IXBI - Integrating X-ray and Biomedical Imaging for Multi-Scale, Molecularly Resolved Medicine

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1) Description of the research area

Recent advances in medical imaging and spatial biology now enable unprecedented, multi-scale analysis of human tissues—from high-precision biopsy guidance to whole-sample phase-contrast X-ray imaging, subcellular reconstruction by volumetric electron microscopy, and comprehensive, spatial molecular profiling. If integrated, these technologies allow precise identification of disease-relevant microenvironments and quantitative characterization of their architecture and molecular composition, transforming our ability to study human pathology.

Today, the technologies are already provided and sometimes even developed by researchers associated to the Swedish research infrastructures MAX IV, SciLifeLab and others, but are used in isolation from each other and not available as integrated services. They can therefore not be systematically validated in clinical research in order to change the everyday health care practice in pathology and allow biomarker and drug target identification. To solve this and ensure a clinically valuable pipeline advancing cutting-edge research for pathology and precision medicine, we will form **the Integrated X-ray and Biomedical Imaging** (IXBI) cluster. More specifically, IXBI will establish interoperable workflows linking **imaging -guided biopsies (CIR)**, **dose -efficient phase-contrast X-ray tomography** of intact tissue (**MAX IV**), **volume electron microscopy (vEM)** and **spatial omics** (**SciLifeLab**), fused by **AIdriven data analysis- (SciLifeLab)**. Together these methods enable correlative characterisation of patient biopsies from organ scale to nanoscale with molecular readouts.

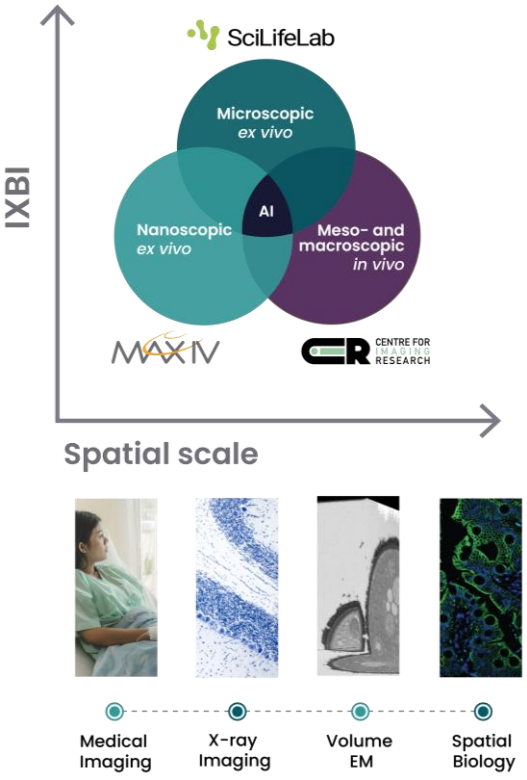

Figure 1. *Our cluster will define how cross-scale imaging/omics can be combined to create comprehensive medical image at all relevant length scales to understand tissue pathologies.*

Relevance to ground-breaking technology. The past decade has witnessed a revolution in in vivo and ex vivo imaging technologies. Several new techniques have very recently been developed and advanced the analytical toolbox for diagnostics. The very recent development of phase contrast imaging with coherent x-rays, enabled by the advent of fourth generation synchrotrons pioneered at MAX IV Laboratory, has also added completely new opportunities for imaging in life science as this type of imaging can deliver very high resolution while keeping the radiation dose at an acceptable level. With the capacities at MAX IV and SciLifeLab, Sweden now has a unique position in the world to build something disruptive and ground-breaking for our capacity to understand and treat future pathologies. IXBI focuses on **integration**—shared sample logistics, metadata, crossmodal registration, dose/throughput envelopes, GPU-based reconstruction and data governance—so that multimodal imaging can be validated in clinical research and scaled as joint services. By combining the most advanced medical imaging diseased tissues can be identified early and biopsies and tissue samples obtained with

unprecedented precision. These can then be reconstructed with cellular resolution in toto with X-ray imaging, to zoom in on the diseased cells. Afterward, the critical disease relevant cell types and their microenvironment can be characterized ultrastructurally and molecularly by volume electron microscopy and spatial biology profiling, generating an unprecedented depth of molecular precision data for AI-powered analysis.

This integrated set of breakthrough technologies thus will enable the future of patient sample and biopsy characterization, to catch disease early, diagnose patients with molecular precision and allow personalized treatment and much better health and disease management. MAX IV's and SciLifeLab's infrastructure and collaborative research networks for technology develoment and their use in clinical research and health care, will ensure that these breakthrough technologies will be openly accessible across Sweden, as well as to international collaborators. This breakthrough technology cluster has the potential to propel Sweden into an internationally leading position for the future of human tissue and biopsy characterization in health care.

2) Network description and mode of cooperation

Collaborating partners and contributions.

MAX IV (phase contrast Xray tomography; acquisition/reconstruction), **SciLifeLab** (vEM, spatial biology, data integration and AI analysis, **NBIS/BIIF**, **Data Centre**), and **CIR** (clinical imaging and imaging guided biopsies) jointly lead the planning, with **LU, UU, KTH, SU and KI** as core universities. A strategic MAX IV–SciLifeLab partnership will align roadmaps and define joint services.

Platforms and methodologies

• MAX IV Laboratory: Sweden's national synchrotron; two beamlines partially support phase-contrast tomography (≈8–35 keV, ≈1–2 µm voxels) for intact human tissues; IXBI will define standardised acquisition (incl. multi-distance propagation) and GPU-accelerated reconstruction and *draft a concept note for a dedicated biomedical imaging beamline* (planning only).

• SciLifeLab: Sweden's national infrastructure for molecular life science technologies

– Cellular & Molecular Imaging (CMI): cryo-EM/cryo-ET; FIB-SEM (room-temperature) and correlative array tomography; complementary nanoSIMS; planning upgrade to plasma FIB-SEM.

– Spatial & Single-Cell Biology (SSCB): spatial transcriptomics and in situ sequencing; targeted spatial proteomics; mass spectrometry imaging; multimodal integration.

– NBIS/BIIF & Data Centre: image/spatial molecular data integration and AI driven analysis, FAIR stewardship, secure access, compute and user support.

• CIR – Centre for Imaging Research: MRI, PET, CT, M/EEG, autoradiography, radiochemistry/radioligands; image-guided biopsies; across-species testbeds and clinical research interfaces.

Participating researchers

• *Marta Carroni* – Head, Swedish National Cryo-EM Facility (SciLifeLab/Stockholm). Role: vEM/cryo-EM workflows, correlative alignment with X-ray and spatial omics.

• *Daniel Lundqvist* – Director, CIR (KI/KUH). Role: clinical multimodal imaging and imaging-guided biopsy pathways; user/testbeds and regulatory interfaces.

• *Mats Nilsson* – Platform Director, Spatial Biology (SciLifeLab/SU). Role: spatial omics integration (ISS/targeted proteomics/MSI) and registration to volumes.

• *Carolina Wählby* – Professor, Quantitative Microscopy (UU; SciLifeLab/NBIS BIIF). Role: AI-based image/spatial data analysis and visualisation (e.g., TissUUmaps).

• *Mia Phillipson* – Co-Director, SciLifeLab; professor (UU). Role: clinical/translation interfaces, ethics/governance alignment, Data Centre strategy.

• *Jan Ellenberg* – Director, SciLifeLab; professor (KI). Role: overall leadership and integration across platforms and Data Centre; governance and international links.

Olof Karis (PI) — Director, MAX IV; Professor (UU). Leads project strategy and integration; oversees phase-contrast tomography and joint service design; accountable for governance, risks and the planning report.

Structure for collaboration

• Executive Project Team (**EPT**): Directors of MAX IV and SciLifeLab with CIR representation—strategic oversight; monthly.

• Breakthrough Technology Development Group (**BTDG**): experts across modalities, AI/data and HSS—define work packages for the next phase; bi-weekly sprints.

• Scientific Project Managers: coordination, documentation, workshops, reporting (relying on staff at the infrastructures' operations offices) These will be paid from the project in full through its duration.

3) Forms of collaboration (planned activities)

Planned activities (planning only; specifying how services should be built and by whom).

• Coordination of research questions: WP-S1 Research agenda & state-of-the-art; WP-S2 interoperable protocols for consent, logistics, sample handling, metadata and cross-modal registration; selection of pathology use-cases. Identify **Standard Operating Procedures (SOPs)** that the project needs to deliver.

• Knowledge exchange: focused method-integration sprints (Oct–Jan) across partners

• Workshops and seminars: two workshops (Nov, Jan) for agenda-setting, workflow integration and service design; seminar series on phase-contrast acquisition/reconstruction and correlative vEM/spatial omics.

• Needs assessment of infrastructure: service-readiness criteria for phase-contrast tomography, vEM and spatial omics; compute/storage and governance needs; *concept note for a biomedical imaging beamline at MAX IV* (planning only).

Six-month workflow

• **M1 – Kick-off & scope:** Inception meeting; confirm < 5 pathology use-cases; EPT/BTDG roster; HSS interview plan; lock workshop dates.

• **M2 – Workshop 1 (agenda & interfaces):** State-of---the-art review; biopsy→X-ray→vEM→spatial omics handoffs; data/AI governance options; launch -methodintegration- sprints.

• **M2–M4 – Technology sprints:** Short staff exchanges (MAX IV ↔ SciLifeLab ↔ CIR); data/AI reference architecture; define/refine requirements.

• **M5 – Workshop 2 (service design):** Joint services/access models; training/mobility plan; beamline concept note (planning only); acceptance criteria; collect LOIs.

• **M6 – Synthesis & reporting:** Finalise the 20 page planning report + annexes (SOP drafts, architecture diagram, governance outline, letters of intent).

Work packages

WP	Planning focus	Lead & partners	Deliverables/Outputs
S1 Research agenda & state-of-the-art	Fix <5 pathology use cases; map capabilities/gaps; international comparators.	*PI*/MAX IV with Ellenberg, Phillipson; CIR	8–10 pp agenda & gap map; use-case sheets with feasibility/risks (EPT-approved).
S2 Sample & metadata interoperability	Consent, biopsy logistics, tissue handling; metadata schema; cross-modal registration; governance.	Phillipson (ethics/clinical), Lundqvist (CIR), Data Centre/NBIS	SOP v1.0; metadata profile (DATS/OME-NGFF); governance note; decision log.
S3 Phase contrast Xray tomography @ MAX IV	Acquisition (incl. multi-distance); dose/throughput envelopes; GPU-based reconstruction; readiness criteria.	*PI*/MAX IV with X-ray & data experts	Requirements spec; readiness checklist; **beamline concept note** (planning only).
S4 Volume EM workflows (vEM)	RT and cryogenic plasma FIB-SEM; targeting from X-ray volumes; QA; compatibility with spatial omics.	Carroni (CMI) with CMI units	SOPs (targeting, milling, acquisition, QA) + interface note to S5.
S5 Spatial omics integration	3D extension (transcriptomics/proteomics/MSI); registration to X-ray/vEM; data products.	Nilsson (SSCB) with SSCB units	Protocol map (2D→3D); registration playbook; data product spec (levels, QC, provenance).
S6 AI & data architecture + governance	Reference architecture for cross-scale fusion; QC, reproducibility; access control; FAIR + pseudonymisation.	Wählby (NBIS/BIIF) with Data Centre	Architecture diagram; MLOps/QC plan; governance options; minimal compute/storage plan.
S7 Cluster & service design	Joint services across MAX IV–SciLifeLab; CIR interfaces; training/mobility; LOIs.	Ellenberg (SciLifeLab), *PI*, Lundqvist (CIR)	Service catalogue (access modes, SLAs), training/mobility plan, LOI packet, risk register.

4) Description of merits (applicant's suitability)

The applicant team combines leadership of national research infrastructures with strengths in coherent X-ray imaging, clinical multimodal imaging/biopsies, vEM, spatial omics and AI-enabled analysis. Complementarity is explicit (CIR ↔ MAX IV ↔ SciLifeLab), supporting realistic planning and credible routes to service readiness in a future cluster.

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