Perspectives of X-ray Fluorescence Imaging (XFI)

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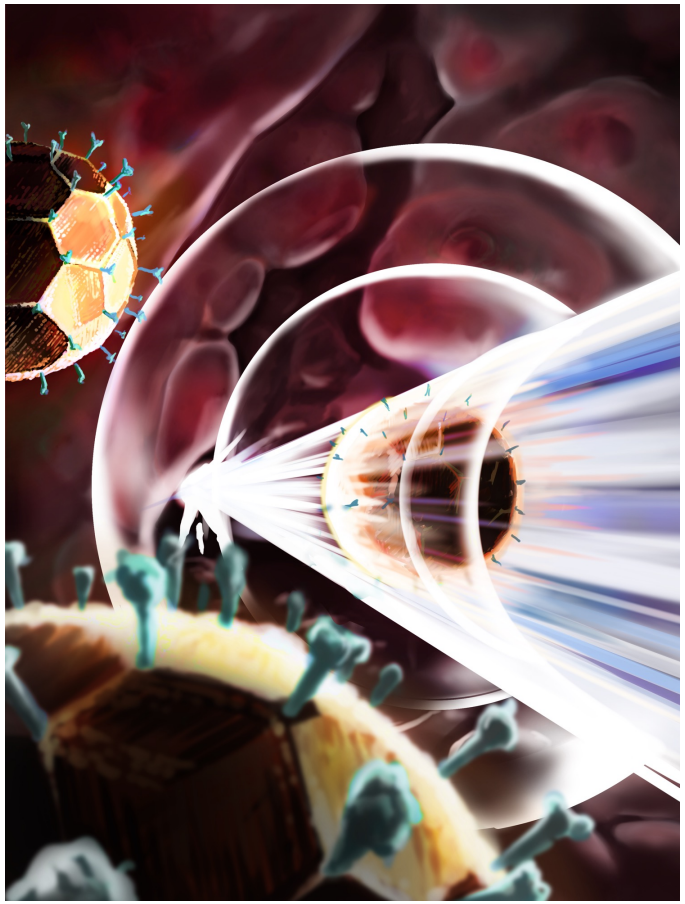
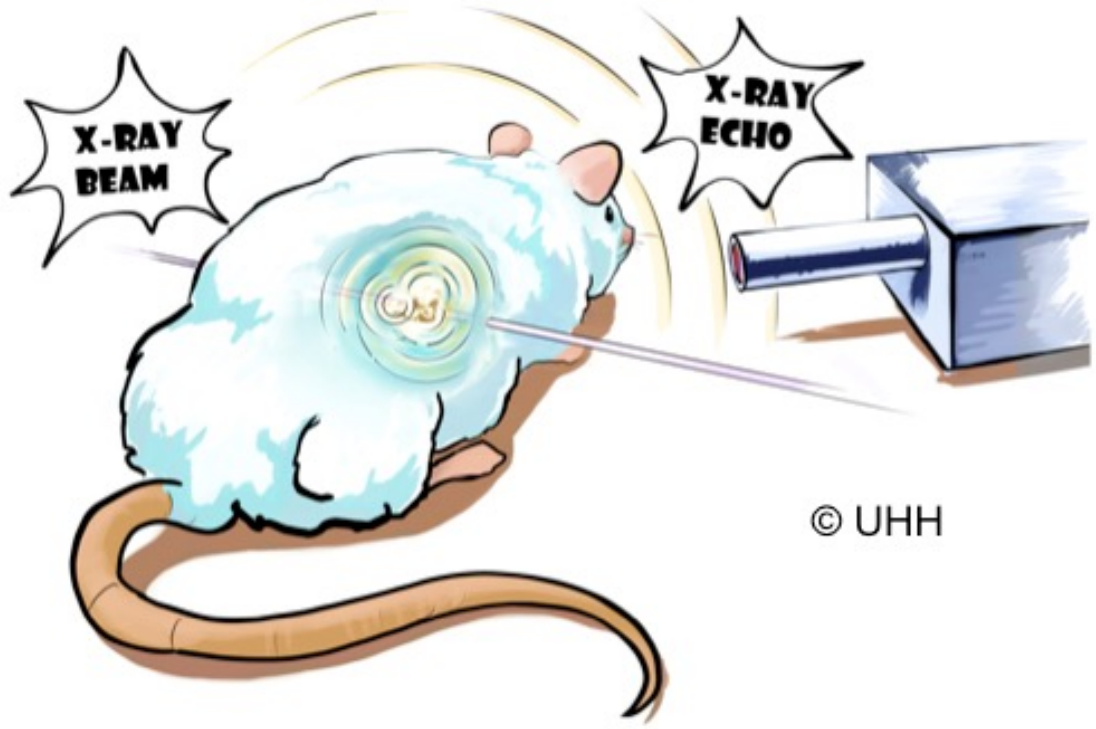


Content

- How does XFI **work**?
- **Added**-values of XFI
- **Data** examples of pilot-studies
- Perspectives of **pre-clinical** applications and need for **compact X-ray source**



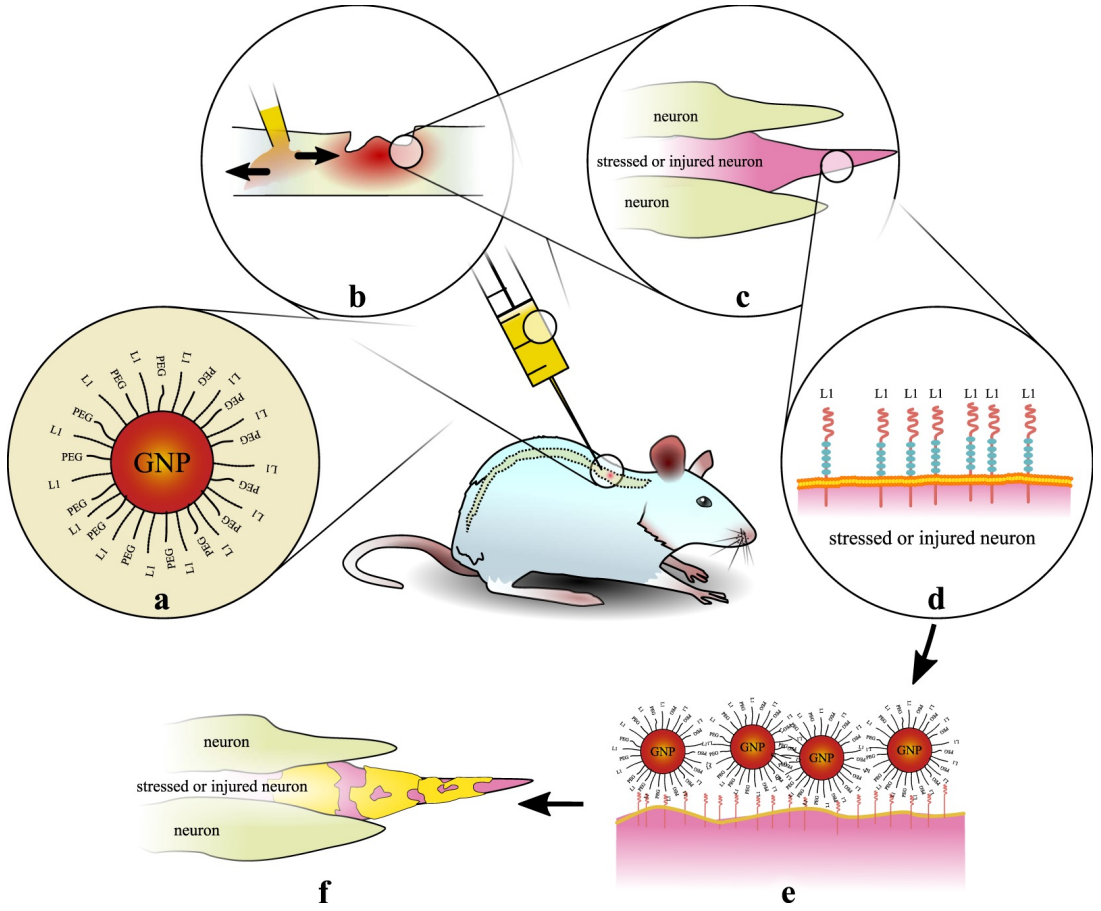
XFI – why and how?

Labeling entities like

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

enables assessing their **biodistribution in space and time**

Pencil X-ray beam **scans** object and creates „**X-ray echos**“ by exciting fluorescence of these **labels**



F. Grüner et al., Sci. Rep. **8**, 16561 (**2018**)

XFI added values

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

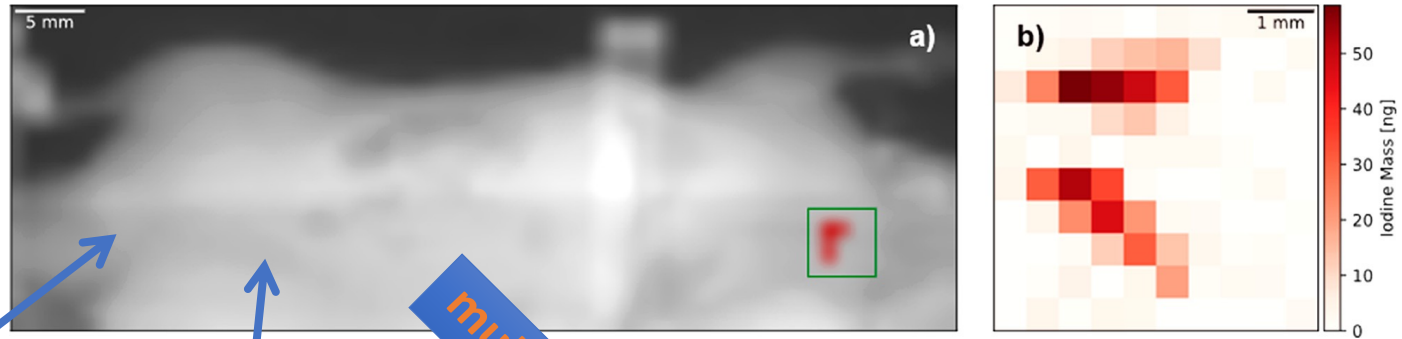
  → in vivo: 0.2...1 **mm,** ex vivo: 80...200 **nm**
- **High sensitivity and quantitative data**

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

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

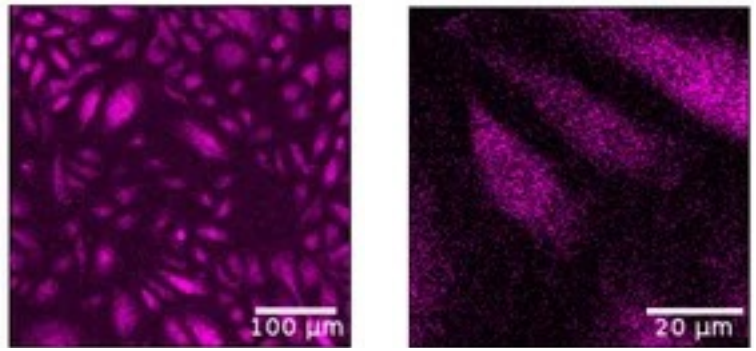
  → measurements on different size scales **from in vivo full-body scans down to ex vivo individual cells**

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



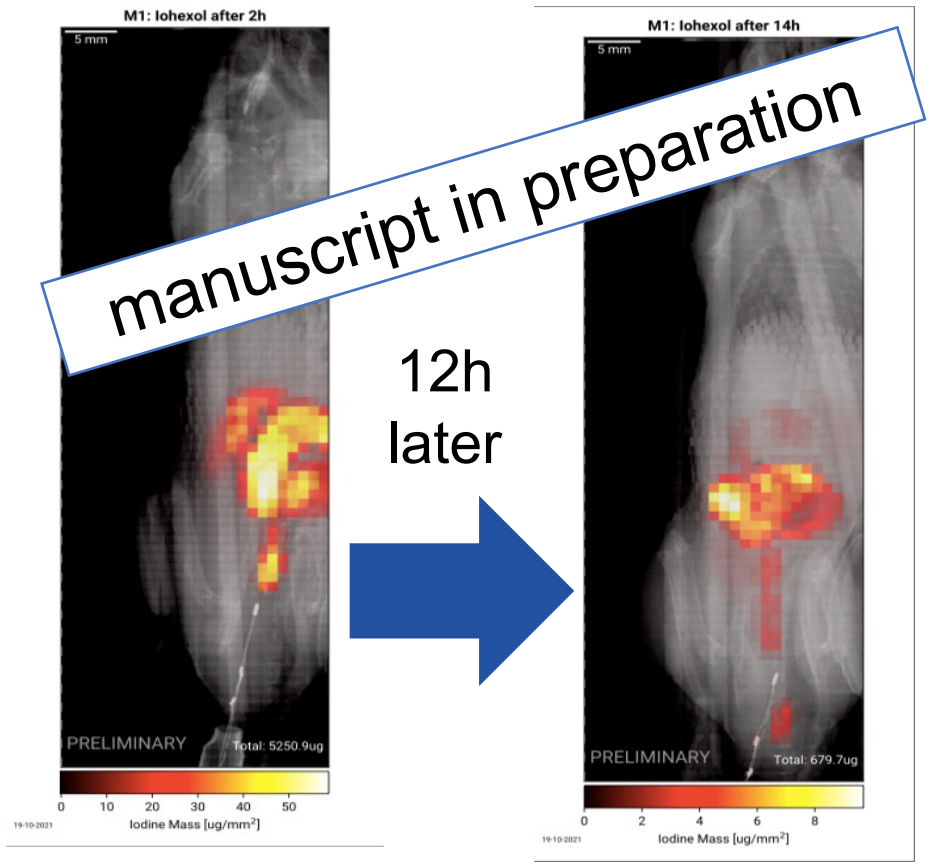
multi-scale

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



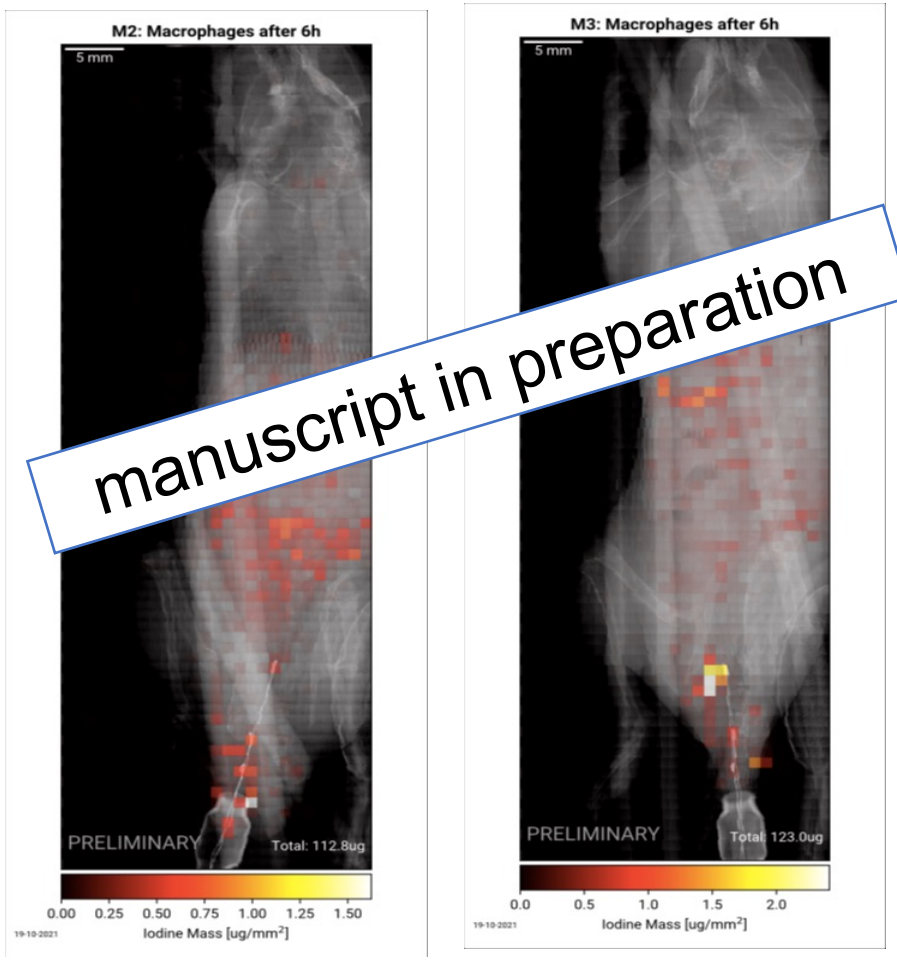
XFI – example 1: in-vivo cell tracking

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

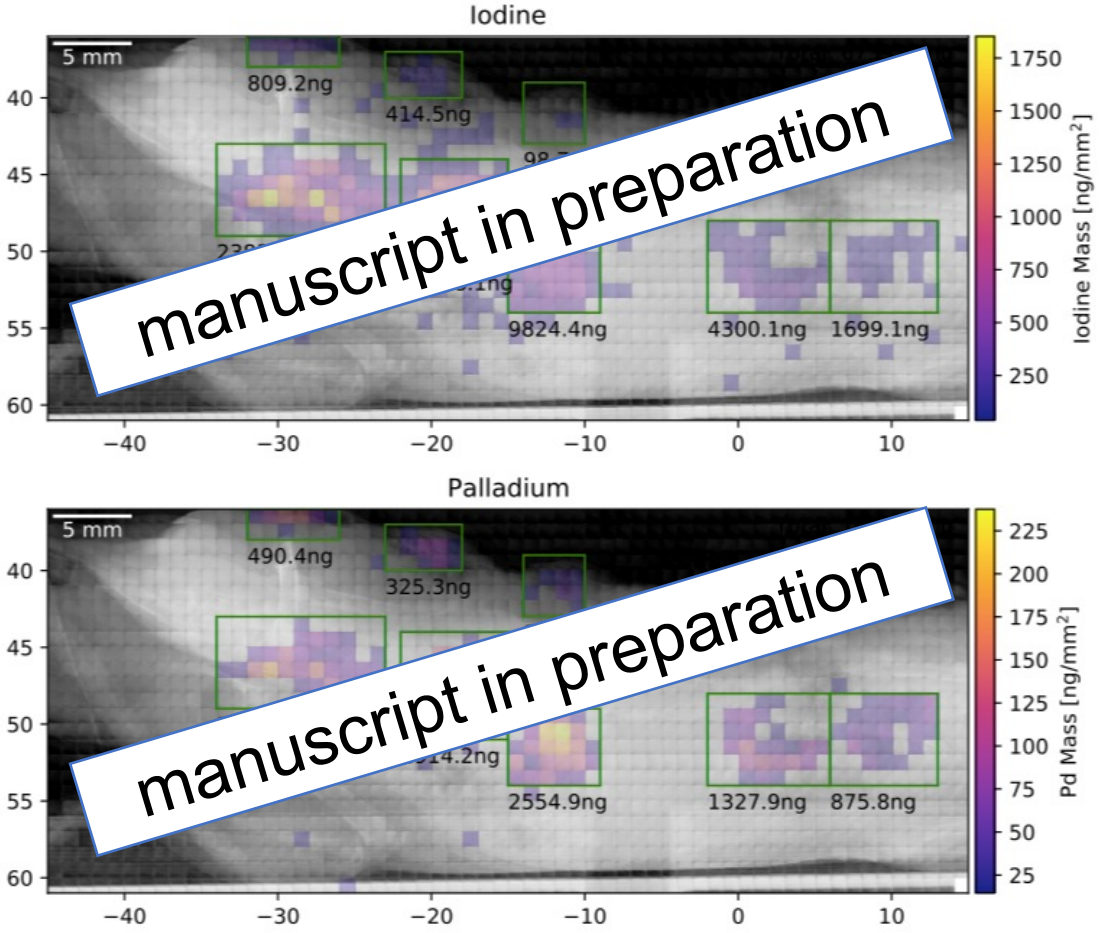


Labeled macrophages,
6h post injection

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



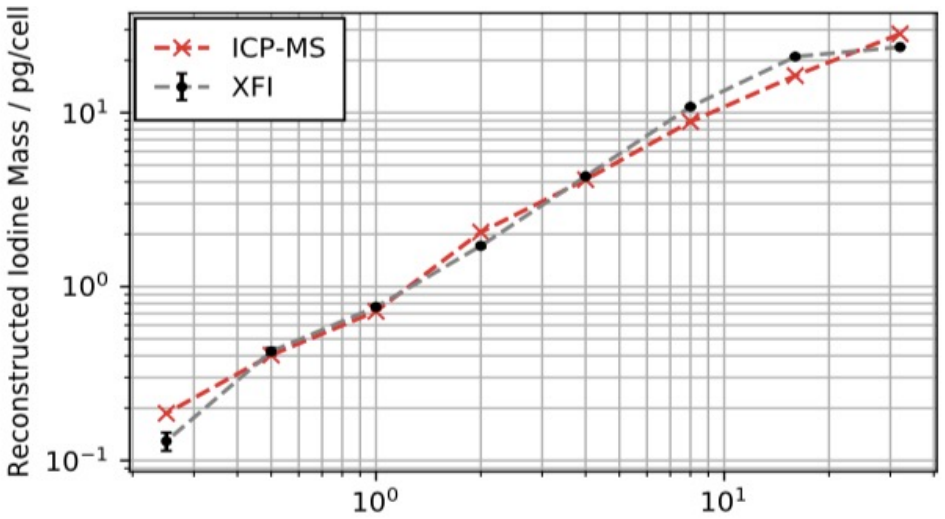
XFI – example 2: multi-tracking



Two different subsets of macrophages injected into same sites:

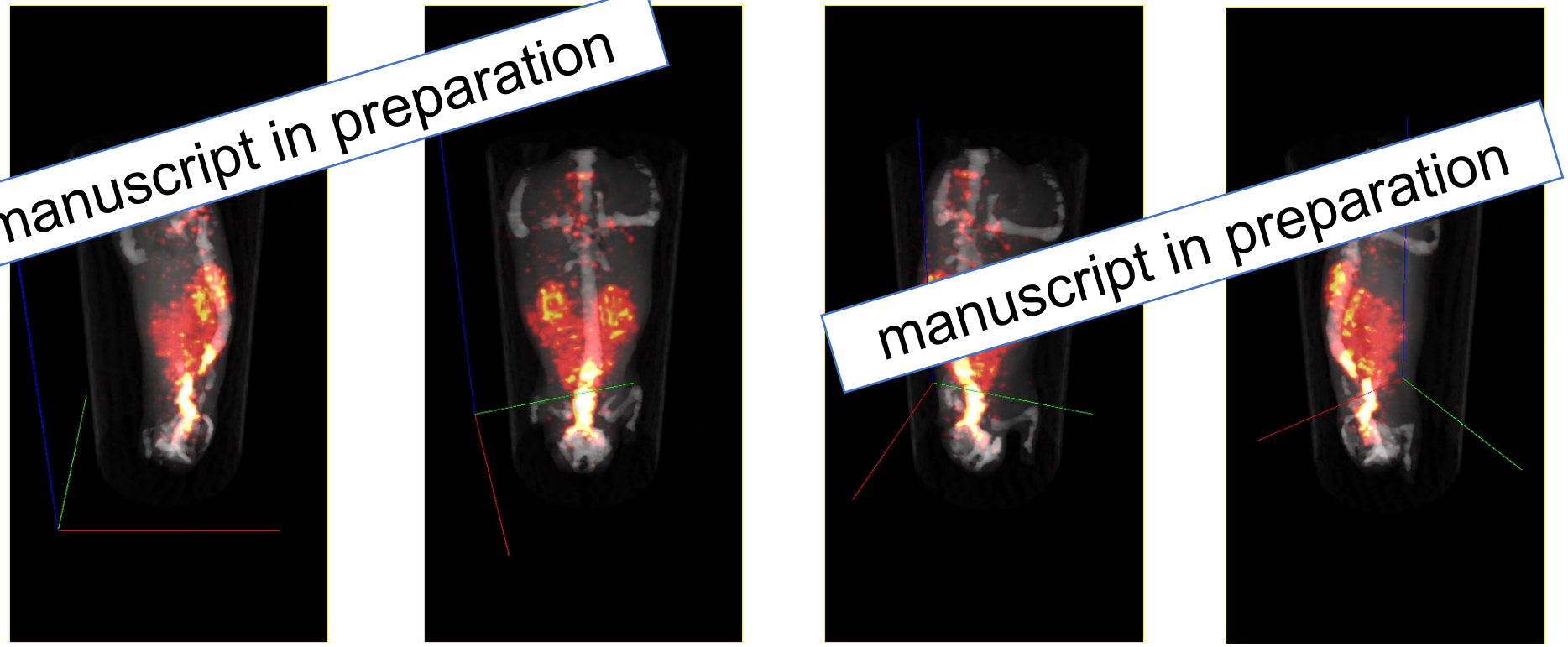
- 50% with molecular Iodine label
- 50% with Pd-nanos as markers

→ cross-check with **ICP-MS**



XFI – example 3: demo of 3D-XFI

Measured with mouse phantom (developed by University Hospital UKE) containing Pd (0.03 mg/ml in kidneys, 0.02 mg/ml in lungs, 0.01 mg/ml in liver)
→ images taken with 6 detectors, applied dose: 62 mGy



XFI – our preclinical R&D goals

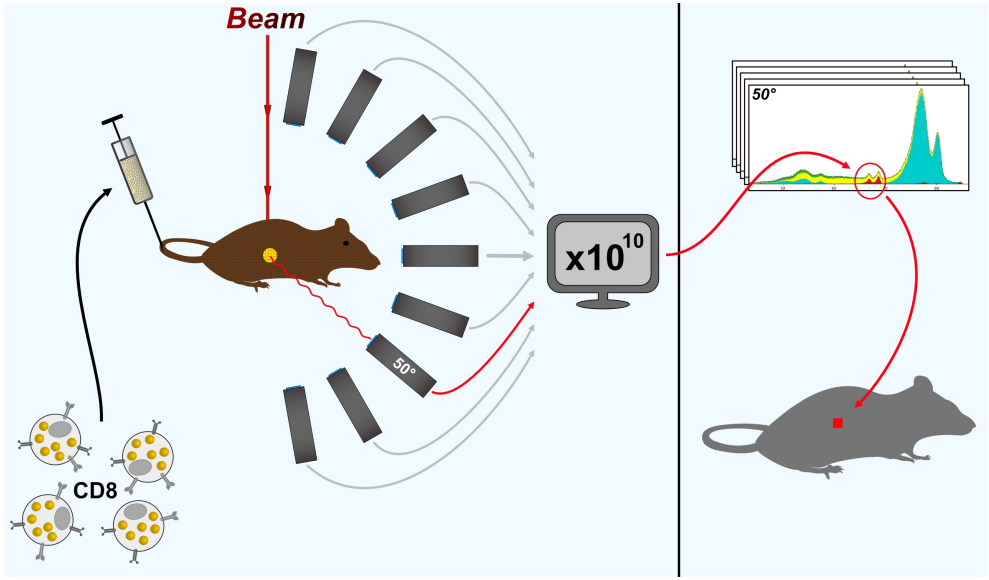
- In vivo – **tracking of medical drugs/nanocarriers**
  → **pharmacokinetics:**

  Do medical drugs reach their target? → efficacy
  Where else do they accumulate? → adverse drug effects

  → can they reach the inner volume of a **tumor**?
  → over what time scale are medical drugs metabolized?

- In vivo – **tracking of immune cells:**

  - monitoring the targeting of T-cells in cell therapy and/or assessing the immune response in immune-mediated inflammatory diseases (e.g. Morbus Crohn) for novel therapies



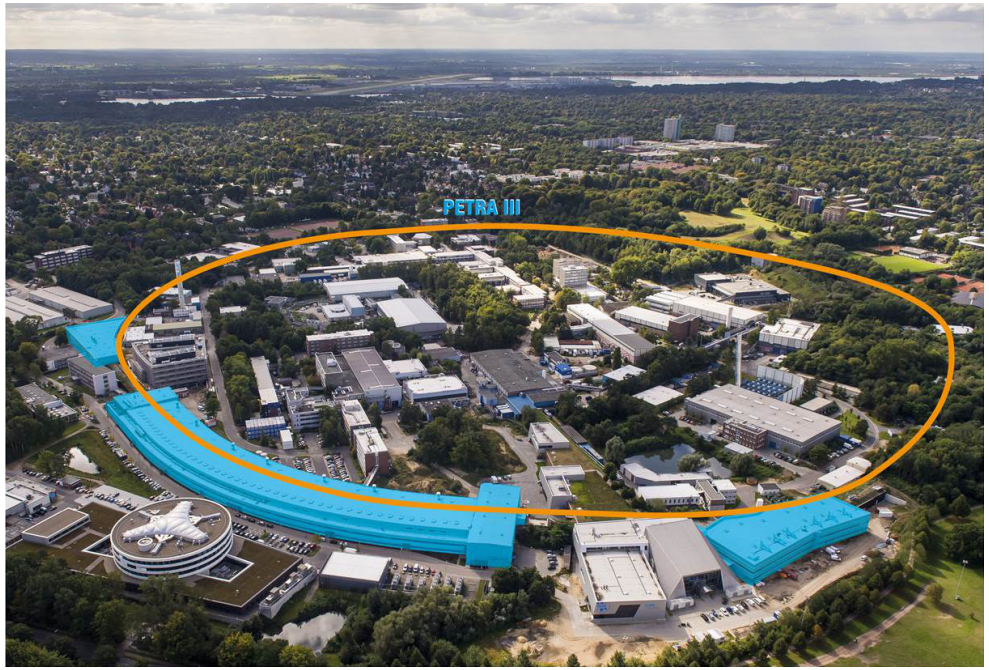
H. Kahl et al., *Int. J. Mol. Sci.* **2021**, *22* (16), 8736

Need for compact X-ray source

- Synchrotrons are highly brilliant X-ray sources but way too large (diameters in the km-range)

➔ **laser - driven X-ray sources**:

- provide pencil beams
- not suited for all imaging modalities but ideal for XFI



https://www.wayforlight.eu/en/facility/20469

PHYSICAL REVIEW ACCELERATORS AND BEAMS **23,** 031601 (2020)

Editors' Suggestion

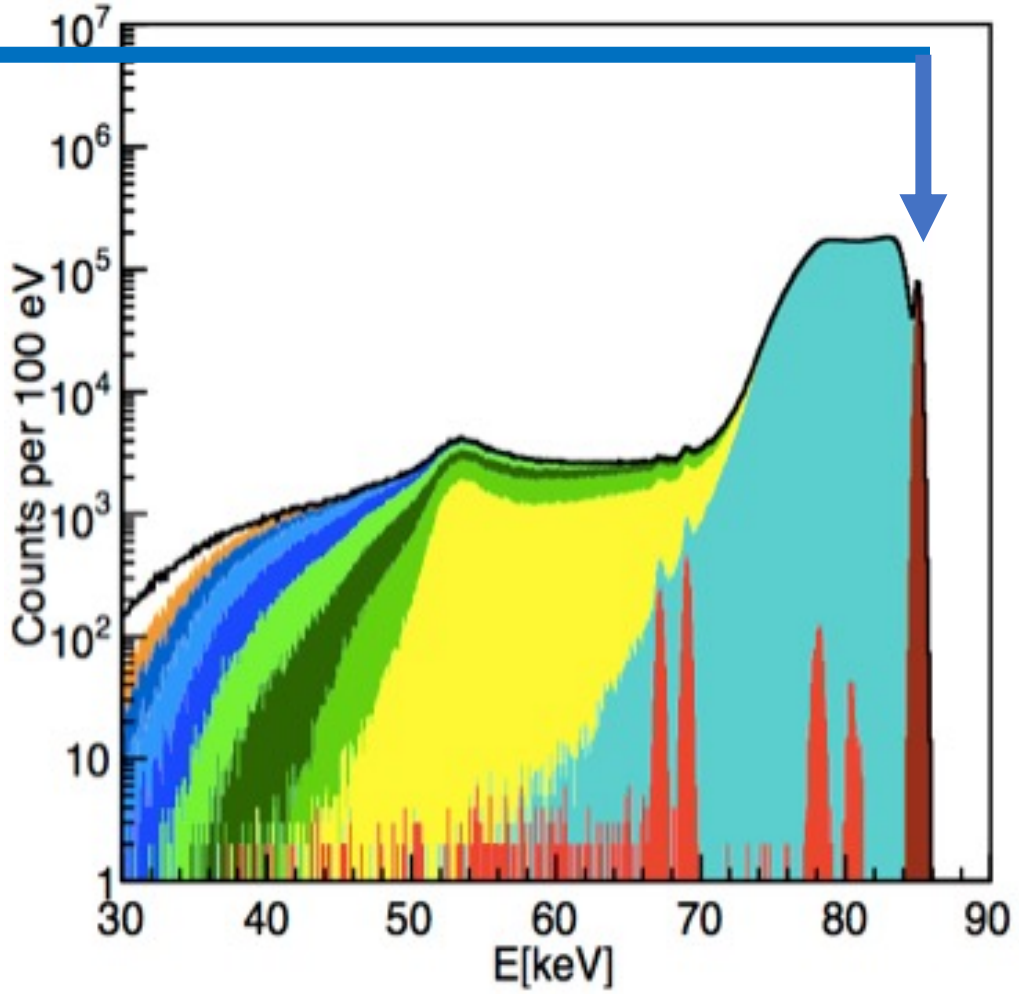
Design study for a compact laser-driven source for medical x-ray fluorescence imaging

Theresa Brümmer,[1,*] Alexander Debus,[2] Richard Pausch,[2,3] Jens Osterhoff,[1] and Florian Grüner[4]

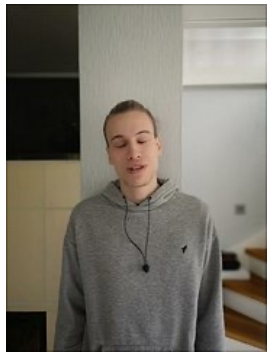
Required beam parameters

- **Bandwidth:**
  conventional X-ray tube spectra too broad
  → should be less than 15% FWHM
- **Pencil beams:**
  beam diameter determines spatial resolution
  → 1 mrad and 1 mm beam size at target
- **Photon flux (within bandwidth and divergence):**
  → ca. 10^9 photons/sec/mm^2
  → Thomson source with high repetition rate (kHz) needed

Cooperation on pilot-study with Gabriele Grittani and Carlo Lazzarini at ALFA end station



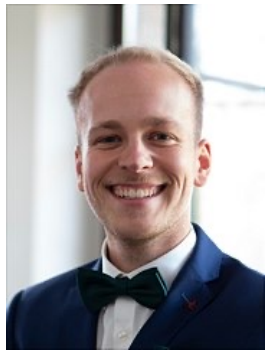



THANK YOU!













Publications by UHH-team on XFI

- Florian Grüner et al. “Localising functionalised gold-nanoparticles in murine spinal cords by X-ray fluorescence imaging and background-reduction through spatial filtering for human-sized objects”, *Scientific Reports*, Volume 8, Issue 1, Article number 16561 (**2018**)
- Carlos Sanchez-Cano et al. “X-ray-Based Techniques to Study the Nano–Bio Interface”, *ACS Nano* **2021**, 15, 3754−3807
- Oliver Schmutzler et al. “X-ray Fluorescence Uptake Measurement of Functionalized Gold Nanoparticles in Tumor Cell Microsamples”, *Int. J. Mol. Sci*. **2021**, 22, 3691
- Henrik Kahl et al. ”Feasibility of Monitoring Tumor Response by Tracking Nanoparticle-Labelled T Cells Using X-ray Fluorescence Imaging—A Numerical Study”, *Int. J. Mol. Sci*. **2021**, 22, 8736.
- A. Ungerer et al. "X-ray-Fluorescence Imaging for In Vivo Detection of Gold-Nanoparticle-Labeled Immune Cells: A GEANT4 Based Feasibility Study", *Cancers* **2021**, 13(22):5759
- C. Körnig et al. " In-situ X-ray fluorescence imaging of the endogenous iodine distribution in murine thyroids“, *Scientific Reports* 12, 2903, **2022**
- J. Baumann et al. “Enabling Coarse X-ray Fluorescence Imaging Scans with Enlarged Synchrotron Beam by Means of Mosaic Crystal Defocusing Optics“, *Int. J. Mol. Sci.* **2022**, *23*(9), 4673
- T. Staufer, M.L. Schulze, O. Schmutzler et al. “Assessing Cellular Uptake of Exogenous Coenzyme Q_{10} into Human Skin Cells by X-ray Fluorescence Imaging“, *Antioxidants* 11, no. 8:1532, **2022**
- Y. Liu et al. “Size- and Ligand-Dependent Transport of Nanoparticles in *Matricaria chamomilla* as Demonstrated by Mass Spectroscopy and X-ray Fluorescence Imaging”, *ACS Nano,* **2022**