ML-10	➔ apoptosis

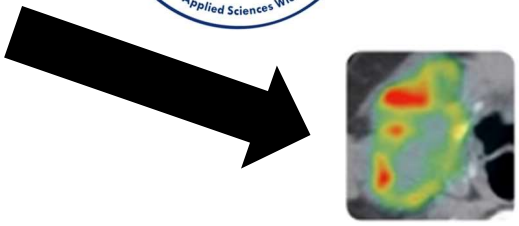




Ghatage DD et al. 2012
http://www.auntminnie.com

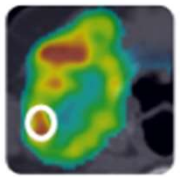
Biomarkerentwicklung und Imaging Methodenvalidierung





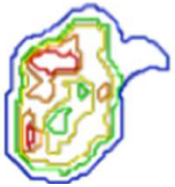
Multimodal/Multiparametric
Preclinical Imaging
µMRI, µCT, µSPECT, µPET

Prescription
Function



Radiomics/Proteomics/Holomics
Machine learning / AI

Dose
Discretization



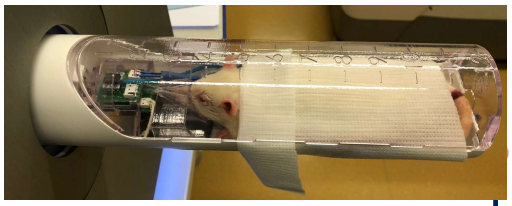
Biological adaptive radiation therapy; investigation of radiobiological effects

Kompetenzzentrum für Präklinische Bildgebung und Medizintechnik

FACHHOCHSCHULE
WIENER NEUSTADT
Austrian Network for Higher Education

Technical integration and establishment of the imaging infrastructure

2017-2021



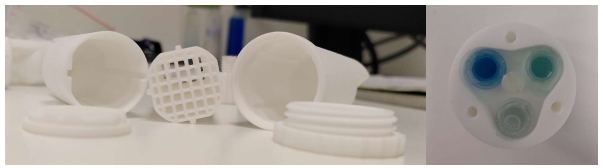
In-vivo experiments

Starting January 2023

Development of robust acquisition and reconstruction protocols for the different imaging modalities

2018-2023

- Ex-vivo system validation
- Performance analysis
- Irradiation workflow development
- Small animal research set-up



Data analysis and image post-processing

Starting Q3 2023

- Method verification in-vitro/in-vivo/ex-vivo
- Fine tuning of imaging protocols
- Treatment monitoring

Development of novel imaging methods and analysis tool

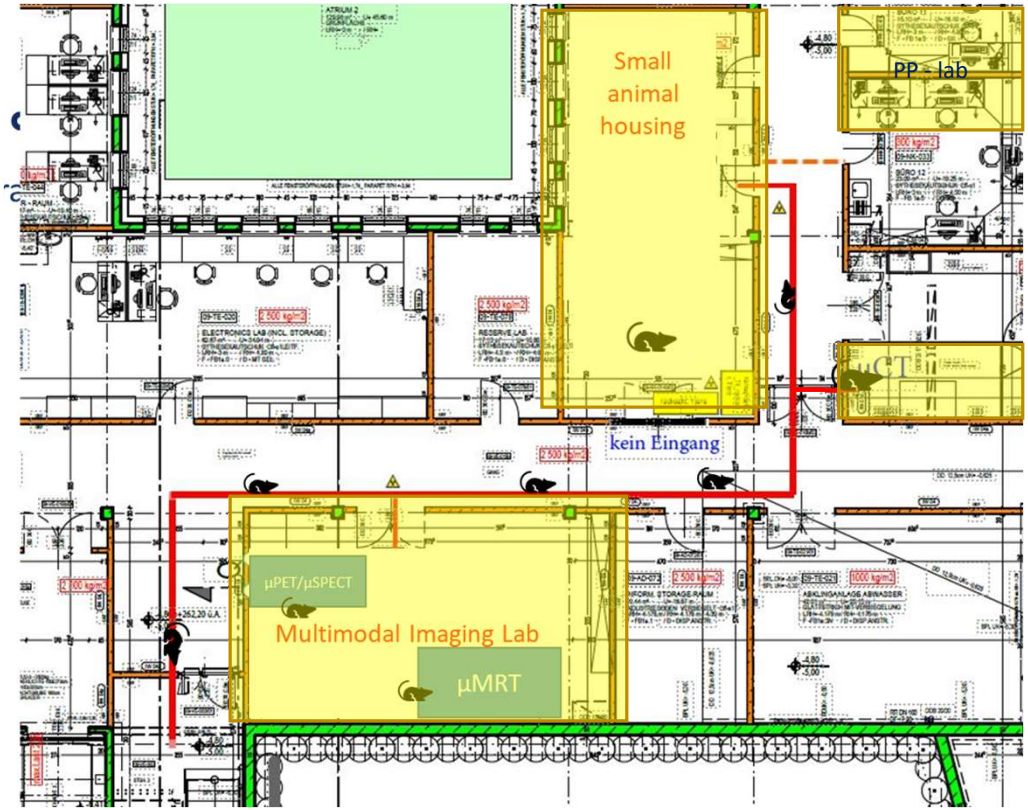
Starting 2023

Kompetenzzentrum für Präklinische Bildgebung und Medizintechnik

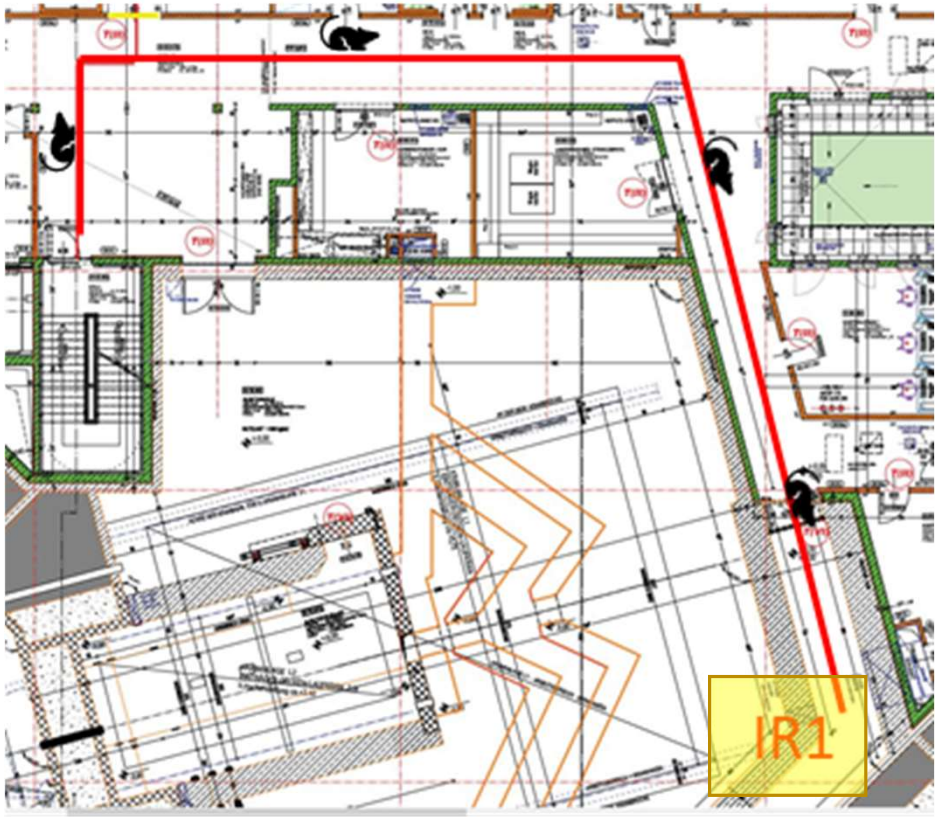
FACHHOCHSCHULE
WIENER NEUSTADT
Austrian Network for Higher Education

Imaging Labs der FHWN am Standort MedAustron

Untergeschoß



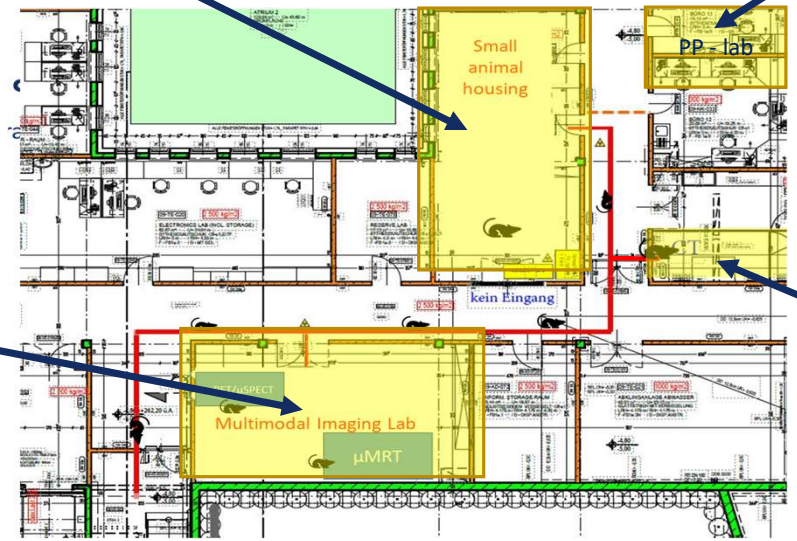
Erdgeschoß



Kompetenzzentrum für Präklinische Bildgebung und Medizintechnik

FACHHOCHSCHULE
WIENER NEUSTADT
Austrian Network for Higher Education

Animal housing unit



Data post-processing lab

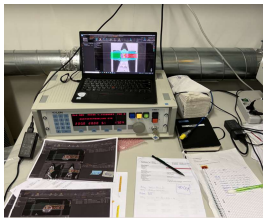
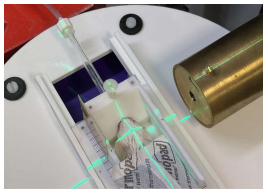
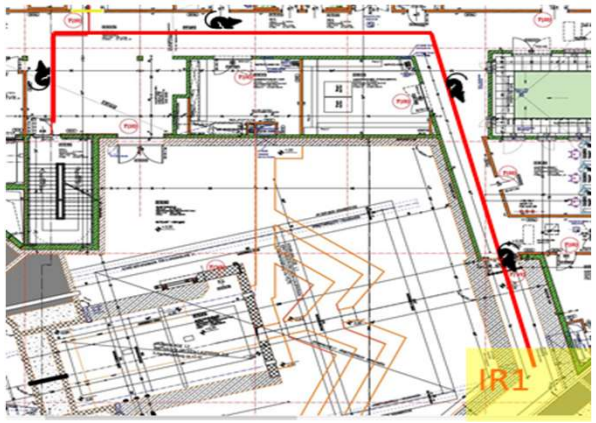
Multimodal imaging lab

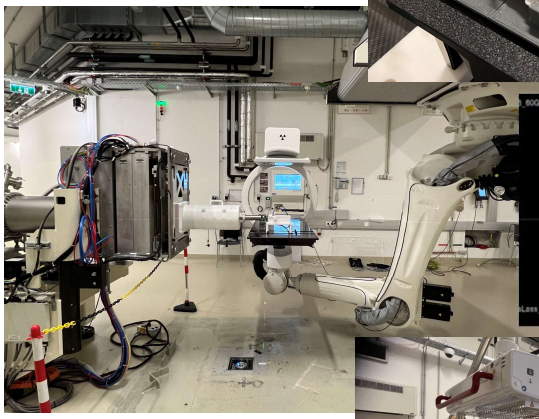
micro-CT lab

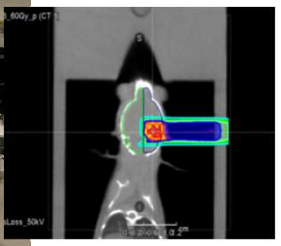
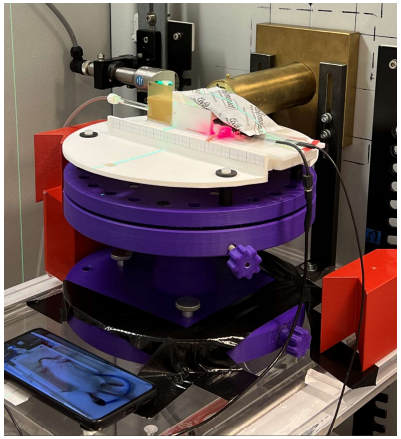
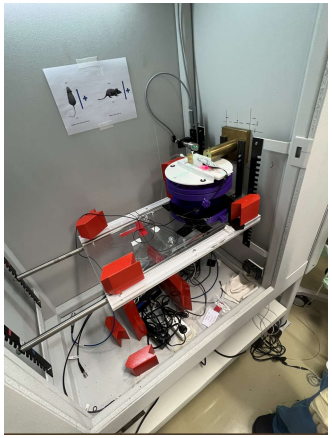
Kompetenzzentrum für Präklinische Bildgebung und Medizintechnik

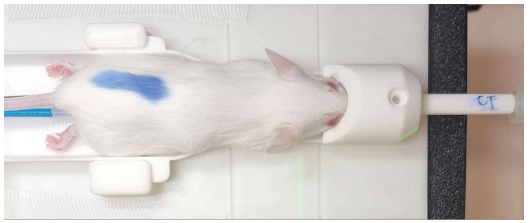
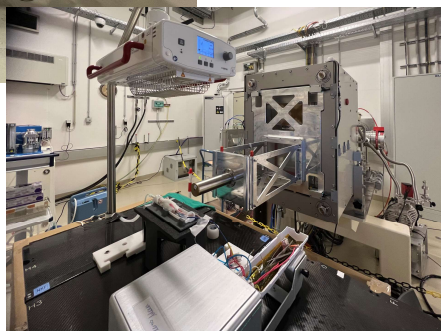
FACHHOCHSCHULE
WIENER NEUSTADT
Austrian Network for Higher Education

Photon beam irradiation set-up vs. ion beam irradiation set-up



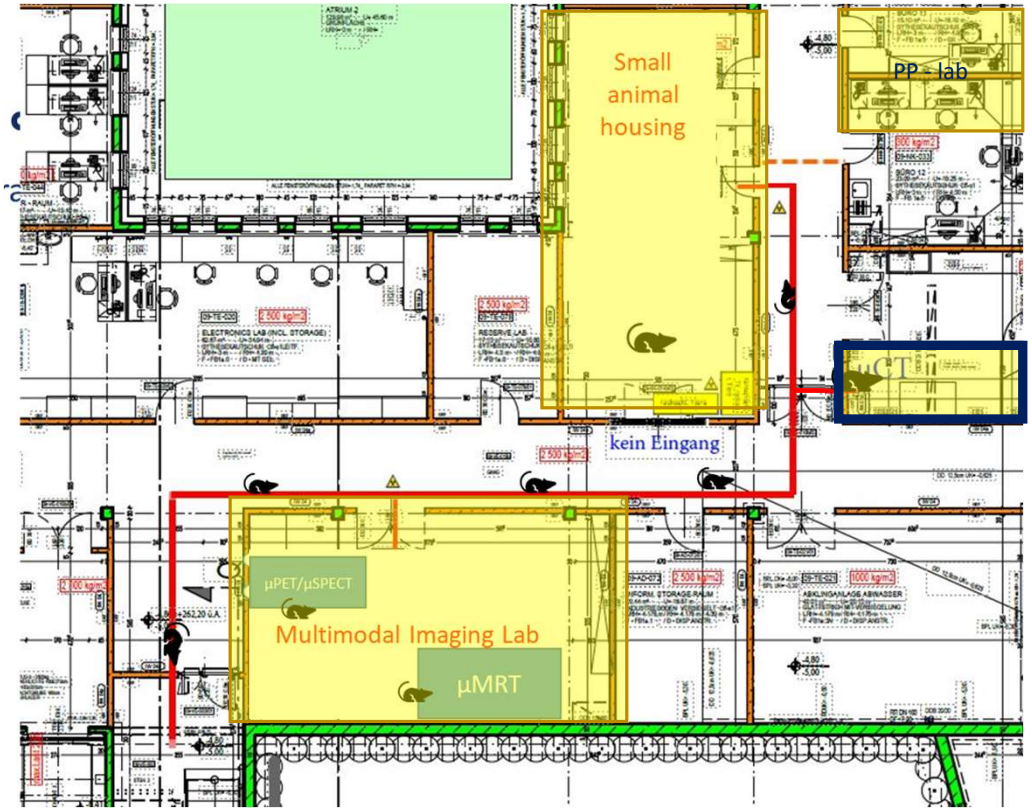




Kompetenzzentrum für Präklinische Bildgebung und Medizintechnik

FACHHOCHSCHULE
WIENER NEUSTADT
Austrian Network for Higher Education

Basement

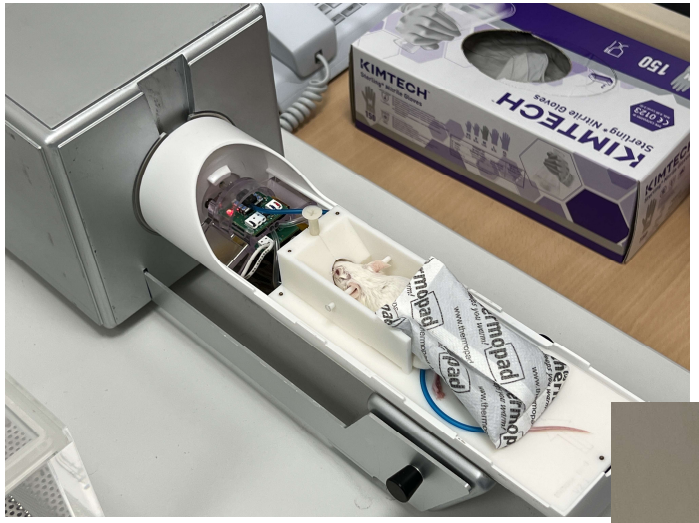


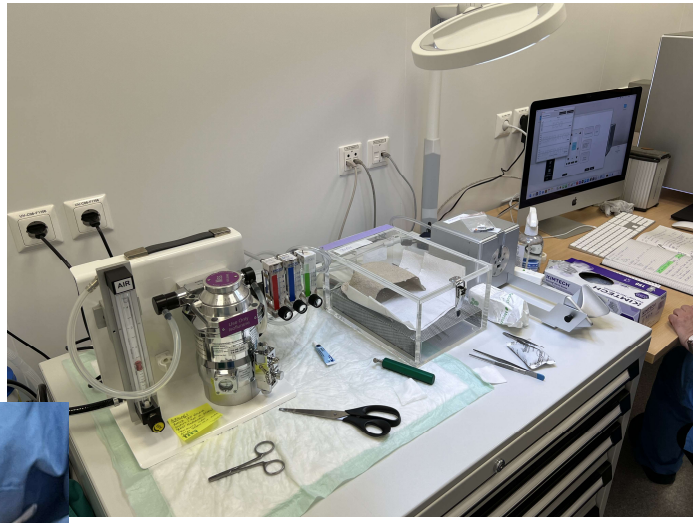
Kompetenzzentrum für Präklinische Bildgebung und Medizintechnik

FACHHOCHSCHULE
WIENER NEUSTADT
Austrian Network for Higher Education

Kompetenzzentrum für Präklinische Bildgebung und Medizintechnik

FACHHOCHSCHULE
WIENER NEUSTADT
Austrian Network for Higher Education

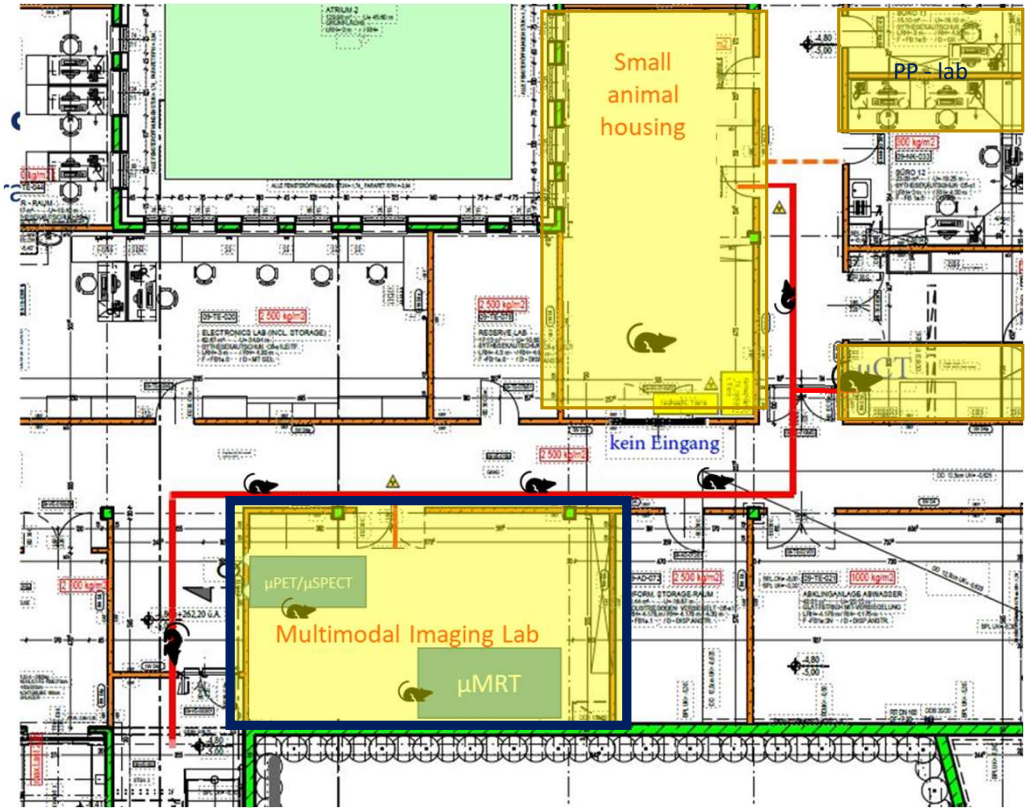


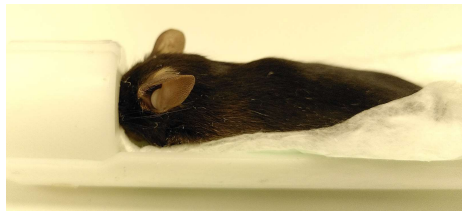


Kompetenzzentrum für Präklinische Bildgebung und Medizintechnik

FACHHOCHSCHULE
WIENER NEUSTADT
Austrian Network for Higher Education

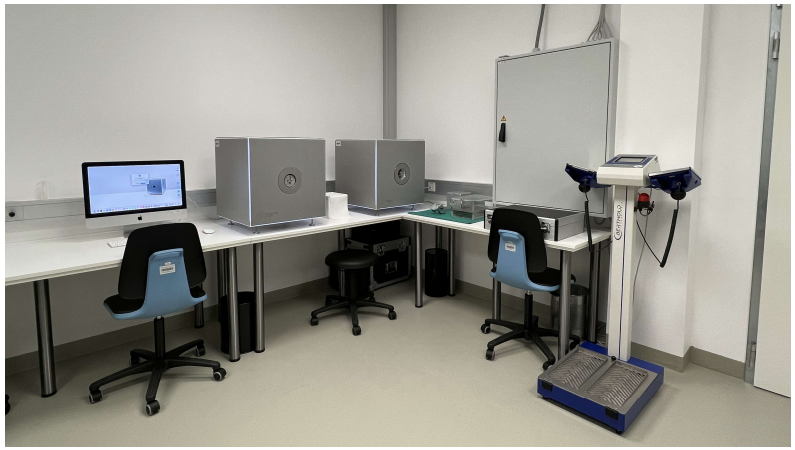
Basement

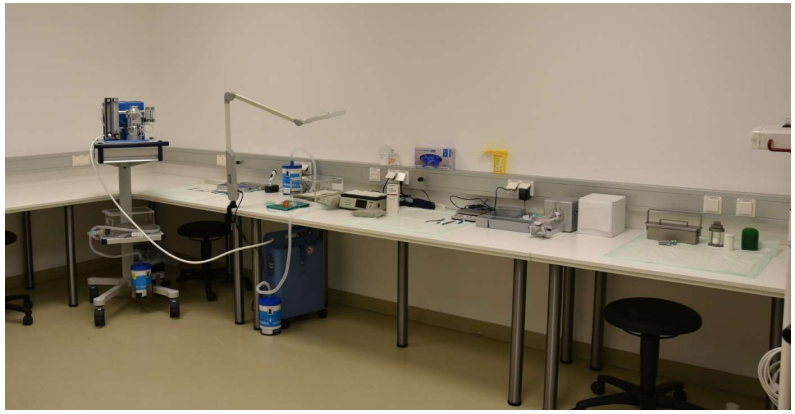




Kompetenzzentrum für Präklinische Bildgebung und Medizintechnik

FACHHOCHSCHULE
WIENER NEUSTADT
Austrian Network for Higher Education

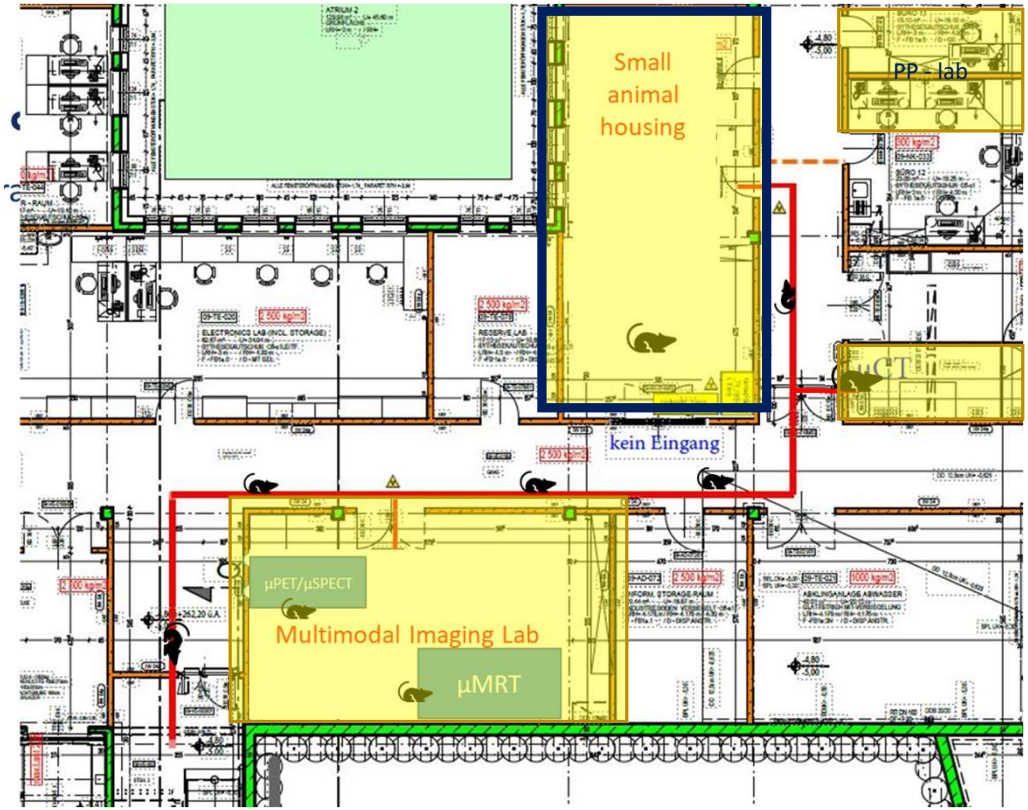




Kompetenzzentrum für Präklinische Bildgebung und Medizintechnik

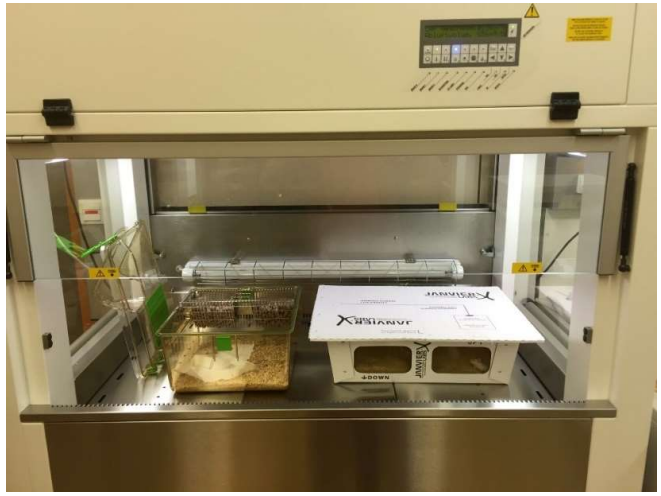
FACHHOCHSCHULE
WIENER NEUSTADT
Austrian Network for Higher Education

Basement



Kompetenzzentrum für Präklinische Bildgebung und Medizintechnik

FACHHOCHSCHULE
WIENER NEUSTADT
Austrian Network for Higher Education

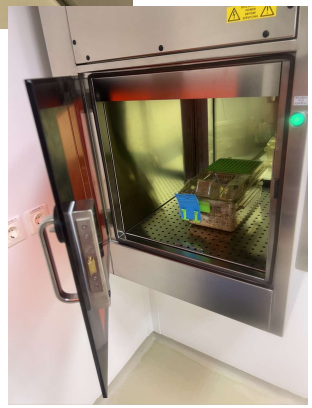
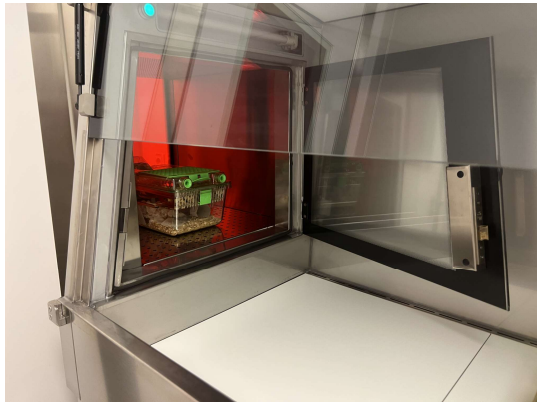


Kompetenzzentrum für Präklinische Bildgebung und Medizintechnik

FACHHOCHSCHULE
WIENER NEUSTADT
Austrian Network for Higher Education





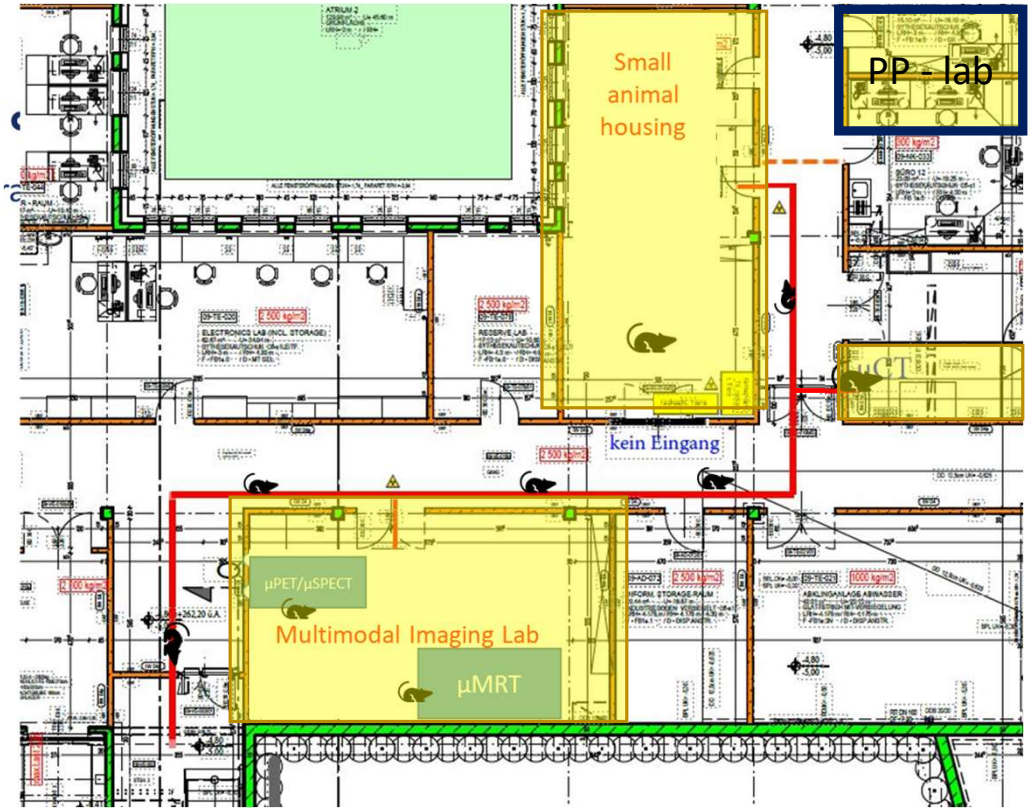




Kompetenzzentrum für Präklinische Bildgebung und Medizintechnik

Competence Center of Preclinical Imaging and Biomedical Engineering / MedAustron

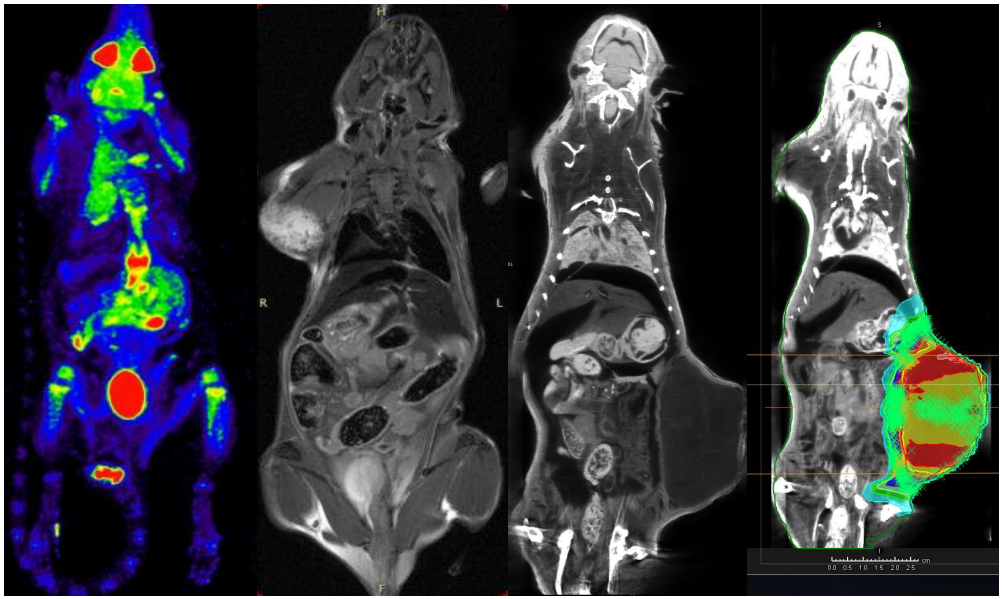
FACHHOCHSCHULE
WIENER NEUSTADT
Austrian Network for Higher Education

Basement



Kompetenzzentrum für Präklinische Bildgebung und Medizintechnik

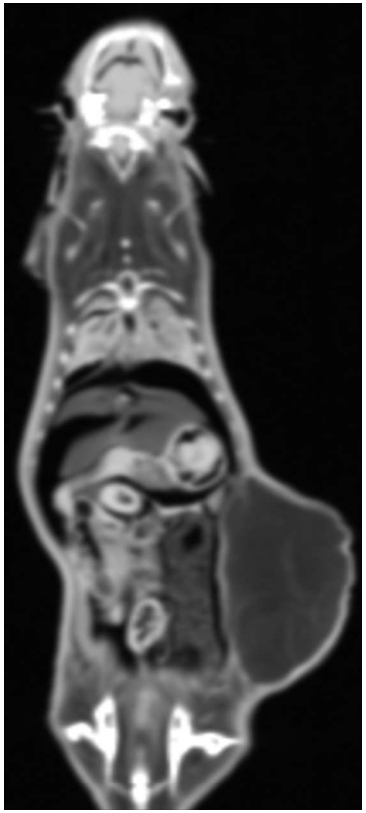
FACHHOCHSCHULE
WIENER NEUSTADT
Austrian Network for Higher Education



Beispiel – präklinische multimodale Bildgebung

FACHHOCHSCHULE
WIENER NEUSTADT
Austrian Network for Higher Education

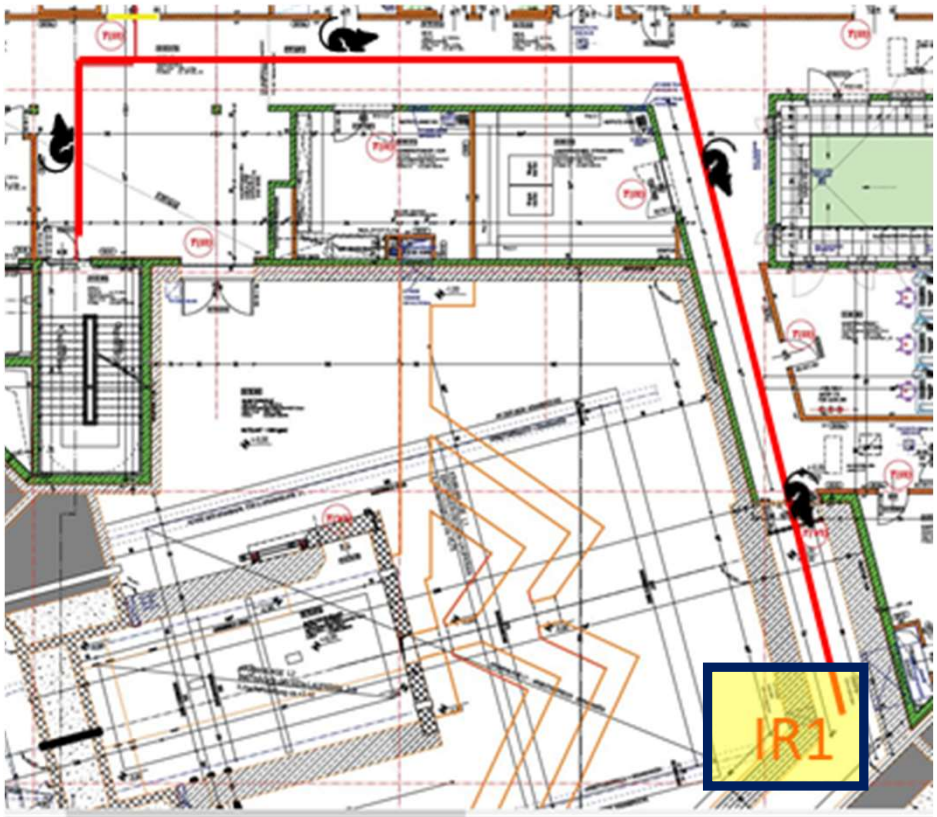
Klinisches CT versus mikroCT

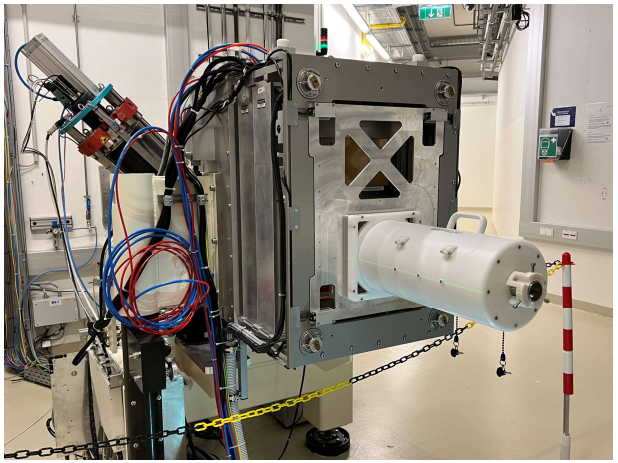


Kompetenzzentrum für Präklinische Bildgebung und Medizintechnik

FACHHOCHSCHULE
WIENER NEUSTADT
Austrian Network for Higher Education

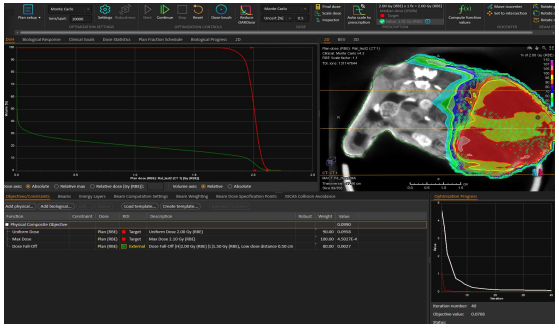
Groundfloor

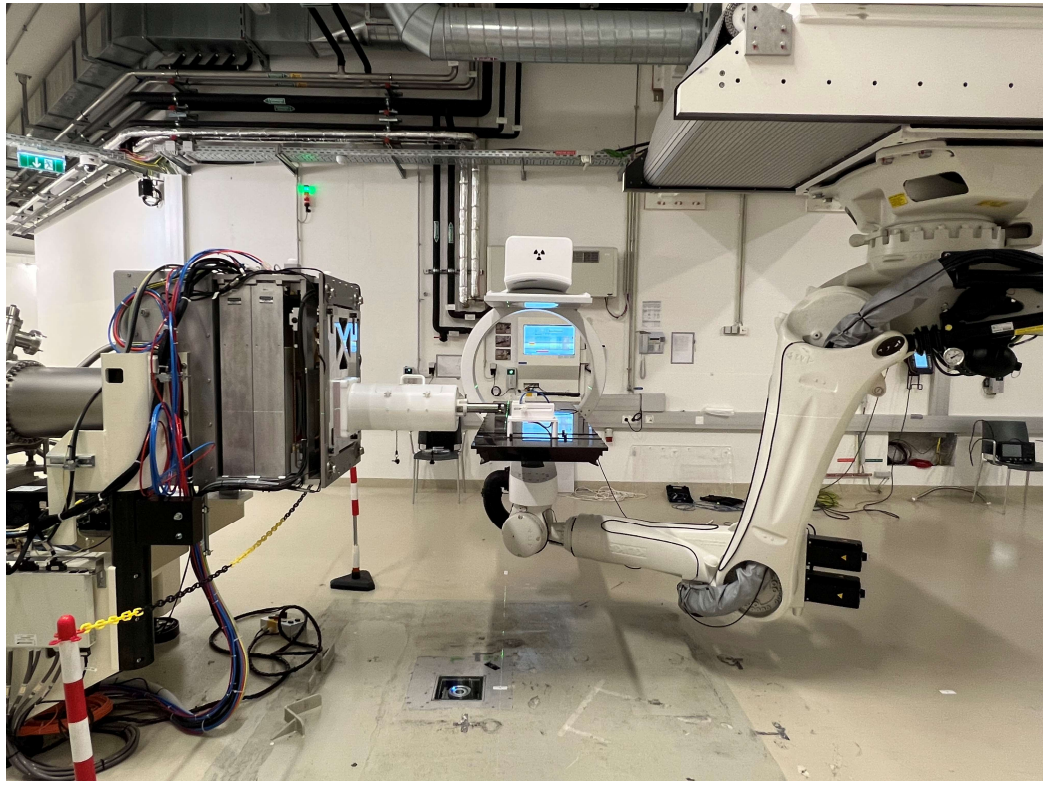


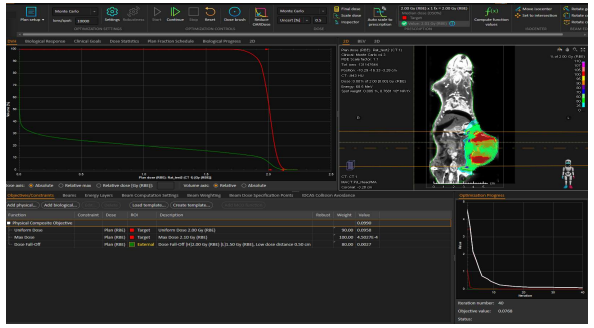


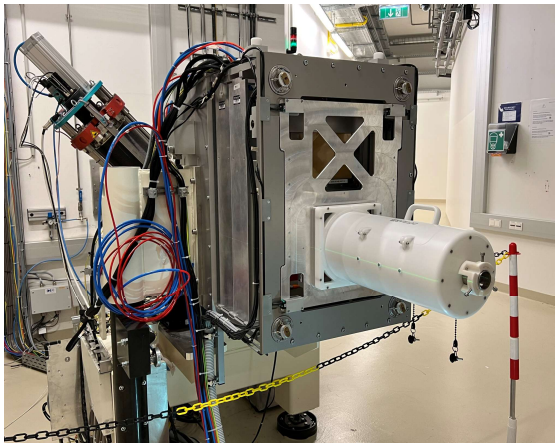
Kompetenzzentrum für Präklinische Bildgebung und Medizintechnik

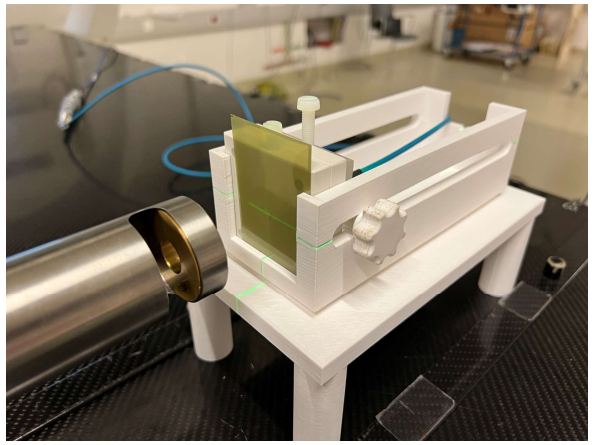
FACHHOCHSCHULE
WIENER NEUSTADT
Austrian Network for Higher Education





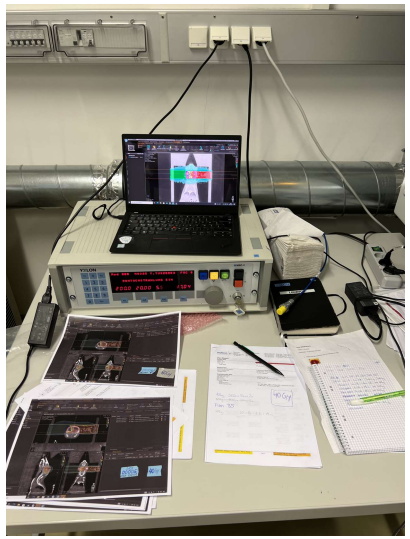


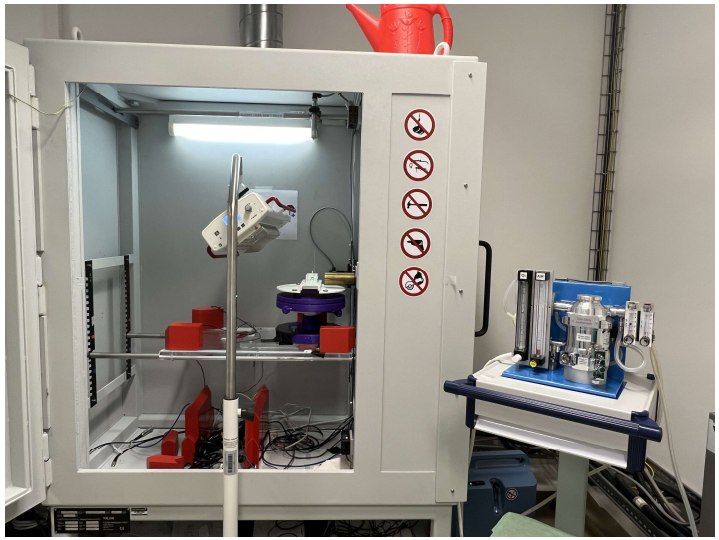


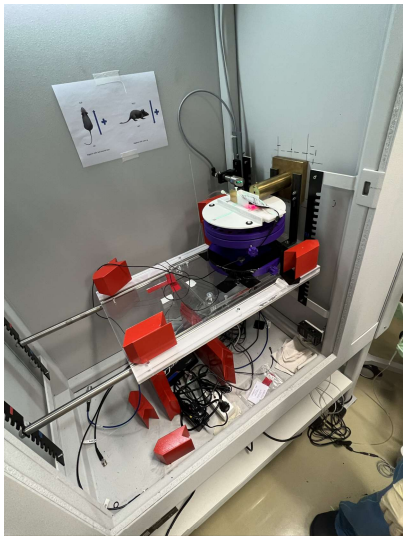


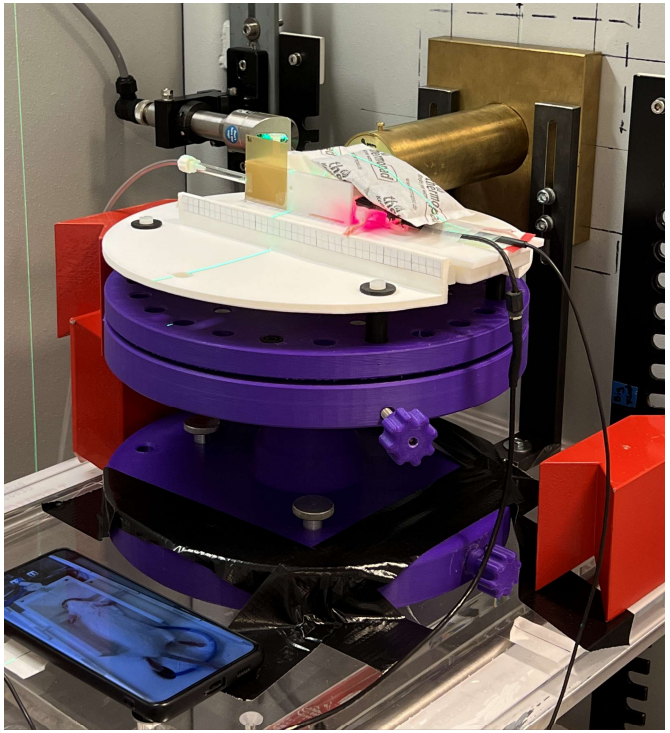
Kompetenzzentrum für Präklinische Bildgebung und Medizintechnik

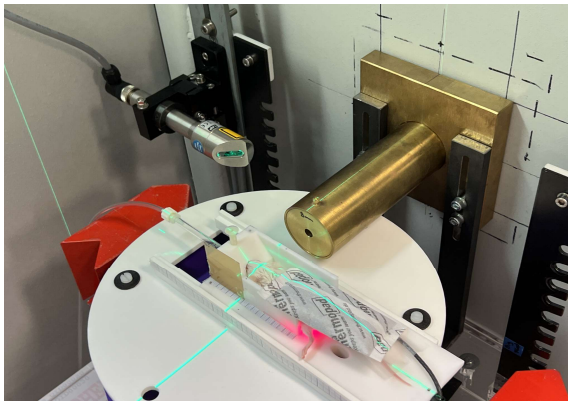
FACHHOCHSCHULE
WIENER NEUSTADT
Austrian Network for Higher Education

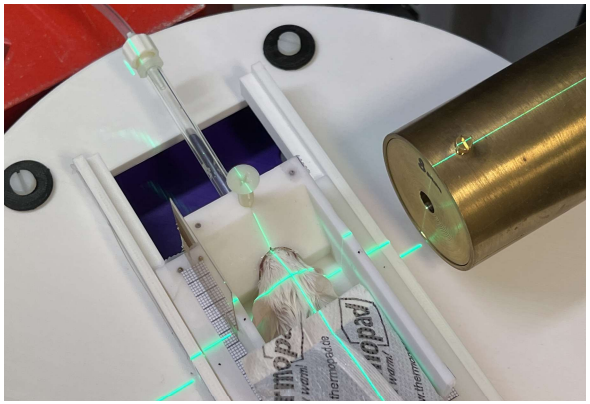












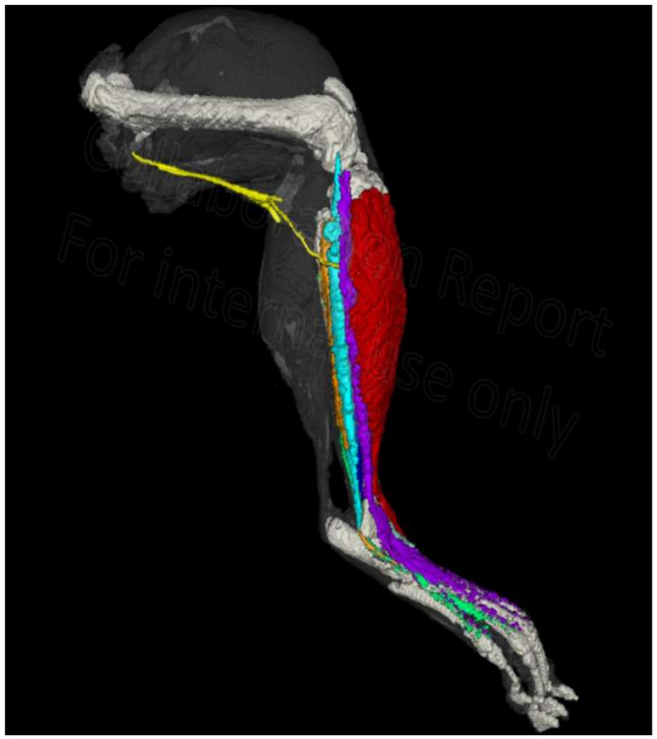
FACHHOCHSCHULE
WIENER NEUSTADT
Austrian Network for Higher Education

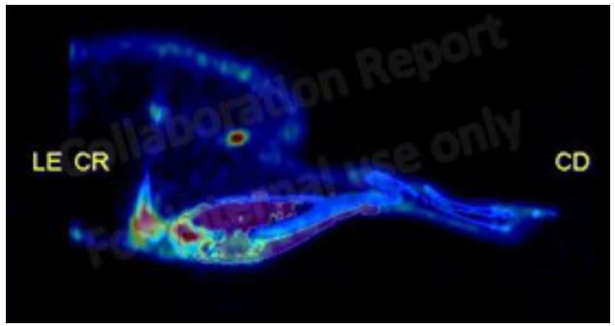
Current research activities
(Selection)

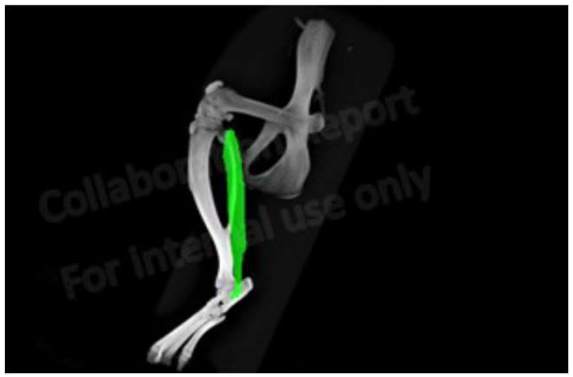
Beispiel – präklinische multimodale Bildgebung

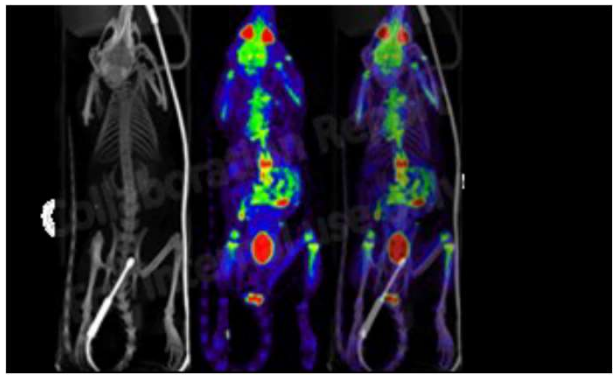
FACHHOCHSCHULE
WIENER NEUSTADT
Austrian Network for Higher Education

Kooperationsprojekt – periphere Nervenregeneration









Beispiel – präklinische multimodale Bildgebung

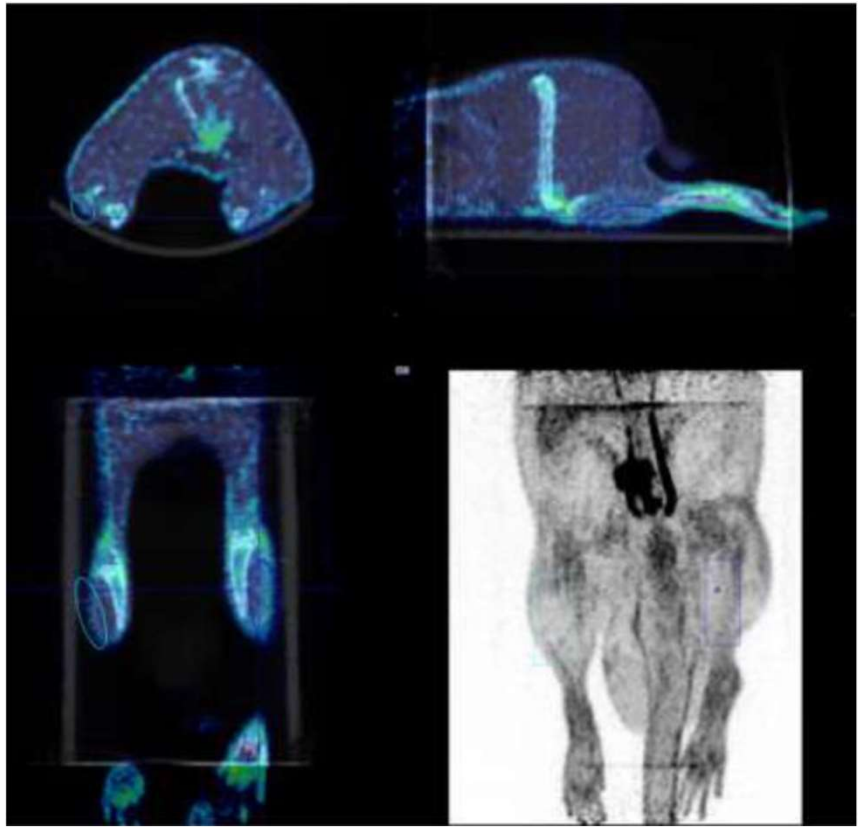
Kooperationsprojekt – periphere Nervenregeneration

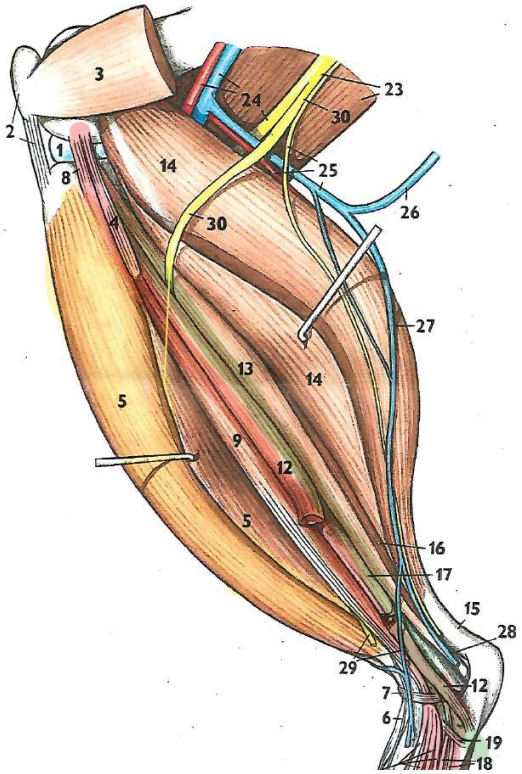
FACHHOCHSCHULE
WIENER NEUSTADT
Austrian Network for Higher Education

Beispiel – präklinische multimodale Bildgebung

FACHHOCHSCHULE
WIENER NEUSTADT
Austrian Network for Higher Education

Kooperationsprojekt – periphere Nervenregeneration

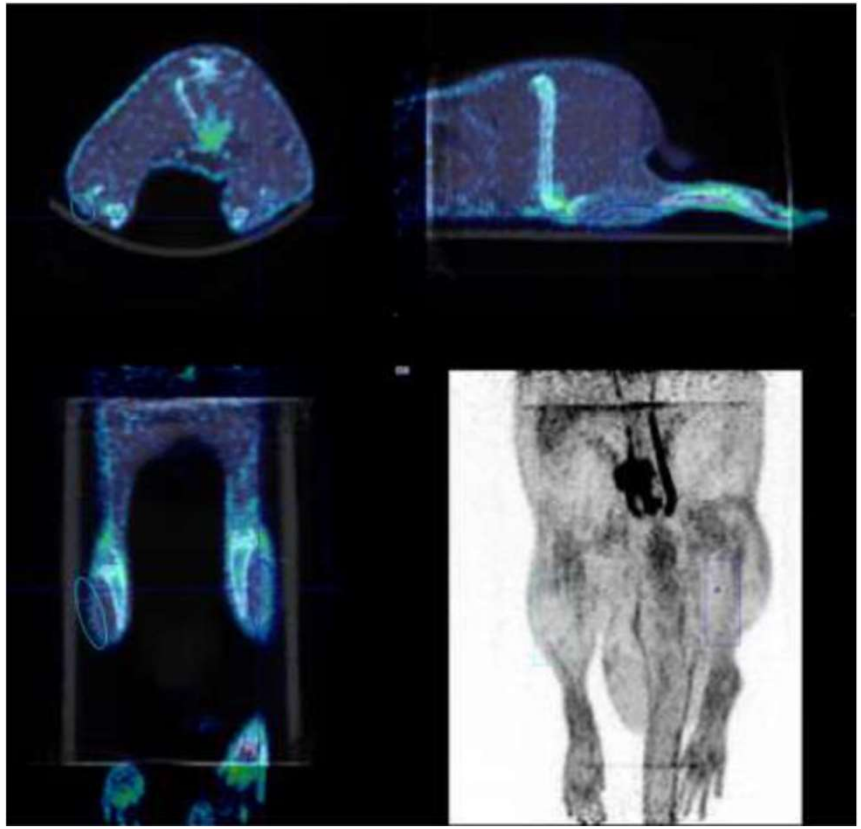


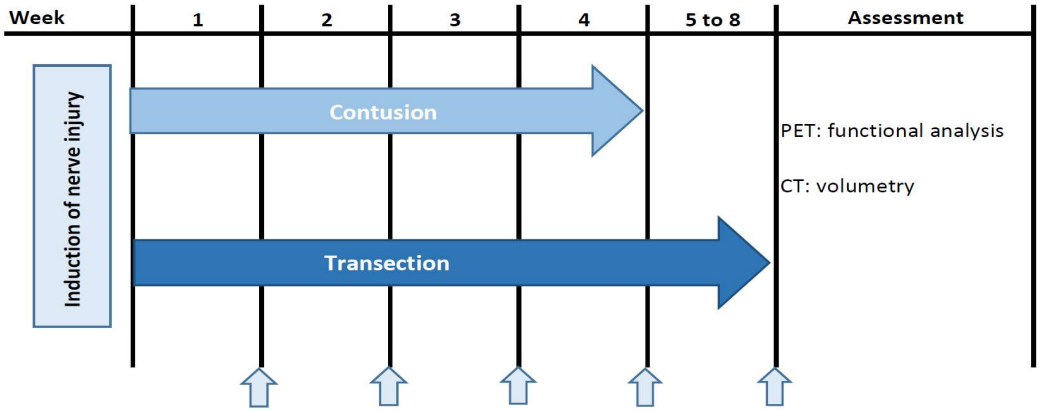


Beispiel – präklinische multimodale Bildgebung

FACHHOCHSCHULE
WIENER NEUSTADT
Austrian Network for Higher Education

Kooperationsprojekt – periphere Nervenregeneration



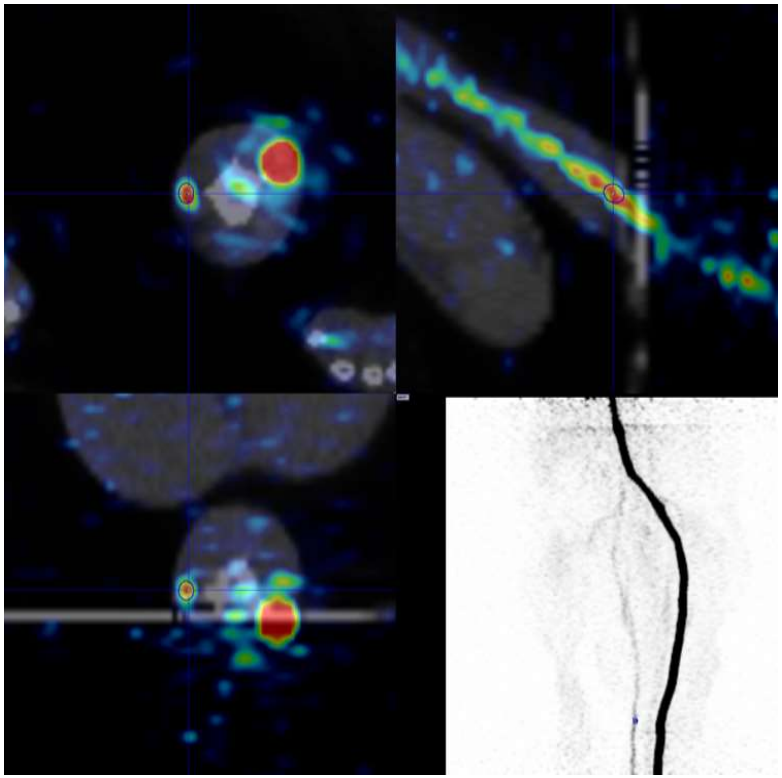


PET	
Axial scan length	127 mm
Injected activity	45 MBq
Time p.i.	60 min
PET scan duration	20 min
Energy window	350-650 keV
Timing window	3.438 ns
Attenuation correction	CT scan
Reconstruction algorithm	OSEM3D/MAP
Resolution	1.5 mm

Beispiel – präklinische multimodale Bildgebung

FACHHOCHSCHULE
WIENER NEUSTADT
Austrian Network for Higher Education

Kooperationsprojekt – periphere Nervenregeneration

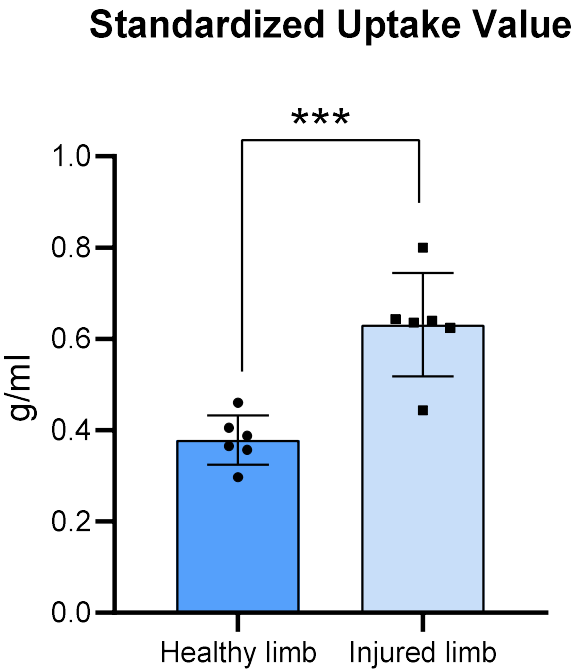


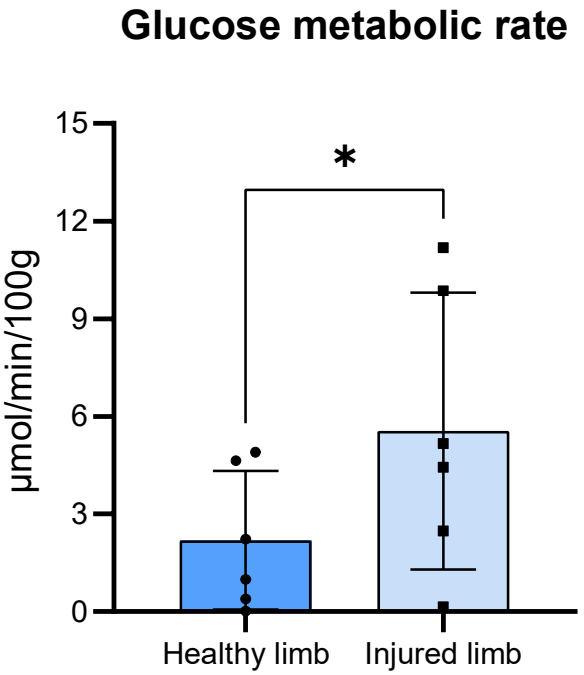
Parameter	Current value	% SE	Conf.low	Conf.high	Unit
Lumped Constant	0.89	---	---	---	1/1
Plasma Gluc.	5.0	---	---	---	mmol/l
vB	0.010178	7.57	0.00846	0.0119	1/1
K1	0.051644	3.33	0.04782	0.05547	ml/ccm/min
k2	0.186626	4.66	0.16724	0.20601	1/min
k3	0.002694	21.91	0.00138	0.00401	1/min
k4	0.0	---	---	---	1/min
Flux	7.34949E-4	19.93	4.08596E-4	0.00106	ml/ccm/min
MRGlu.	0.397012	19.93	0.22072	0.5733	µmol/min/100g
Vs	NaN	---	---	---	ml/ccm
Vt	NaN	---	---	---	ml/ccm

Parameter	Current value
DOF	10.0
SumSquared	0.870949
ChiSquare	0.517325
AIC	-1.493352
SC	-3.381567
MSC	5.622161
R2	0.997958
Sy.x	0.295118
Runs test p	0.760237
AUC	60568.695138

Beispiel – präklinische multimodale Bildgebung

Kooperationsprojekt – periphere Nervenregeneration

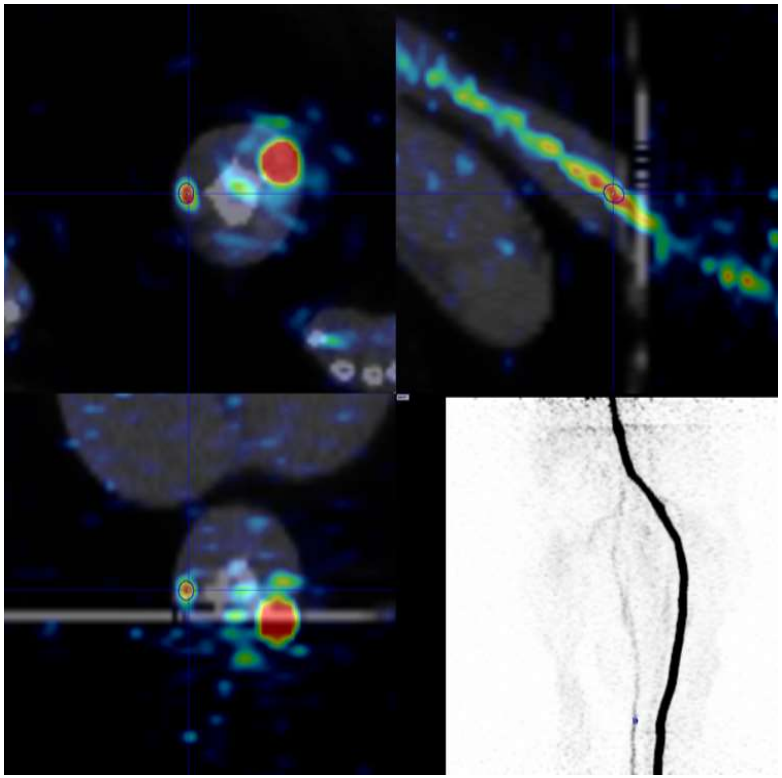


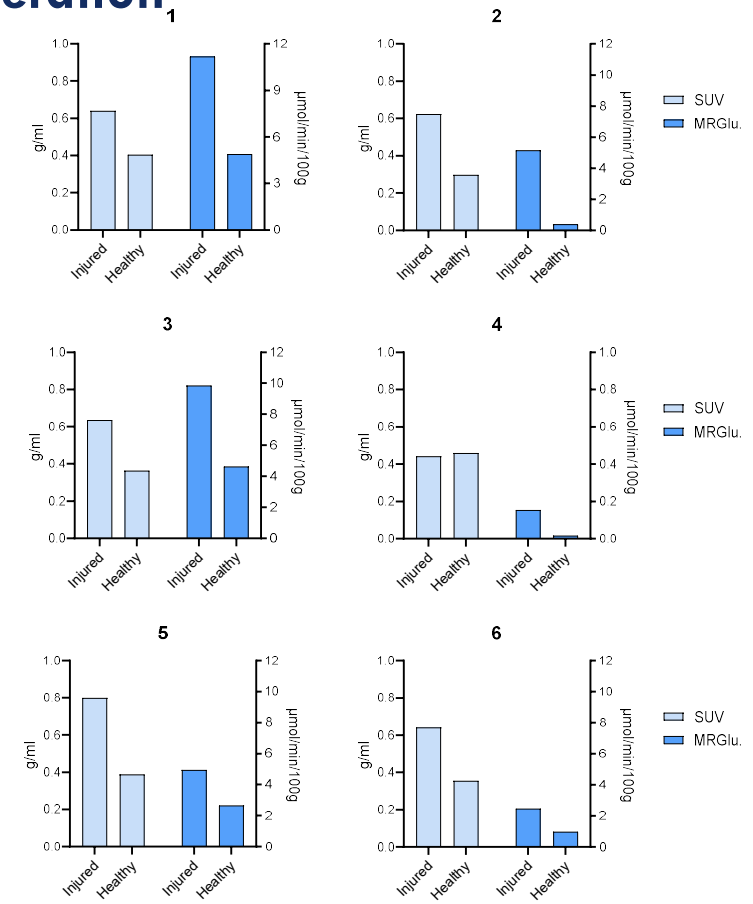


Beispiel – präklinische multimodale Bildgebung

FACHHOCHSCHULE
WIENER NEUSTADT
Austrian Network for Higher Education

Kooperationsprojekt – periphere Nervenregeneration



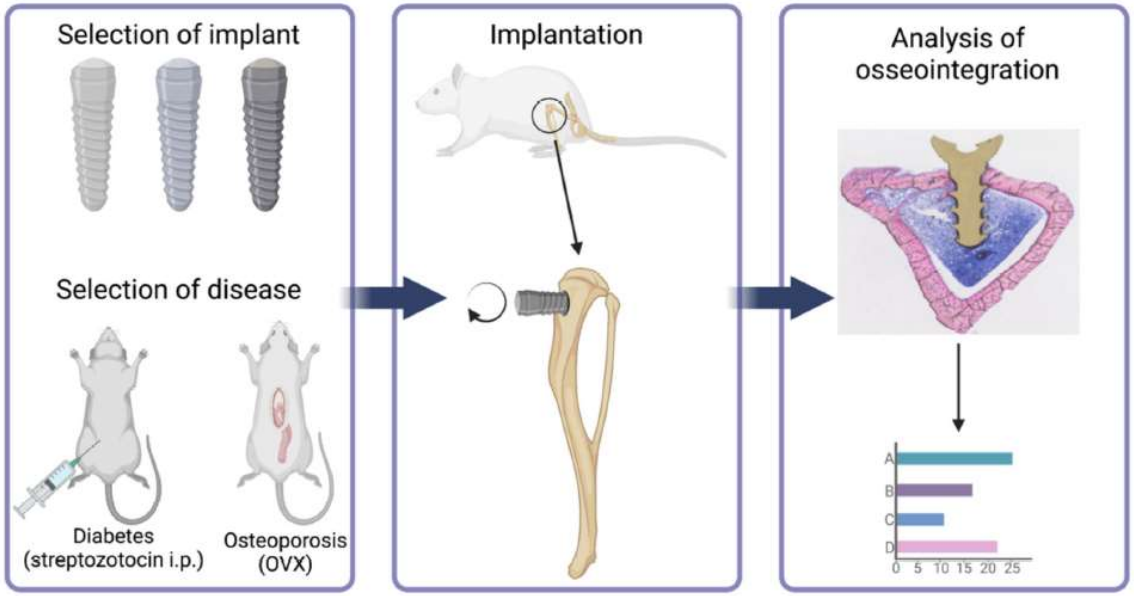


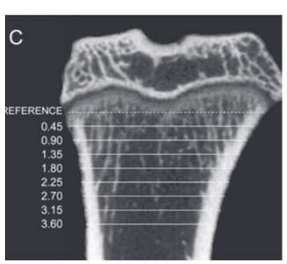
Beispiel – präklinische multimodale Bildgebung

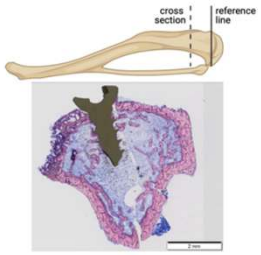
FACHHOCHSCHULE
WIENER NEUSTADT
Austrian Network for Higher Education

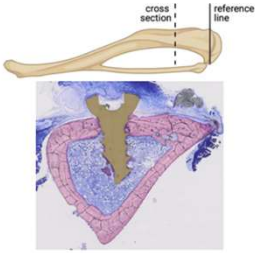
FWF Project

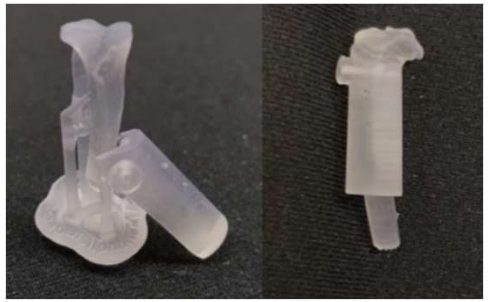
“PRECISE – Development of 3D-printed surgical guides to standardize, refine and reduce animal experiments in osseointegration research“









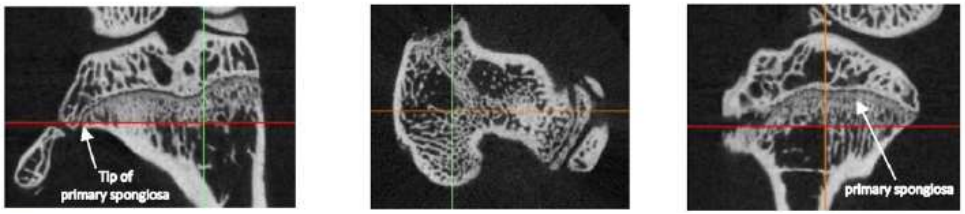


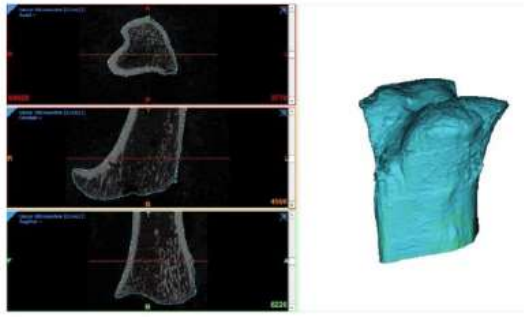
Beispiel – präklinische multimodale Bildgebung

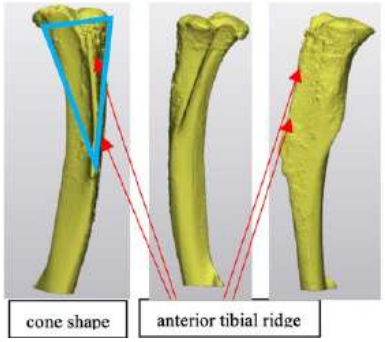
FACHHOCHSCHULE
WIENER NEUSTADT
Austrian Network for Higher Education

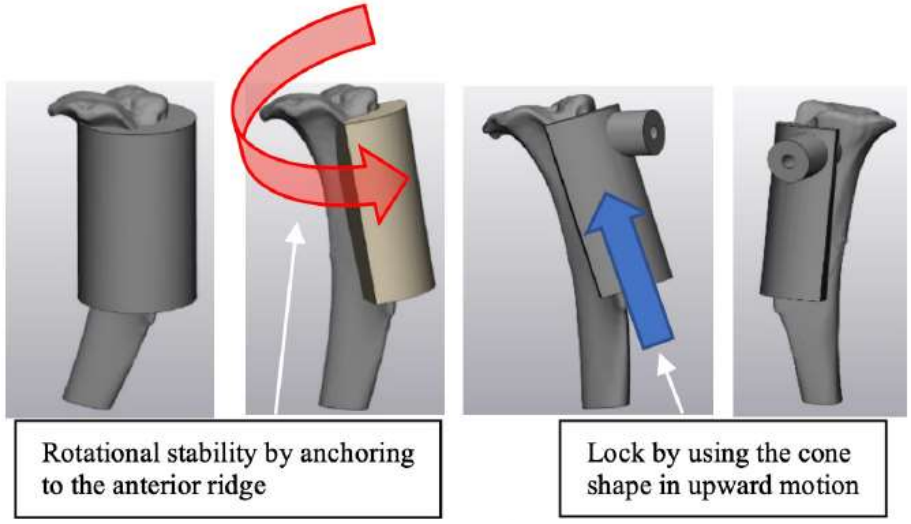
FWF Project

“PRECISE – Development of 3D-printed surgical guides to standardize, refine and reduce animal experiments in osseointegration research“



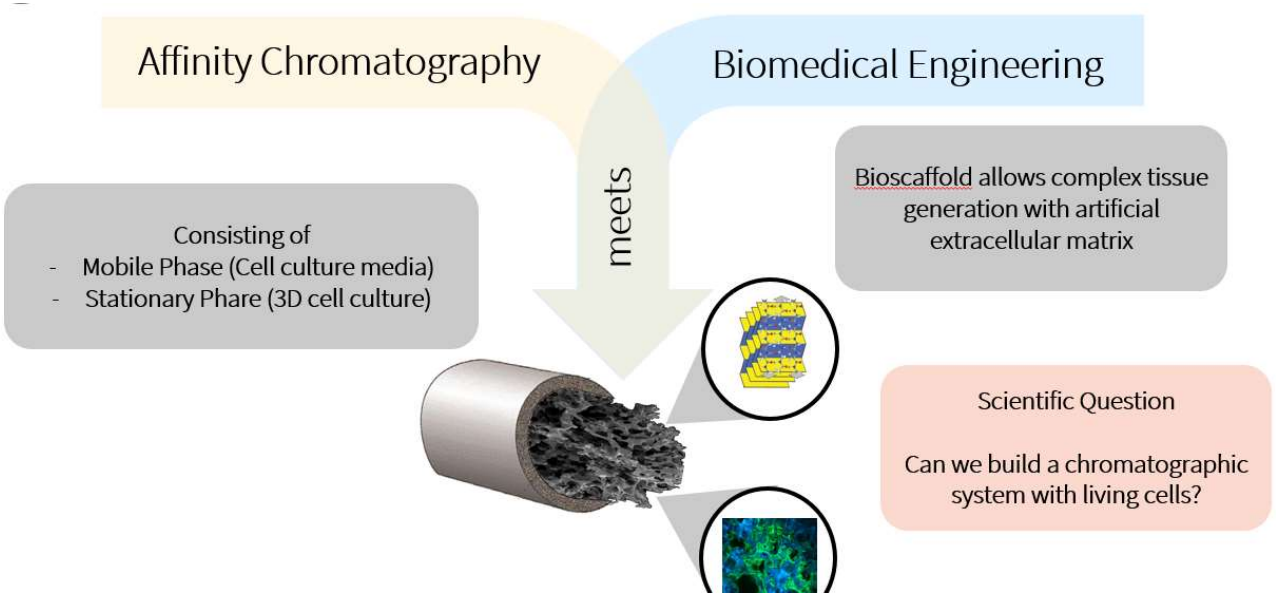


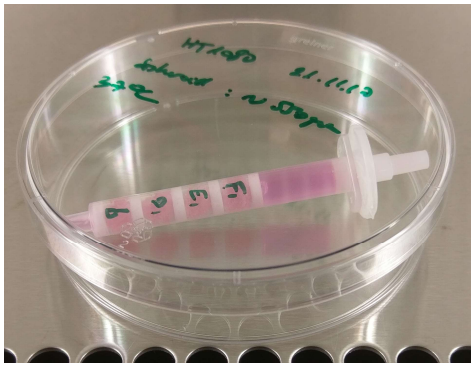




Beispiel – präklinische multimodale Bildgebung

Spheriograph





Beispiel – präklinische multimodale Bildgebung

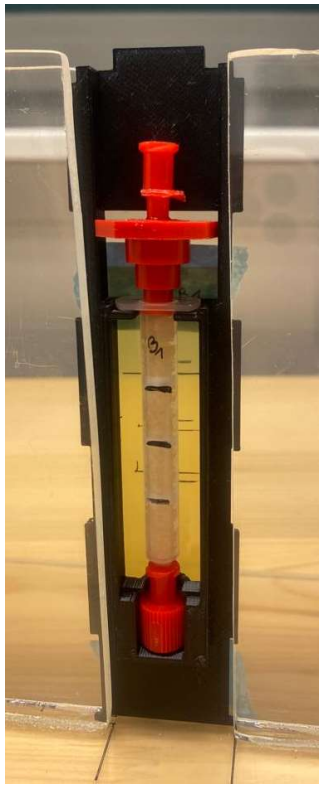
Spheriograph

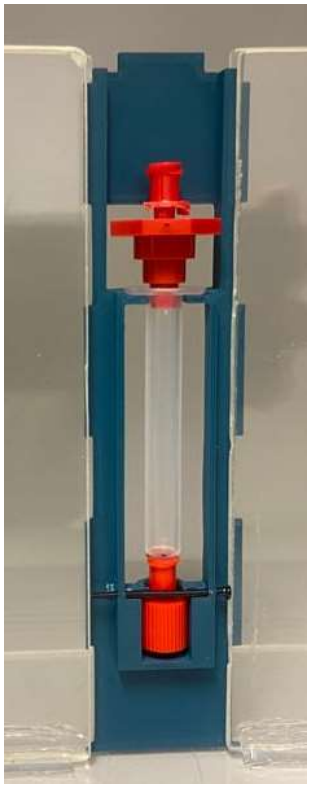
3 different groups of 3 spheriographs with 4 compartments each (silk incl. Colon Ca cells)

- Group A – Photons
- Group B – Protons
- Group C – Control Group

1 group à 3 spheriographs containing only silk

- Group E





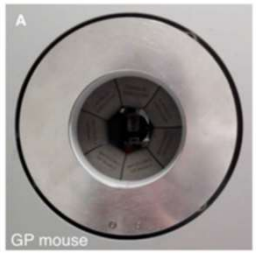
Beispiel – präklinische multimodale Bildgebung

FACHHOCHSCHULE WIENER NEUSTADT
Austrian Network for Higher Education

Spheriograph

µSPECT (γ – Cube) System, Molecubes, Ghent	
Generator	Curium, 2,15 GBq
Nuclide	[Tc^{99m}]
Tracer	Sestamibi (MIBI)
Accumulation period	30 min
Acquisition duration	10 min
FOV	4,5 – 8nenn
Reconstruction parameter	MLEM, iterative, 500µm und 250 µm

µSPECT



	GP mouse
FOV	31 x 196 mm
Spatial resolution	0.7 mm
Bore size	32 mm

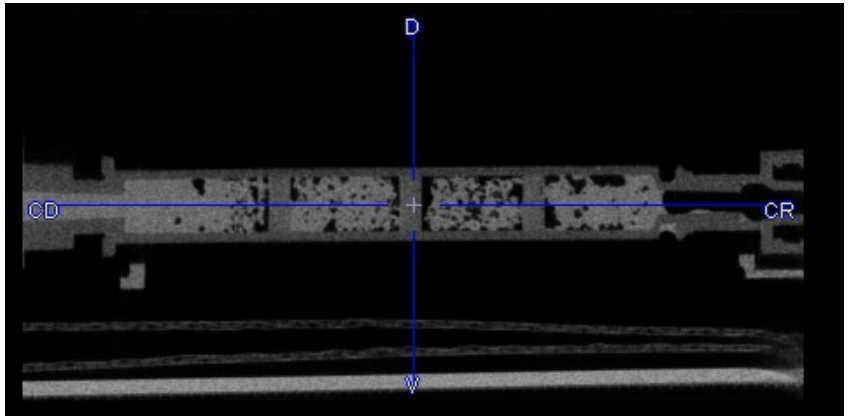
Beispiel – präklinische multimodale Bildgebung

FACHHOCHSCHULE
WIENER NEUSTADT
Austrian Network for Higher Education

Spheriograph

µCT (X-Cube) System, Molecubes, Ghent	
Acquisition	HR Scan (High resolution)
Reconstrucion	iterative, 200µm und 100 µm

- One x-ray source
- Cone shaped X-ray beam
- Fixed geometry
- Focal spot size: 33µm
- Tungsten anode
- Filter: 0.8 mm Aluminium filter
- Detector material: CsI



Beispiel – präklinische multimodale Bildgebung

FACHHOCHSCHULE
WIENER NEUSTADT
Austrian Network for Higher Education

Set up - Biology

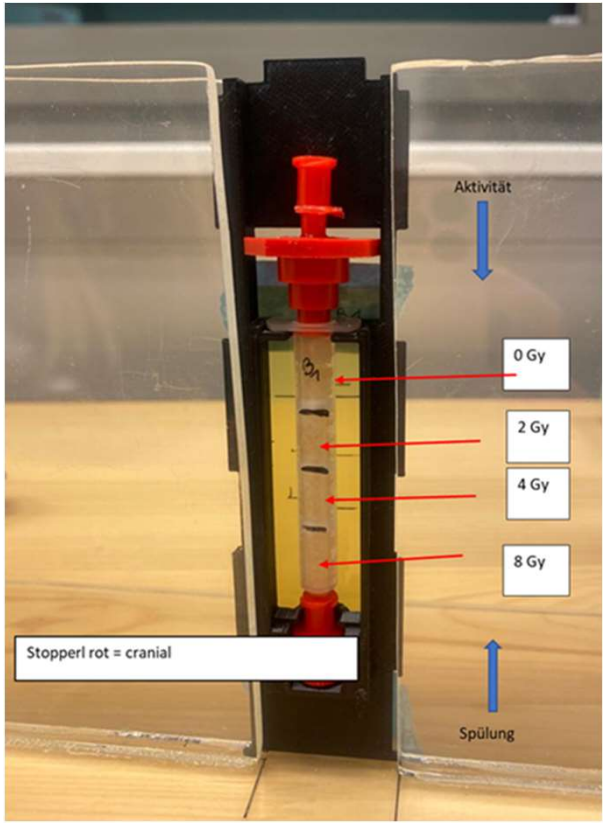
- Flushing with RPMI (Cell culture medium)
- Inducing activity: caudo – cranial
- Flushing: cranio - caudal
- No sterile filter used
- Incubation chamber at37°C, without CO2
- Cell death with MTT Essay

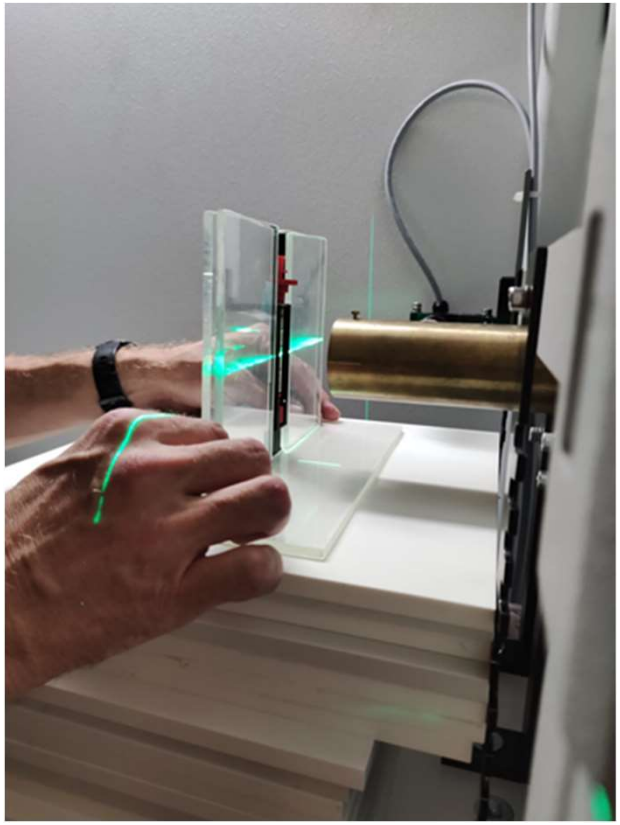
Beispiel – präklinische multimodale Bildgebung

FACHHOCHSCHULE
WIENER NEUSTADT
Austrian Network for Higher Education

Irradiation with photons and protons

- Photon irradiation group A
- Proton irradiation group B
- Same positioning for imaging and irradiation
- Start with 2 Gy
- Usage of plates for adjusting the height

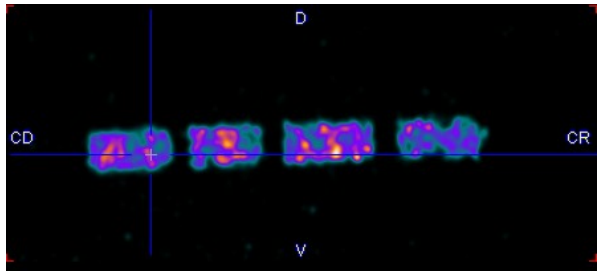




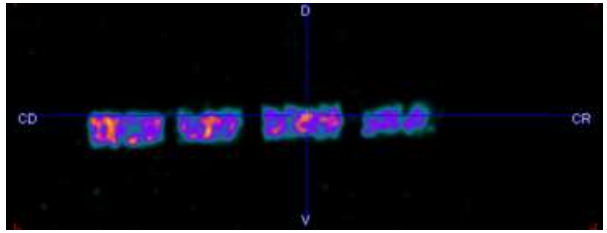
Beispiel – präklinische multimodale Bildgebung

FACHHOCHSCHULE
WIENER NEUSTADT
Austrian Network for Higher Education

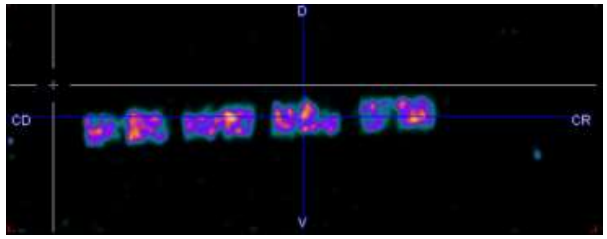
Unspecific binding



E1 – Silk only, without colon ca cells – 5,2 MBq



A1_PI_Tag1 – irradiation with photons – 5,5 MBq



B1_PI_Tag1 – irradiation with protons – 5,4 MBq

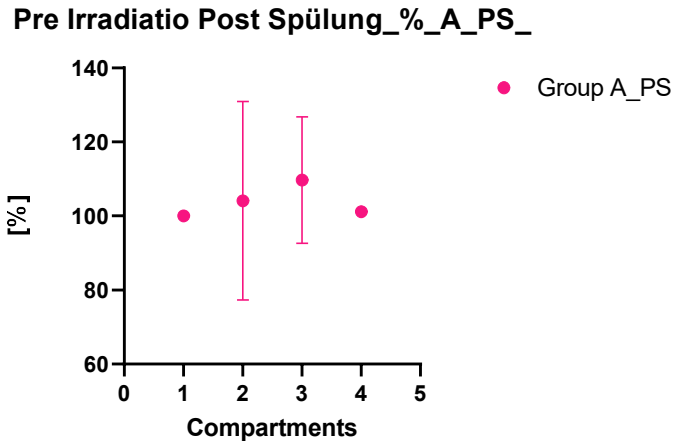
Beispiel – präklinische multimodale Bildgebung

FACHHOCHSCHULE WIENER NEUSTADT
Austrian Network for Higher Education

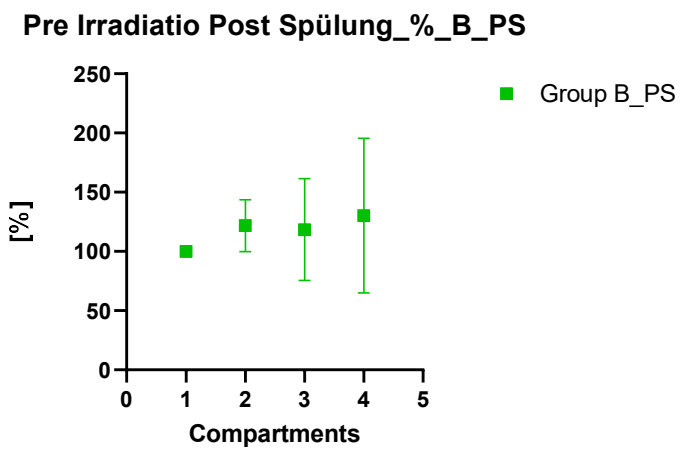
Graph Pad Prism

Day 0 – Pre irradiation % normalisation to compartment 1

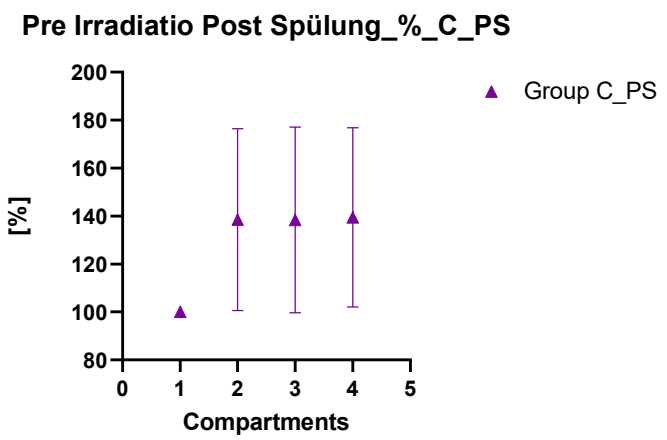
Group A



Group B



Group C



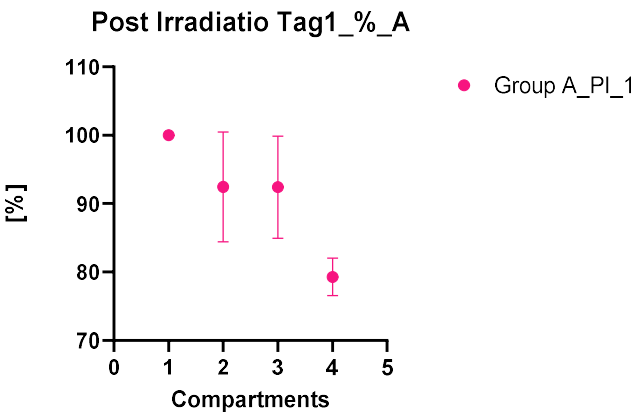
Beispiel – präklinische multimodale Bildgebung

FACHHOCHSCHULE WIENER NEUSTADT
Austrian Network for Higher Education

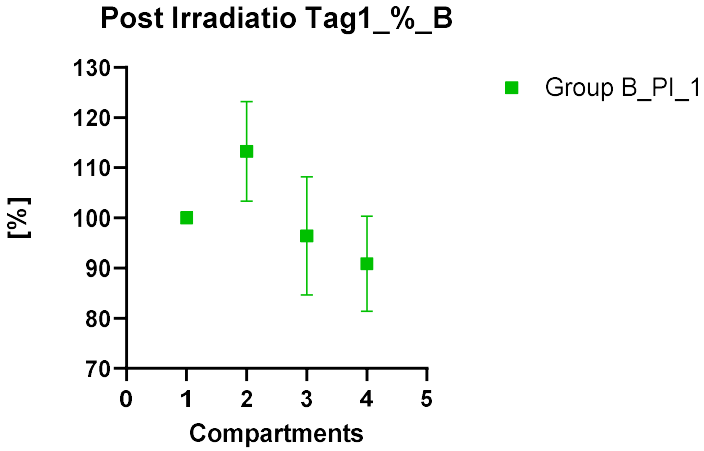
Graph Pad Prism

Day 1 – Post irradiation % normalisation to compartment 1

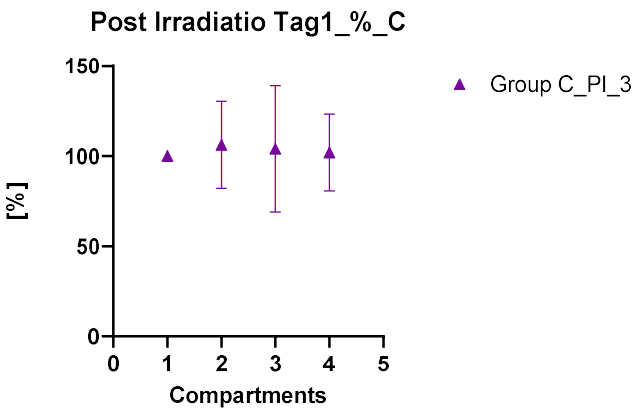
Group A



Group B



Group C



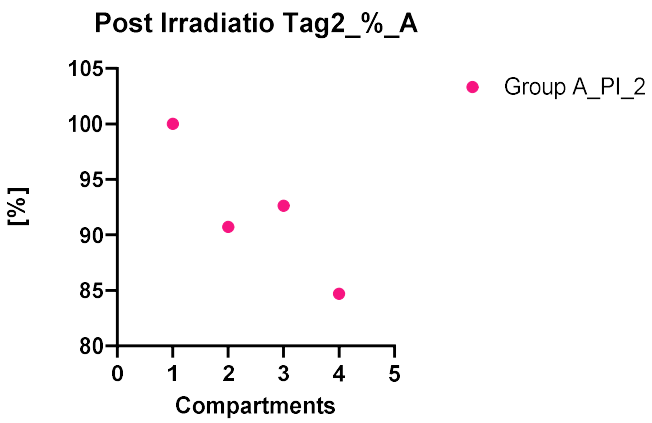
Beispiel – präklinische multimodale Bildgebung

FACHHOCHSCHULE WIENER NEUSTADT
Austrian Network for Higher Education

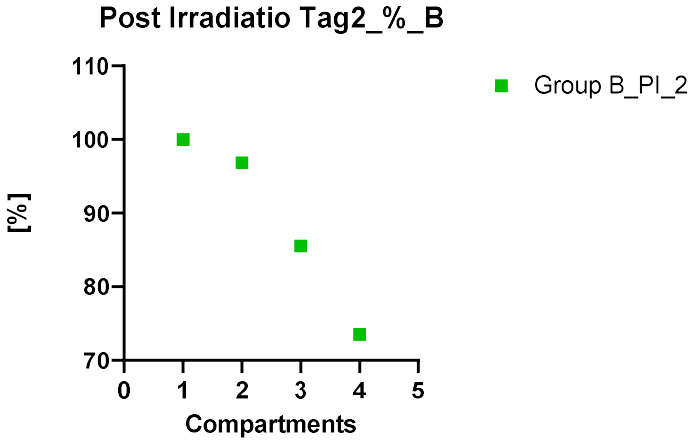
Graph Pad Prism

Day 2 – Post irradiation % normalisation to compartment 1

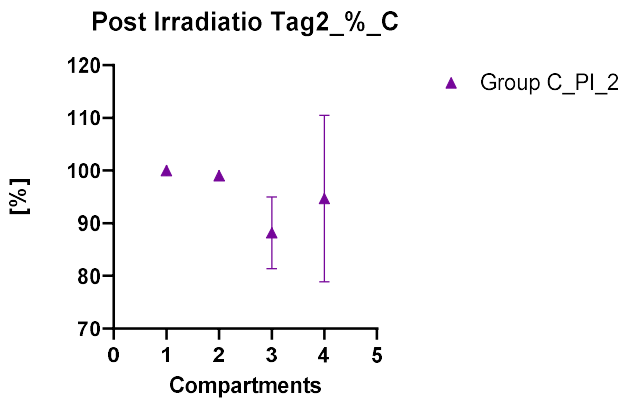
Group A



Group B



Group C



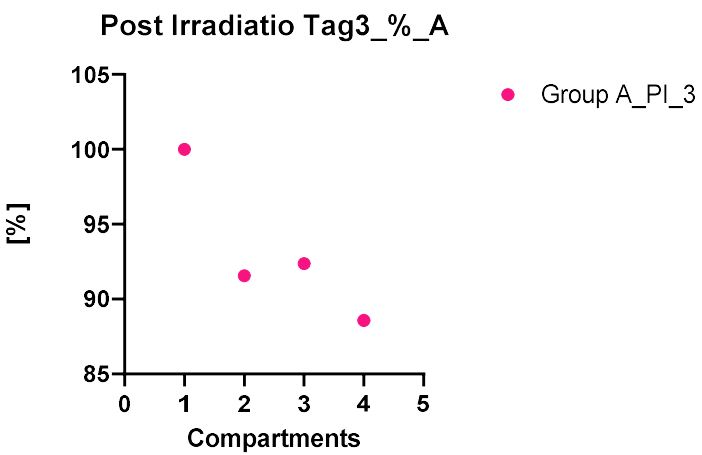
Beispiel – präklinische multimodale Bildgebung

FACHHOCHSCHULE WIENER NEUSTADT
Austrian Network for Higher Education

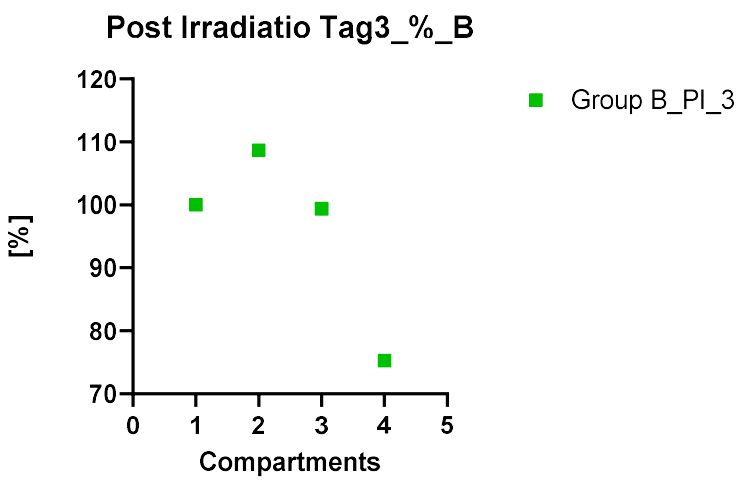
Graph Pad Prism

Day 3 – Post irradiation % normalisation to compartment 1

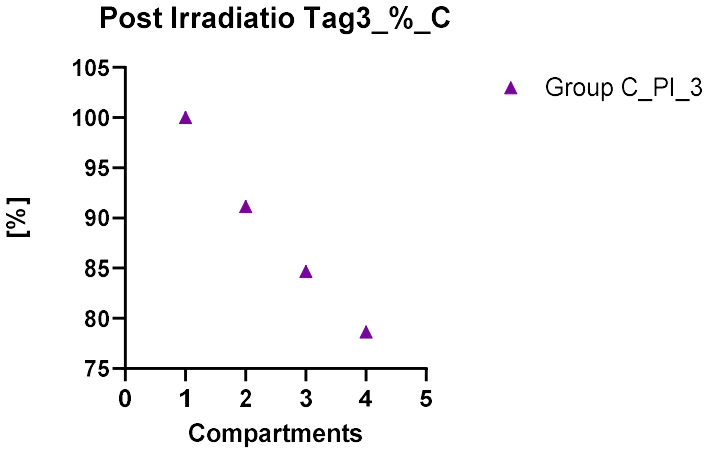
Group A



Group B



Group C



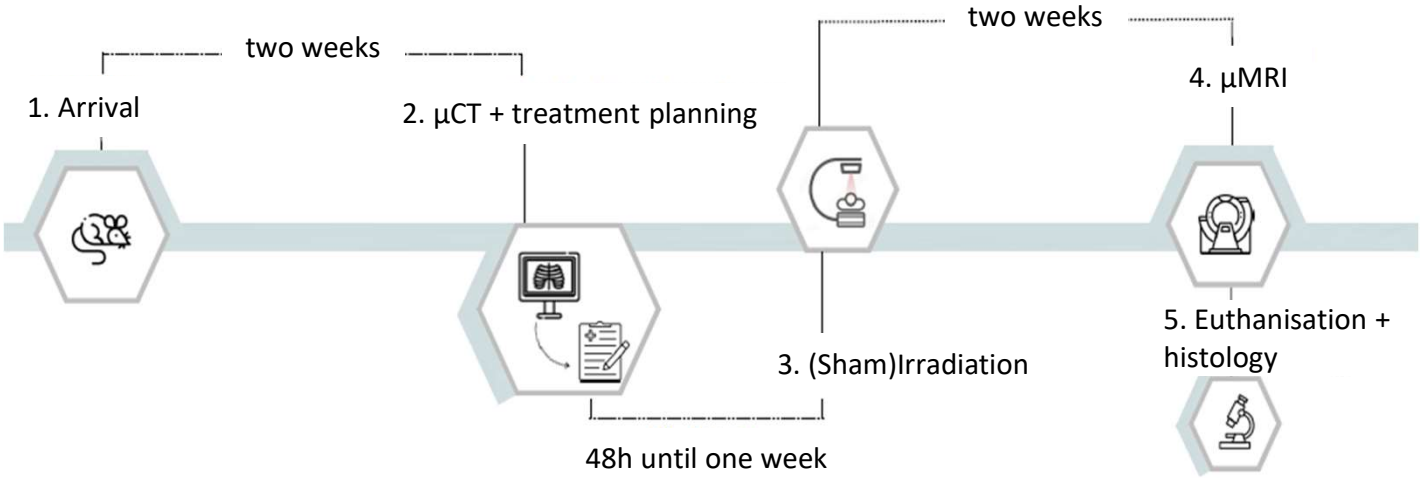
Beispiel – präklinische multimodale Bildgebung

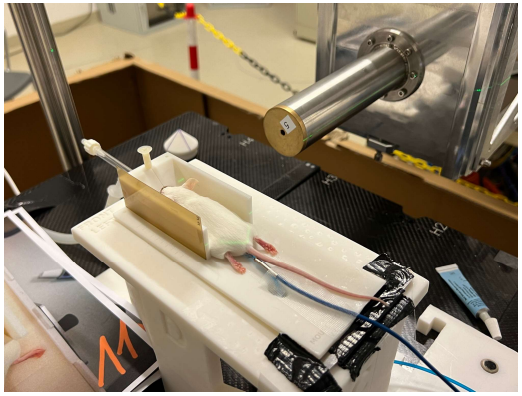
FACHHOCHSCHULE WIENER NEUSTADT
Austrian Network for Higher Education

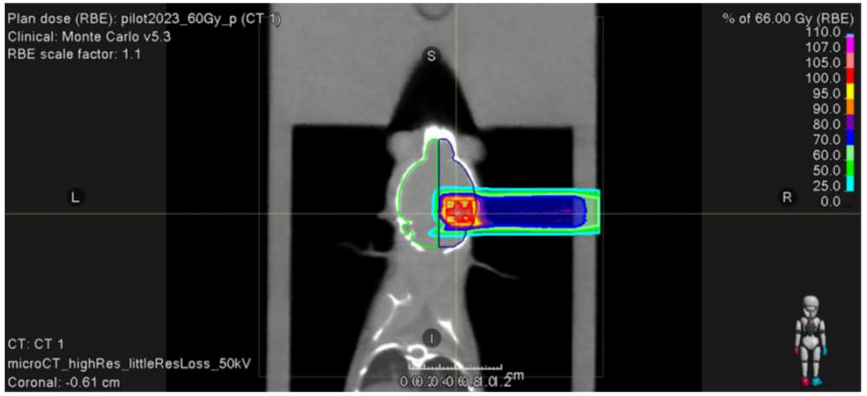
Whole-Brain mouse irradiation to study normal tissue complications (NTC)

PILOT study:

- 15 female Balb/c mice, 6-8 Wochen
- Evaluation of potential pain with MGS scoring
- Pain management with Carprofen: s.c. (10mg/kg BW) via tip water (5mg/L)
- Evaluation of normal tissue complications after brain irradiation with photons and protons
- Validation of the methodological and technical set-up







Beispiel – präklinische multimodale Bildgebung

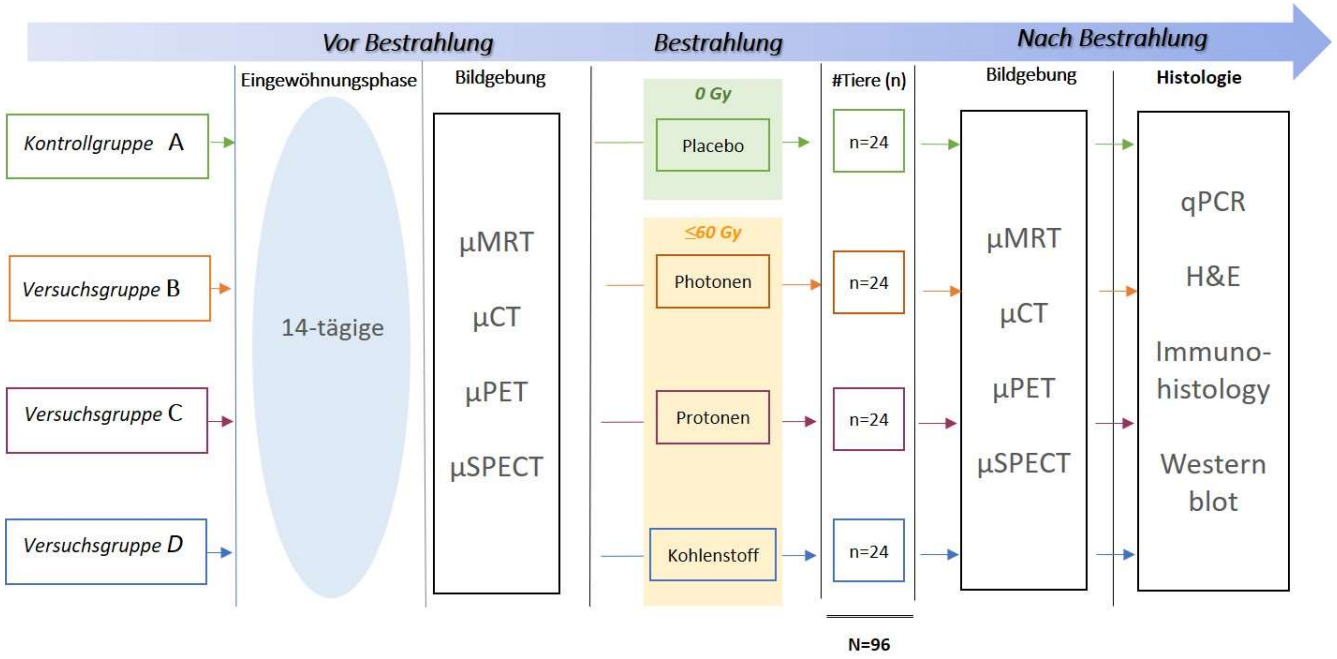
FACHHOCHSCHULE WIENER NEUSTADT
Austrian Network for Higher Education

Whole-Brain mouse irradiation to study normal tissue complications (NTC)

Main study:

- 102 Balb/c mice, 8-12 Wochen
- Pain management with Carprofen: s.c. (10mg/kg BW) via tip water (5mg/L)
- Evaluation of normal tissue complications after brain irradiation with photons and protons and carbon ions
- Validation of the methodological and technical set-up

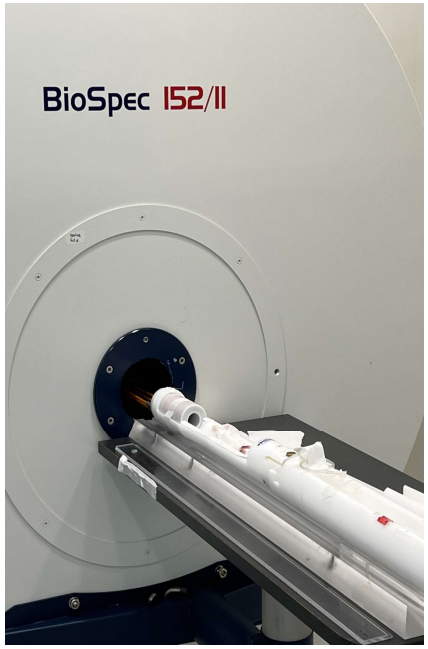
Study design

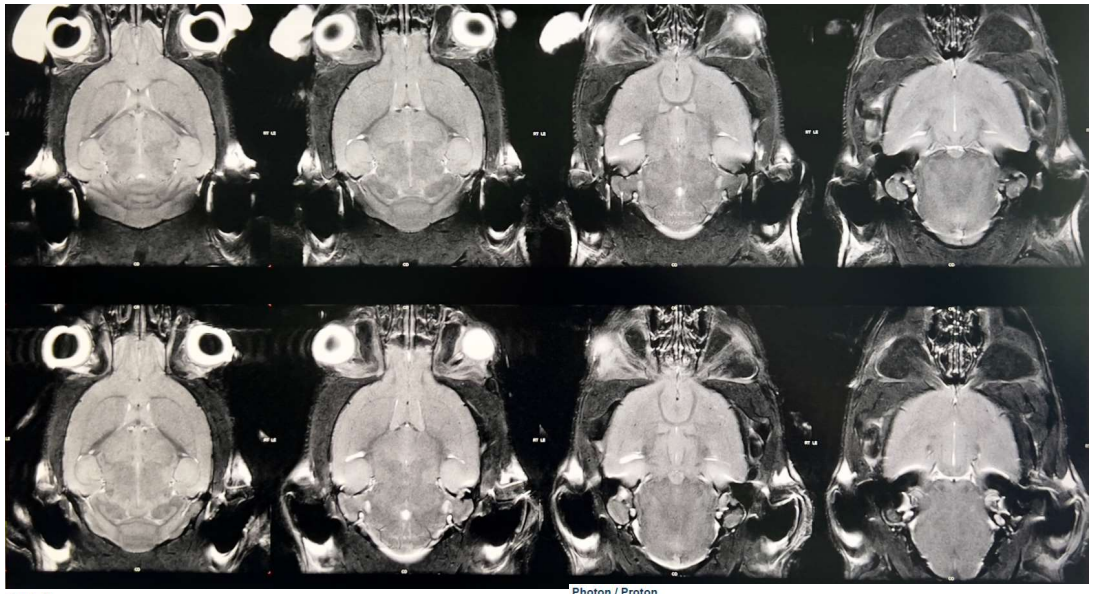


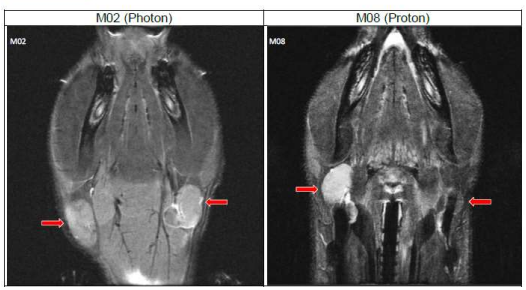
Beispiel – präklinische multimodale Bildgebung

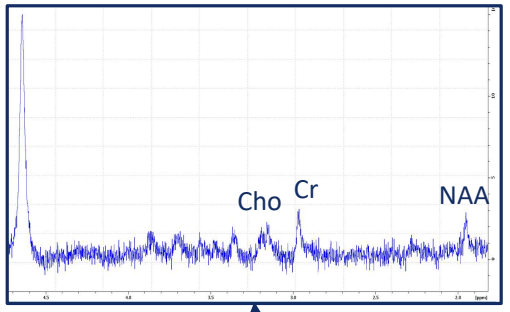
FACHHOCHSCHULE
WIENER NEUSTADT
Austrian Network for Higher Education

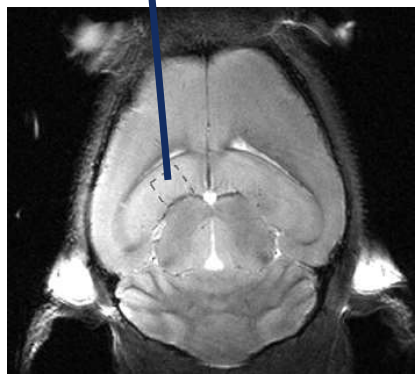
Whole-Brain mouse irradiation to study normal tissue complications (NTC)







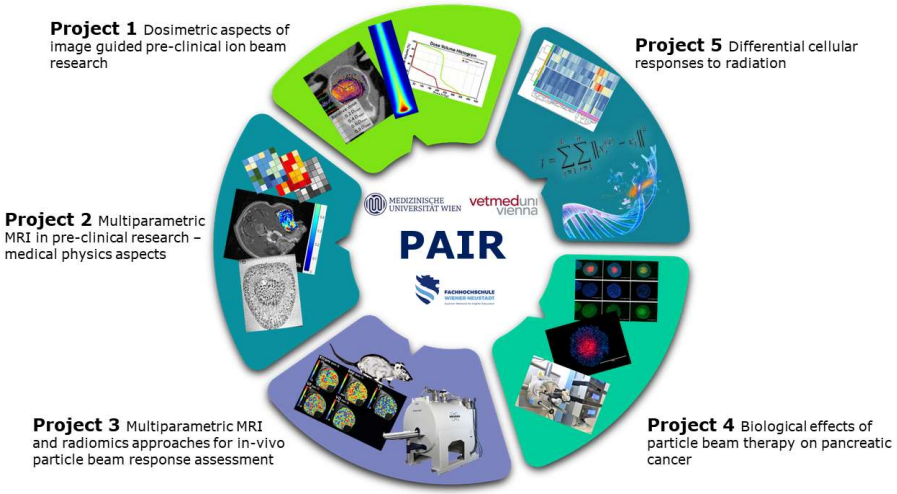


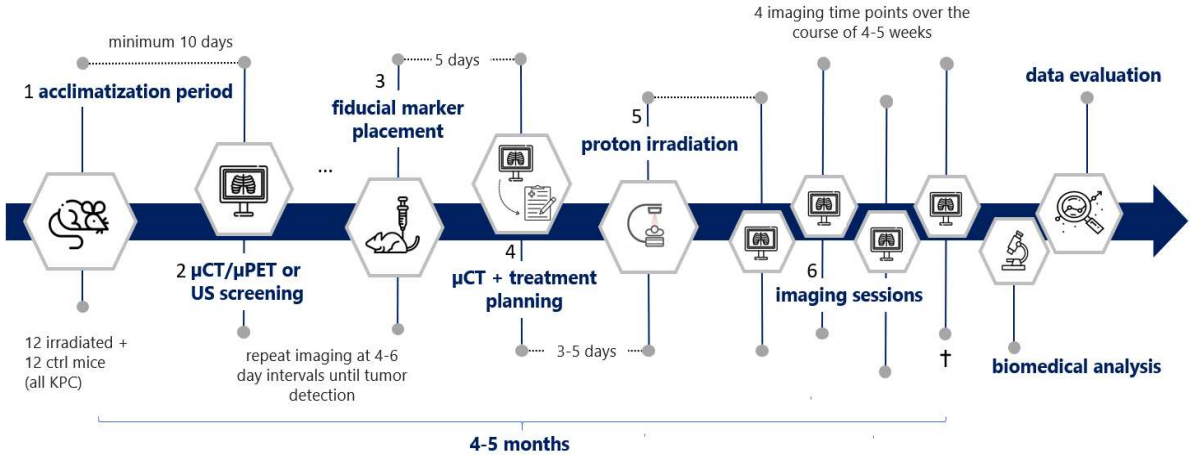


Beispiel – präklinische multimodale Bildgebung

FACHHOCHSCHULE
WIENER NEUSTADT
Austrian Network for Higher Education

FWF PAIR project – Preclinical Ion Beam Research





Beispiel – präklinische multimodale Bildgebung

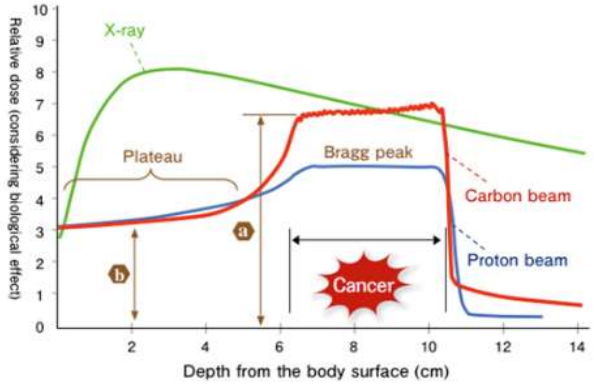
FACHHOCHSCHULE
WIENER NEUSTADT
Austrian Network for Higher Education

PDAC:

- >90% of all pancreatic carcinomas
- Late diagnosis
- Aggressive tumor growth
- high risk of metastatic spreading
- Dire prognosis
- Increasing incidence world-wide
- Heterogenic tissue composition, hypoxic
- Limited therapy options due to high toxicity

Particle Therapy:

- Promising therapeutic option
- high radio-biological effect
- Better tumor control = survival rate
- Better sparing of normal/healthy tissue
- Precise dose deposition
- Better utilization of therapeutic dose



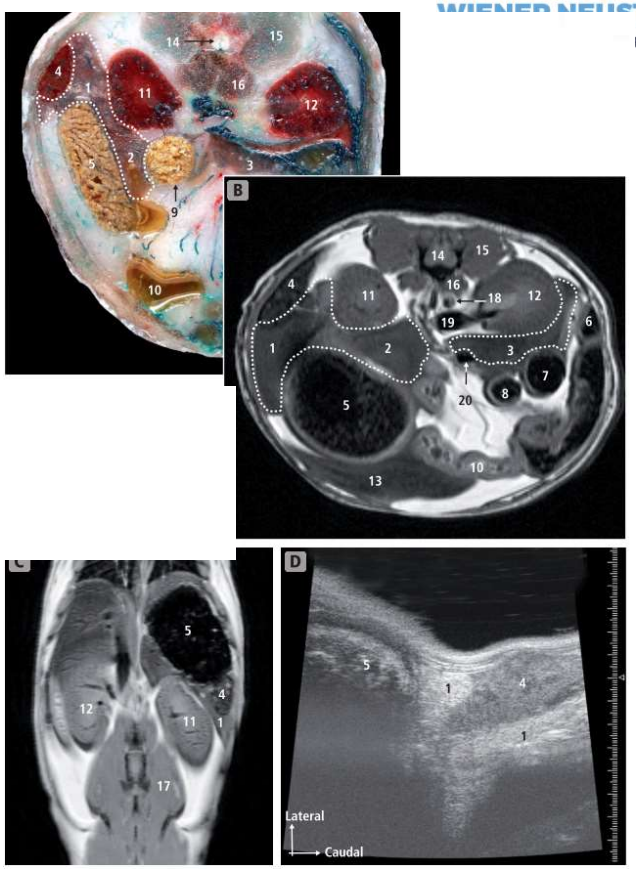
Beispiel – präklinische multimodale Bildgebung

FACHHOCHSCHULE WIENER NEUSTADT
Education

- Establishing a robust in vivo tumor model for PDAC:
  - Heterotopic allograft model
  - Orthotopic transgenic model

- Worklfow testing and optimization:
  - Irradiation (reproducable positioning, fiducial marker placement, imaging-guided irradiation, etc.)
  - Imaging (sequence and protocol optimization, respiratory gating, immobilization/positioning bed, etc.)

Example of flank tumors



Navarro, M., Ruberte, J., Carretero, A., Nacher, V., & Domínguez, E. (2017). Digestive tract. *Morphological Mouse Phenotyping: Anatomy, Histology and Imaging*, 89–146. https://doi.org/10.1016/B978-0-12-812972-2.50005-2

Beispiel – präklinische multimodale Bildgebung

FACHHOCHSCHULE
WIENER NEUSTADT
Austrian Network for Higher Education

- 20 C57BL/6J mice 4-6 weeks, Janvier Labs
- 36 KPC mice 4-6 weeks, Shanghai Model Organisms

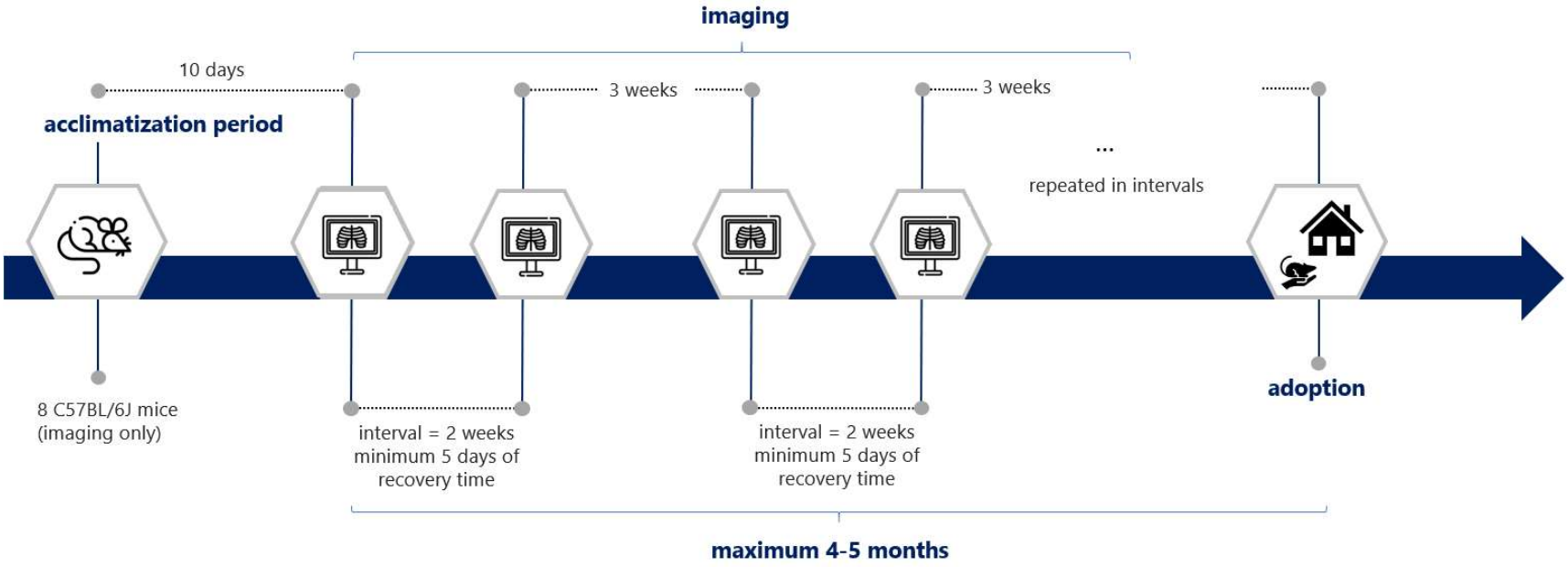
- Max. 20Gy proton irradiation for both tumor models

- Imaging prior to IR = µPET/µCT and/or US
- Imaging during IR = CBCT
- Imaging after IR = µPET/µMRI, µCT or US

- Health assessment score sheet daily and when needed; therafter twice a week
- Weighing mice daily
- Caliper measurement in flank model daily
- Orthotopic tumors measured in size @ imaging time points

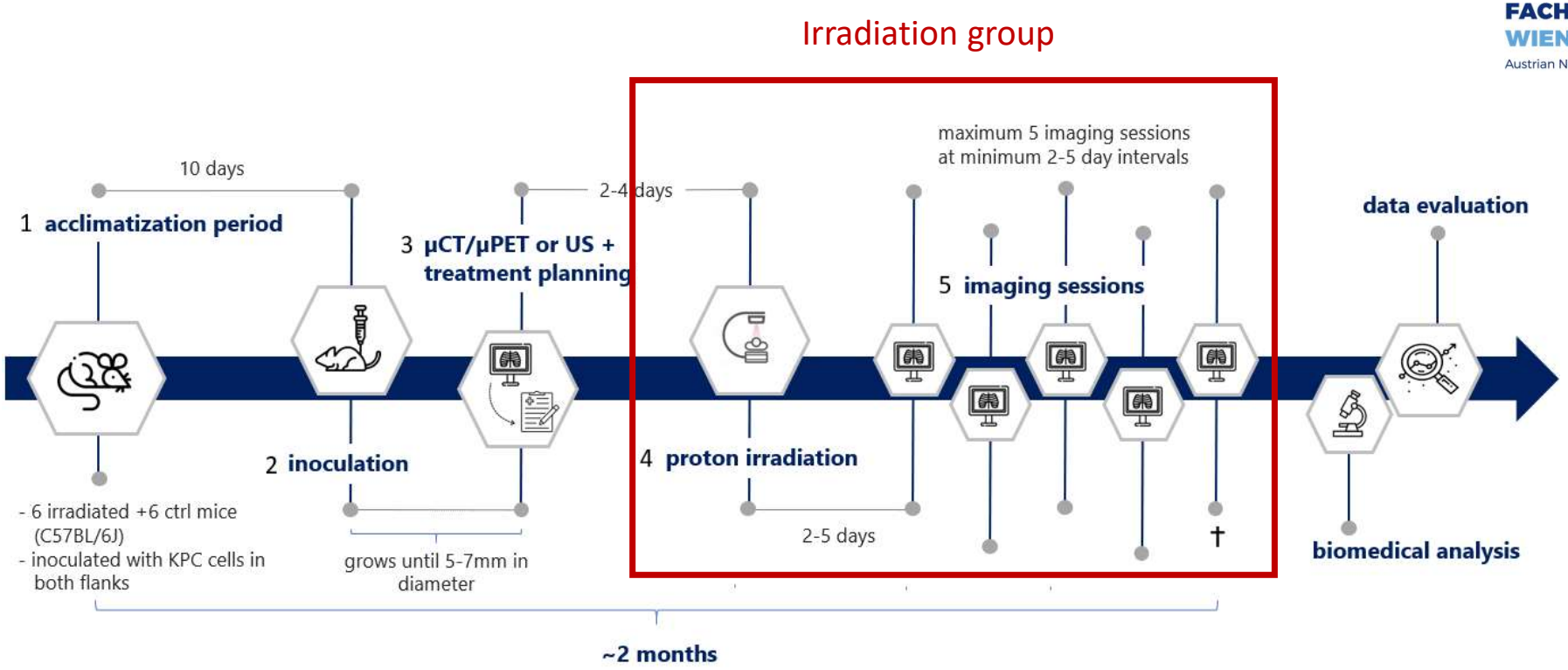
Beispiel – präklinische multimodale Bildgebung

FACHHOCHSCHULE
WIENER NEUSTADT
Austrian Network for Higher Education



ONLY IMAGING AND WORKFLOW

Beispiel – präklinische multimodale Bildgebung

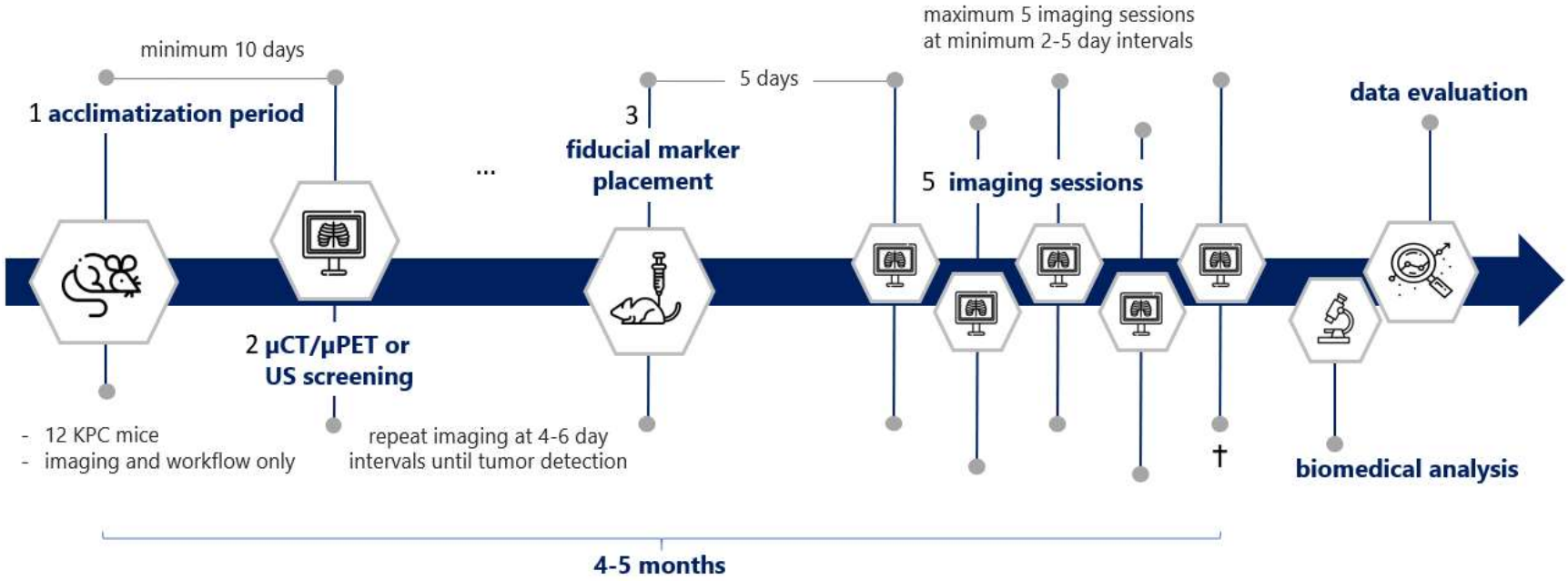


Outcome:

tumor progression, morphological, functional, molecular and immunobiological information

Beispiel – präklinische multimodale Bildgebung

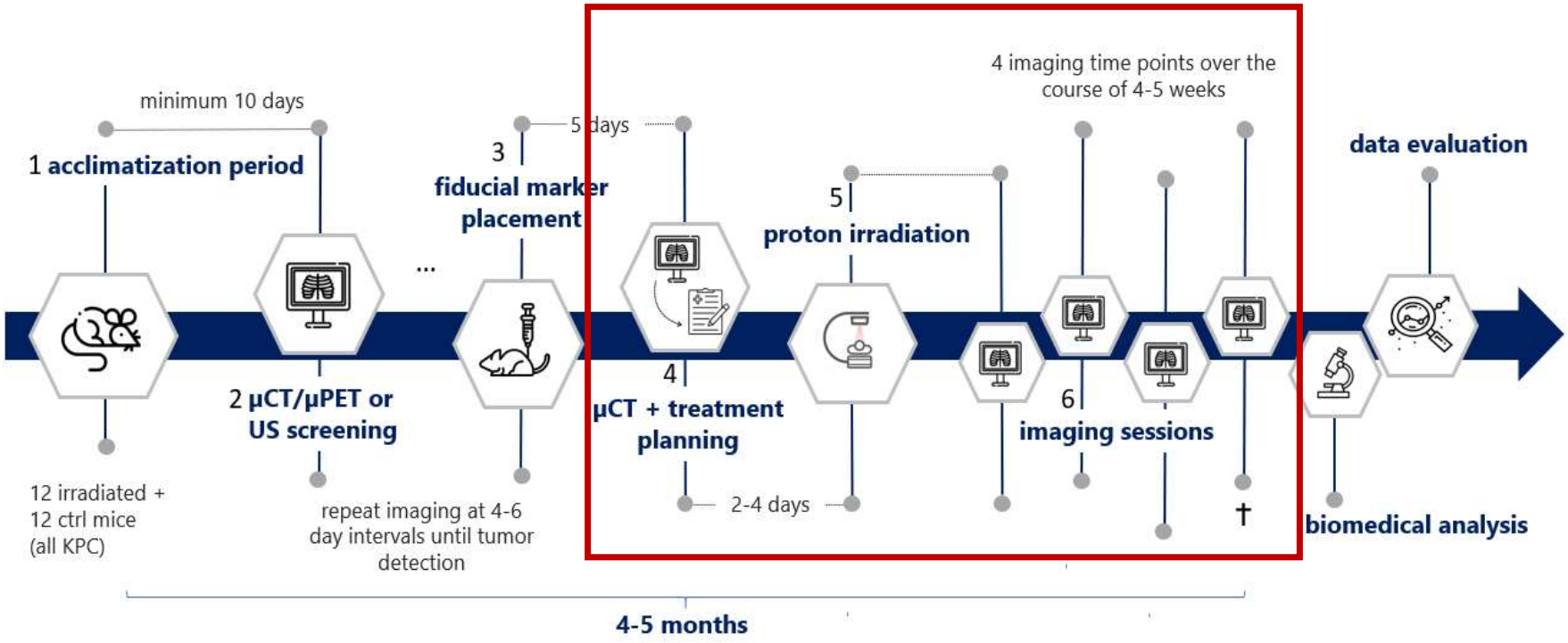
FACHHOCHSCHULE
WIENER NEUSTADT
Austrian Network for Higher Education



Outcome:

positioning verification, fiducial markers, optimizing imaging sequences and protocols to minimize duration of anesthesia, tumor detection and progression, immunibiological effects

Beispiel – präklinische multimodale Bildgebung

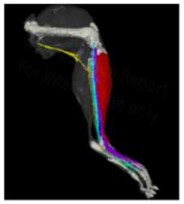
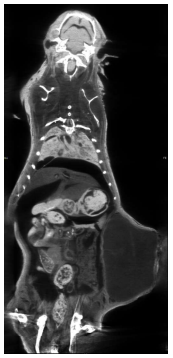


Outcome:

therapeutic response of tumor, angiogenesis/vascularization, metabolism, immuno-response

Vielen Dank für eure Aufmerksamkeit!

FACHHOCHSCHULE
WIENER NEUSTADT
Austrian Network for Higher Education

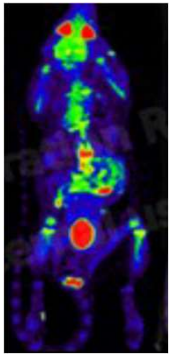














Competence Center for Preclinical Imaging and Biomedical Engineering

University of Applied Sciences Wiener Neustadt

Vielen Dank für eure Aufmerksamkeit!

FACHHOCHSCHULE
WIENER NEUSTADT
Austrian Network for Higher Education

„Science should be one of the great unifying forces in a world of diversity.“

Peter Ratcliff

Competence Center for Preclinical Imaging and Biomedical Engineering

University of Applied Sciences Wiener Neustadt