CNS Cyberinfrastructure for Network Science Center

LUDDY SCHOOL OF INFORMATICS, COMPUTING, AND ENGINEERING Bloomington

Explore Human Reference Atlas Data in 3D VR

Andreas "Andi" Bueckle, Ph.D.
Research Lead

Cyberinfrastructure for Network Science Center
Department of Intelligent Systems Engineering
Luddy School of Informatics, Computing, and Engineering
Indiana University, Bloomington, IN, USA

3rd Annual XR Symposium | Johns Hopkins University Applied Physics Laboratory | Laurel, MD | July 27, 2022

Vision…

https://www.reddit.com/r/Thatsabooklight/comments/kf2ve0/the_medical_infusion_devices_center_background/

https://medcitynews.com/2019/09/the-benefits-of-ar-in-healthcare/

…and Reality

https://www.mobihealthnews.com/news/asia/ndmc-partners-htc-deepq-build-largest-mr-anatomy-classroom-taiwan

https://cgvr.cs.uni-bremen.de/research/atlas_19/

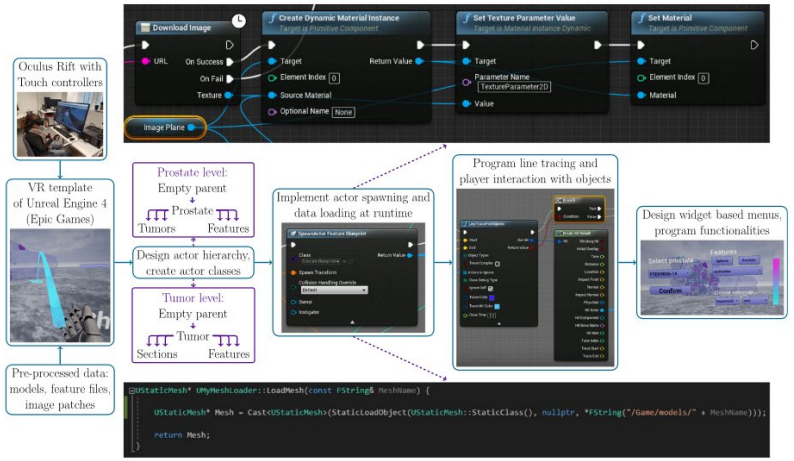


Fig. 3 VR implementation steps illustrated. The example on top shows how images (cropped serial sections) are loaded with Blueprint nodes. The example in bottom is the C++ function used for loading meshes

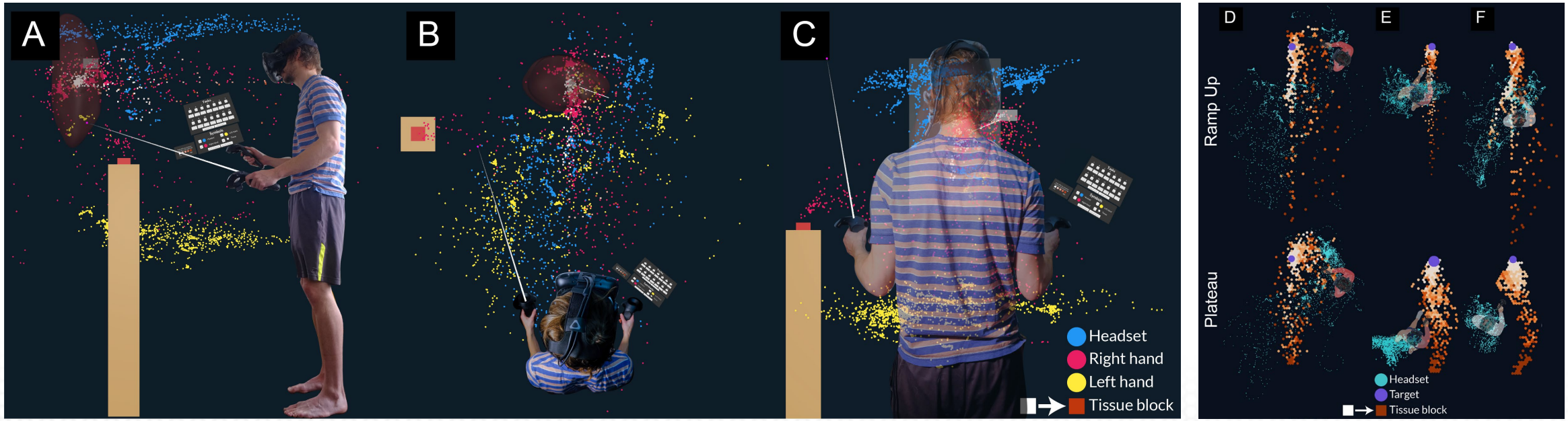
Liimatainen, Kaisa, Leena Latonen, Masi Valkonen, Kimmo Kartasalo, and Pekka Ruusuvuori. "Virtual Reality for 3D Histology: Multi-Scale Visualization of Organs with Interactive Feature Exploration." *BMC Cancer* 21, no. 1 (December 2021): 1133. https://doi.org/10.1186/s12885-021-08542-9.

Where is the Data?

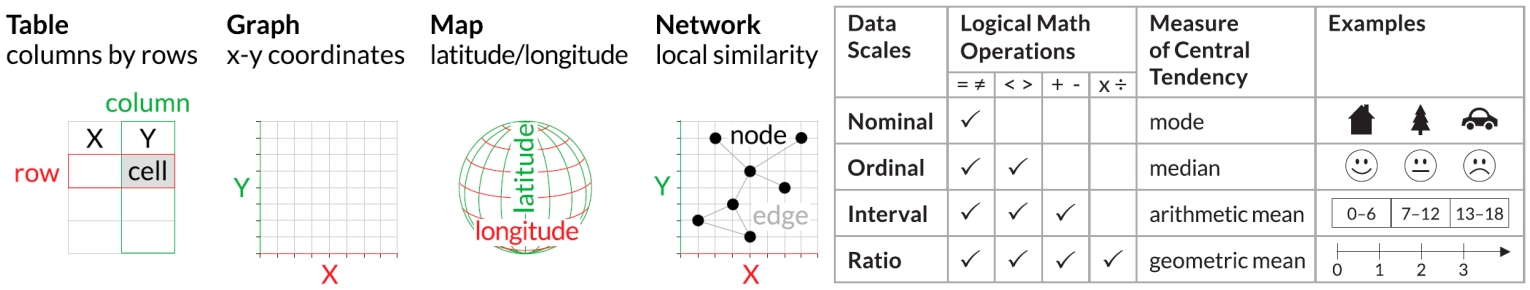
Data Visualization in VR: Vision

"Visual data exploration seeks to integrate humans in the data exploration process, applying their perceptual abilities [...]. The basic idea is to present the data in some visual form, allowing data analysts to [...] interact with it." (Keim, 2001)

- Symbiosis of computers and humans
- Visualization is for humans only
- Many formalizations for making, interpreting, and teaching data visualization



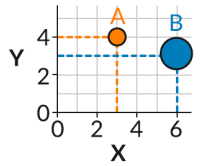
Data Visualization Literacy Framework

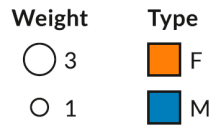


Data Scales	Logical Math Operations = ≠	< >	+ -	x ÷	Measure of Central Tendency	Examples
Nominal	✓				mode	
Ordinal	✓	✓			median	
Interval	✓	✓	✓		arithmetic mean	0–6 | 7–12 | 13–18
Ratio	✓	✓	✓	✓	geometric mean	0 1 2 3

	Outlier	Trend	Clustering
Position			
Size			
Color			

Label	X	Y	Weight	Type
A	3	4	1	F
B	6	3	3	M





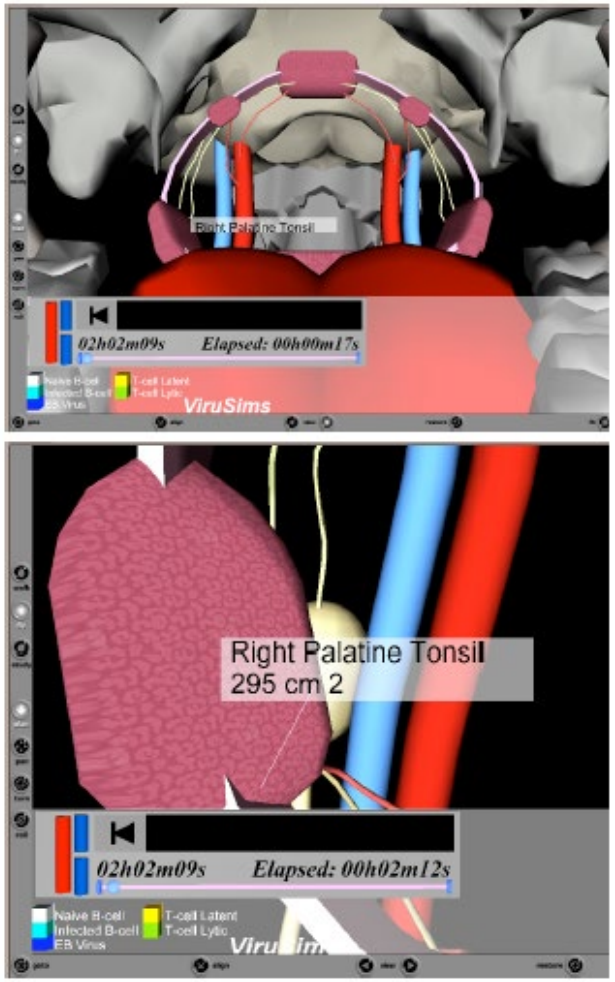
Qualitative	Quantitative		
Categorical	Sequential	Diverging	Cyclic

			Geometric Symbols: Point	Geometric Symbols: Line	Linguistic Symbols	Pictoral Symbols
Spatial	Position	X, Y				
Retinal	From	Size				
		Shape				
	Color	Value				
		Hue				
		Saturation				
	Texture	Granularity				
		Pattern				
	Optics	Blur				
	Motion	Speed				

Börner, Katy, Andreas Bueckle, and Michael Ginda. "Data Visualization Literacy: Definitions, Conceptual Frameworks, Exercises, and Assessments." *Proceedings of the National Academy of Sciences* 116, no. 6 (2019): 1857–64. https://doi.org/10.1073/pnas.1807180116.

Information-Rich Virtual Environments (IRVE)

- “An information-rich virtual environment (IRVE) is a realistic VE that is enhanced with the addition of related abstract information.”
- Bowman, Doug A, Chris North, Jian Chen, Nicholas F Polys, Pardha S Pyla, and Umur Yilmaz. “Information-Rich Virtual Environments: Theory, Tools, and Research Agenda,” 81–90. New York City, NY: ACM, 2003. https://doi.org/10.1145/1008653.1008669.

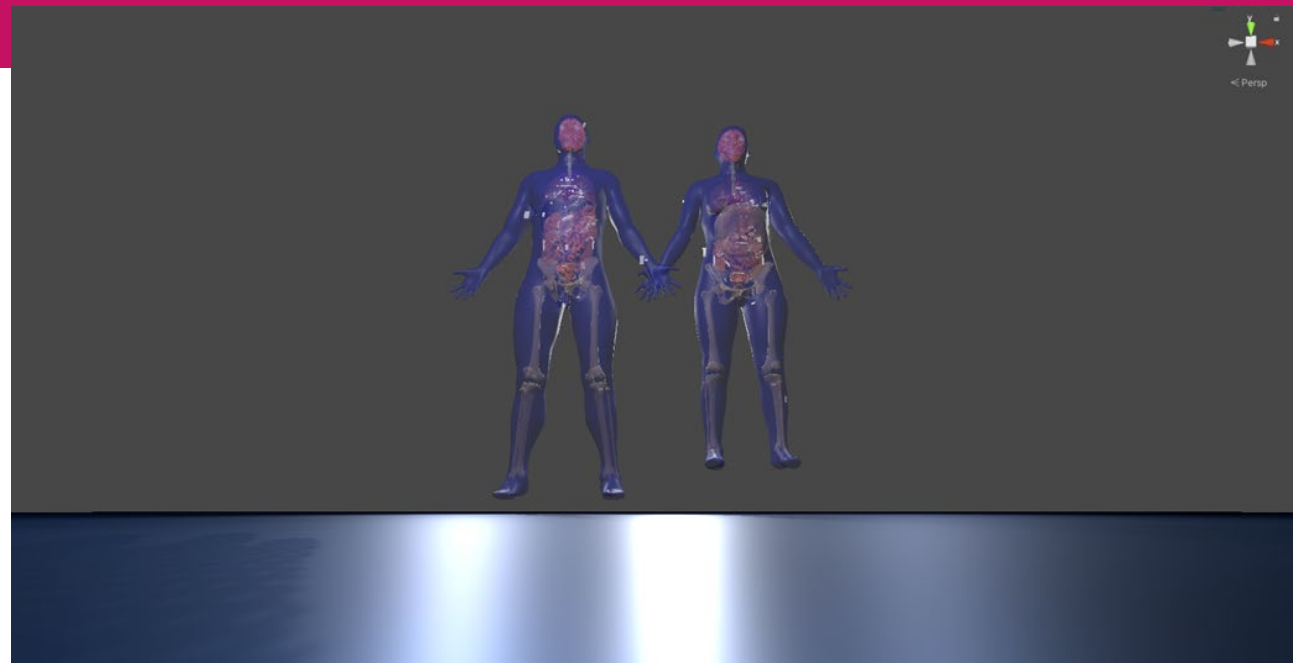


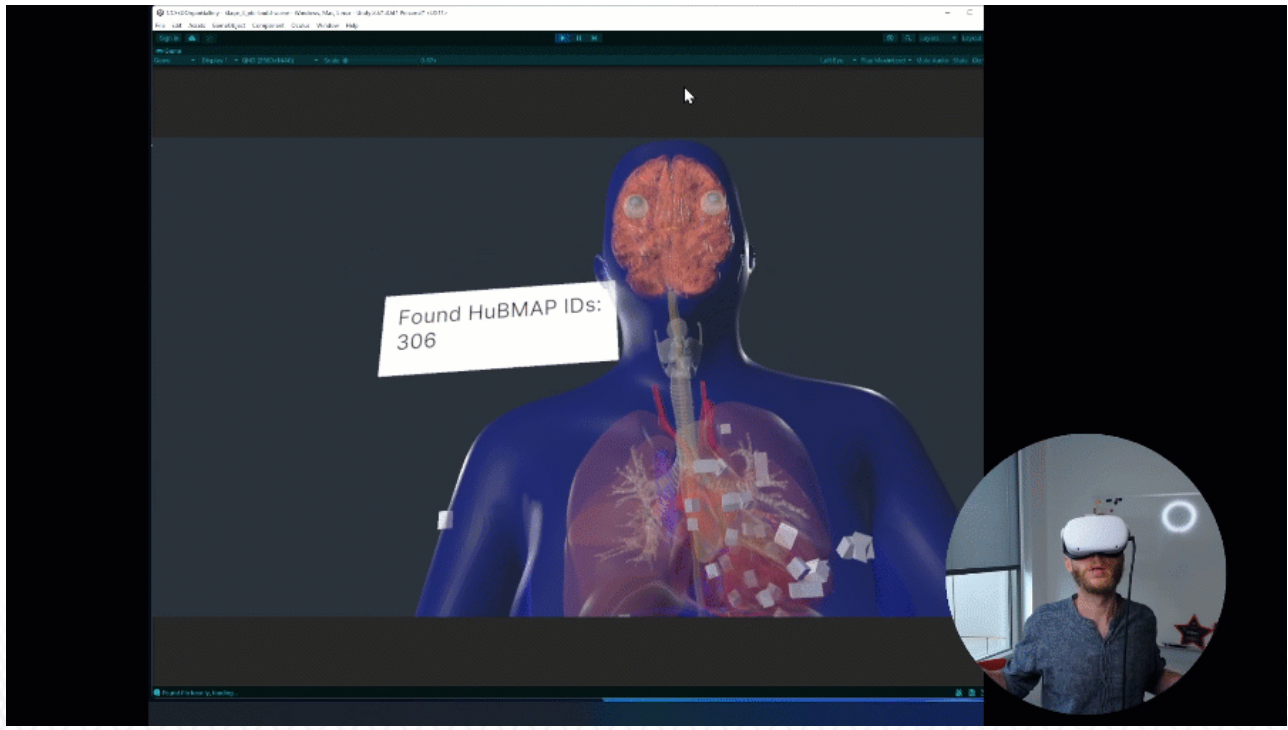
The Common Coordinate Framework (CCF) Organ VR Gallery

Also called the “Human Reference Atlas in 3D VR”

The CCF Organ VR Gallery

- Human BioMolecular Atlas Program (HuBMAP) and other single-cell mapping efforts
- Integrates 3 data types for human tissue:
  - **Spatial**
  - **Biological structure**
  - Specimen/clinical metadata (not covered in this talk)
- Code: https://github.com/cns-iu/ccf-organ-vr-gallery
- Preprint: Bueckle, Andreas, Kristen M Browne, Bruce W Herr II, and Katy Börner. “The Common Coordinate Framework (CCF) Organ VR Gallery.” OSF, January 12, 2022. https://doi.org/10.31219/osf.io/z9gm3.



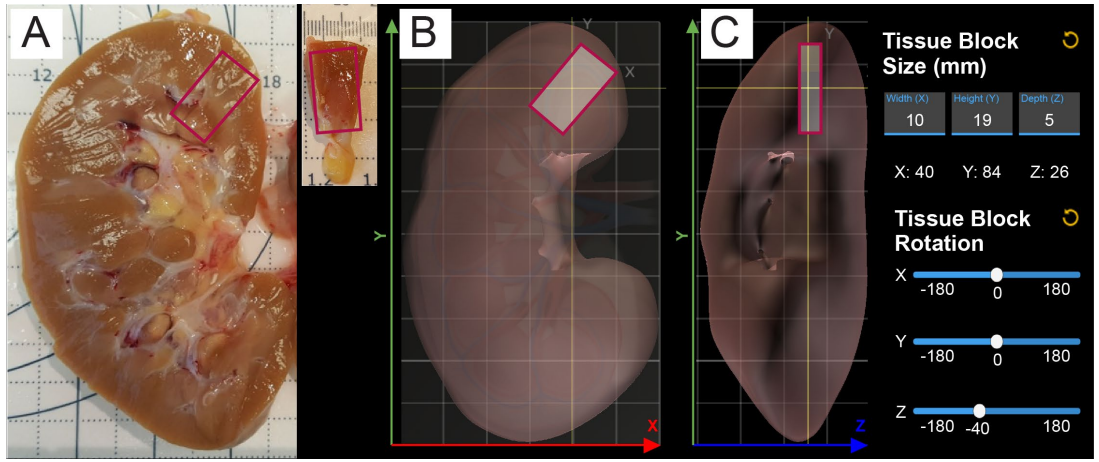


Spatial Data

Warning: graphical image of a kidney coming up!

The Meat of the Matter

- Documenting tissue extraction sites is non-trivial
- Photos of reference organs (if available) on cutting boards with spatial markers
- We used the Visible Human male, left kidney (100 mm high, 60 mm wide, 40 mm deep)
- Spitzer, V., M. J. Ackerman, A. L. Scherzinger, and D. Whitlock. “The Visible Human Male: A Technical Report.” *Journal of the American Medical Informatics Association* 3, no. 2 (March 1996): 118–30. https://doi.org/10.1136/jamia.1996.96236280.



Mapping to the CCF

NIH NATIONAL CANCER INSTITUTE
BBRB Biorepositories and Biospecimen Research Branch

GTEx Tissue Harvesting Work Instruction

PR-0004-W1	VER. 03.05	Effective Date: mm/dd/yyyy	Page 13 of 21

4.3.6.20 **Colon**

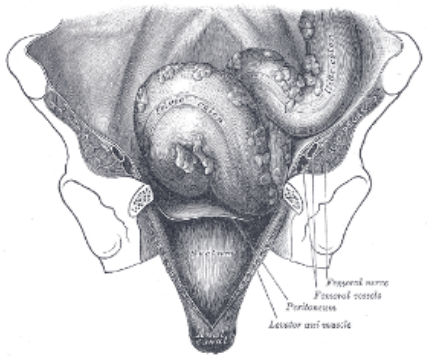
4.3.6.20.1 **Preferred Location: Transverse colon**. Gently rinse mucosa with normal saline before aliquot preparation. Aliquots should contain the full thickness of the colonic wall, i.e., **mucosa and muscularis propria**. **Trim adjacent adipose tissue.**

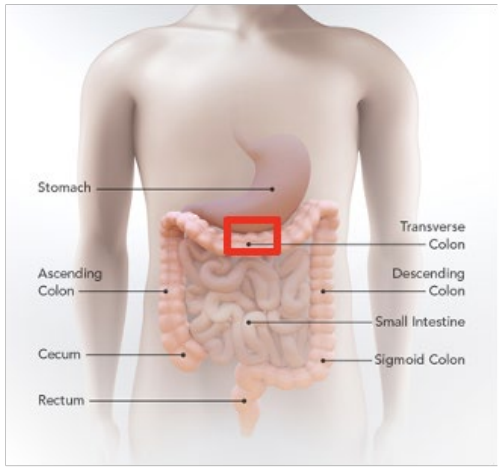
4.3.6.20.2 **Preferred Aliquot:** 20 mm x 10 mm x thickness (≤4 mm), divided into two adjacent 10 mm x 10 mm x thickness aliquots. Each cassette should contain two 10 mm x 10 mm x thickness aliquots.

4.3.6.20.3 **Preferred Location: Sigmoid colon.** Preferred Location: Sigmoid colon. Gently rinse mucosa with normal saline before aliquot preparation. **Obtain only muscularis propria**; discard mucosa and any serosal adipose tissue.

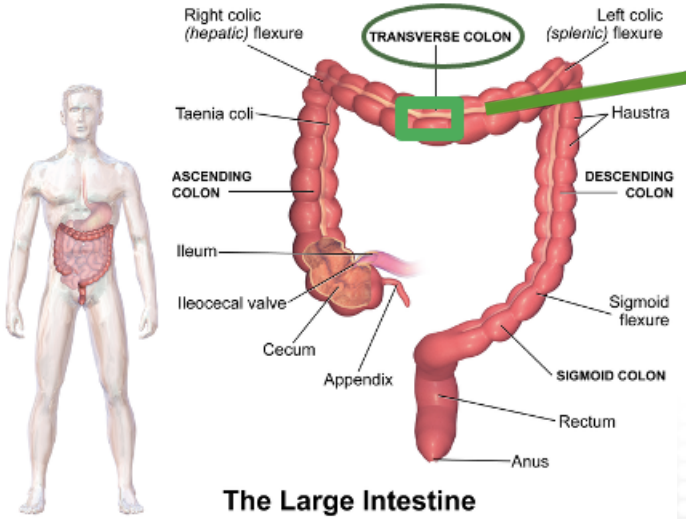
4.3.6.20.4 **Preferred Aliquot:** 20 mm x 10 mm x thickness (≤4 mm), divided into two adjacent 10 mm x 10 mm x thickness aliquots. Each cassette should contain two 10 mm x 10 mm x thickness aliquots.

Sigmoid Colon ('pelvic colon') Dissection Guide (Diagram 4)

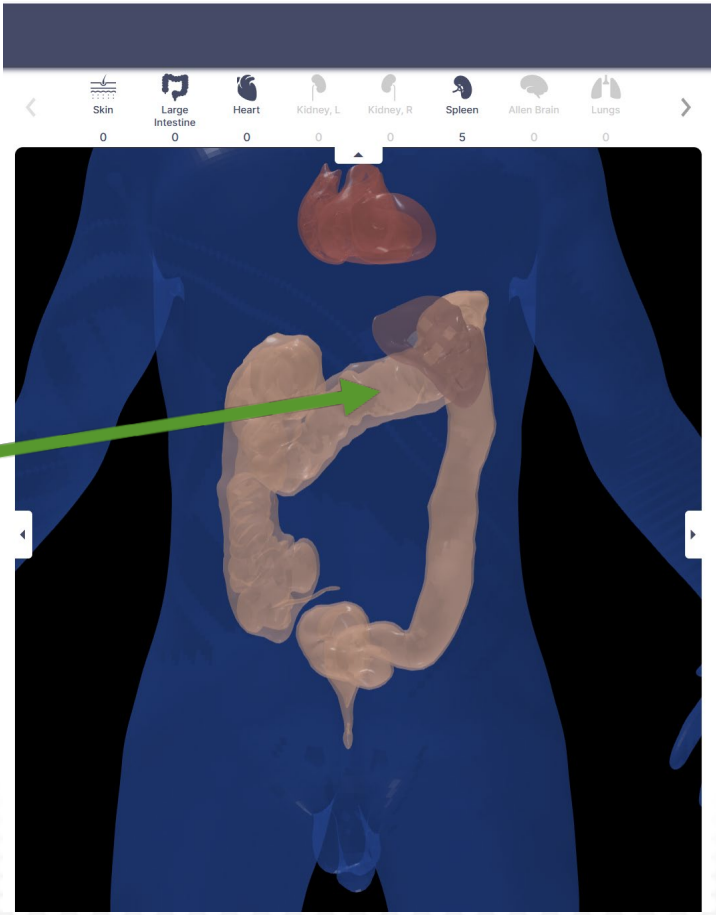




Recover the transverse colon starting 10 cm back from the right colic (hepatic) flexure.

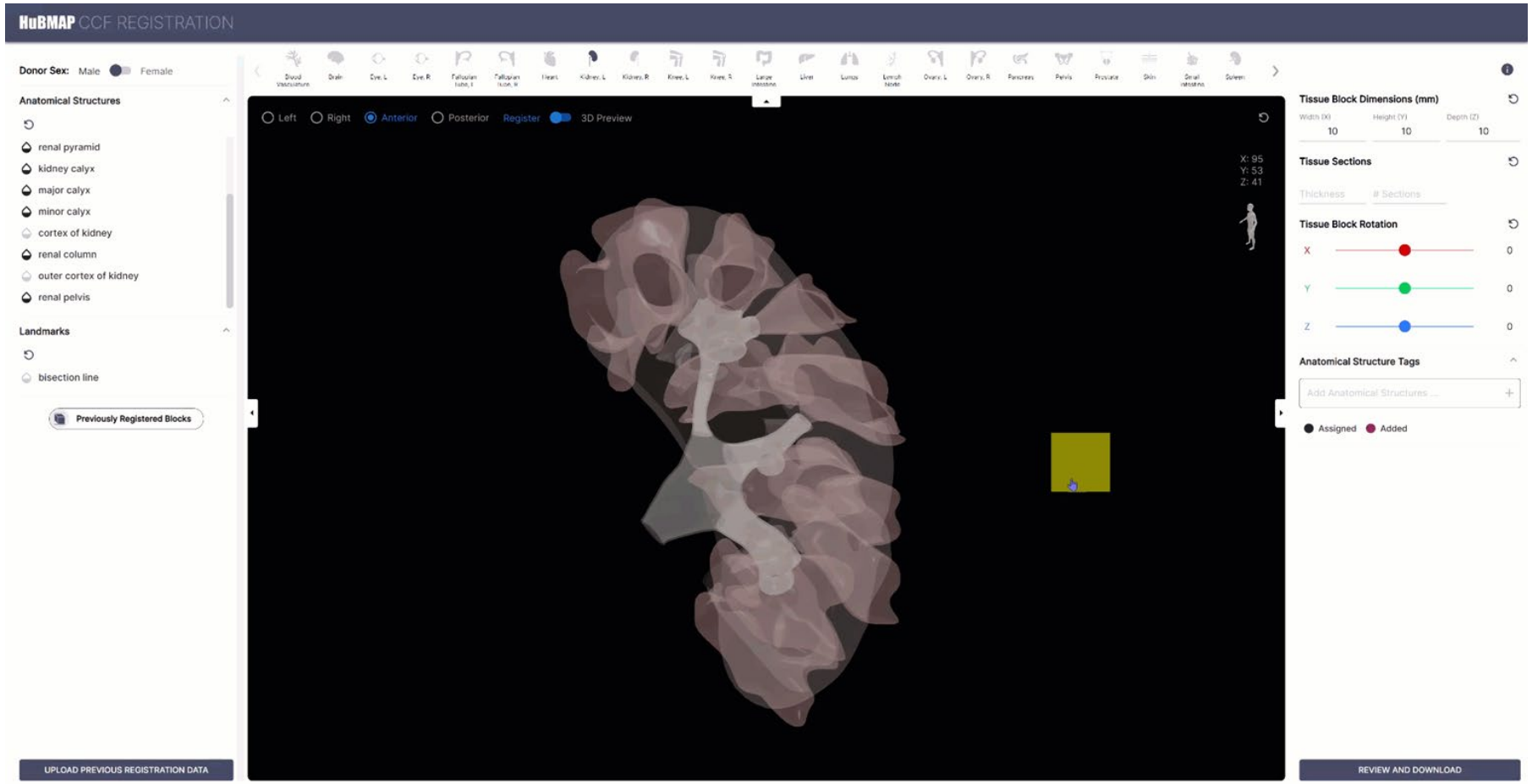


The Large Intestine



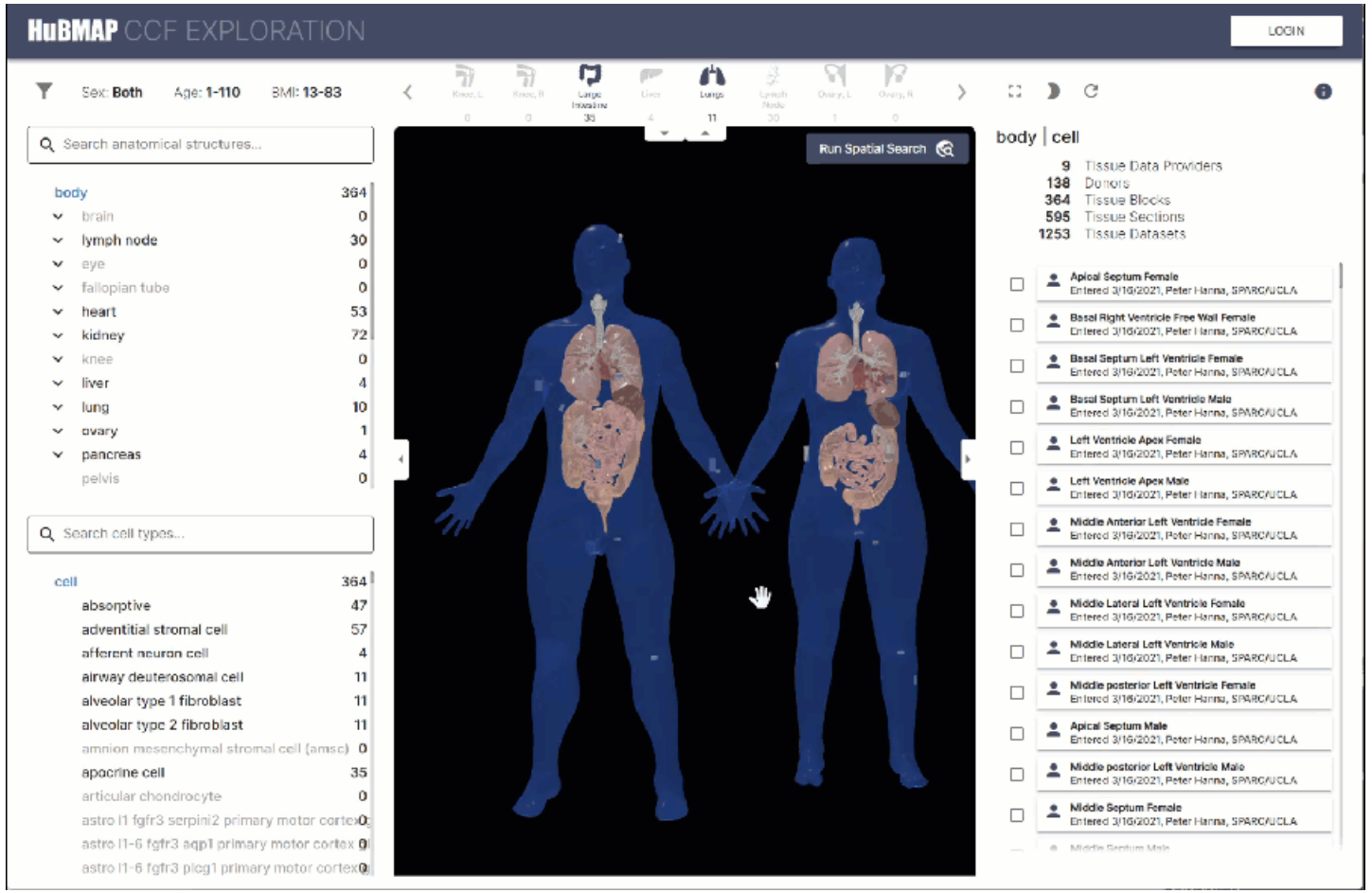
CNS Cyberinfrastructure for Network Science Center

CCF Registration User Interface (RUI)



https://hubmapconsortium.github.io/ccf-ui/rui/

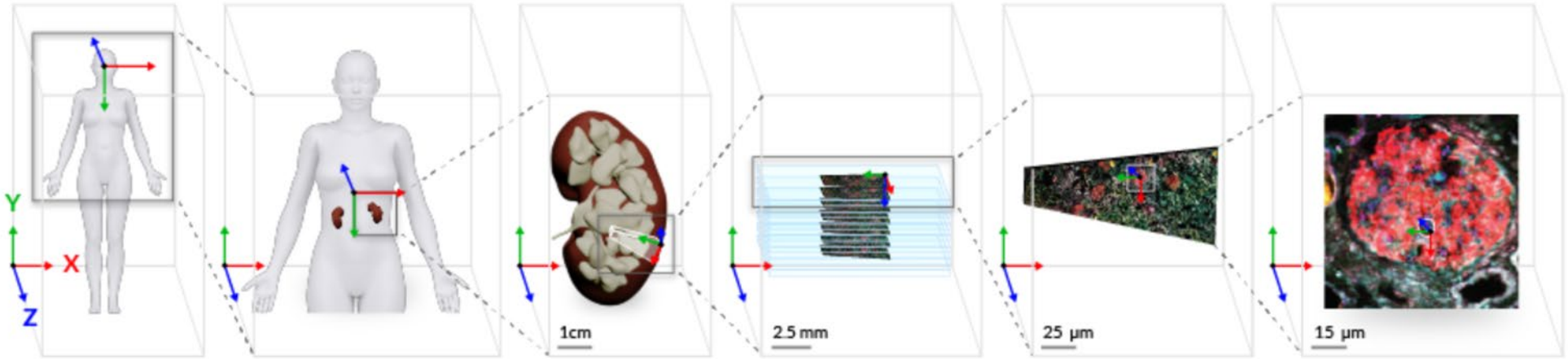
CCF Exploration User Interface (EUI)



https://portal.hubmapconsortium.org/ccf-eui

CCF

Allows us to 3D register tissue and explore tissue blocks spatially and semantically across macro-, meso-, and micro-scale.



Biological Structure

Linked Open Data (LOD)

Anatomical Structure, Cell Type, Plus Biomarker (ASCT+B) Table

Background–Structuring Knowledge: What does an ASCT+B Table Do?

Unstructured knowledge sources ~80% of biomedical knowledge

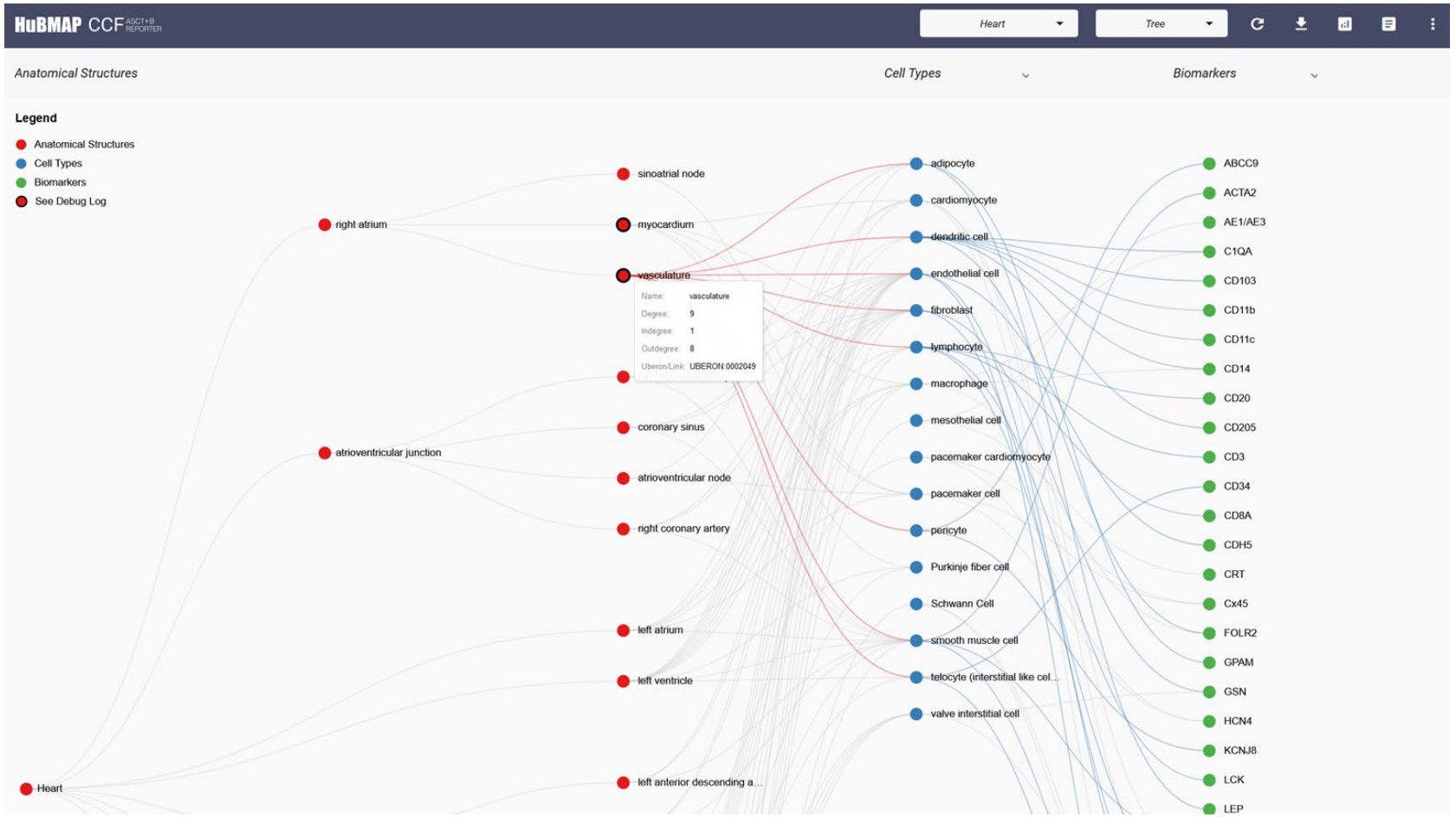
Standardize how information is captured, formatted, labeled

Knowledge about organs, anatomical structures, cell types, biomarker sets that uniquely define cell types

Ontologies like the multi-species Uber Anatomy (Uberon) and Cell Ontology (CL) capture nomenclature, synonyms, descriptions, relationships between entities, provenance for knowledge, assigns unique ID for this unit of knowledge

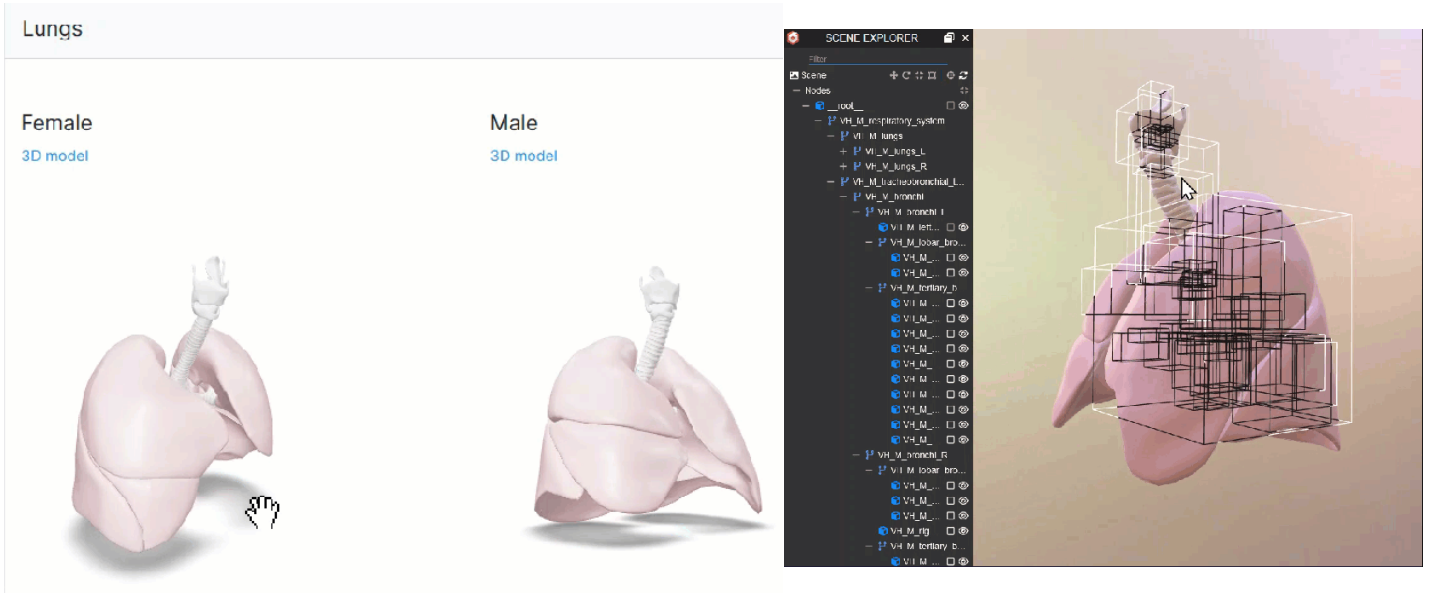
Structured knowledge unifies nomenclature that describes datasets so we are all speaking in the same language

ASCT+B Reporter Vis of ASCT+B tables



https://hubmapconsortium.github.io/ccf-asct-reporter

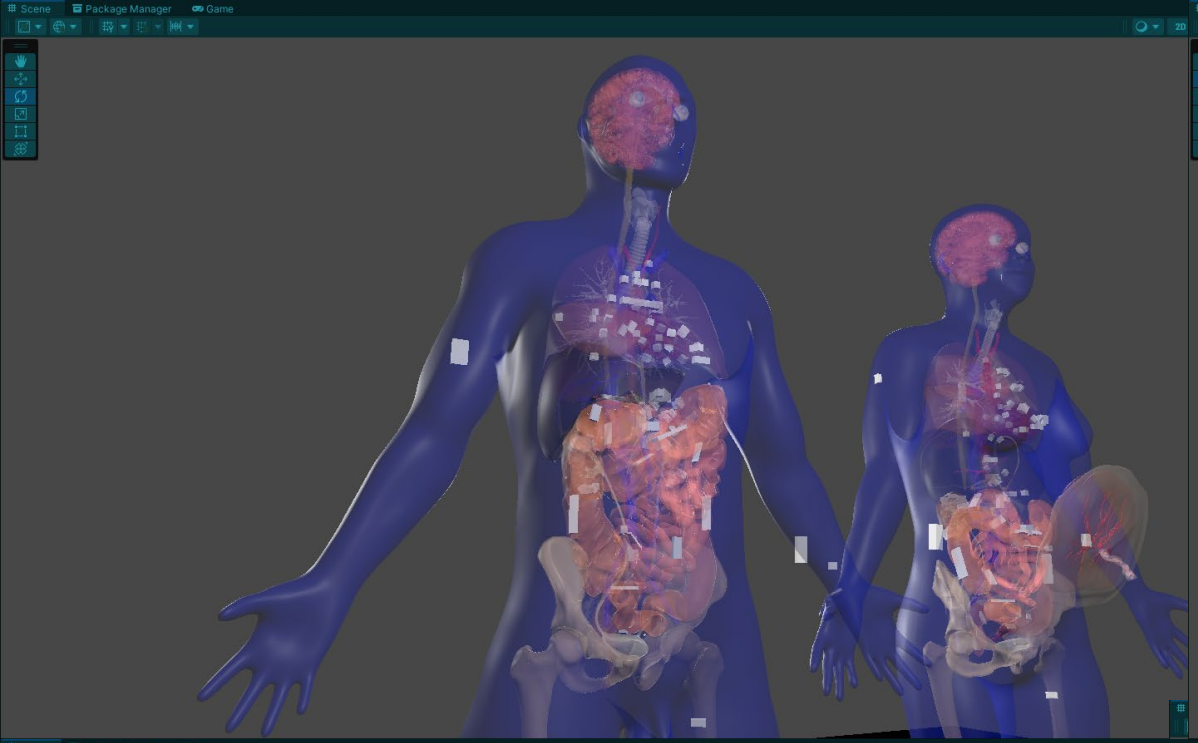
Tie to Spatial Data: 3D Reference Models

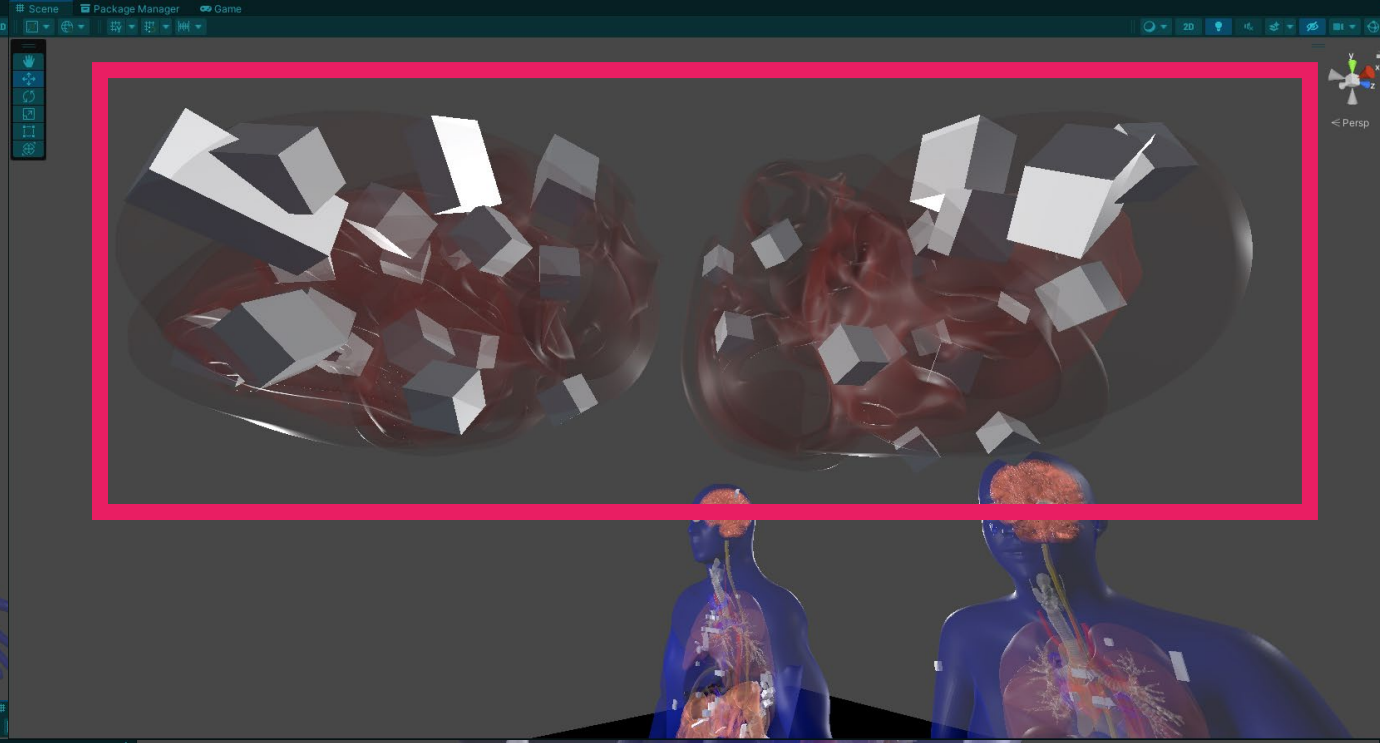


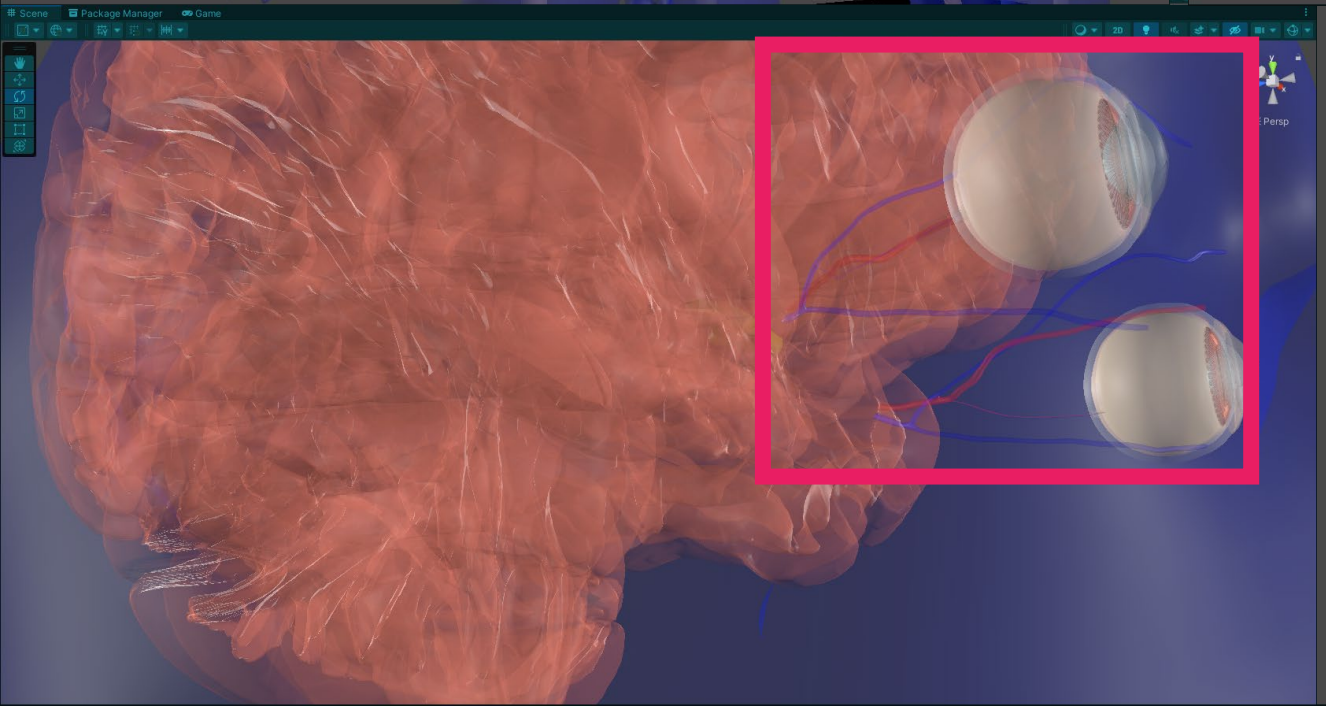
- Custom built by our medical illustrator team with input from subject matter experts
- Support the RUI, EUI, and CCF Organ VR Gallery
- Anatomical structures labeled with ontology IDs

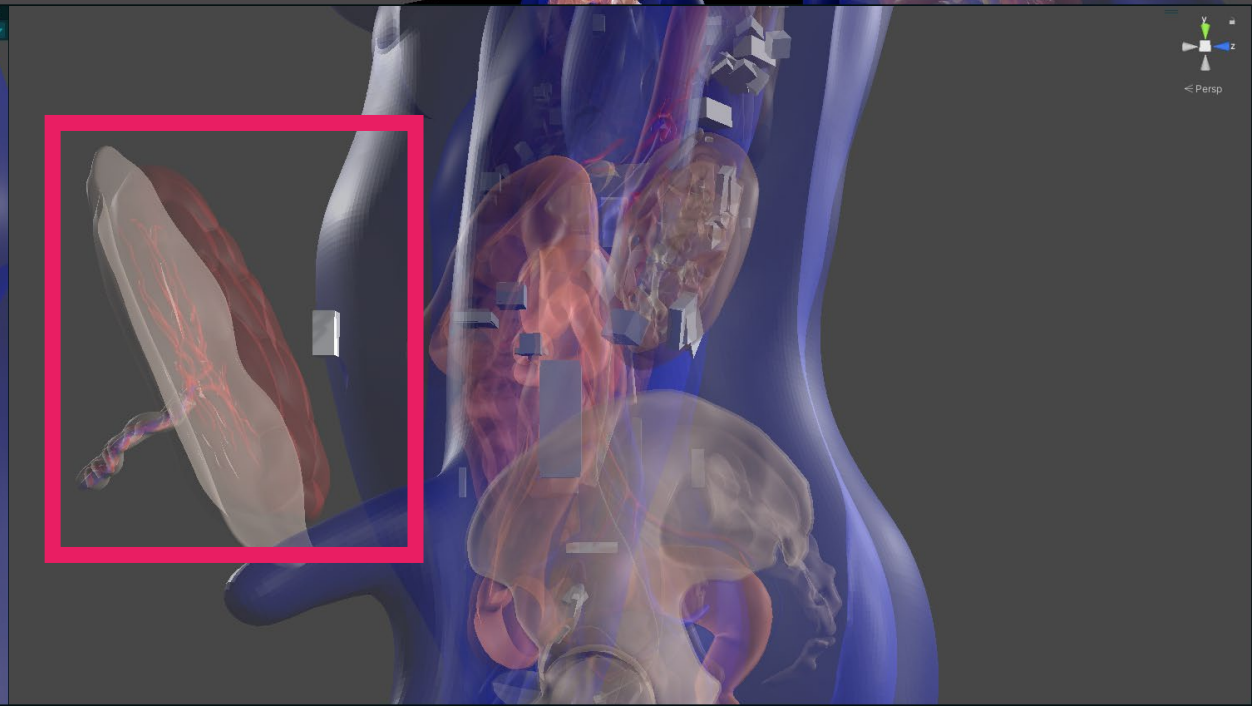
https://hubmapconsortium.github.io/ccf/pages/ccf-3d-reference-library.html

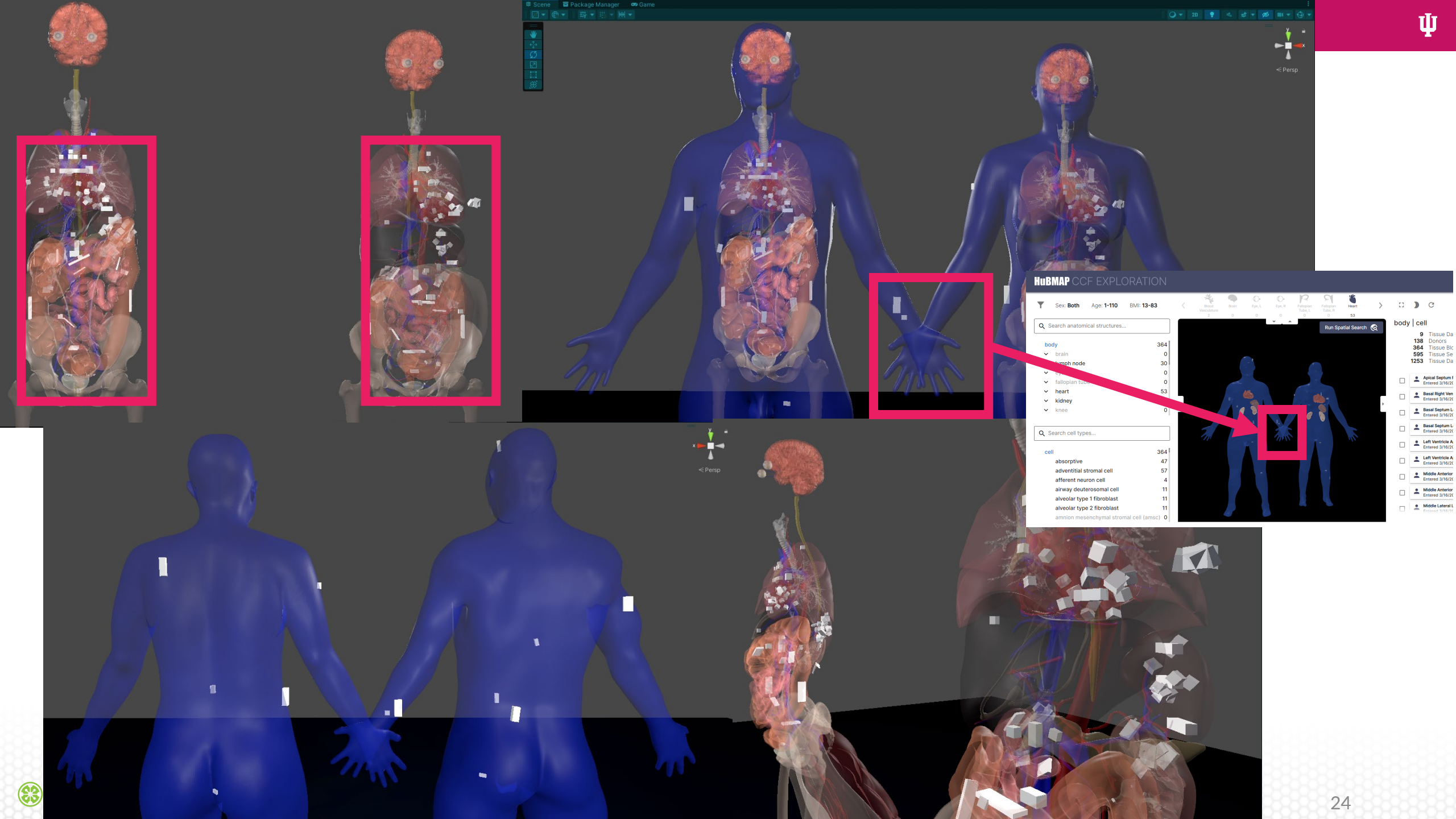
A Closer Look at the Gallery

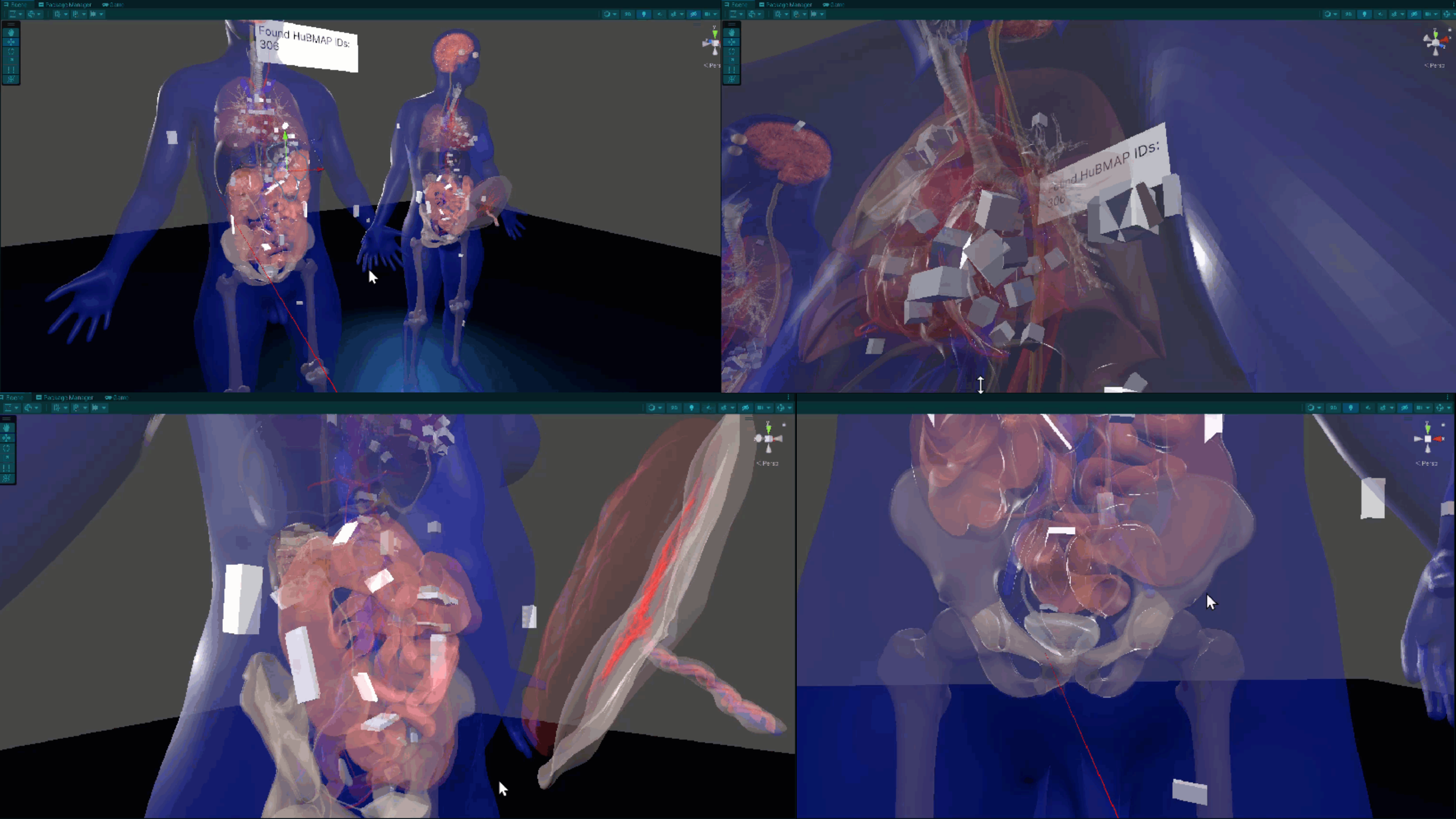

Scene
Package Manager
Game


Scene
Package Manager
Game
Persp

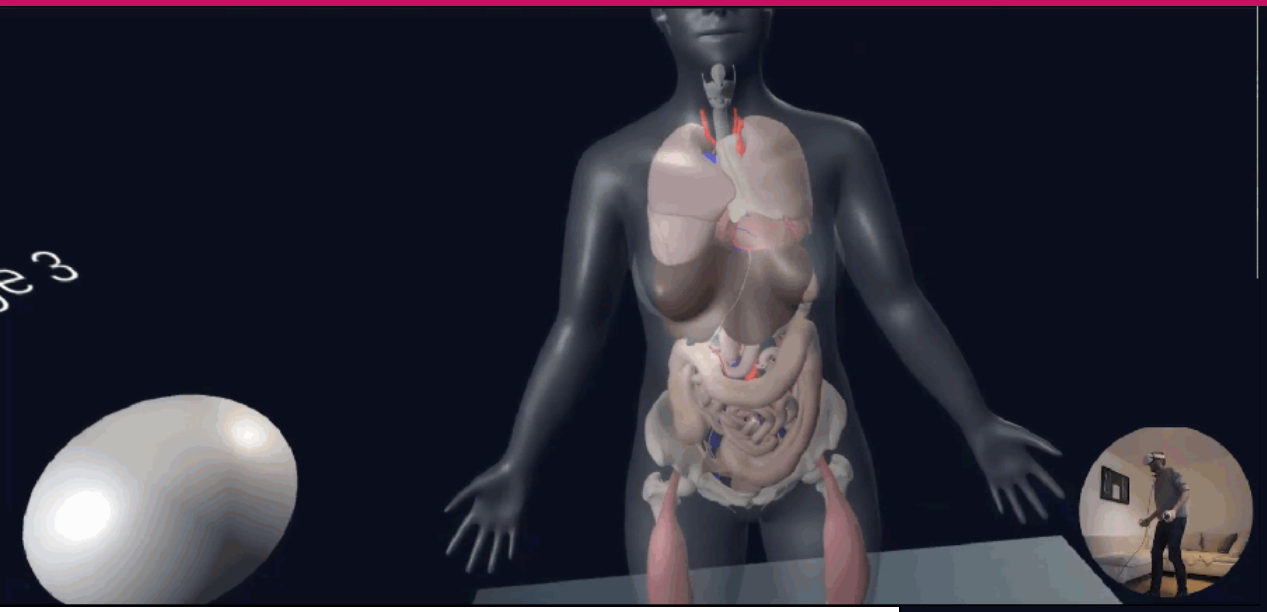

Scene
Package Manager
Game
Persp

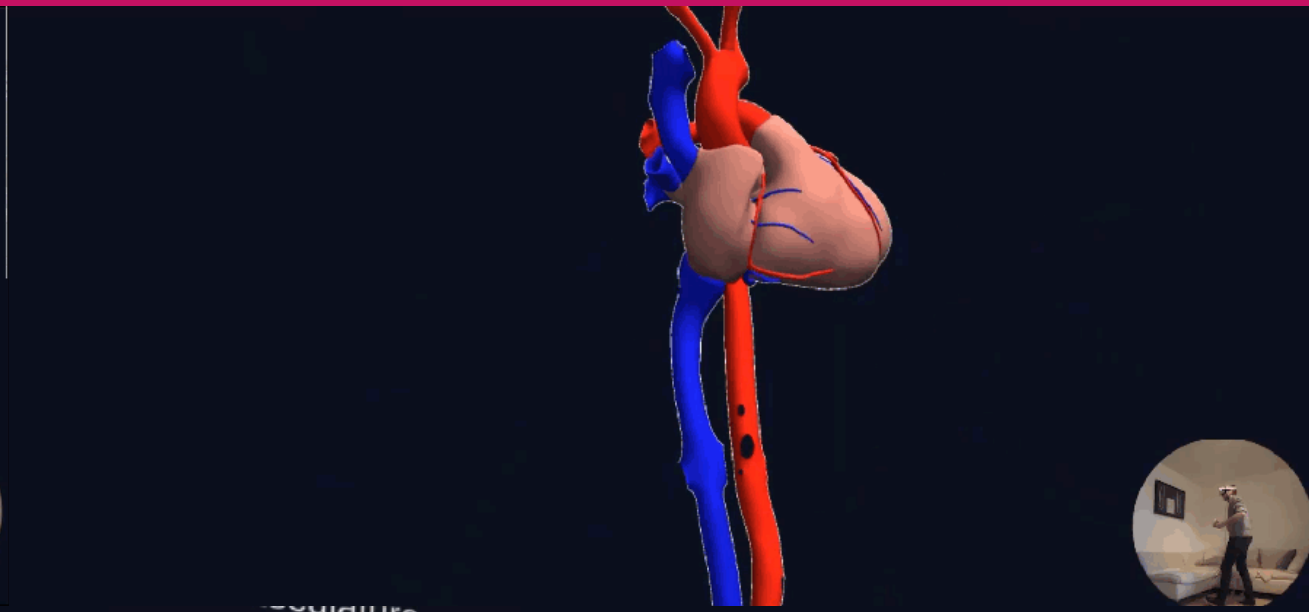

Persp


Scene
Package Manager
Game
Persp
HuBMAP CCF EXPLORATION
Sex: Both
Age: 1-110
BMI: 13-83
Search anatomical structures...
body 364
brain 0
lymph node 30
fallopian tube 0
heart 53
kidney
knee 0
Search cell types...
cell 364
absorptive 47
adventitial stromal cell 57
afferent neuron cell 4
airway deuterosomal cell 11
alveolar type 1 fibroblast 11
alveolar type 2 fibroblast 11
amnion mesenchymal stromal cell (amsc) 0
Run Spatial Search
body | cell
9 Tissue Da
138 Donors
364 Tissue Blc
595 Tissue Se
1253 Tissue Da

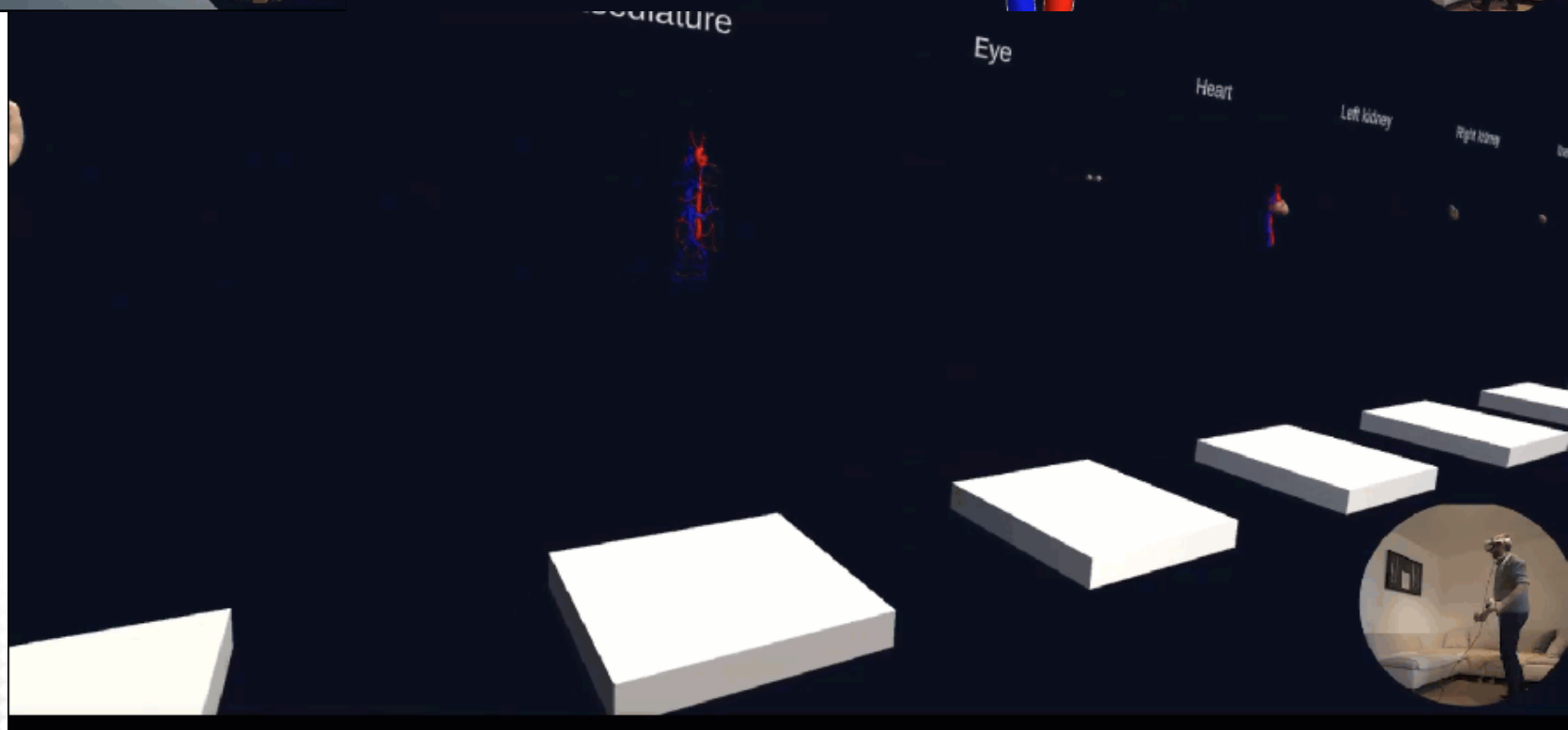

Found HuBMAP IDs:
306


Large intestine
Blood vasculature
Spleen





Try it out yourself in the demo session today!



CNS Cyberinfrastructure for Network Science Center

Data from CCF API

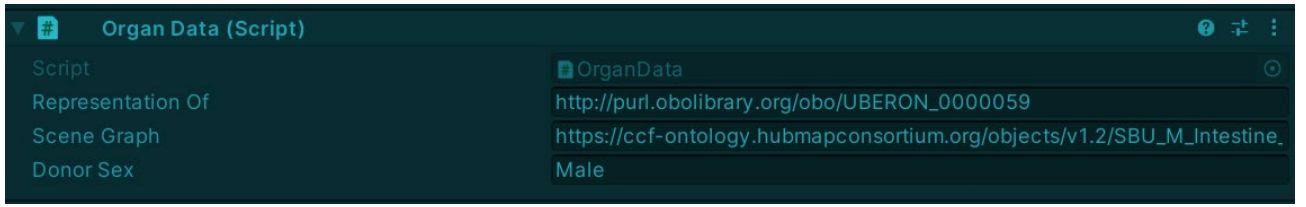
- https://ccf-api.hubmapconsortium.org/#/
- Endpoints for individual organs, tissue blocks, entire scene
  - /scene to get all 3D objects
  - /reference-organs to get organ sex
- Query strings to refine search for sex, organ, age, etc.

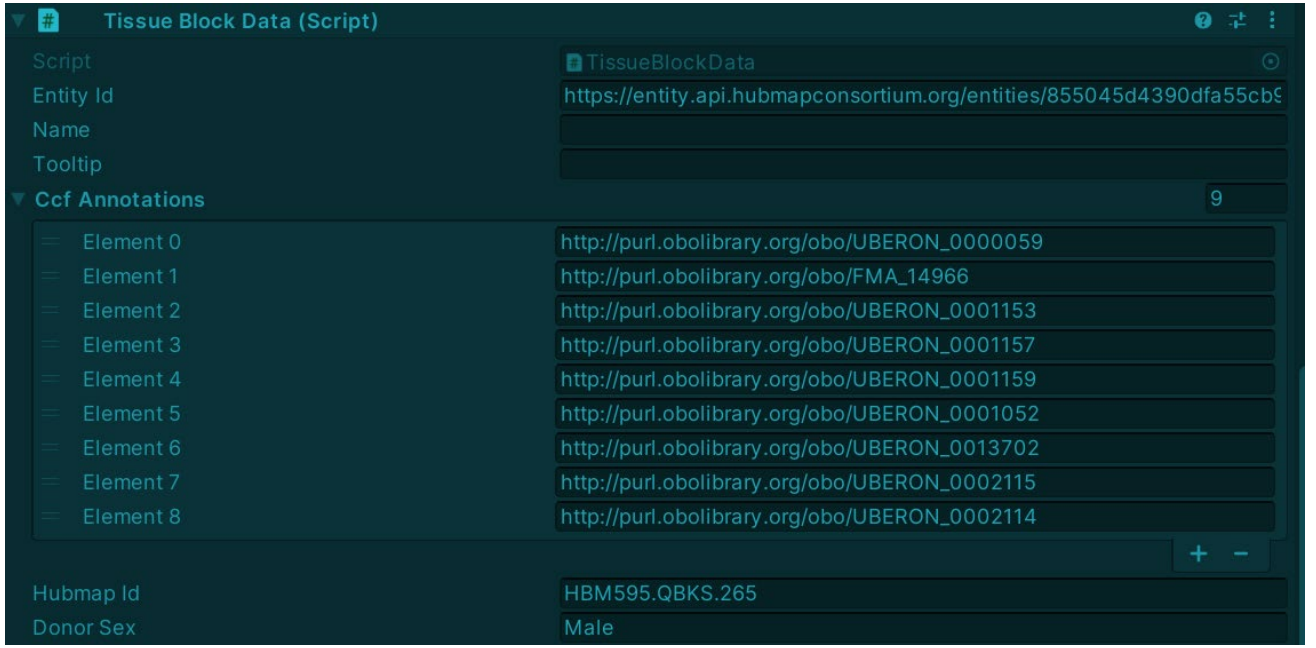

```
[
  {
    "@id": http://purl.org/ccf/latest/ccf.owl#VHMSkinV1.1,
    "@type": "SpatialSceneNode",
    representation_of: http://purl.obolibrary.org/obo/UBERON_0002097,
    reference_organ: http://purl.org/ccf/latest/ccf.owl#VHMSkinV1.1,
    scenegraph: https://ccf-ontology.hubmapconsortium.org/objects/v1.2/VH_M_Skin.glb,
    scenegraphNode: "VH_M_skin",
    transformMatrix: [
        1,
        0,
        0,
        0,
        0,
        1,
        0,
        0,
        0,
        0,
        1,
        0,
        -0.4,
        0,
        0,
        1
    ],
    tooltip: "Skin",
    color: [
        255,
        255,
        255,
        255
    ],
    opacity: 0.5,
    unpickable: true,
    _lighting: "pbr",
    zoomBasedOpacity: false
  },
```

```
  {
    "@id": http://purl.org/ccf/1.5/fe26f171-fdd4-4293-bfe0-2a8c1e84c7fa,
    "@type": "SpatialSceneNode",
    entityId: https://entity.api.hubmapconsortium.org/entities/386c2f0387641f395fe040546e05abf5,
    ccf_annotations: [
        http://purl.obolibrary.org/obo/UBERON_0010396,
        http://purl.obolibrary.org/obo/UBERON_0002370,
        http://purl.obolibrary.org/obo/UBERON_0002049,
        http://purl.obolibrary.org/obo/UBERON_0002194,
        http://purl.obolibrary.org/obo/UBERON_0002007,
        http://purl.obolibrary.org/obo/UBERON_0013702,
        http://purl.obolibrary.org/obo/UBERON_0010417,
        http://purl.obolibrary.org/obo/UBERON_0010397,
        http://purl.obolibrary.org/obo/UBERON_0010748,
        http://purl.obolibrary.org/obo/UBERON_0005457,
        http://purl.obolibrary.org/obo/UBERON_0005469
    ],
    transformMatrix: [
        0.003121494278664074,
        0,
        0.003466770610852044,
        0,
        0,
        0.00557,
        0,
        0,
        -0.003466770610852044,
        0,
        0.003121494278664074,
        0,
        0.39044315440000005,
        0.4904139740000001,
        -0.027701225,
        1
    ],
    color: [
        255,
        255,
        255,
        229.5
    ]
  },
```

Data from CCF API

- OrganData.cs
- TissueBlockData.cs

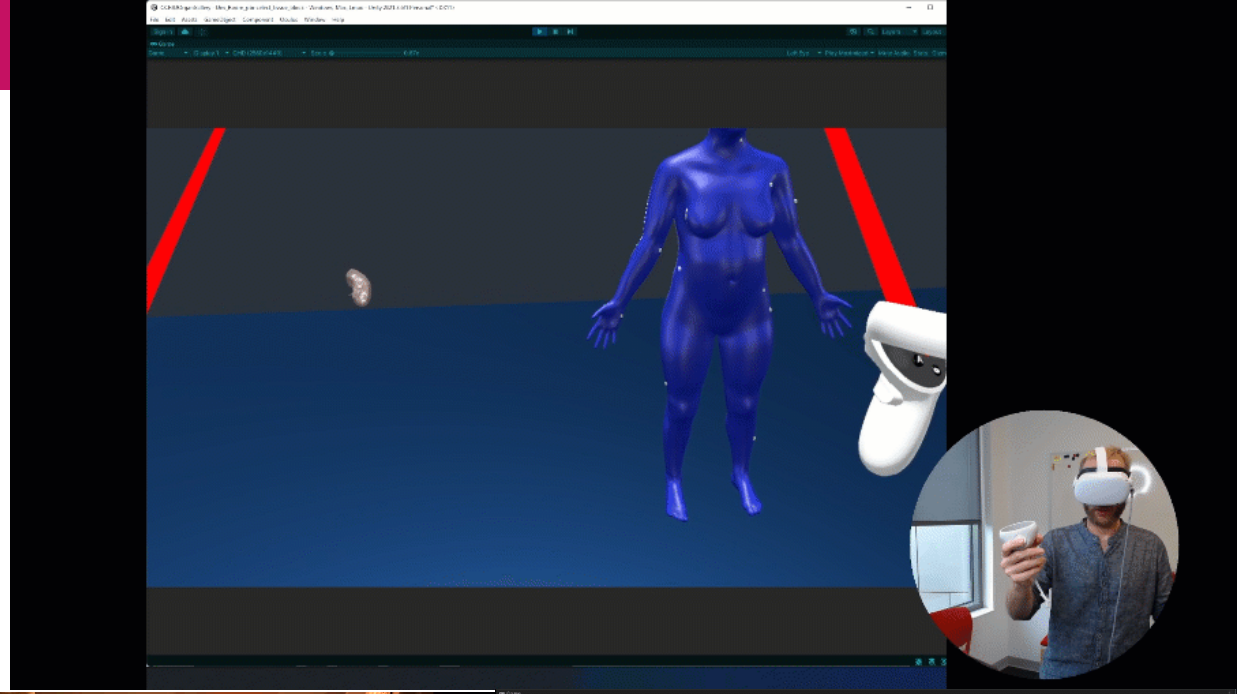


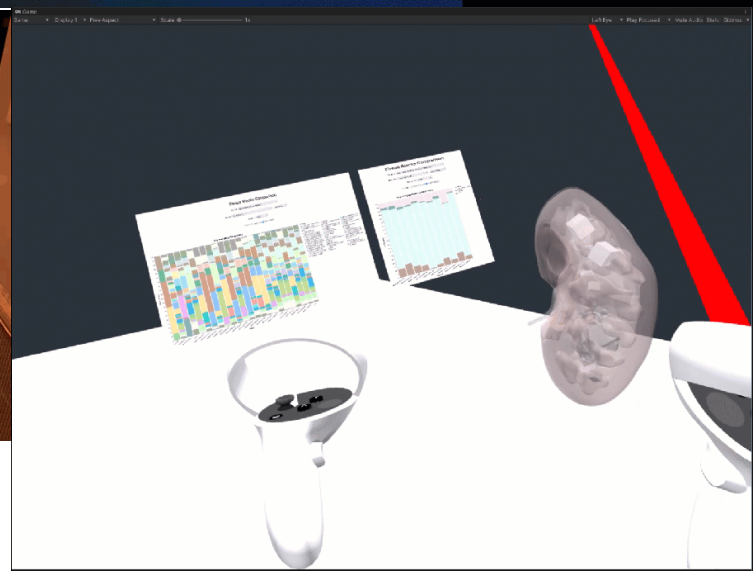


Future Work

Future Work

- Organ pullout
- Utility glove
- Visualizations
- Deploy version 1.0 by the end of 2022

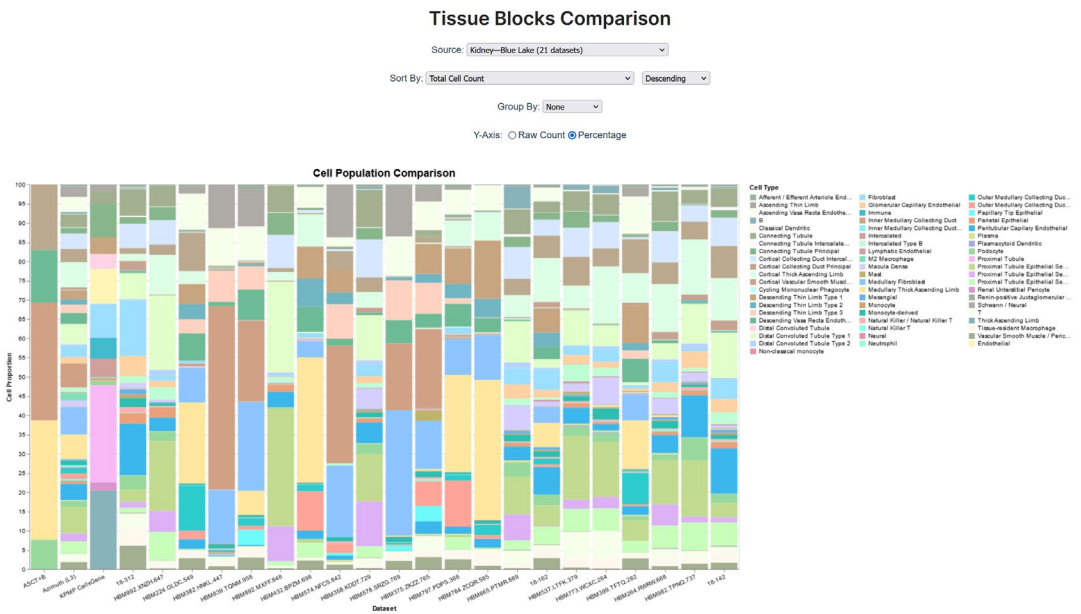




https://www.youtube.com/watch?v=g_PQB6JRlIU

Valve Corporation. “Half Life: Alyx.” Valve Corporation, 2020. https://www.half-life.com/en/alyx/.

Retrieving Cell Counts on User Input (in Development)

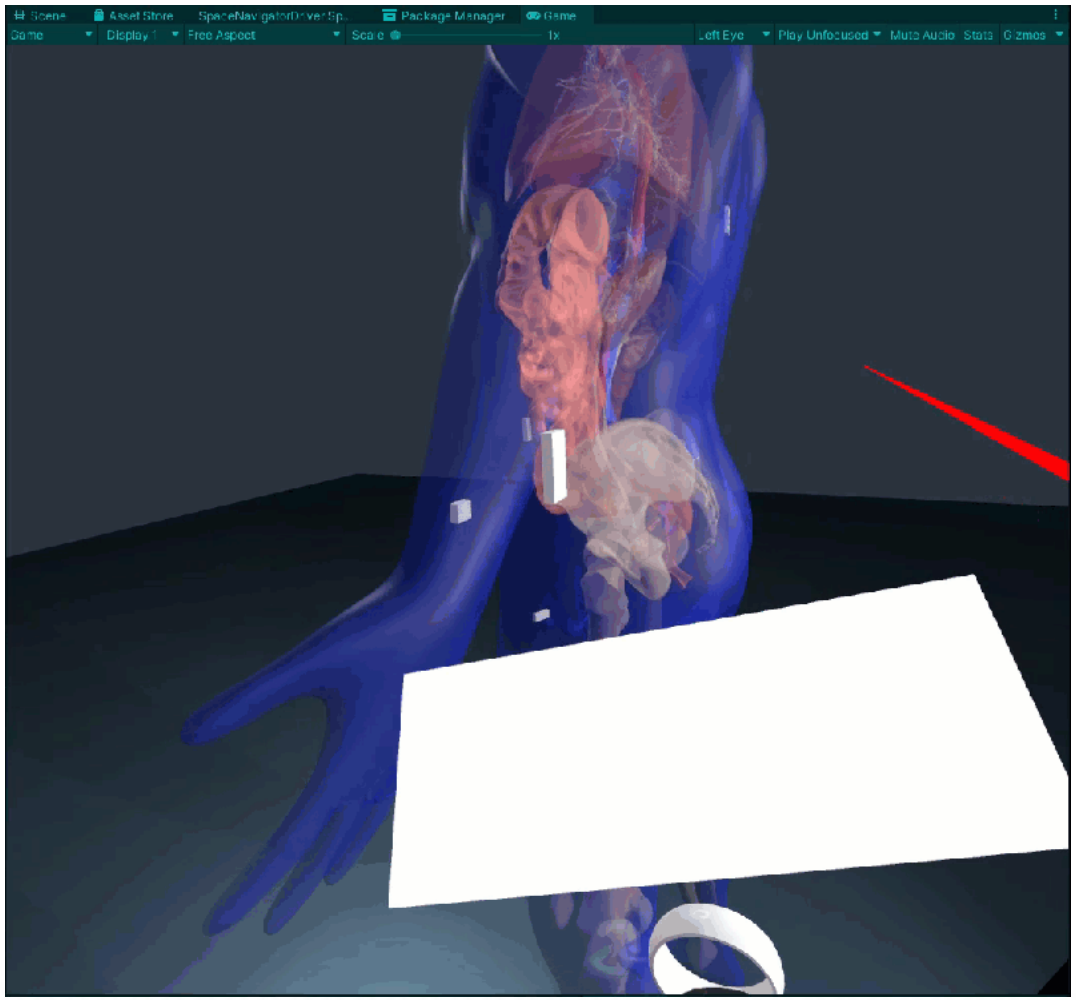


https://hubmapconsortium.github.io/tissue-bar-graphs/

Search this file...

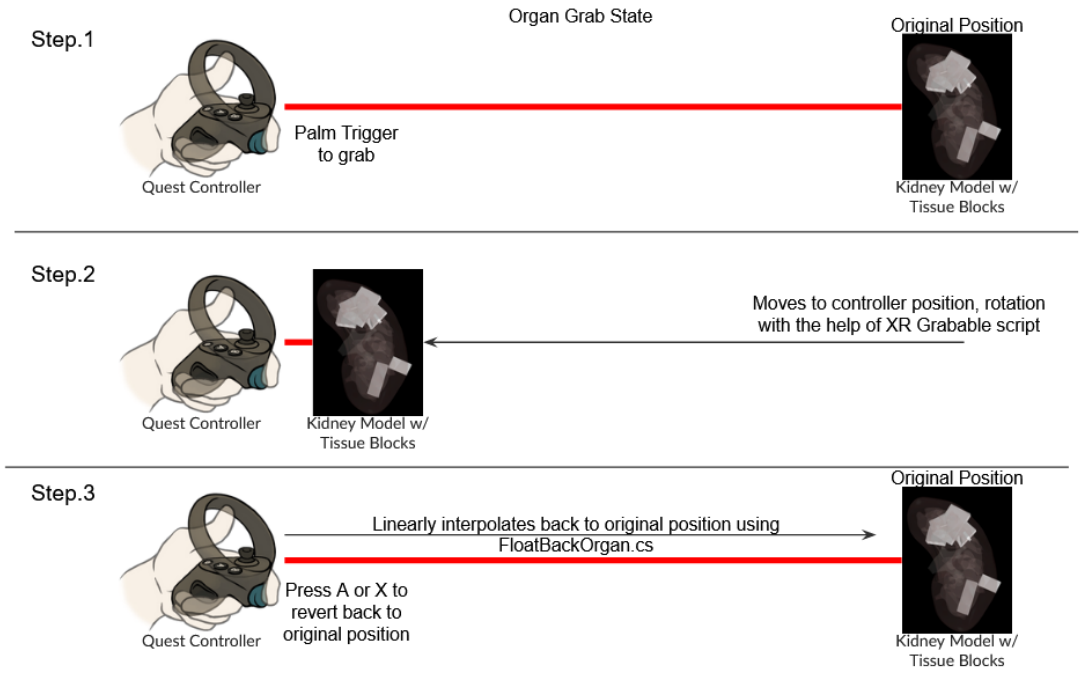
		cell_type	count	percentage	cat	sex	exp	age	y_pos	dataset_name
2	0	CD68 / Macrophage	76	6.109324	young / sun	f	sun	22	1330.214	General Electric RTI_Liz McDonough_undefined
3	1	T-Killer	47	3.778135	young / sun	f	sun	22		General Electric RTI_Liz McDonough_undefined
4	2	T-reg	63	5.064308	young / sun	f	sun	22		General Electric RTI_Liz McDonough_undefined
5	3	T-helper	1058	85.048231	young / sun	f	sun	22		General Electric RTI_Liz McDonough_undefined

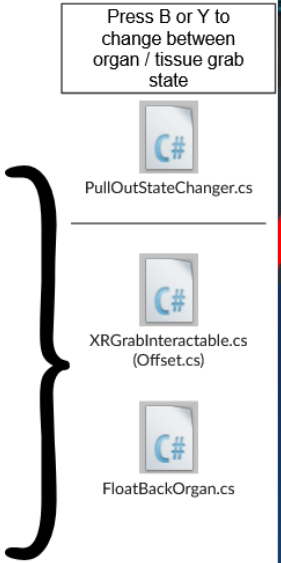
https://github.com/hubmapconsortium/tissue-bar-graphs/blob/static/csv/Skin_Soumya_et_al__paper/HBM229.HKHH.537.csv

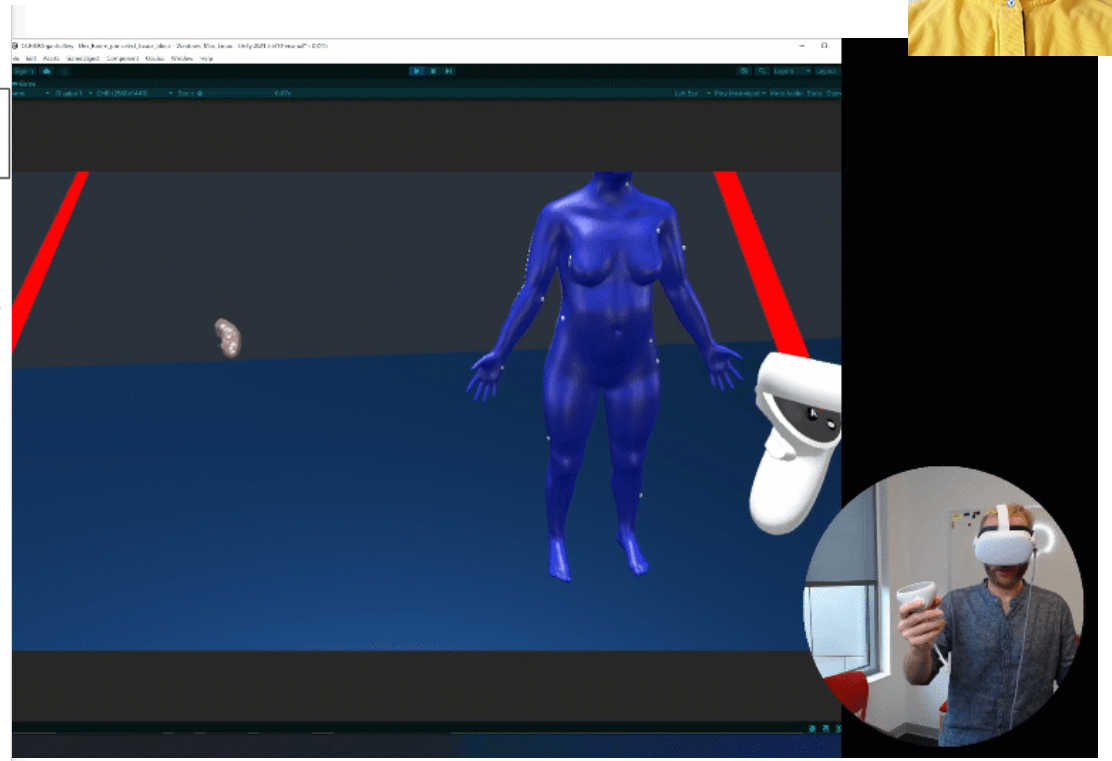


Organ Pullout (in Development)

(V) Input Action: (A) Pull-out / Float Back to source position functionality for Organs



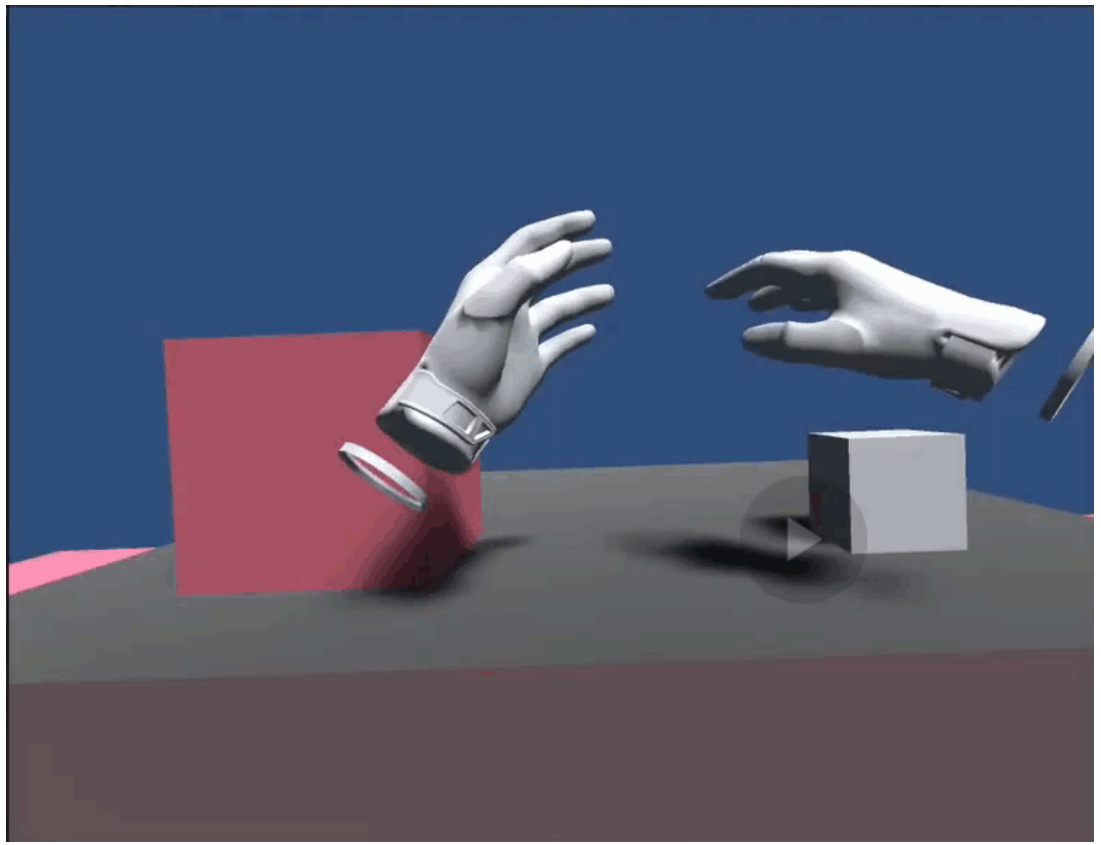




Wrist Pockets (in Development)

XRSocketInteractor.cs

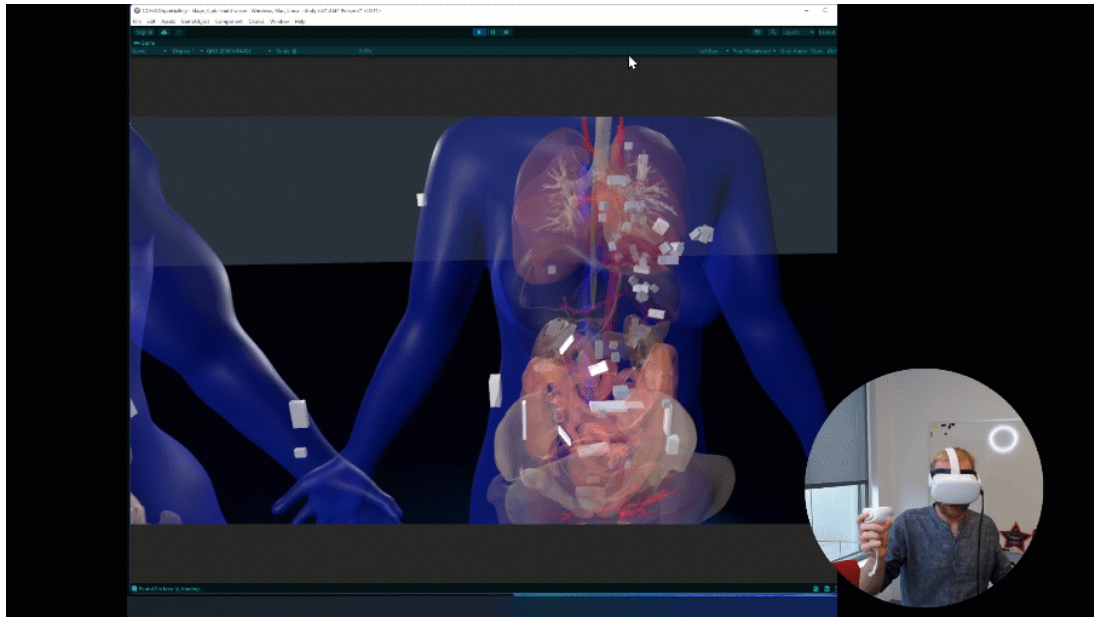
TissueBlockFloatBack.cs



https://www.youtube.com/watch?v=JmaAHyNvA98

Conclusion

- Preserve spatiality
- Visualize biological structure
- Use specimen data as filters
- Create Information-Rich Virtual Environment in VR
- Integrate spatial and abstract data in one continuous immersive environment



Become a Tester!

- Documentation: https://www.figma.com/file/TopdFvriKNcV9Af2Hgo8aK/Documentation-Organ?node-id=0%3A1
- Feedback: https://forms.gle/wnGnZLyDvU9MEs5o8
- Meta Quest 2 setup (general introduction): https://www.figma.com/file/0MgWkoPyuWLWb8esFsYya5/CNS-Documentation?node-id=0%3A1
- GitHub issues: https://github.com/cns-iu/ccf-organ-vr-gallery/issues
- Please contact Andreas Bueckle at abueckle@iu.edu!

Acknowledgements

- Red Pill Blue Pill VR R&D team:
  - Catherine Qing
  - Yash Ramesh Kumar
  - Naval Pandey
  - Riley Halloran
- Katy Börner

CNS Cyberinfrastructure for Network Science Center

INDIANA UNIVERSITY
LUDDY SCHOOL OF INFORMATICS, COMPUTING, AND ENGINEERING

Relevant Papers for HuBMAP

Börner, Katy, Sarah A. Teichmann, Ellen M. Quardokus, James C. Gee, Kristen Browne, David Osumi-Sutherland, Bruce W. Herr, et al. “Anatomical Structures, Cell Types and Biomarkers of the Human Reference Atlas.” *Nature Cell Biology* 23, no. 11 (November 1, 2021): 1117–28. https://doi.org/10.1038/s41556-021-00788-6.

Börner, Katy, Andreas Bueckle, Bruce W. Herr, Leonard E. Cross, Ellen M. Quardokus, Elizabeth G. Record, Yingnan Ju, et al. “Tissue Registration and Exploration User Interfaces in Support of a Human Reference Atlas,” 2021. https://doi.org/10.1101/2021.12.30.474265. (accepted to Nature Communications Biology)

Bueckle, Andreas, Kilian Buehling, Patrick C. Shih, and Katy Börner. “3D Virtual Reality vs. 2D Desktop Registration User Interface Comparison.” *PLOS ONE* 16, no. 10 (2021): e0258103. https://doi.org/10.1371/journal.pone.0258103.

Bueckle, Andreas, Kilian Buehling, Patrick C. Shih, and Katy Börner. “Optimizing Performance and Satisfaction in Matching and Movement Tasks in Virtual Reality with Interventions Using the Data Visualization Literacy Framework.” *Frontiers in Virtual Reality*, 2021. https://doi.org/10.3389/frvir.2021.727344

Your Turn