X-ray Fluorescence Imaging (XFI)

as a tool to monitor gold nanoparticle distributions in targeted alpha therapy

cooperation project between
U Osaka and UHH

Dr. rer. nat. Theresa Staufer, Prof. Dr. rer. nat. Florian Grüner
Accelerator Physics, Institute for Experimental Physics, University of Hamburg (UHH) and Center for Free Electron Laser Science (CFEL)

Our UHH imaging team

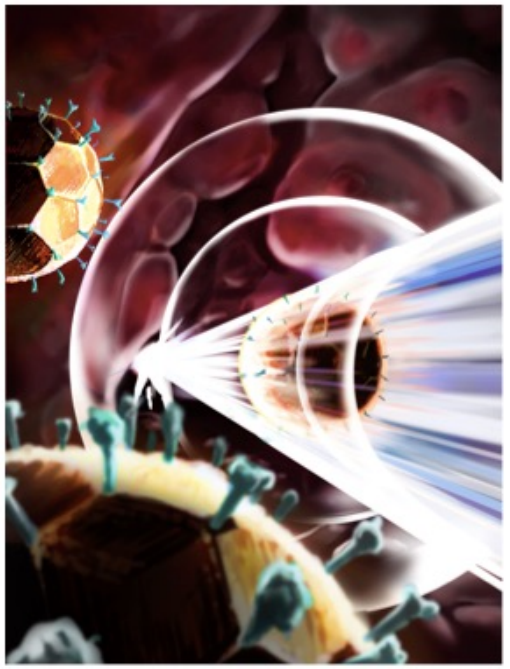
XFI LifeScience – why and how?

Labeling entities like

- immune cells (cell therapy)
- medical drug compounds, e.g. for cancer treatment
- nanoparticle carriers for mRNA-delivery
- antibodies

enables assessing their
biodistribution in space and time

Scanning X-ray beam creates
„**X-ray echos**“ by exciting
fluorescence of these **labels**



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XFI - added values

- **Non-invasive** → in vivo measurements
- **High spatial in-vivo resolution**

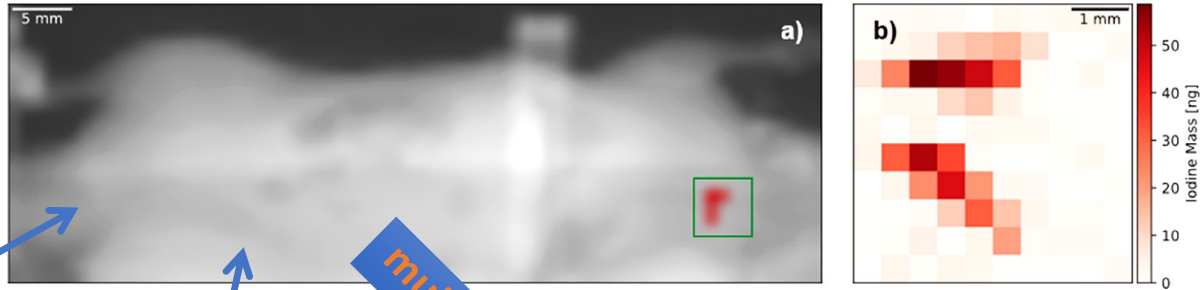
  → in vivo: 0.2...1 **mm,** ex vivo: 80...200 **nm**
- **High sensitivity and quantitative data**

  → smallest local amounts detectable + anatomy
- **Longitudinal studies** possible → no decay of signal
- **Multi-tracking (unique for XFI)**

  → different entities can be tracked simultaneously
- **Multi-scale (unique for XFI)**

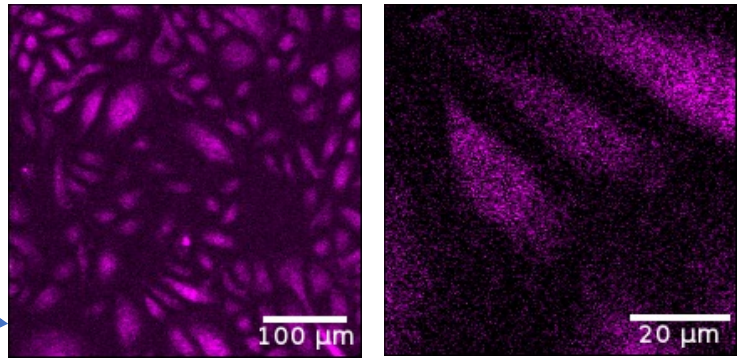
  → measurements on different size scales **from in vivo full-body scans down to ex vivo individual cells**

C. Sanchez-Cano et al., *ACS Nano* **2021**, 15, 3754−3807
C. Körnig et al., *Scientific Reports* 12, 2903, **2022**



multi-scale

T. Staufer et al., *Antioxidants* 11, 1532, **2022**



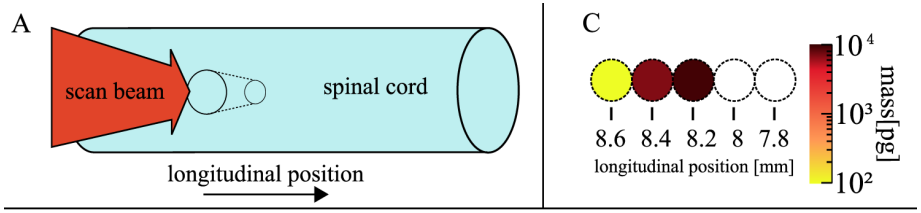
XFI – biological use cases I

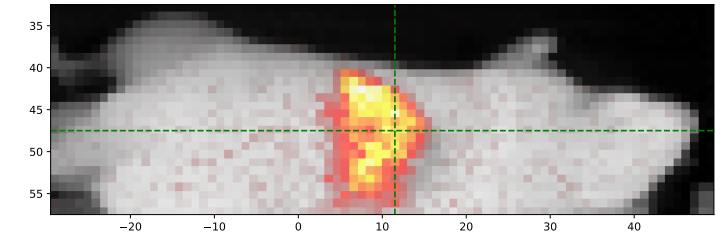
- Localization of L1-functionalized gold nanoparticles in a murine spinal cord to localize damaged neurons
  → high spatial resolution

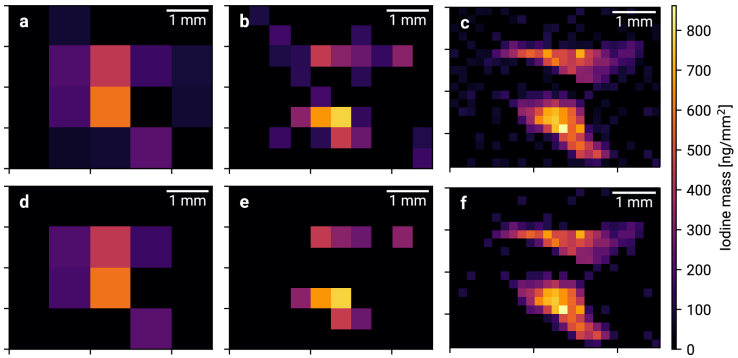
- Full-body scans of mice after injection of free unfunctionalized palladium nanoparticles
  → 80% of PdNPs end up in the liver

- Measurement of endogenous iodine content in murine thyroid
  → just 1.8 μg iodine mass per thyroid, high spatial resolution under in-vivo conditions;
  no difference between wildtype and Rag1-deficient mice

F. Grüner et. al, Scientific Reports 8,1,16561 (**2018**)







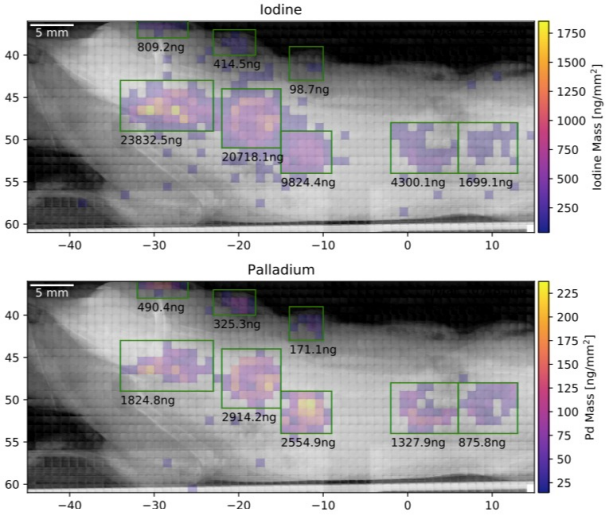
C. Körnig et al., *Scientific Reports* 12, 2903 (**2022**)

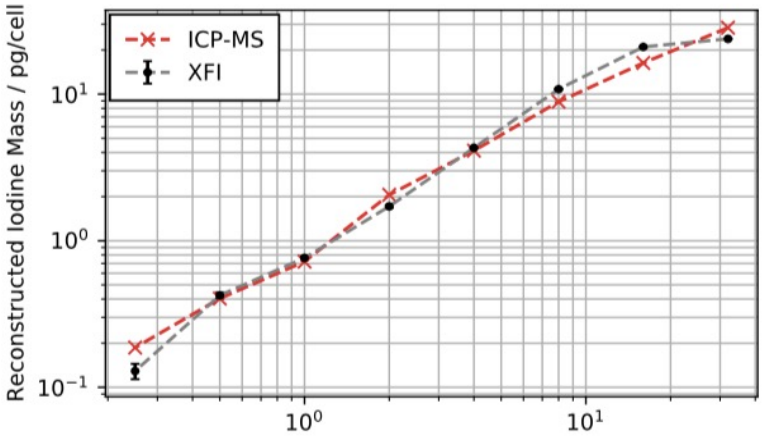
XFI – biological use cases II

- Back injection of differently labelled macrophages
  → two maps, but from **same** mouse: 50% labelled with molecular tracer, other 50% with nanoparticles
  → XFI is a quantitative modality
  → XFI allows multi-tracking

- In-situ measurements of macrophage distribution in mice with colitis model
  → signals so far from up to 72 hours after intraperitoneal injection

- Comparison with invasive ICP-MS
  → very good agreement



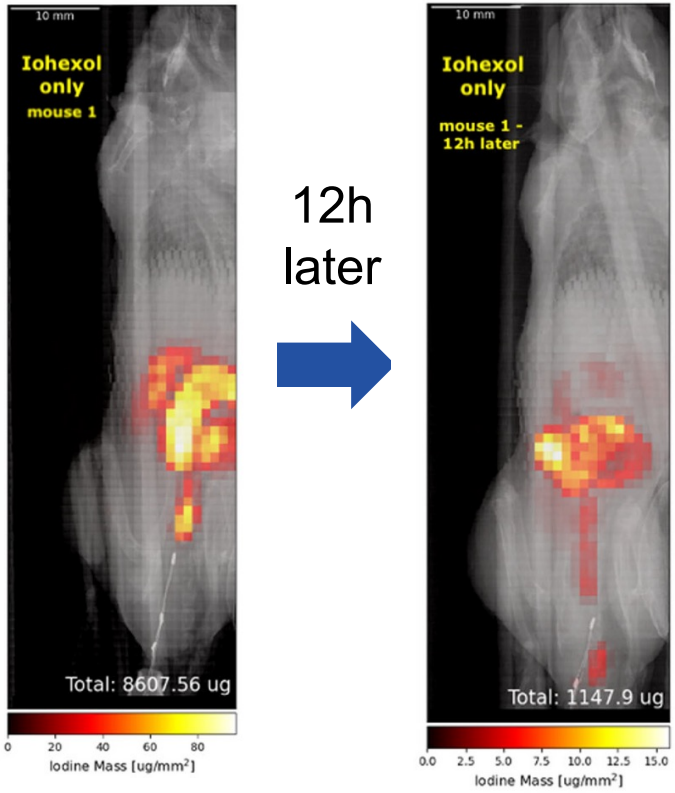


T. Staufer et al., *Scientific Reports* 13,11505 (**2023**)

In vivo cell tracking with XFI

Molecular contrast agent **without** cells
1 mouse scanned **twice**

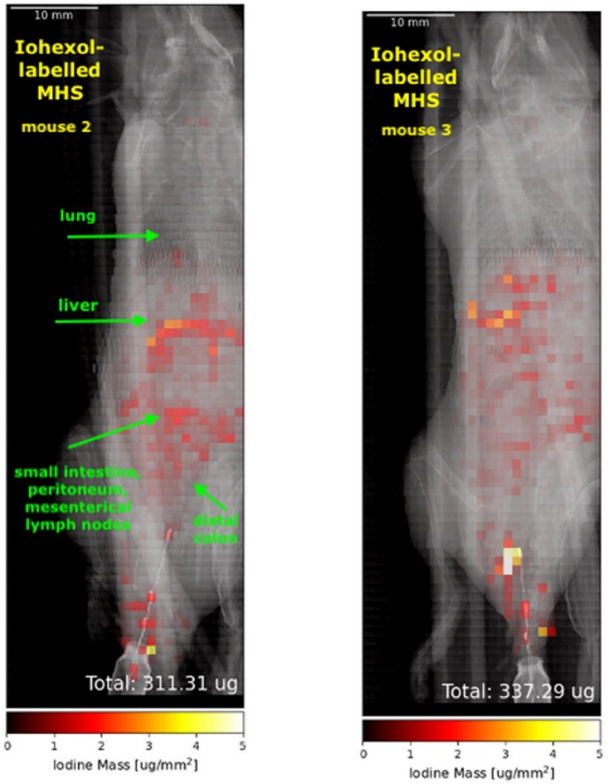
T. Staufer et al., *Scientific Reports* 13,11505 (**2023**)



Labeled macrophages, 6h post injection

→ **Distribution** of labels different

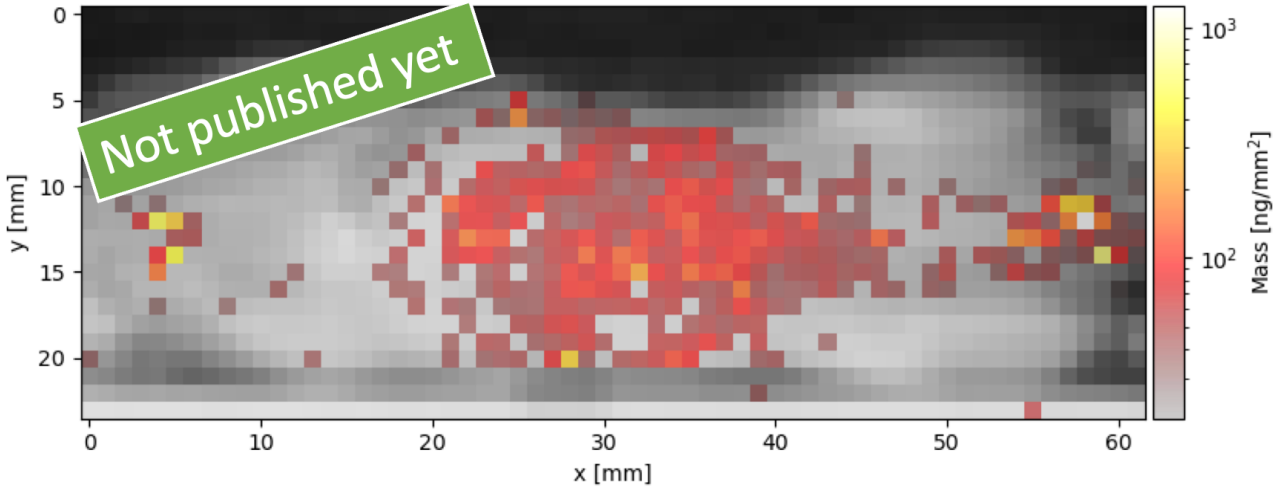
→ **Reconstructed** total mass = injected mass of labels



Tracking of an anti-cancer drug

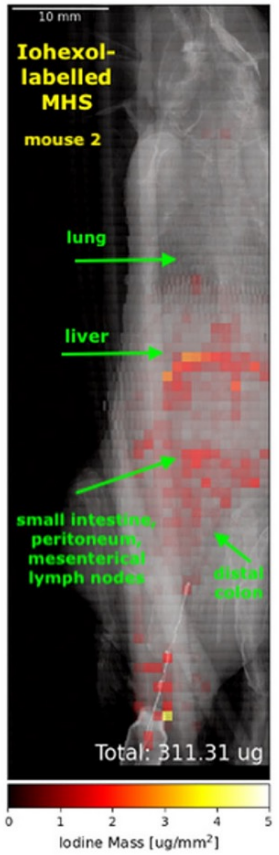
our first **pharmacokinetic** case study:

- intra-peritoneal injection of a **labeled cytostatic compound**
- scanning mouse like in in vivo study



Prof. Huber
PD Dr. Frenzel
Dr. Bosurgi

quite **different** biodistribution

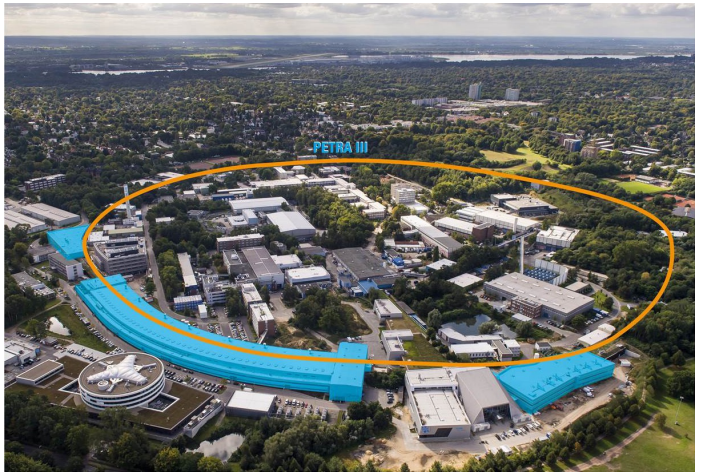


T. Staufer et al., *Scientific Reports* 13,11505 (**2023**)

Which X-ray source for XFI?

Necessary parameters:

- **pin beam** with small diameter (**1 mm**)
- **narrow bandwidth spectrum** (max. 15% FWHM)
- **continuous** photon flux of ca. $10^{9...10}$ photons per second
- **tunable** energy



→ currently only provided by **large synchrotron** facilities

http://photon-science.desy.de

➔Compact, inexpensive sources needed:
technology transfer from basic research into society via industry

SIEMENS Healthineers + UH

Enabling XFI for small-scale labs

https://roentgenmuseum.de/november-2017/

\+

dedicated novel X-ray optics

=

- **dedicated X-ray optics** fulfills XFI-requirements as already demonstrated in UHH-lab with "**SCOTTI**" (**S**uper **C**ompact **O**ptics-based **T**unable **T**estbed for **I**maging)

- **X-ray spectra** already **XFI-enabling**, photon **flux** too little for in-vivo/clinical applications
  → Joachim Hertz Stiftung for SCOTTI **2.0** (**even more compact than SCOTTI**)
  → cooperation with Siemens Healthineers for SCOTTI **3.0**

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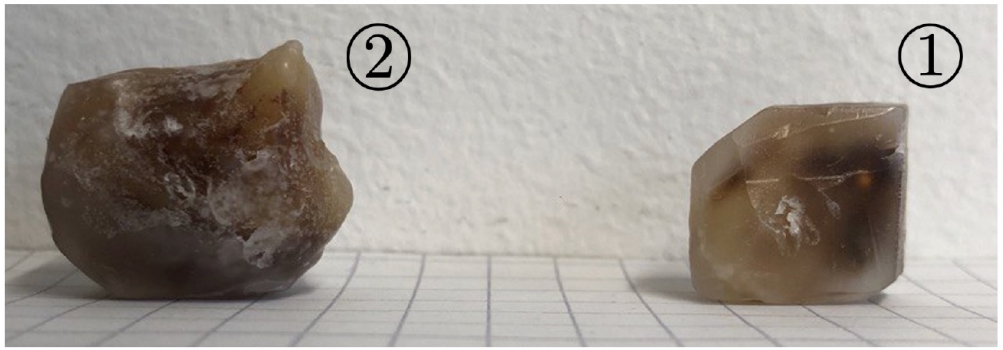
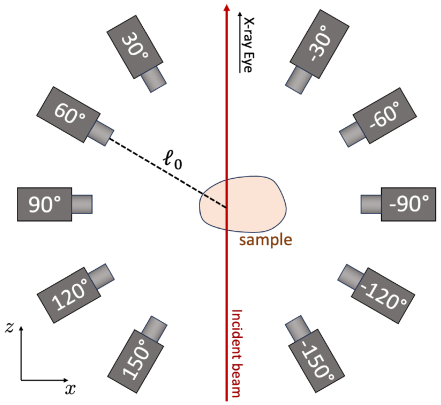
- Huang Xuhao
- Prof. Kazuya Kabayama
- Prof. Koichi Fukase

Scanning tumor samples from Osaka

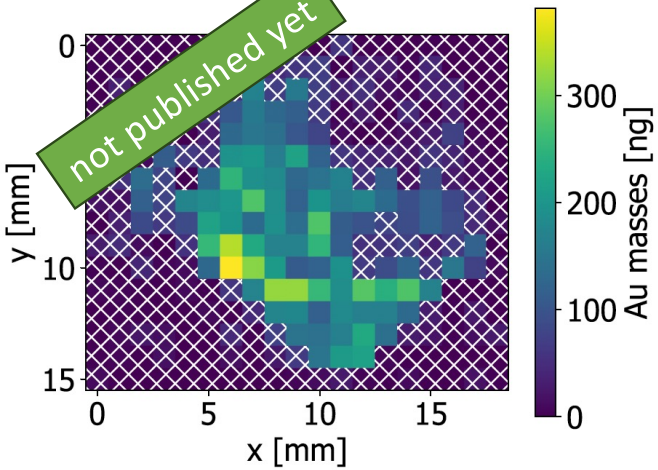
photos



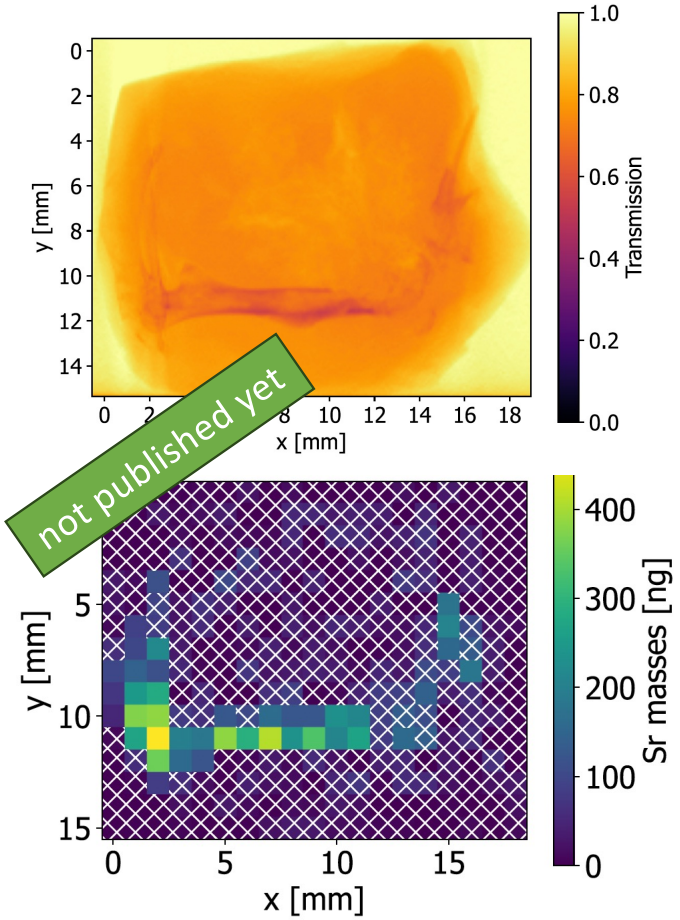
schematic of experimental setup at synchrotron:



First results on gold distribution in tumor 2



Cross-check XFI with micro-CT



micro-CT:
bone present?

XFI:
strontium map
indicates bone

Next steps:

- XFI above K-edge
- tomosynthesis-XFI with our lab system

Summary:

from **preclinical XFI** to first **tumor sample** scans