

Harmonizing KPMP / HuBMAP Data: Developing Novel Common Coordinate Framework User Interfaces

Bruce W. Herr II, Katy Börner, and MC-IU Team

Intelligent Systems Engineering, School of informatics,
Computing and Engineering
Indiana University, Bloomington, IN; Harvard Medical School,
Boston, MA

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Katy Börner
MC-IU PI, Faculty, CNS Director
katy@indiana.edu
CNS projects and ambitions,
science maps, MOOCs
Enjoys: Fashion design, movies,
German food



Griffin M. Weber
Associate Professor of Medicine
and Biomedical Informatics
Department of Medicine, Harvard
Medical School
griffin_weber@hms.harvard.edu



Lisel Record
MC-IU PM, CNS Assoc. Director
recorde@indiana.edu
Project management, user
research, public outreach
Enjoys: Growing the perfect tomato



Ellen M. Quardokus
MC-IU Research Scientist
ellenmq@indiana.edu
Molecular biology, microscopy,
anatomy, scientific software,
usability, interdisciplinary
communication



Bruce W. Herr II
CNS Senior System Architect / PM
bherr@indiana.edu
Scrum, visualization, technology
trends
Enjoys: Meditation, hot sauce,
family



Leonard Cross
Senior Interaction Designer
lccross@iu.edu
User interface specification and
design



Andreas Bueckle
PhD Candidate in Information Science
abueckle@indiana.edu
HuBMAP RUI, visualization, virtual
reality, filmmaking
Enjoys: Traveling, photography,
sailing



Matthew Martindale
CNS Center Assistant
masmarti@iu.edu
Travel, purchasing, event
organization
Enjoys: Spending time with family

The Human Body at Cellular Resolution: The NIH Human Biomolecular Atlas Program.

Snyder et al. *Nature*. 574, p. 187-192.

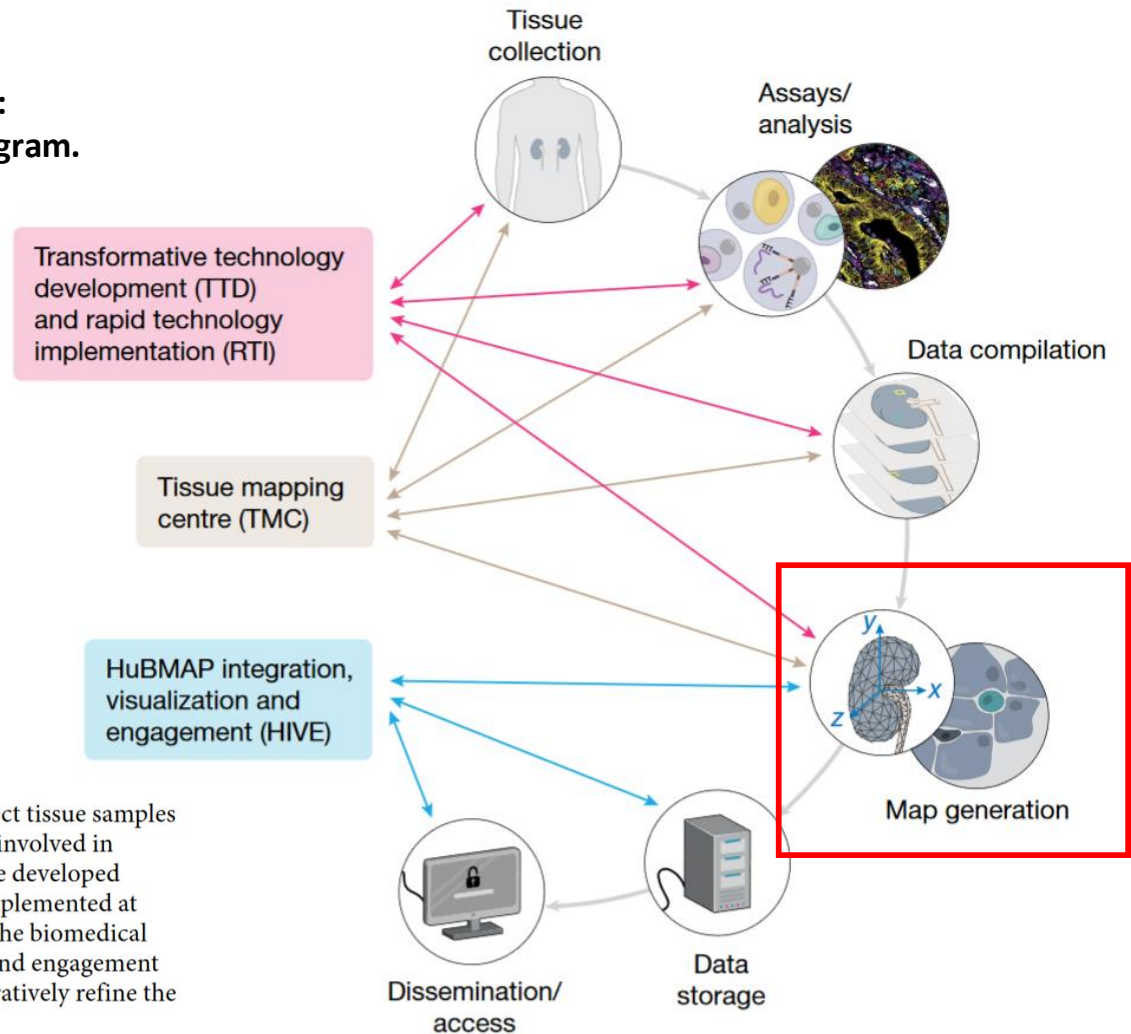


Fig. 1 | The HubMAP consortium. The TMCs will collect tissue samples and generate spatially resolved, single-cell data. Groups involved in TTD and RTI initiatives will develop emerging and more developed technologies, respectively; in later years, these will be implemented at scale. Data from all groups will be rendered useable for the biomedical community by the HuBMAP integration, visualization and engagement (HIVE) teams. The groups will collaborate closely to iteratively refine the atlas as it is gradually realized.

The Human Body at Cellular Resolution: The NIH Human Biomolecular Atlas Program.
 Snyder et al. *Nature*. 574, p. 187-192.

- Landmarks are**
- **Anatomical structures**
 - **Biomolecular markers**

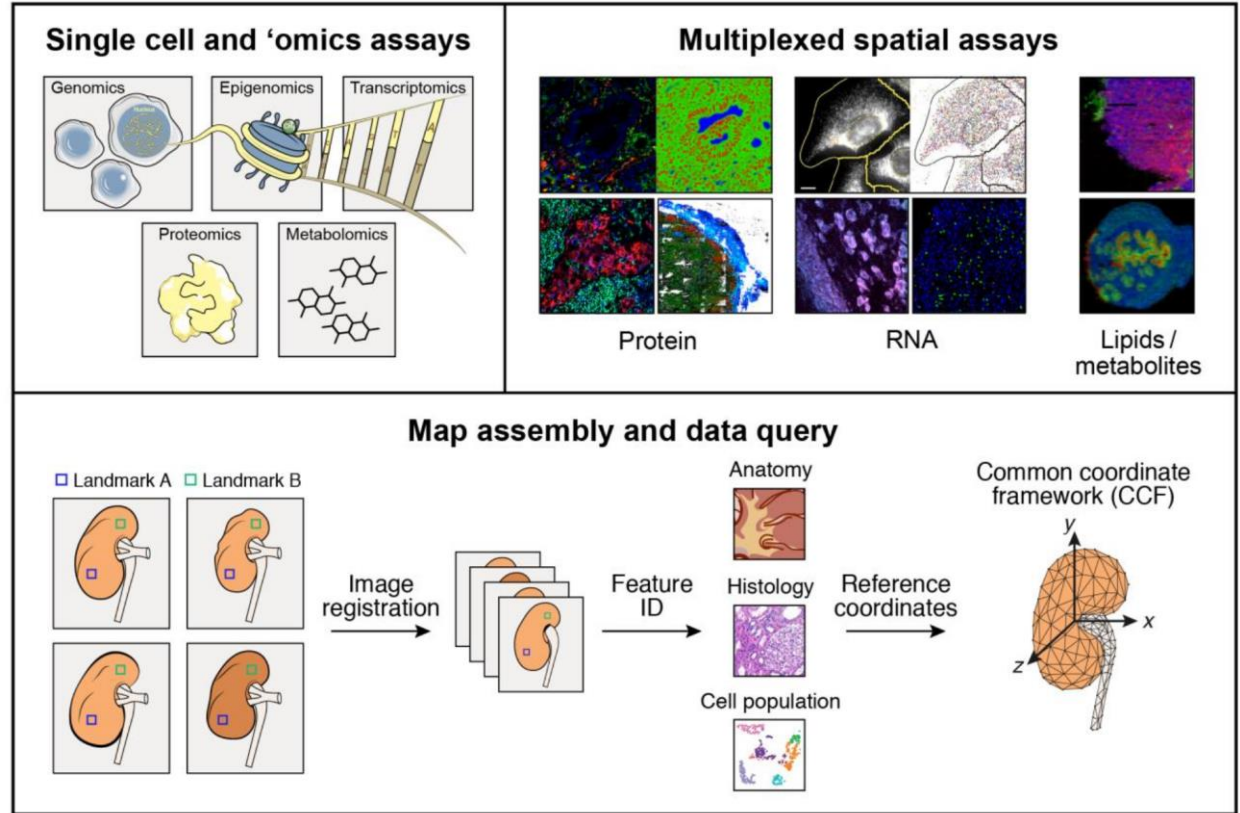
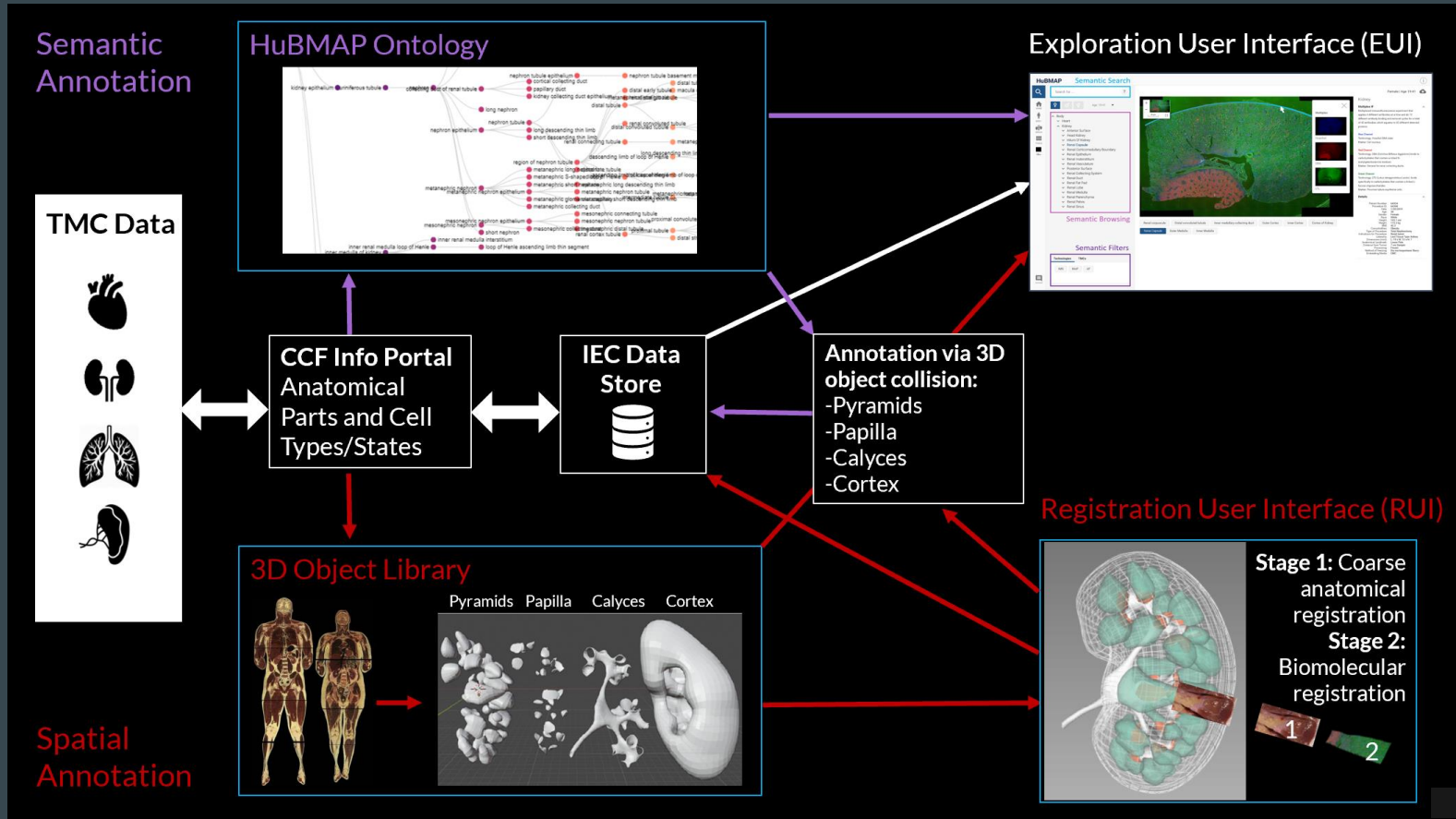


Fig. 3 | Map generation and assembly across cellular and spatial scales. HuBMAP aims to produce an atlas in which users can refer to a histological slide from a specific part of an organ and, in any given cell, understand its contents on multiple 'omic levels—genomic, epigenomic, transcriptomic, proteomic, and/or metabolomic. To achieve these ends, centres will apply a combination of imaging, 'omics and mass spectrometry

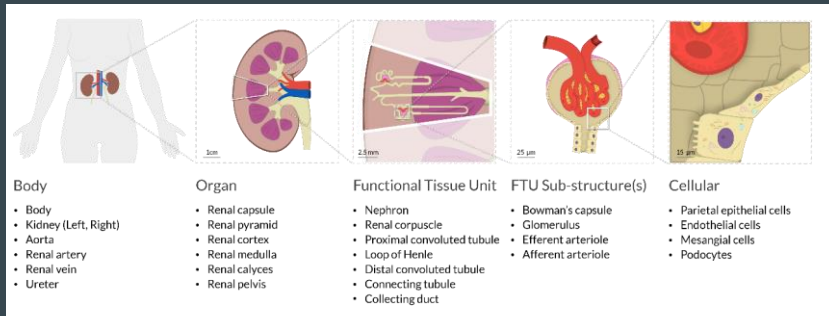
techniques to specimens collected in a reproducible manner from specific sites in the body. These data will be then be integrated to arrive at a high-resolution, high-content three-dimensional map for any given tissue. To ensure inter-individual differences will not be confounded with collection heterogeneity, a robust CCF will be developed.

MC-IU: CCF Registration to CCF Exploration Workflow

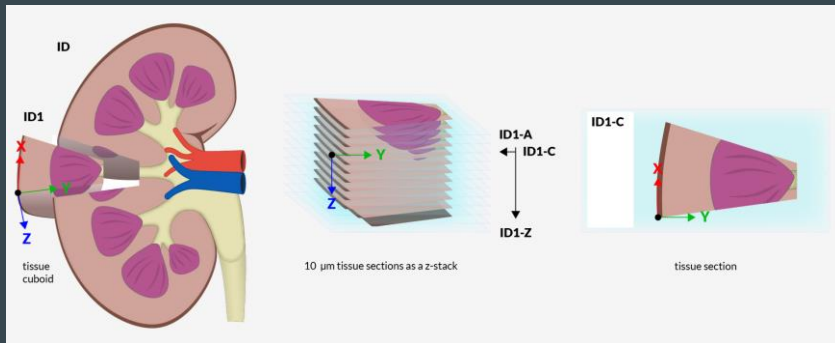


MC-IU: Common Coordinate Framework (CCF)

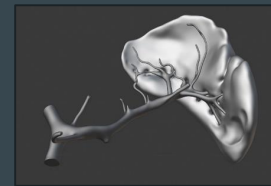
A common coordinate framework (CCF) is a conceptual and computational framework for the storage, analysis, and (visual) exploration of spatially and semantically indexed data—across individuals, technologies, labs.



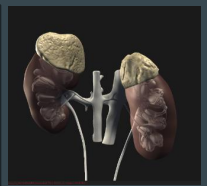
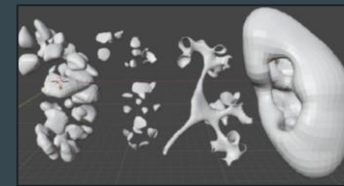
Semantic zoom from whole human body, to organ, to functional tissue units (FTUs), to single-cell level.



Three-step spatial registration of single cells in relation to reference organs.



VH Spleen



VH Kidney

MC-IU: CCF Relevant Metadata















HuBMAP

HuBMAP CCF Information Portal

This portal links to information that is critical for constructing Common Coordinate Frameworks (CCFs) for the National Institutes of Health Human Biomolecular Atlas Program (HuBMAP).

The information was provided by individual organ-specific Tissue Mapping Centers (TMCs), Transformative Technology Development (TTD), or Rapid Technology Implementation (RTI) efforts in close collaboration with the Mapping Component at Indiana University (MC-IU).

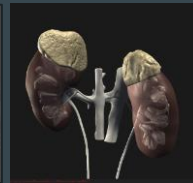
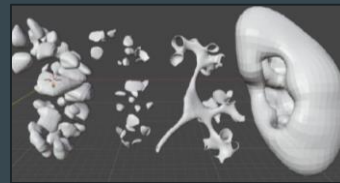
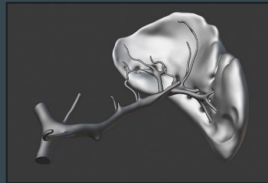
For questions, please contact MC-IU via info@iuhbmap.org.

Organ	TMC	Technology
 Kidney	TMC-Vanderbilt	MALDI Imaging Mass Spectrometry (MALDI IMS) LC-MS
 Kidney	TTD-Berkeley	nanoDESI IMS LC-MS
 Kidney	TMC-UICSD	SNARE-seq2; psRNAseq SNARE-seq2; Chromatin Accessibility seq Bulk RNA-seq
 Spleen	TMC-Caltech-UW	seq-FISH
 Spleen	TMC-Florida	Light Sheet Microscopy (LSM) CODEX Imaging Mass Cytometry (IMC) Single Cell scRNA-Seq 10x Genomics
 Heart	TMC-Caltech-UW	seq-FISH
 Lung	TMC-UICSD	Bulk RNA-seq SNARE-seq2; psRNAseq SNARE-Seq2; Chromatin Accessibility seq
 Large Intestine	TMC-Stanford	CODEX Bulk RNA-seq Bulk ATAC-seq Bulk Whole Genome Sequencing (WGS) Metabolomics/Lipidomics
 Small Intestine	TMC-Stanford	CODEX snRNA-seq Bulk RNA-seq Bulk ATAC-seq Bulk Whole Genome Sequencing (WGS) Metabolomics/Lipidomics
 Small Intestine	TMC-Caltech-UW	SeqFISH
 Bladder	TMC-UICSD	SNARE-seq2; Chromatin Accessibility seq
 Ureters	TMC-UICSD	SNARE-seq2; Chromatin Accessibility seq
 Thymus	TMC-Florida	Light Sheet Microscopy (LSM) CODEX Imaging Mass Cytometry (IMC) Single Cell scRNA-Seq 10x Genomics
 Lymph Nodes	TMC-Florida	Light Sheet Microscopy (LSM) CODEX Imaging Mass Cytometry (IMC) Single Cell scRNA-Seq 10x Genomics

Information critical for CCF design but not yet captured in the data on Globus is documented in the [CCF Info Portal](#).

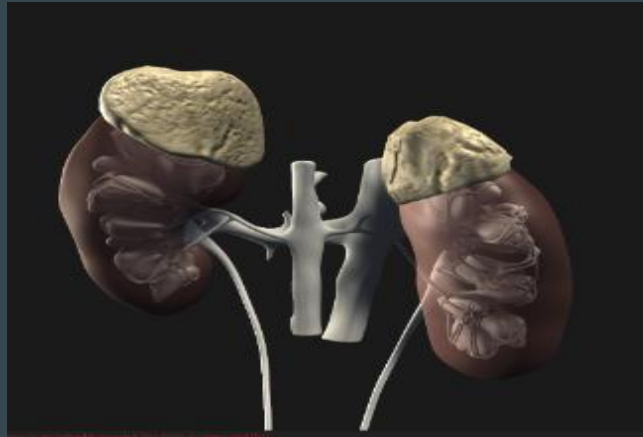
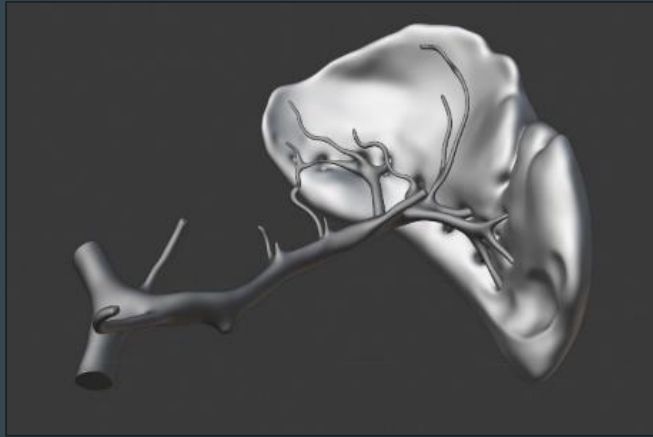
The CCF Info Portal also captures details for the CCF reference organs. Completed organs, approved by TMC organ experts:

- Kidney (left and right) for male and female Visible Human
- Spleen for male and female Visible Human



Anatomical and cell type data from the anatomical structures and cell types (ASCT) tables for the kidney and spleen have been linked to UBERON, Foundational Model of Anatomy (FMA), Kidney Tissue Anatomy Ontology (KTAO), and Cell Ontology (CL).

MC-IU: CCF Object Library



3D models by Kristen Browne, NIH. Rendering by MC-IU.

File Formats

Basic image/object: OME-Tiff (raster) and OBJ (vector)

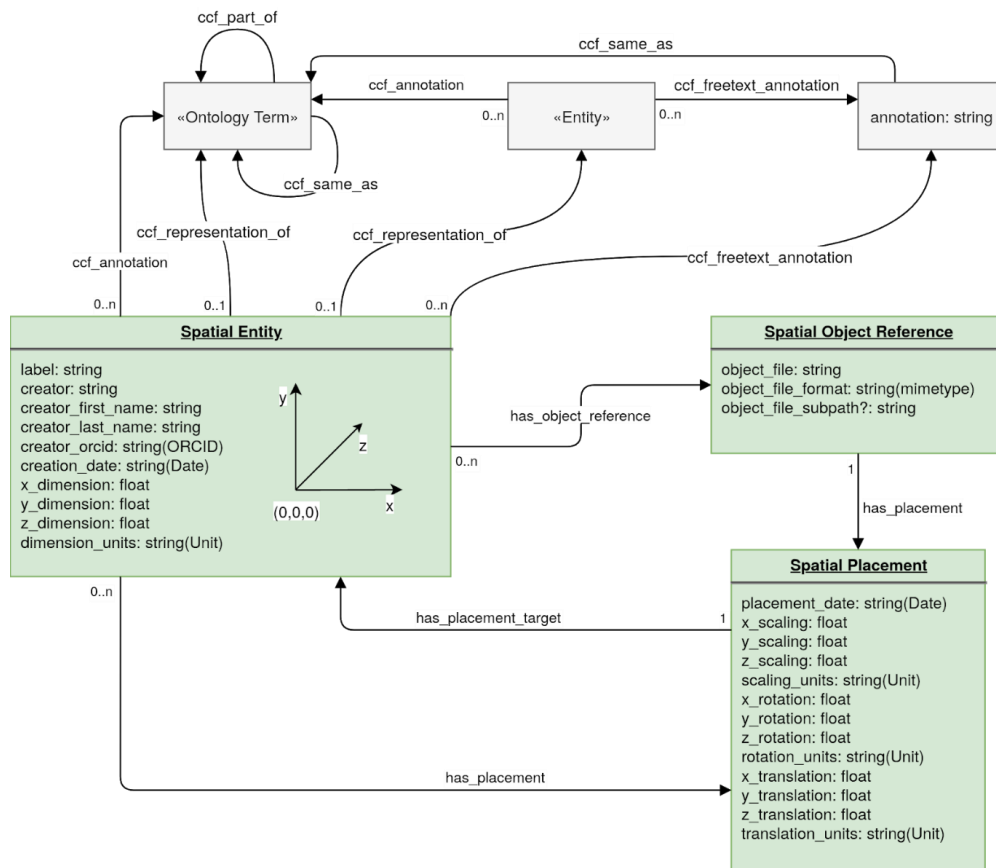
Regions: SVG annotations for 2D, OBJ regions in 3D (aligned with reference model for the organ)

Reference Organs

Kidney: Male and female kidneys from NLM VH
ImageVU 5/50/500 kidneys by Dec. 2019/Feb. 2020/June 2020

Lung: Lung D175 (June 2020)

MC-IU: ER Diagram of CCF Core Model

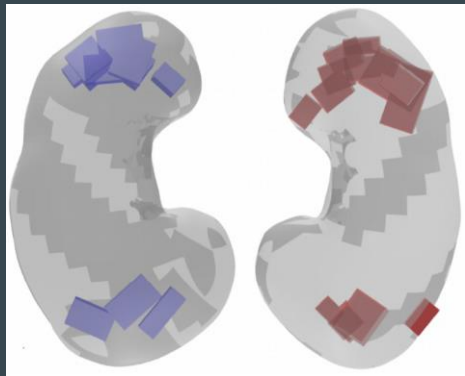


Current sources of ontology terms are: UBERON, Foundational Model of Anatomy (FMA), Kidney Tissue Anatomy Ontology (KTAO), and Cell Ontology (CL).

<http://purl.org/ccf/latest/ccf.owl>

- ▼ body
 - heart
 - ▼ kidney
 - ▼ renal pelvis
 - right renal pelvis
 - metanephric renal pelvis
 - mucosa of renal pelvis
 - kidney calyx
 - renal papilla
 - left renal pelvis
 - perihilar interstitium
 - kidney pelvis smooth muscle
 - kidney pelvis urothelium
 - ▼ renal parenchyma
 - cortex of kidney
 - ▼ kidney vasculature
 - kidney blood vessel
 - ▲ kidney capsule

MC-IU: CCF Metadata Captured



Kidney: right

left

Kidney data by VU:

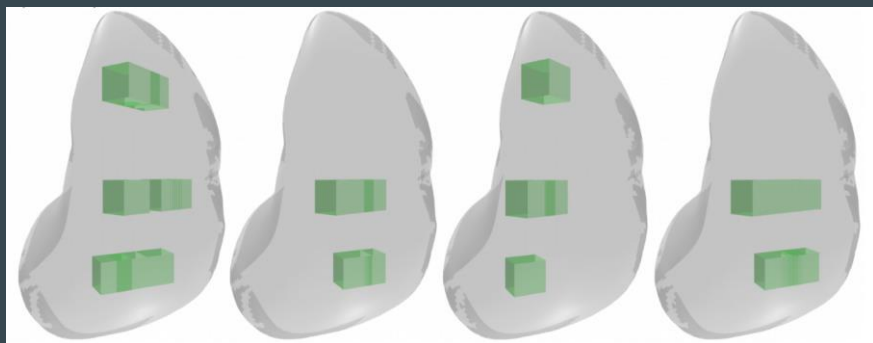
25 tissue cuboids were registered using the RUI. Data is on Globus.

Spleen data by UFL:

Data comes from 4 spleens. There exist 3 sampling sites (CC1-CC3).

Each CC is subdivided into 6 cuboids. 24 cuboids were registered.

All $25 + 24 = 49$ cuboid registrations were confirmed with TMC experts.

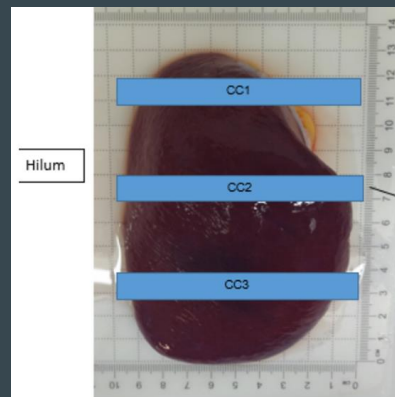


Spleen: UFL0001

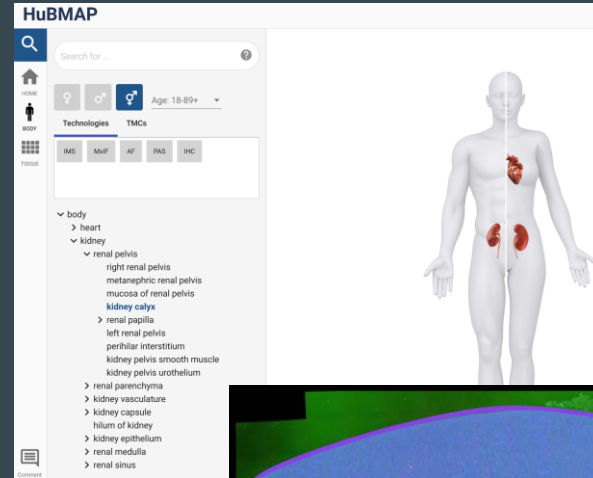
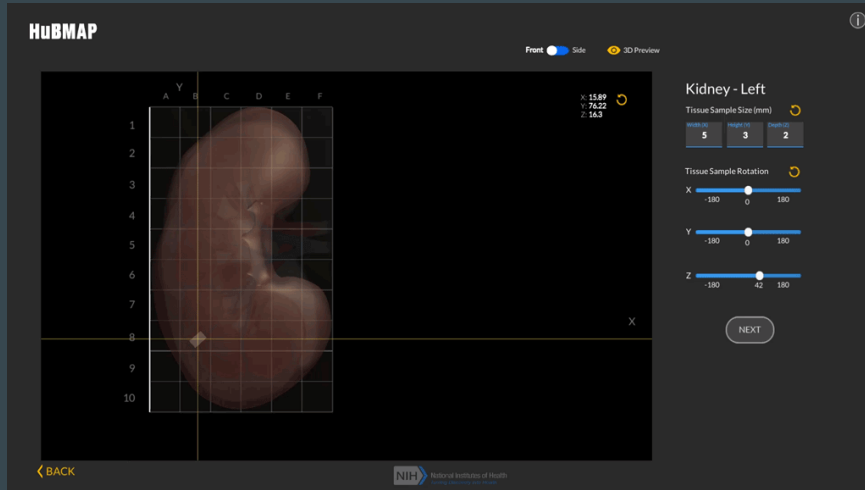
UFL0002

UFL0003

UFL0004



MC-IU: CCF Registration UI (RUI) and Exploration UI (EUI)

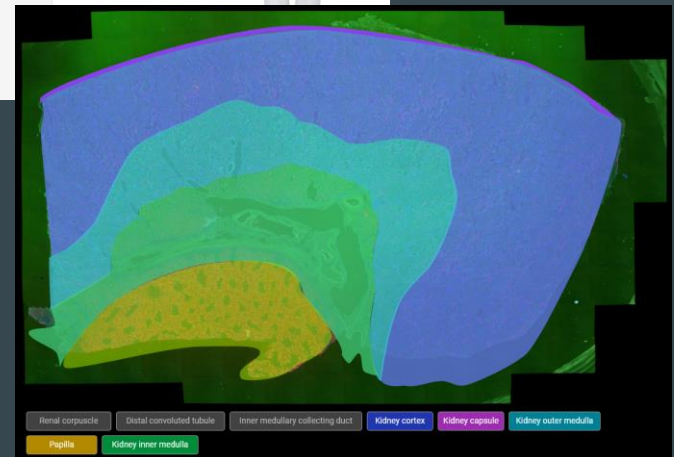


RUI was designed for experts that collect human tissue and need to document the tissue extraction site.

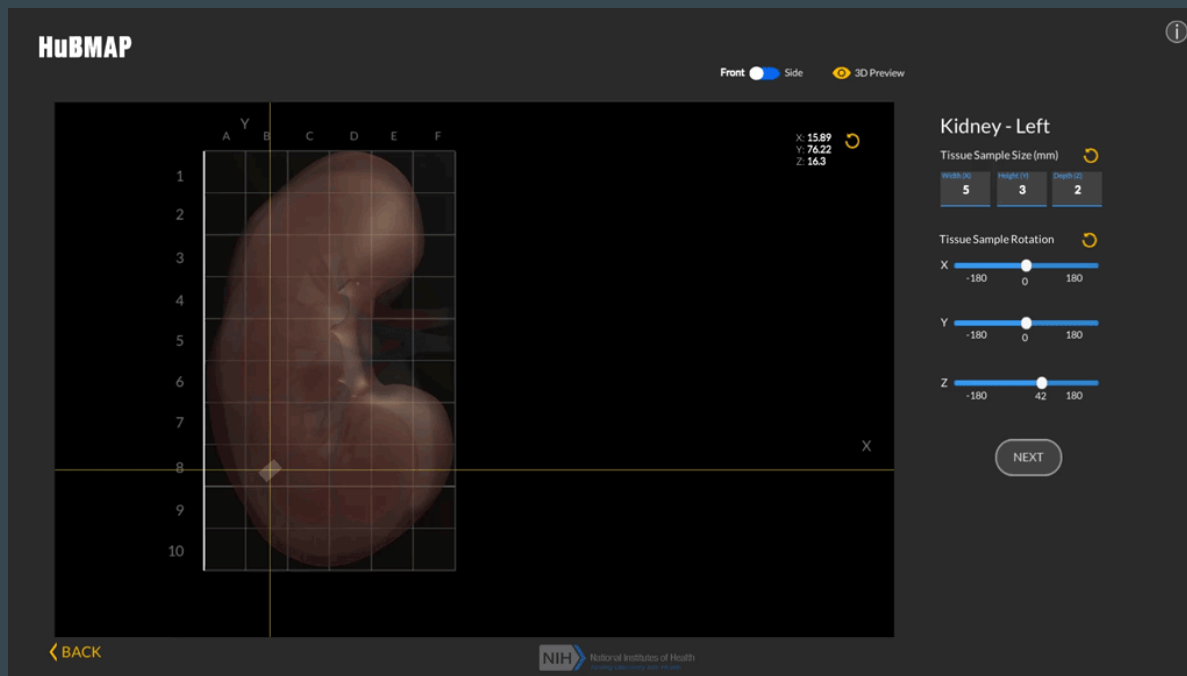
<https://hubmapconsortium.github.io/ccf-3d-registration>

EUI makes it possible to explore 2D/3D tissue samples semantically and spatially across multiple scales.

<https://hubmapconsortium.github.io/ccf-ui/>



CCF Registration UI (RUI) DEMO



Registration UI: <https://hubmapconsortium.github.io/ccf-3d-registration>

RUI Tutorial: <https://www.youtube.com/watch?v=-ABY5leCEk4>

RUI Tech Demo: <https://www.youtube.com/watch?v=E8GGcpPsohc>

RUI Semantic Annotation Using Collision Detection: <https://www.youtube.com/watch?v=6SLqUBEJALE>

Acknowledgements

HuBMAP Consortium (<https://hubmapconsortium.org>)



Thanks go to all the **patients** that agreed to volunteer healthy tissue and open use of their data.



TMCs



Jeffrey Spraggins
TMC-Vanderbilt
Vanderbilt University



Sanjay Jain
TMC-UCSD
Washington University
St. Louis



Clive Wasserfall
TMC-UFL
University of Florida



Kristen Browne
Medical Imaging and
3D Modeling Specialist
NIAID

3D Models

MC-IU HIVE Team



Katy Börner
MC-IU PI
CHS Director



Griffin Weber
Assoc. Professor of Medicine
Harvard Medical School



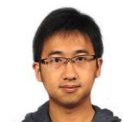
Lisele Record
MC-IU PI
CHS Associate Director



Bruce Herr II
Sr. Systems Architect/PII



Ellen Quardokus
Sr. Research Analyst



Yingnan Ju
PhD Student



Andreas Bueckle
PhD Candidate



Leonard Cross
Sr. UX/UI Designer



Matthew Martindale
Center Assistant