2.1 Common Coordinate Framework (CCF) Session

Organizers
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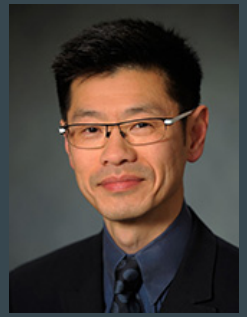
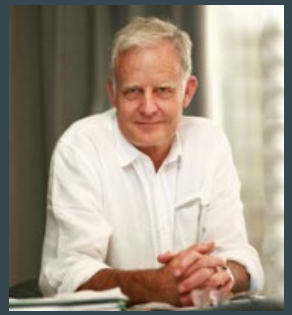



NIH-HCA Virtual Meeting

March 30, 2020

2.1 Common Coordinate Framework (CCF) Session

Subtopics
(1) CCF User Interfaces & Anatomical Structures and Cell Types (ASCT) Tables - Katy Börner
(2) Computational physiology - Peter Hunter
(3) Data localizations to CCF - James Gee

Overall Goal
Create cross-consortia collaborations and programs in areas where this community needs to build a stronger international ecosystem for single cell analysis work.

(1) CCF User Interfaces & Anatomical Structures and Cell Types (ASCT) Tables (Katy Börner)

Major anatomical terms and 3D structures in human

- Which organs are studied by which of the 12+ consortia attending the NIH-HCA meeting?
- What gross and micro anatomical terms are most important for the R&D in the 12+ consortia?
- What are common sampling sites from which tissue is sampled for the different organs?

Major human cell types, sizes, and “calling cards”

- What cell types are most important for the organs studied by the 12+ consortia attending the NIH-HCA meeting?
- Which of the 25+ sc assay types are most indicative for identifying these cell types?
- What is known about cell type sizes and distribution in human micro and macro anatomy?

Taxonomy nomenclatures and standardization

- What nomenclature conventions are available?
- Recognizing there won't be a 'perfect' solution, what are priorities to consider for cross-system cell class nomenclatures?

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**

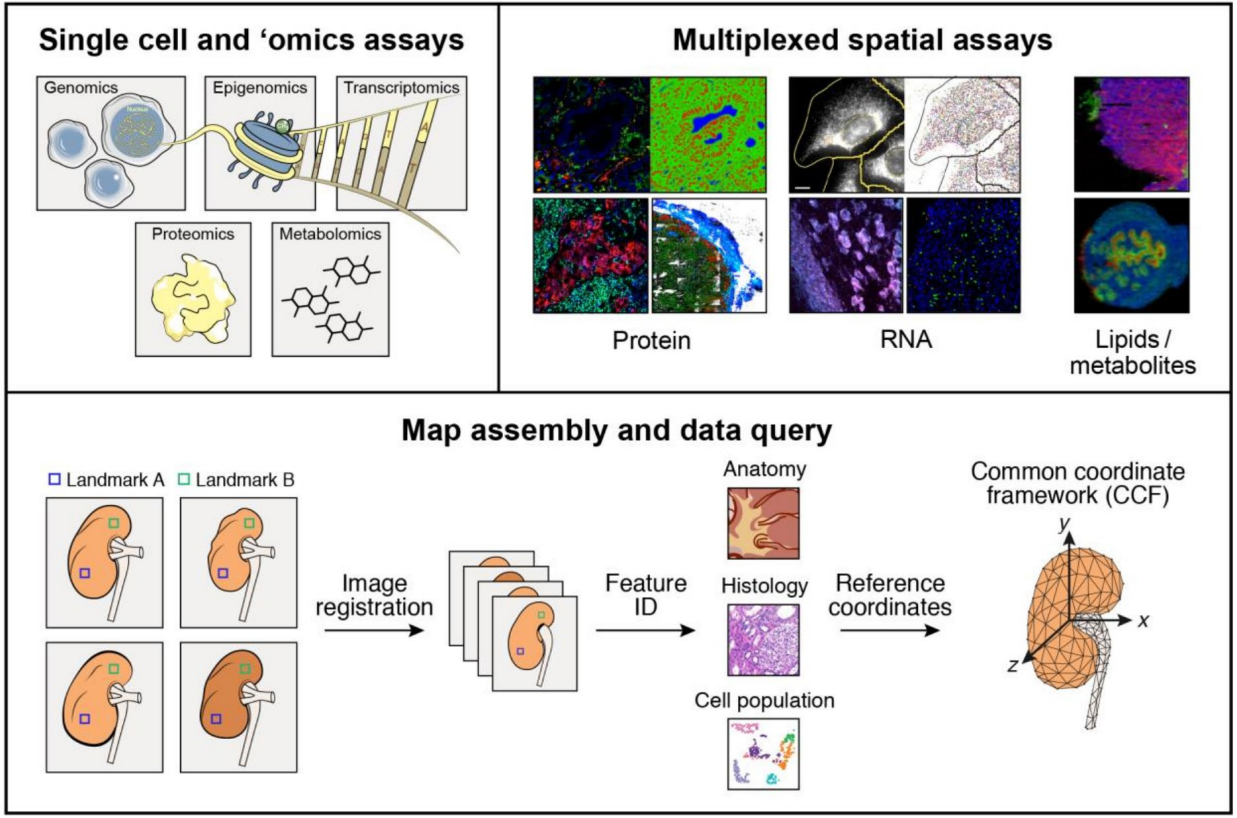
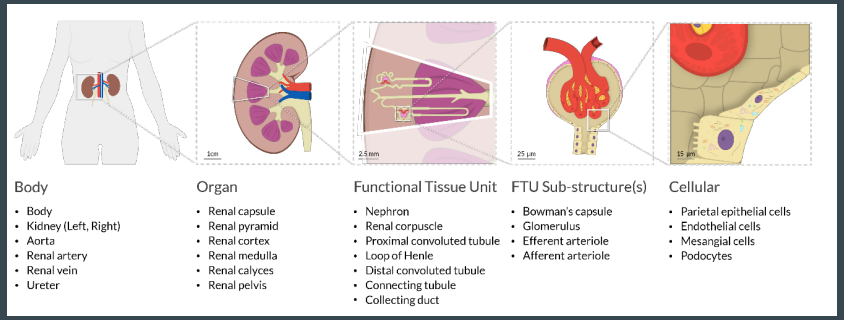


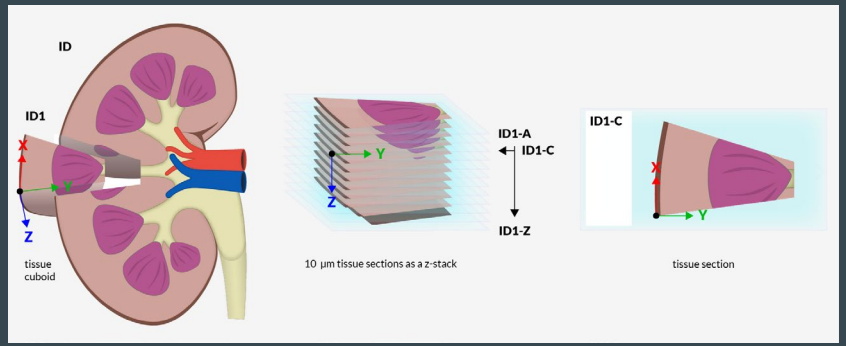
Fig. 3 | Map generation and assembly across cellular and spatial scales. HuBMAP aims to produce an atlas in which users can refer to a histological slide from a specific part of an organ and, in any given cell, understand its contents on multiple 'omic levels—genomic, epigenomic, transcriptomic, proteomic, 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.

Common Coordinate Framework (CCF)

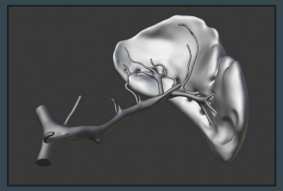
A common coordinate framework (CCF) is a conceptual and computational framework for the storage, analysis, and (visual) exploration of spatially and semantically indexed data—across individuals, technologies, labs.



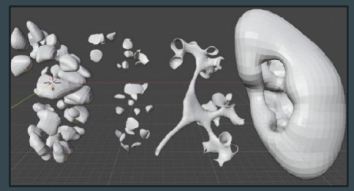
Semantic zoom from whole human body, to organ, to functional tissue units (FTUs), to single-cell level.

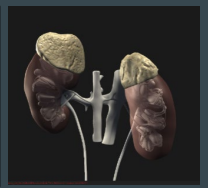


Three-step spatial registration of single cells in relation to reference organs.



VH Spleen





VH Kidney

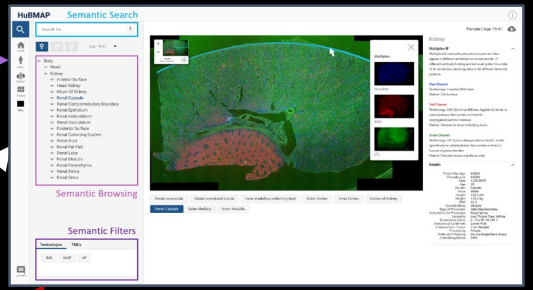
Semantic Annotation

Partonomy

kidney
kidney capsule
cortex of kidney
outer cortex of kidney
renal medulla

Knowledge Graph

Exploration User Interface (EUI)



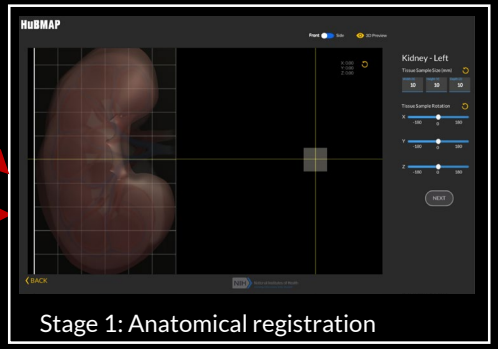
CCF Info Portal
Anatomical Structures and Cell Types (ASCT)

TMC Data

IEC Data Store

Semantic Annotation via 3D Object Collision
- Cortex
- Medullary Pyramids
- Calyces

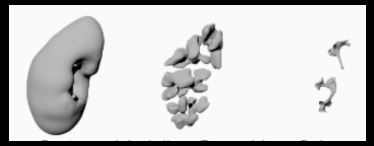
Registration User Interface (RUI)



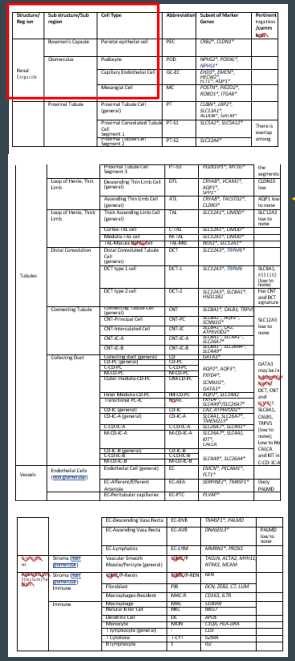
Spatial Annotation

3D Object Library

Cortex Medullary Pyramids Calyces

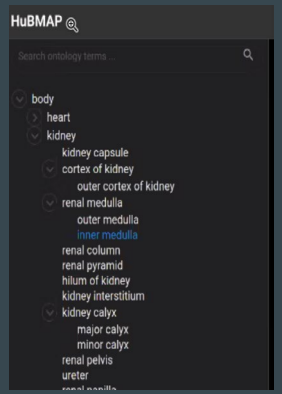


ASCT Table



Ontology Design

Partonomy



Knowledge Graph

3D Object Design

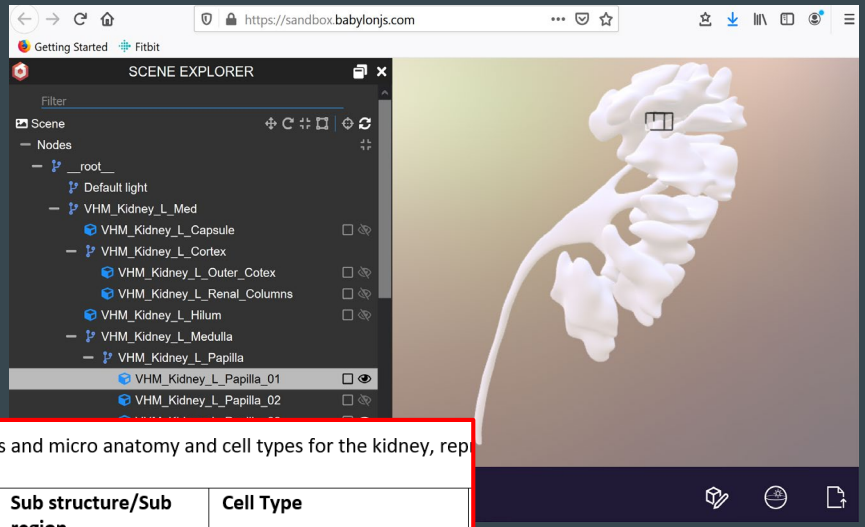


Table S2: Gross and micro anatomy and cell types for the kidney, rep

Structure/ Reg ion	Sub structure/Sub region	Cell Type
Renal Corpuscle	Bowman's Capsule	Parietal epithelial cell
	Glomerulus	Podocyte
		Capillary Endothelial Cell
		Mesangial Cell

A Multimodal and Integrated Approach to Interrogate Human Kidney Biopsies with Rigor and Reproducibility: The Kidney Precision Medicine Project https://www.biorxiv.org/content/10.1101/828665v1

Table 5: Cell types and associated markers from KPMP Pilot 1 transcriptomic studies. Asterisk denotes genes detected by more than one technology. *Italics*, genes detected by a single technology.

Structure/Region	Sub structure/Sub region	Cell Type	Abbreviation	Subset of Marker Genes	Pertinent negatives/comments
Renal Corpuscle	Bowman's Capsule	Parietal epithelial cell	PEC	*CRB2*, CLDN1**	
	Glomerulus	Podocyte	POD	*NPHS2*, PODXL*, NPHS1**	
		Capillary Endothelial Cell	GC-EC	*EHD3*, EMCN*, HECW2*, FLT1*, AQP1**	
		Mesangial Cell	MC	*POSTN*, PIEZO2*, ROBO1*, ITGA8**	
Tubules	Proximal Tubule	Proximal Tubule Cell (general)	PT	*CUBN*, LRP2*, SLC13A1*, ALDOB*, GATM**	
		Proximal Convoluted Tubule Cell Segment 1	PT-S1	*SLC5A2*, SLC5A12**	There is overlap among the segments
		Proximal Tubule Cell Segment 2	PT-S2	*SLC22A6**	
		Proximal Tubule Cell Segment 3	PT-S3	*PDZK1IP1*, MT1G**	
	Loop of Henle, Thin Limb	Descending Thin Limb Cell (general)	DTL	*CRYAB*, VCAM1*, AQP1*, SPP1**	CLDN10 low
		Ascending Thin Limb Cell (general)	ATL	*CRYAB*, TACSTD2*, CLDN3**	AQP1 low to none
	Loop of Henle, Thick Limb	Thick Ascending Limb Cell (general)	TAL	*SLC12A1*, UMOD**	SLC12A3 low to none
		Cortex-TAL cell	C-TAL	*SLC12A1*, UMOD**	
		Medulla-TAL cell	M-TAL	*SLC12A1*, UMOD**	
		TAL-Macula Densa cell	TAL-MD	*NOS1*, SLC12A1**	
	Distal Convolution	Distal Convoluted Tubule Cell (general)	DCT	*SLC12A3*, TRPM6**	
		DCT type 1 cell	DCT-1	*SLC12A3*, TRPM6*	SLC8A1, HSD11B2 (low to none)
		DCT type 2 cell	DCT-2	*SLC12A3*, SLC8A1*, HSD11B2*	Has CNT and DCT signature
	Connecting Tubule	Connecting Tubule Cell (general)	CNT	*SLC8A1*, CALB1, TRPV5*	
		CNT-Principal Cell	CNT-PC	*SLC8A1*, AQP2*, SCNN1G**	

Anatomical Structures and Cell Types (ASCT) Table Example for

Kidney

Also called Pathology and Cell Ontology Table in UK

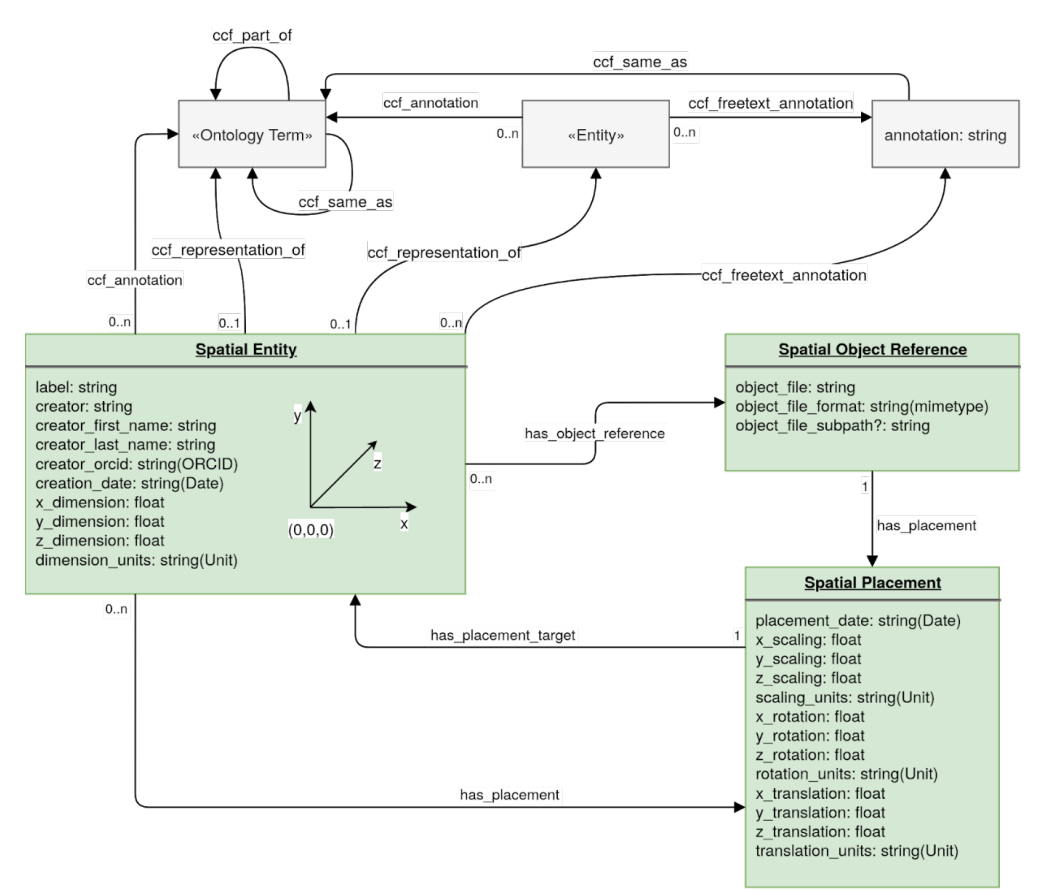
ASCT Table compiled by Clive H. Wasserfall and Marda L. Jorgensen Department of Pathology, University of Florida

Structure/Region	Substructure/Sub-region			Cell Types	Marker Subset
Splenic Pulp	Red Pulp	Venous Sinuses	Pulp Arteries	Vascular endothelium	CD34, SMA
			Penincillar Arterioles	Vascular endothelium	CD34
			Sheathed Arterioles	Vascular endothelium, macrophages, sheath cells	CD34
			Arterial Capillaries	Vascular endothelium	CD34
			Sinuses	Littoral cells	CD8a, CD68, LYVE-1
				Endothelial	CD141
			Veins	Vascular endothelium	CD34
			Stroma	Stromal Cells	Collagen IV, MadCAM-1, CD271
		Splenic Cords		Macrophages	CD68, CD163
				Monocytes	CD11b, CD11c, CD14
				Reticular Myofibroblasts	SMA, CK8/18, CD271
				Erythrocytes	CD235a
				B Lymphocytes	CD20, CD19

Anatomical Structures and Cell Types (ASCT) Table Example for

Spleen

Entity Relationship Diagram of CCF Core Model

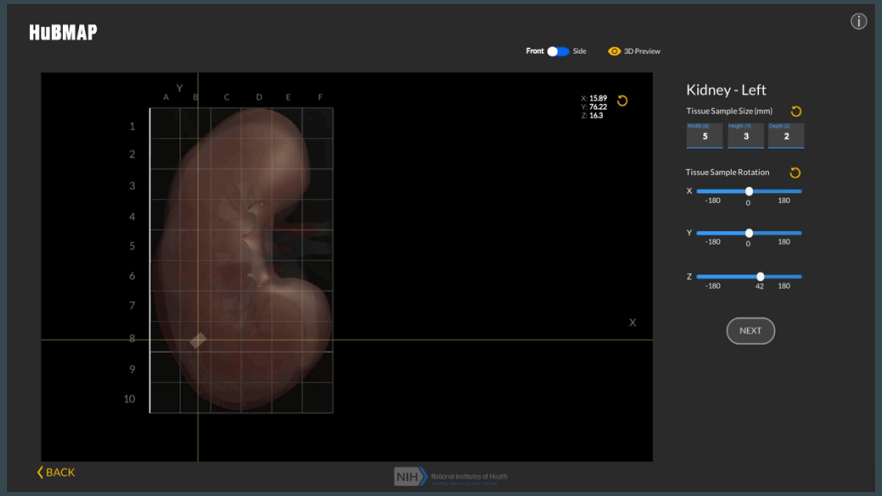


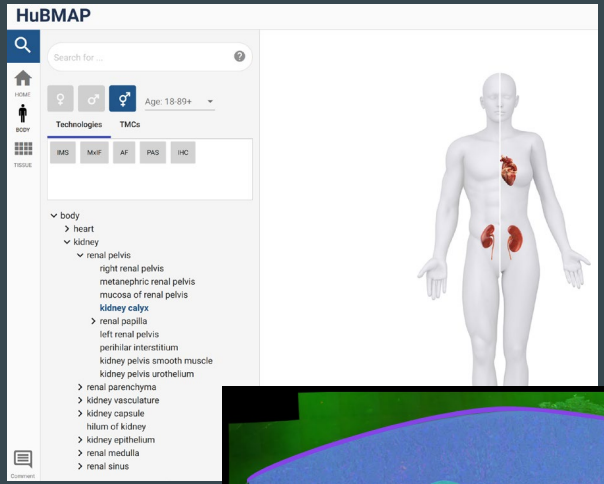
Current sources of ontology terms are: UBERON, Foundational Model of Anatomy (FMA), Kidney Tissue Anatomy Ontology (KTAO), and Cell Ontology (CL).

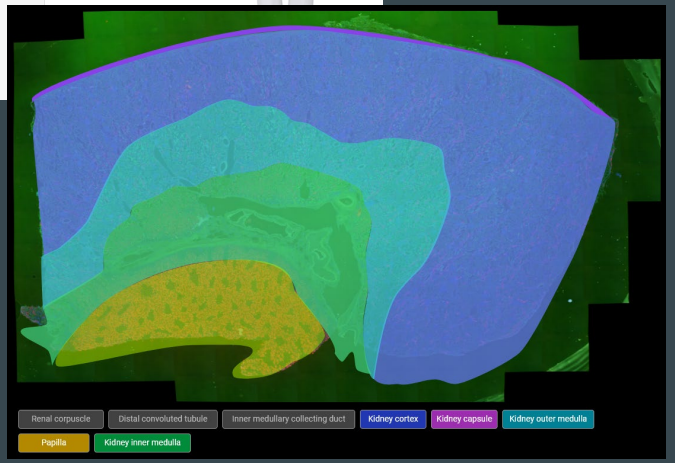
http://purl.org/ccf/latest/ccf.owl

- 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

CCF Registration UI (RUI) and Exploration UI (EUI)



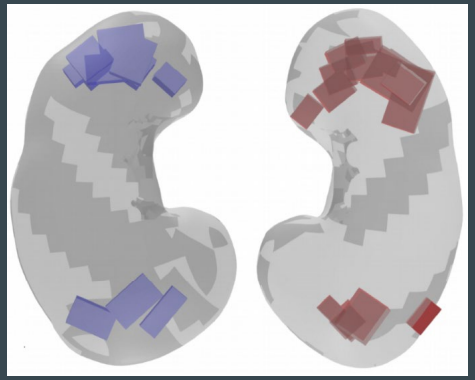




RUI was designed for experts that collect human tissue and need to document the tissue extraction site.
https://hubmapconsortium.github.io/ccf-3d-registration

EUI makes it possible to explore 2D/3D tissue samples semantically and spatially across multiple scales.
https://hubmapconsortium.github.io/ccf-ui/

CCF Metadata Captured

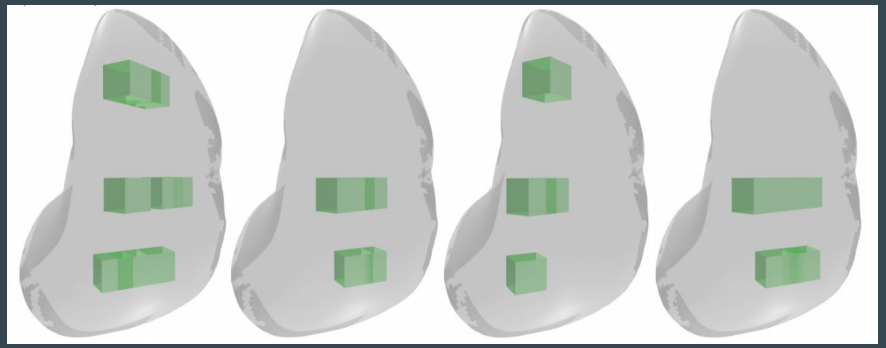


Kidney: right left

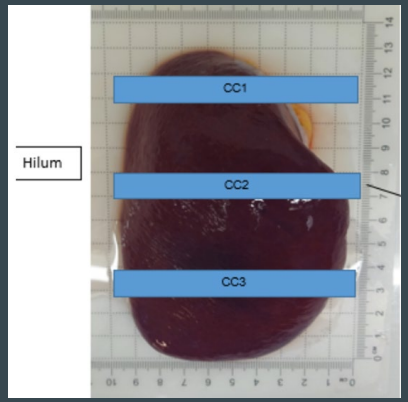
Kidney data by VU:
25 tissue cuboids were registered using the RUI. Data is on Globus.

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



Anatomical Structures and Cell Types (ASCT) Table - DRAFT!

10 Organs x 10 Consortia Effort to Agree on Anatomical Structures and Cell Types (ASCT) Tables for Human

	HuBMAP	RBK	KPMP	SPARC	LungMAP	HTAN	HCA	GUDMAP	t Cell Atl	BICCN	len Brain Atl	TCGA	Total
Kidney	1	S cells, organ	1	0	0	0	1	1	0	0	0	1	5
Liver	0	0	0	0	0	0	1	0	0	0	0	1	2
Spleen	1	0	0	0	0	0	1	0	0	0	0	0	2
Heart	1	0	0	1	0	0	1	0	0	0	0	0	3
Lung	1	0	0	1	1	1	1	0	0	0	0	1	6
L intestine/Colon	1	0	0	1	0	1	1	0	1	0	0	1	6
S intestine	1	0	0	0	0	0	0	0	0	0	0	0	1
Bladder	1	0	0	1	0	0	0	1	0	0	0	1	4
Ureters	1	0	0	0	0	0	0	1	0	0	0	0	2
Thymus	1	0	0	0	0	0	0	0	0	0	0	1	2
Lymph nodes	1	0	0	0	0	0	1	0	0	0	0	0	2
mediastinal lymph node	0	0	0	0	0	0	1	0	0	0	0	0	1
Eye	1	0	0	0	0	0	1	0	0	0	0	0	2
Brain	0	0	0	0	0	0	1	0	0	1	1	1	4
Cerebellum	0	0	0	0	0	0	1	0	0	0	1	0	2
Pancreas	0	0	0	0	0	1	1	0	0	0	0	1	3
Breast	0	0	0	0	0	1	1	0	0	0	0	1	3
Skin	0	0	0	0	0	1	0	0	0	0	0	1	2
Pediatric systems	0	0	0	0	0	1	0	0	0	0	0	0	1
Ovaries	0	0	0	0	0	0	0	0	0	0	0	1	1
Eyes	0	0	0	0	0	0	1	0	0	0	0	0	1
Testes	0	0	0	0	0	0	0	0	0	0	0	1	1
Cervix	0	0	0	0	0	0	0	0	0	0	0	1	1
Uterus	0	0	0	0	0	0	0	0	0	0	0	1	1
Blood	0	0	0	0	0	0	1	0	0	0	0	1	2
Bone	0	0	0	0	0	0	1	0	0	0	0	0	1
Placenta	0	0	0	0	0	0	1	0	0	0	0	0	1
Decidua	0	0	0	0	0	0	1	0	0	0	0	0	1
Embryo	0	0	0	0	0	0	1	0	0	0	0	0	1
esophagus	0	0	0	0	0	0	1	0	0	0	0	1	2
hematopoietic system	0	0	0	0	0	0	1	0	0	0	0	0	1
immune system bulk	0	0	0	0	0	0	1	0	0	0	0	0	1
Stomach	0	0	0	1	0	0	0	0	0	0	0	1	2
Thyroid	0	0	0	0	0	0	0	0	0	0	0	1	1
Postate	0	0	0	0	0	0	0	0	0	0	0	1	1
Adrenal gland	0	0	0	0	0	0	0	0	0	0	0	1	1
Totals	**11**	**0**	**1**	**5**	**1**	**6**	**22**	**3**	**1**	**1**	**2**	**20**	

Please review table at https://tinyurl.com/ASCT10x10

Please suggest other

- consortia/efforts (columns)
- organs (rows)

that should be added.

CCF User Interfaces & Anatomical Structures and Cell Types (ASCT)

Please review table at https://tinyurl.com/ASCT10x10

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