HuBMAP

SOP: Using the CCF Registration User Interface

How to register tissue blocks to 3D reference organs using the CCF RUI

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Introduction

This document contains instructions for spatially registering human tissue blocks to a 3D reference organ using the Common Coordinate Framework (CCF) Registration User Interface (RUI). This SOP is written for HuBMAP members that would like to upload tissue data via the [HuBMAP Ingest Portal](#) and for users not affiliated with the HuBMAP consortium who would like to register tissue data using the [public, standalone RUI](#).

The latest video demo of RUI version 3.0.0 can be found at https://youtu.be/gY3_-LIoKaU.
A video demonstrating how you can double-check your tissue block registrations with the Exploration User Interface (EUI) can be found here: https://youtu.be/UloDIG0S64w.

Roles and Responsibilities

The **User** is the person utilizing the RUI to register tissue blocks. The primary goal of this SOP is to document how to register tissue correctly and efficiently.

The **RUI Support** Person is the MC-IU contact who assists users with tissue registrations. The RUI Support Person also reports bugs and feature requests to the development team via [GitHub issues](#) as needed.

Role	Name	Email
User	Depends on organ	

RUI Support Person	Andreas Bueckle	abueckle@iu.edu

Versions of the Registration User Interface

Two versions of the RUI exist. Which one you access depends on whether you are registering tissue blocks via the HuBMAP Ingest Portal or not.

1. If you would like to register a tissue block for HuBMAP, go to the HuBMAP Ingest Portal and follow the instructions below. The RUI is embedded in the sample registration page. Metadata such as author name, date, etc. is captured as part of the tissue ingest process and RUI data is automatically associated with the tissue block on Globus. Use the CCF Exploration User Interface (EUI) to check data accuracy.
   Note that if the HuBMAP sample for which you register a RUI location is unpublished, you need to be logged into the HuBMAP Portal to see it in the EUI.
2. If you are not affiliated with HuBMAP, go to the public RUI. You will need to enter your first and last name and select the relevant organ (including making selections for male/female and left/right for some organs). After completing registration, download the RUI data in JSON format and share it with the MC-IU team. The RUI data will then be placed into this folder and be made available via the public CCF Exploration User Interface so you can check data accuracy. Instructions on how to use the RUI can be found below.
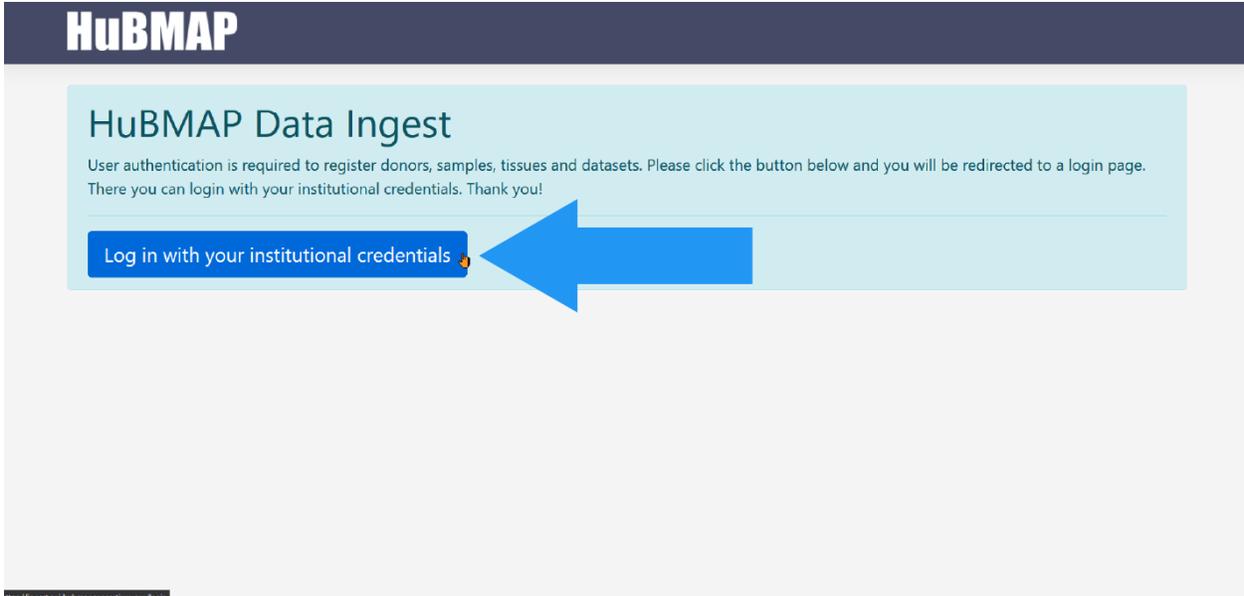
Accessing the RUI from within the HuBMAP Ingest Portal

DISCLAIMER: Although current at the time this SOP was adopted, the steps outlined here may change with future updates to the Ingest Portal. Screenshots may not always reflect what you see when you access the Ingest Portal.

Case 1: Register a new sample and get a RUI location

This section outlines how to access the RUI from the HuBMAP Ingest Portal to register a new sample with HuBMAP and register its location via the RUI at the same time.

1. Visit https://ingest.hubmapconsortium.org
2. If needed, log in using your institutional credentials.

3. Click the Sample tab on the top to see existing samples or to register a new sample.

4. Click the Source ID text input field. This will prompt a search for a Source ID for your Sample.

5. Click the Group dropdown menu and choose your component.
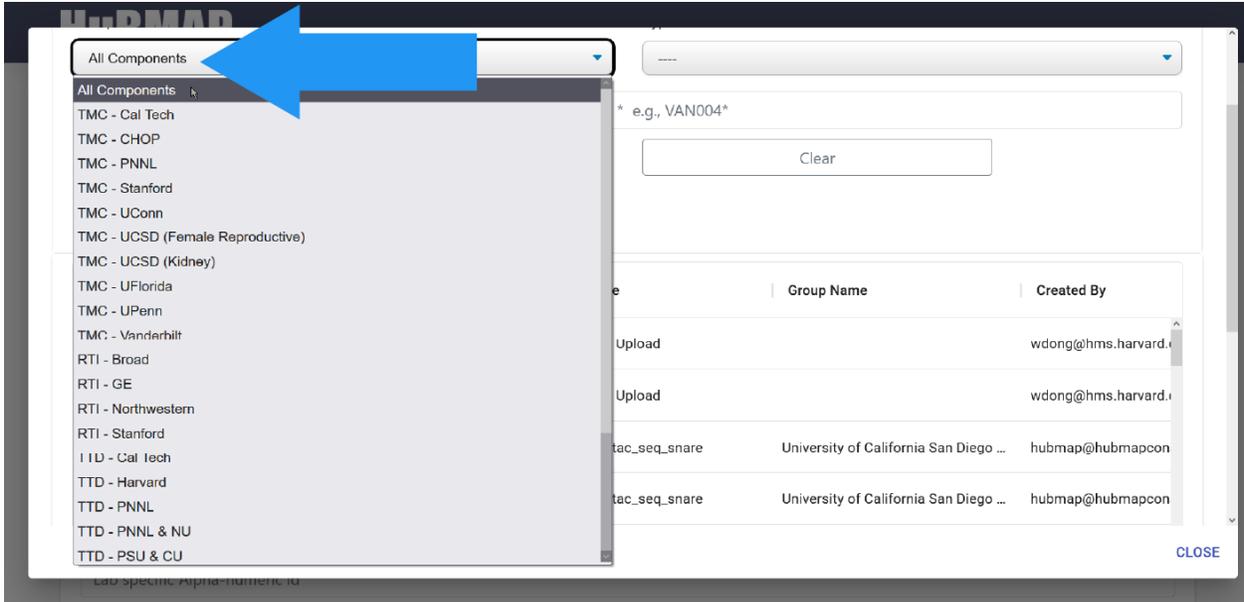
6. Click the Type dropdown menu and select Organ.

7. Click Search.

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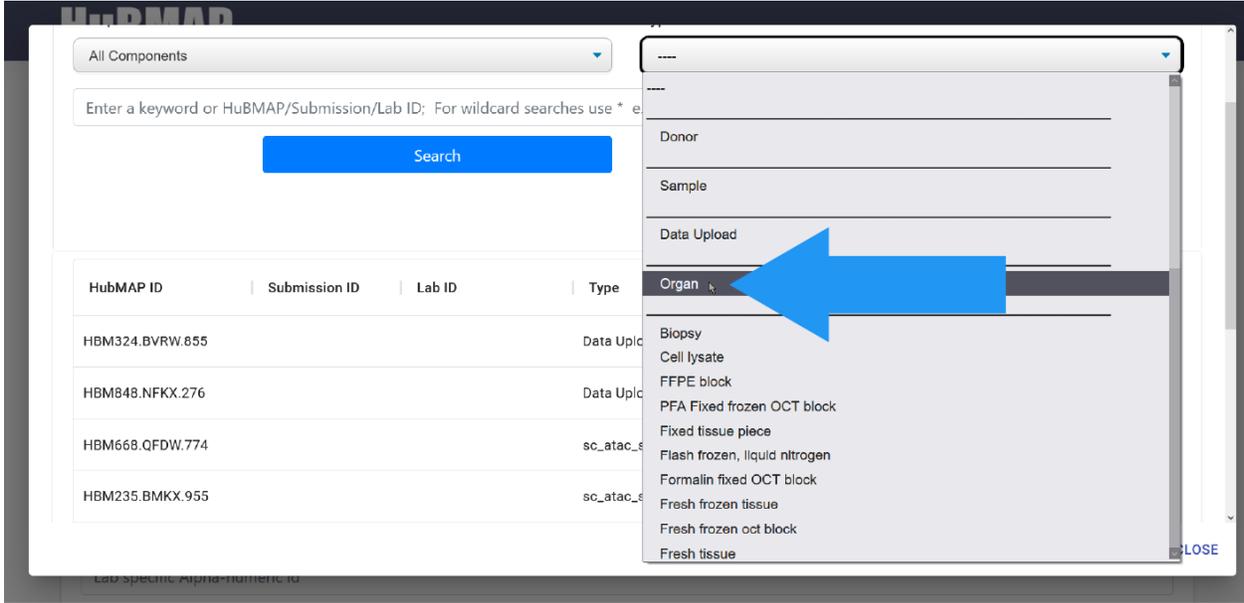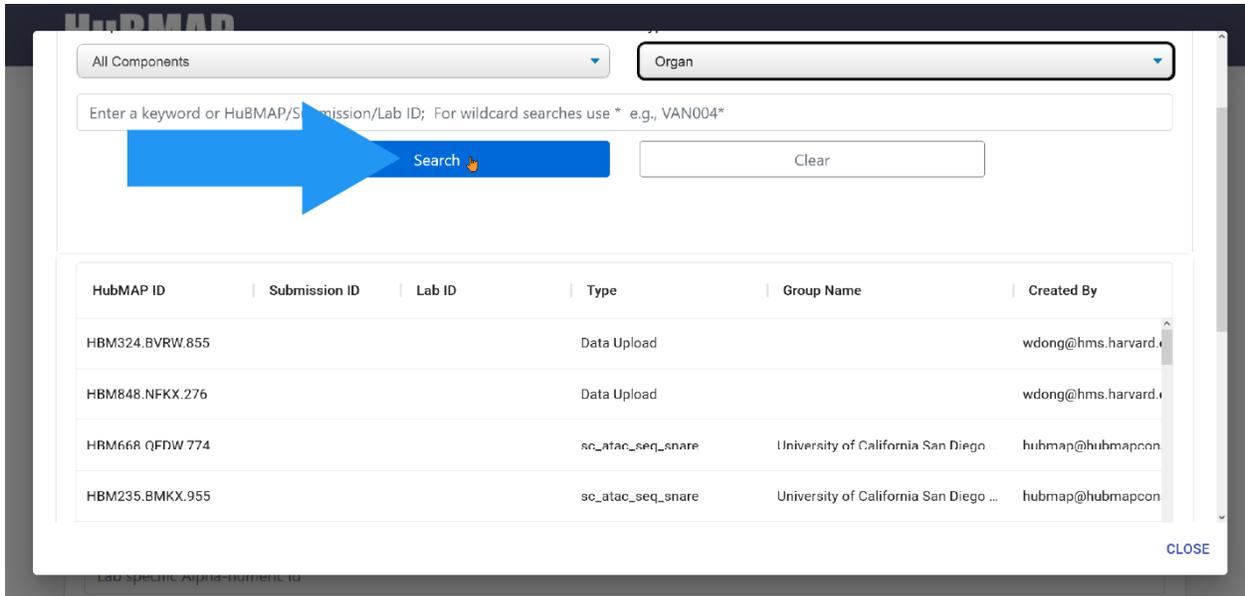
8. A list of organs is displayed. Pick one by clicking its row.
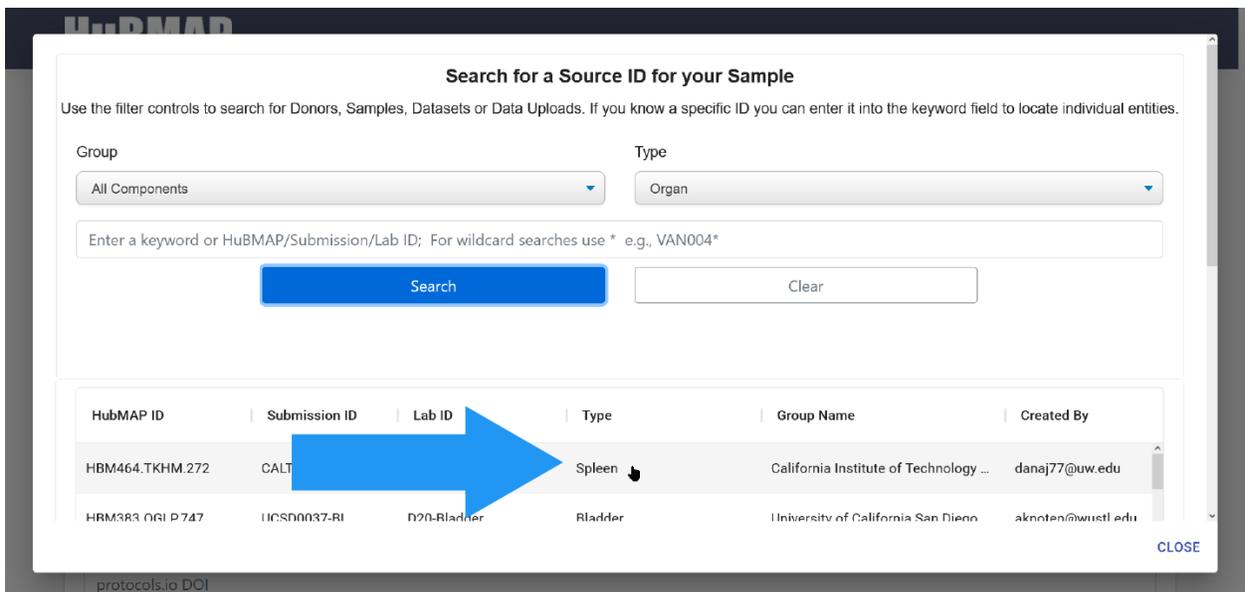
9. This returns you to the Sample Information page, displaying the newly added Source ID. Click the Tissue Sample Type dropdown menu and select the appropriate entr, then fill out the other fields as needed. You can start the registration process by pressing the blue Register Location button.

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10. The RUI is displayed, embedded into the page, with the organ of your choice as well as organ laterality and the donor sex selected based on the organ.
11. Follow the steps outlined in the Tissue Placement section for the next steps to place tissue.
12. When done, click the Generate ID button in the Ingest Portal.

Case 2: Adding a RUI location to an existing sample

Note: This only works if the sample is unpublished.

13. Repeat steps 1, 2, 5, from the section on [registering a new sample with RUI location](#).
14. Then, instead of selecting "Organ" like in step 6, select "Sample," and click the Search button (step 7). You will then see a listing of all the already registered samples for the selected team.
    a. Sidenote: You can also enter a HuBMAP ID to find the sample in question.
15. Select the tissue for which you would like to register a RUI location. Click the Register Location button to access the RUI.
16. Follow steps 11-12 from the section on [registering a new sample with RUI location](#).

Checking your Registration with the Exploration User Interface (EUI)

After having performed a registration using the RUI via the HuBMAP Ingest Portal, it is important to verify the 3D size, position, and rotation of the tissue blocks using the Exploration User Interface (EUI, https://portal.hubmapconsortium.org/ccf-eui). The EUI allows the user to inspect all registered tissue blocks in a 3D interface similar to the 3D Preview mode in the RUI. This video outlines the procedure (https://youtu.be/UloDIG0S64w).

If tissue sections were cut from the tissue blocks make sure to review and approve the number, thickness, and sequence of tissue sections using the listing on the right hand side, see Fig. 2.

If different assay types were run on tissue sections (e.g., CODEX) or suspensions (e.g., scRNAseq analysis) make sure all data is available for each tissue section or suspension on the right hand side.
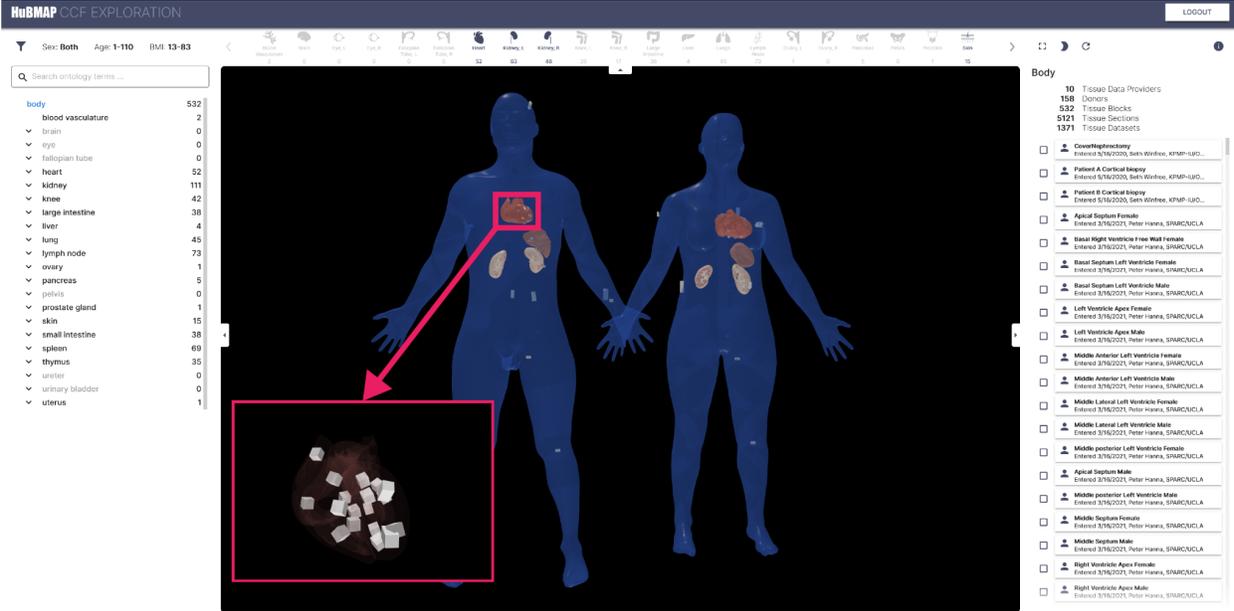
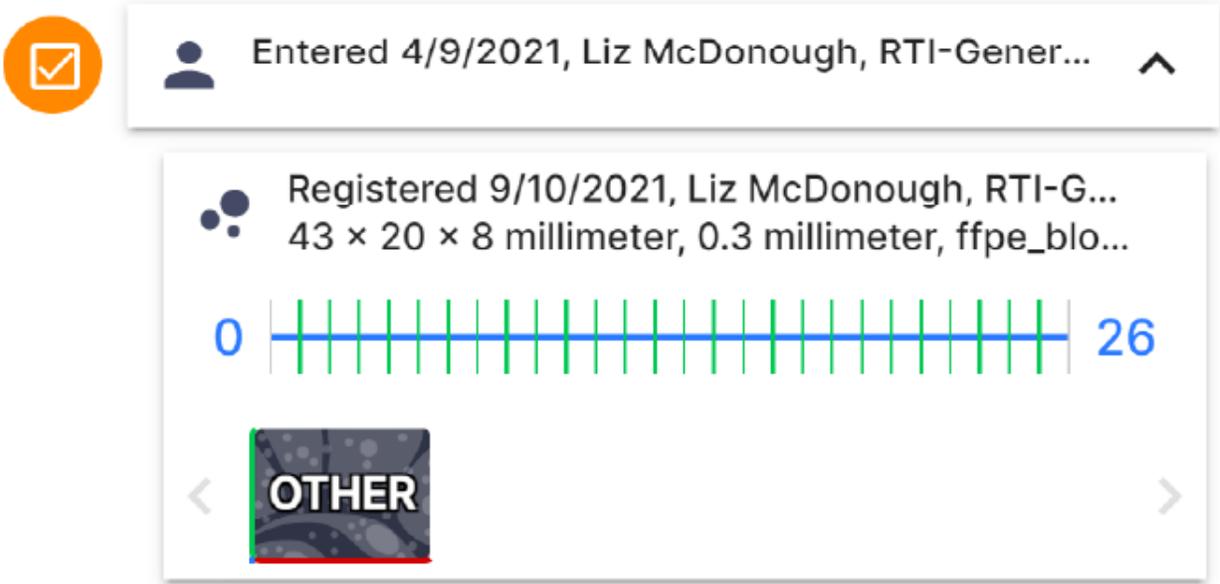**Figure 1:** The Exploration User Interface (EUI).

Figure 2: One tissue block with tissue sections and their associated datasets.

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References and Definitions

The below references and definitions were used in writing this Standard Operating Procedure. When available, definitions were taken from the [HuBMAP Dictionary](#), and aligned with standard terminologies used in relevant fields.

References

- The public Common Coordinate Framework Registration User Interface (CCF RUI): https://hubmapconsortium.github.io/ccf-ui/rui. Accessed on Feb 20, 2021.
- HuBMAP Ingest Portal: https://ingest.hubmapconsortium.org.
- RUI ingest flowchart: https://docs.google.com/presentation/d/1bCX0XusohrvLqoo44ygob3-aAQB6-ei7MMiog7Q75ag/edit#slide=id.p1 . Accessed on Aug 30, 2021.
- The CCF Portal: https://hubmapconsortium.github.io/ccf. Accessed on Feb 20, 2021.

Glossary

Globus: Globus is software-as-a-service for research data management, used by hundreds of research institutions and HPC facilities worldwide for secure, reliable file transfer, sharing and publication. (Globus.org)

HuBMAP: The Human BioMolecular Atlas Program is a consortium composed of diverse research teams funded by the [Common Fund at the National Institutes of Health](#) . HuBMAP is developing the tools to create an open, global atlas of the human body at the cellular level. These tools and maps will be openly available, to accelerate understanding of the relationships between cell and tissue organization and function and human health.

HuBMAP Ingest Portal: The HuBMAP Ingest Portal is where HuBMAP members generate HuBMAP IDs.

Reference Organ: A reference organ is a 3D model based on a variety of potential data sources produced by MC-IU. 3D models are created with the involvement of subject matter experts.

Standard Operating Procedures (SOPs): SOPs are issued to specifically instruct team members in areas of responsibility, procedural steps, appropriate specifications and required records. SOPs outline procedures, which must be followed to support the reproducibility of scientific research. Procedures can take the form of a narrative, a flow chart, a process map, computer screen

printouts or combination of all or any other suitable form, however must be written in appropriate, effective grammatical style. (e.g. plain English).

Tissue Block: A tissue block is a digital, 3D representation of a tissue sample. In the RUI, tissue blocks are cuboids that you can spatially register to a reference organ.

Tissue Section: A tissue section is a slice of a tissue block. Tissue sections inherit the location and rotation of their parent tissue block. The thickness and number of tissue sections is captured with an input field inside the RUI.

Tissue Suspension: A tissue prepared for bulk analysis.

Appendix

Description of the User Interface (UI)
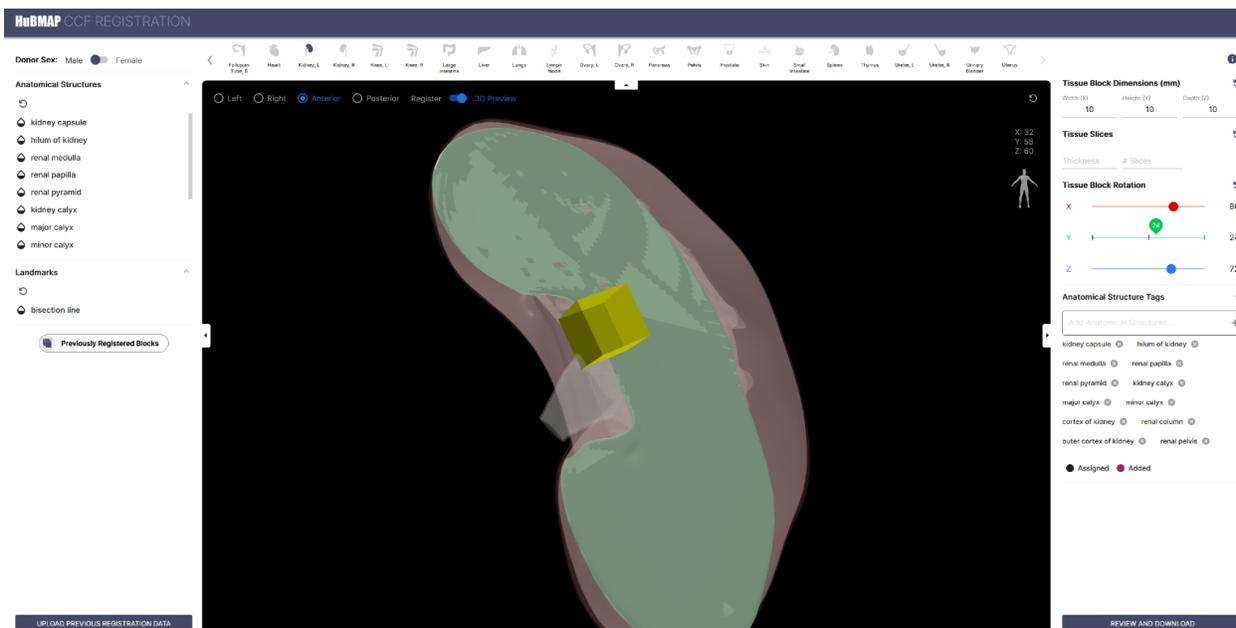
Figure 3: The stand-alone CCF Registration User Interface (RUI).

The RUI currently supports tissue registration for the organs listed in the CCF 3D Reference Object Library (https://hubmapconsortium.github.io/ccf/pages/ccf-3d-reference-library.html) . The yellow cuboid represents the tissue block. The green slide indicates the **bisection line** inside the **kidney**.

Figure 4: The RUI has three panes: metadata (pink), 3D (yellow), and manipulation (blue).

The RUI consists of three panes: the **metadata** pane on the left, the **3D** pane in the middle, and the **manipulation** pane on the right. Here are brief explanations of what can be accomplished in each pane:

    a.   The metadata pane contains the following elements:
        i.   Donor Sex
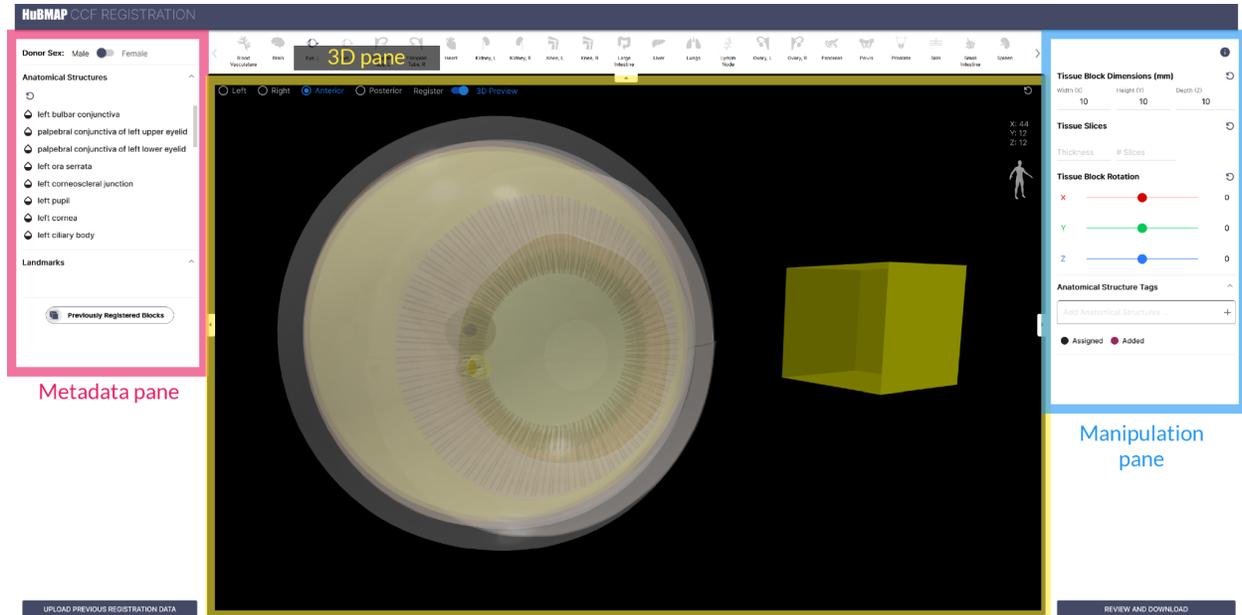   ii.   Anatomical Structures menu: The anatomical structures listed here correspond to 3D structures inside the reference organ. A slider appears when you hover over the drop icon to the left of the anatomical structure text entry, making it possible to adjust the opacity of the structure. This allows you to make certain parts of the organ more transparent than others and to retain certain structures as landmarks while omitting others to ease placing the tissue block. Also, clicking the eye icon to the right of the slider will hide the structure. It can be turned on by clicking the icon again.
        iii.   The Landmarks menu reveals visual cues to allow you to recognize the anatomy of the organ (such as the bisection line for the kidney). All extraction sites are hidden by default. Extraction sites are rendered green.
        iv.   Previously Registered Blocks toggle button: This button allows you to view tissue blocks you have registered before, which show as blue in the 3D pane. This information is taken from your browser cache. When previously registered blocks are shown, anatomical structure opacity is reduced to 20%.

    b.   The 3D pane contains the reference organ and the tissue block. It is a 3D window, similar to what one would find in 3D modeling software or a video game. In the top left corner, a set of radio buttons allow you to control the 3D camera of the scene.

i. Using the radio buttons labeled Left, Right, Anterior, and Posterior, you can rotate the camera around the reference organ in increments of 90 degrees. The current camera view is visually indicated by a small human icon on the right side of the 3D pane.

ii. When Left, Right, Anterior, or Posterior are clicked, the camera movement is restricted to 90 degree increments, and the mouse is used to move the tissue block. Select 3D Preview to verify tissue placement. When in 3D Preview mode, you can rotate the camera at two degrees of freedom while clicking and dragging the left mouse button. You can also zoom in by using the mouse scroll wheel (or whatever input method is assigned to scrolling) and pan the camera (i.e., move it laterally) by clicking and dragging the right mouse button.
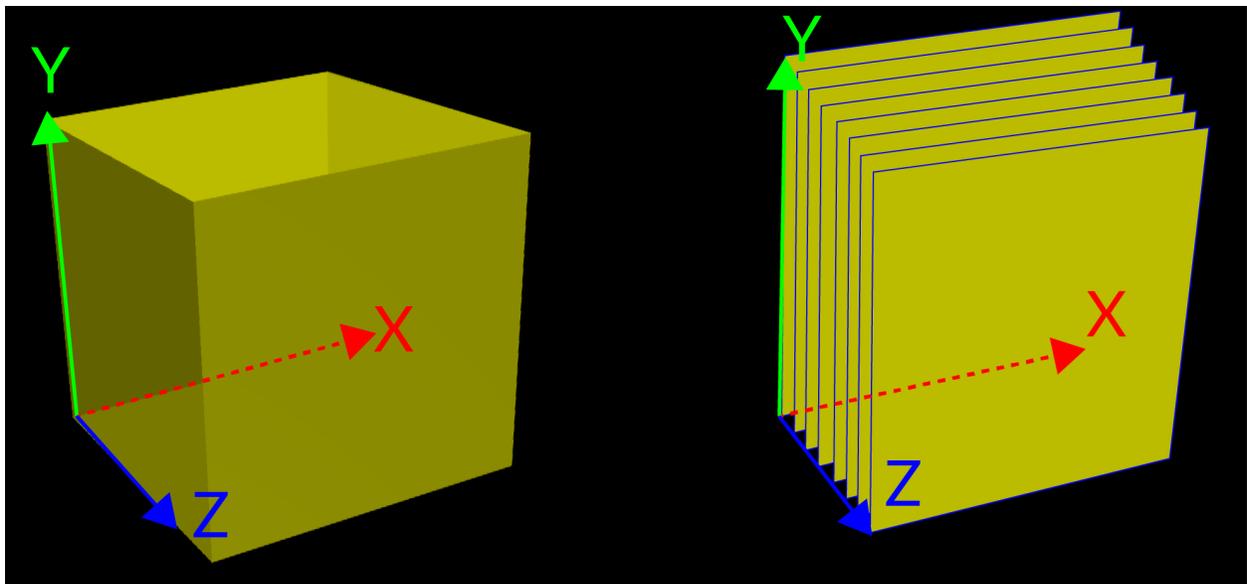
Figure 5: The z-axis should correspond to the cutting direction of the tissue block.

iii. In the top right corner, the current x, y, z-coordinates of the tissue block are shown, with the origin in the back bottom left corner of the reference organ.
Note: When adjusting the Tissue Block Dimensions, please bear in mind that the z-axis (see Fig. 5, blue arrow) represents the cutting direction of the tissue block. This means that when you set the dimensions of your cube, and subsequently the rotation (see below), you must ensure that the depth (Z) value represents the length of the side of the tissue block along which you cut the block into sections.

iv. The circular arrow in the top right corner of the 3D pane can be used to reset the position of the tissue block.

c. The manipulation pane on the right allows you to resize and rotate the tissue block, indicate thickness and number of tissue sections, and review anatomical structure

tags generated via collision detection between the tissue block and the anatomical structures in the reference organ.

    i. On the top of the manipulation pane, the Tissue Block Dimensions fields allow you to define the size of the tissue block in millimeters (mm). These fields can be reset by clicking the small circular arrow button in the top right.

    ii. Below that, the Tissue Sections fields let you indicate the thickness and number of sections for the tissue block. Note that the thickness is indicated in micrometers (μm). These fields can be reset by clicking the small circular arrow button in the top-right.

    iii. The Tissue Block Rotation sliders allow you to add rotation to each axis of the tissue block individually. The sliders are color coded (red: x, green: y, blue: z). All slider values can be reset by clicking the small circular arrow button in the top-right. Note that the RUI is a "y-up" 3D application where the y-axis corresponds to the global "up" vector.

    iv. The Anatomical Structure Tags menu can be expanded via a click. This section is empty by default but is automatically filled as you move the tissue block into the reference organ. Once a collision between an anatomical structure and the tissue block has been detected, the name of the anatomical structure is added to the Anatomical Structure Tags section as a tag. Tags can be removed by clicking on the little x to the right of the tag. Tags can also be added manually using AS terms as they appear in the Anatomical Structures list on the left. Anatomical structures must be selected from the auto-complete suggestions provided.

Registration Process

The registration process works as follows:

1. The RUI currently supports more than 50 of organs as of February 2022. Check whether the RUI supports your organ by opening the standalone version of the RUI and checking the organ carousel: https://hubmapconsortium.github.io/ccf-ui/rui/
2. Gather any materials needed to document where the tissue block was extracted from.
3. Open the relevant version of the RUI (see above to determine which version of the RUI you need to use).

Add Metadata

4. When opening the public RUI, you are presented with a small window,see Fig. 6. You need to enter the required data before you can start the registration process. If you use the RUI embedded in the Ingest Portal, you can skip to the next step.

Figure 6: The window opens when you first land on the RUI webpage.

- a. Name
    - i. In the public version, enter your first and last name into the corresponding text entry fields.
    - ii. Note: In the Ingest Portal version, your name is already captured on the back end based on data from your user profile.
- b. Donor sex and organ selection:
    - i. Select the donor's sex.
    - ii. In the public version, select an organ from the organ carousel. Make sure to select the right or left version as appropriate. The organ might take a few seconds to load.
    - iii. In the Ingest Portal version, the organ is pre-selected.

Click OK to complete this step and see the RUI, see Figure 1

Tissue Placement

If this is your first time using the RUI, please read through the Description of the User Interface (UI) section first.

1. Resize the tissue block using the Tissue Block Dimensions text input fields in the top right corner. The default is a 10x10x10 mm block.
2. Enter tissue section thickness in micrometers.
3. Move the tissue block into position.
4. When using the mouse, the tissue block can only be moved in two dimensions at a time.
    - a. To make "looking inside" the reference organ easier, all anatomical structures are set to 20% opacity as the default. You can adjust the opacity using the Anatomical Structures accordion menu in the metadata pane (see below).
    - b. To inspect tissue blocks you placed before (for reference), click the Previously Registered Blocks toggle button in the metadata pane on the left. Clicking this

toggle button will show all previously registered tissue blocks based on your browser's local cache. This feature is supported on all major browsers.

    c. To change the perspective, use the radio buttons in the 3D pane (see [below](#)).

    d. To verify the placement, switch to 3D Preview mode using the corresponding toggle switch at the top of the 3D pane (see [below](#)).

5. At any time, the tissue block can be moved by pressing the W, A, S, D, Q, or E keyboard buttons, see Fig. 7. Each button moves the tissue block by 0.5 mm either into the positive or negative direction of an axis. The WASDQE buttons can be used at any time, regardless of whether the application is in Register or 3D Preview mode.
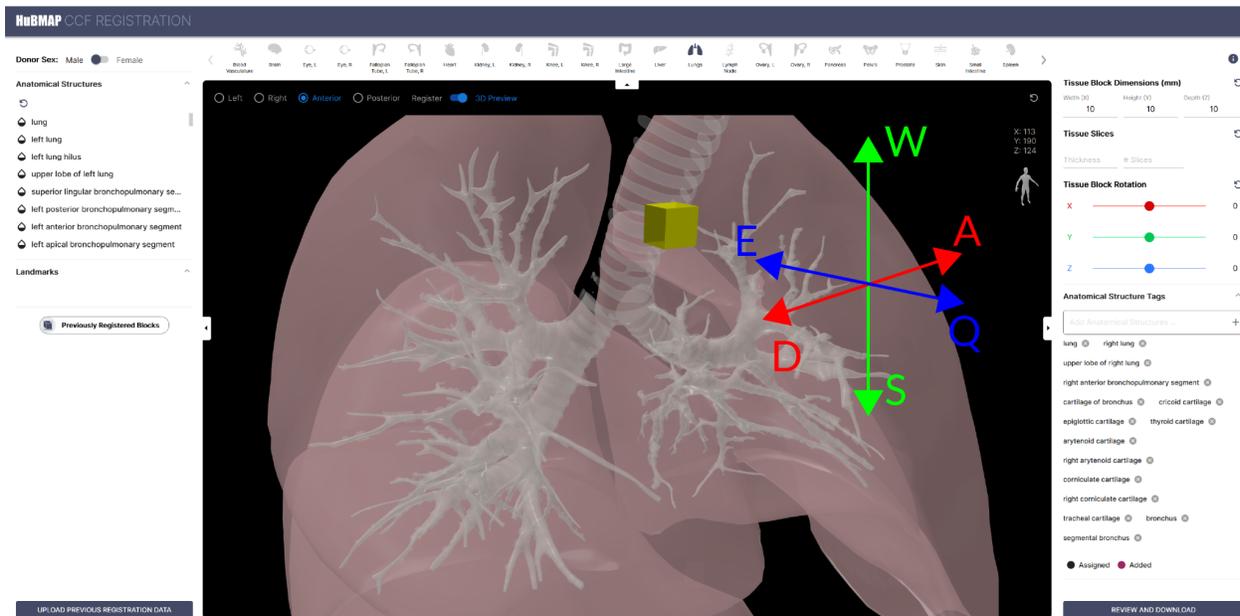
Figure 7: The WASDQE buttons move the tissue block along individual axes.

6. Adjust the rotation of the tissue block by using the rotation sliders in the manipulation pane on the right.

Review, Save, and Share Registration Data

7. If you are using the Ingest Portal version of the RUI, click the Register Location button. The RUI window will then close automatically.

8. If you are using the public version of the RUI, click the Review and Download button in the bottom right corner of the screen to review the data and download it as a JSON file.

9. A Registration Review window pops up so you can check the validity of the data you generated. **You need to then download the JSON file to your hard drive.**

10. You can then share the registration data with the RUI Support Person listed in the [Roles and Responsibilities section](#) above, who will work with you to facilitate its downstream usage.