Getting Started with Lesion Tracing

Stroke is one of the leading causes of adult disability worldwide, and despite intensive physiotherapy, up to 2/3 of stroke survivors never fully recover. There are still many unknowns about the recovery from stroke but growing areas such as neuroimaging and big data are helping to inform the field. Many neuroimaging studies are interested in understanding how different properties of lesions (e.g., their size and location in the brain) relate to various aspects of stroke recovery, such as motor recovery after stroke. However, many of the current studies rely on manually traced lesions for their analysis and therefore, the sample size of their analysis might be limited. More recently, techniques have been developed to automatically trace stroke lesions which could allow the potential of running analysis on large datasets. However, there currently are limited ways to test the accuracy of these techniques (i.e. a large set of manually traced lesions reference for comparison). Our goal is to create a large dataset of manually traced lesions in order to have a set guideline for comparing automatically traced lesions techniques and to help provide a training/test dataset for researchers who are trying to improve their automated techniques. We are hoping that this set of manually traced lesions will serve as a useful resource for researchers, providing them with manually traced lesions to assess the accuracy for their own methods. The brains that you will use to trace these lesions are from datasets collected through the ENIGMA Stroke Recovery working group. You can also read prior publications from our lab that have resulted from this manually traced dataset:

- Liew, S. L., Zavaliangos-Petropulu, A., Jahanshad, N., Lang, C. E., Hayward, K. S., Lohse, K. R., ... & Bigjahan, B. (2020). The ENIGMA Stroke Recovery Working Group: Big data neuroimaging to study brain–behavior relationships after stroke. Human Brain Mapping.
- Liew, S. L., Anglin, J. M., Banks, N. W., Sondag, M., Ito, K. L., Kim, H., ... & Lefebvre, S. (2018). A large, open source dataset of stroke anatomical brain images and manual lesion segmentations. Scientific data, 5, 180011. (Currently 49 citations using this published dataset).

Training

Before you start tracing lesions independently, you will first trace five practice lesions that will be compared to our gold-standard lesions (Inter-rater reliability). In addition, you will re-trace these same five practice lesions, as well as two additional, that will be compared to your initial traced lesions (Intra-rater reliability). Note: do no look at the lesions you first traced when you re-trace lesions for intra-rater reliability.

To get started with this training, complete the following steps:

1. Download itk-SNAP
2. Read through sections 1-4 in this tutorial
3. Watch this tutorial video
4. Watch LesionTracing_Example.mov (in *c0013_lesion_training*)
5. Begin tracing the lesions in *c0013_enimga* → *YourName_Training* → *Training_Set_1*
    a. Make a folder on your desktop called Lesion_Tracing (or something similar)
    b. Download the T1 into your desktop folder
    c. Save your lesion mask locally, then upload to Google Drive folder:
        i. *YourName_Training* → *Training_Set_1*
    d. When you save your lesion mask, save them with the date you traced them (i.e. sub-r000s001_20210817

    e. Reach out to the checker (Bethany) with any questions along the way or if you want to review a lesion tracing before continuing
6. After completing lesion tracings, schedule a meeting with the checker to discuss
7. Once these are approved, you will start tracing the 7 lesions in the folder called *Training_Set_2*
8. After completing these lesion tracings, schedule a meeting with the checker to discuss

Once the practice lesions you have drawn are verified, you will be ready to start independently tracing lesions.

Keeping Notes
Throughout your training and when you begin independently tracing lesions, it will be vital that you keep detailed notes in your notes document, titled *YourName_Training_Notes*.

This is especially important for any trouble images that you may come across. Examples of trouble lesions might be if there were multiple lesions in the brain, odd lesions that you may be unsure about the accuracy of many small white matter lesions, etc. You can refer to your notes when you discuss with your team and this can be referred to during quality checking.

Using a Tablet
It can be useful to trace lesions using an electronic pen and tablet. There are several Wacom tablets located in the lab that can be used and checked out. Alternatively, if you have a tablet (Microsoft Surface, iPad, etc.) you may prefer tracing with a stylus/pen. Others prefer using a normal mouse or trackpad. See what works for you.

Tracing Checklist:
1. Open itk-SNAP
2. Click “Open Image” in the bottom right corner
3. Browse and select the raw brain image file
4. Click Next; Click Finish
    a. Image of a T1 brain should be loaded
5. Locate lesion (easier said than done in some cases. If there are multiple lesions, trace all and include in the same mask)
    a. In the axial (or coronal) view, scroll through the cerebellum
    b. Then scroll through and focus on the brainstem
    c. Then scroll through and focus on the left hemisphere
    d. Then scroll through and focus on the right hemisphere
6. Begin drawing lesion
    a. May be easiest to start in the center of the lesion (however this based on preference)
    b. Use one plane/view to start. Choose the plane/view where you see the lesion most clearly. Even if you are tracing in one view, check the other views frequently to see if what you are tracing looks like lesion in those views as well.
    c. Select polygon mode and ‘smooth curve’ option
    d. Outline the lesion by clicking or dragging around the borders of the lesion
    e. Once an outline is made, click complete, then accept if there are no further changes to make; you should now see a filled slice
    f. For medium to large lesions, trace in *either* coronal or axial view, and then go and clean up the borders (if needed) in the *other* view
    g. For large lesions, the ‘interpolate’ tool can be used:

        i. Trace every 2 or 3 slices, repeating until slices have been traced throughout the entirety of the lesion
        ii. Go to Tools > Interpolate Labels (only click ONCE)
7. Once lesion is complete, go to Segmentation > Save Segmentation Image
8. Save as sub-rXXXsXXX_ses-1_desc-T1-lesion_mask.nii.gz

If you are having trouble determining the lesion border:

1. Use the crosshairs and click on the border you're unsure about, then look in the other views and scroll through to see if that area is "connected" to anything
2. Look at the general shape and "movement" of the lesion

When Finished, Review:

1. Turn the mask opacity down to about 20%, look for any additional lesions
2. Scroll through in both the coronal and axial views, watching the edge of the mask - note where there might be large "jumps" or very straight edges and go fix them
3. Don't trace *any* of the insula
4. Don't trace *any* of the ventricles
5. Don't trace *any* of the dura mater (white border on the skull)
6. Border of the mask should be right on the edge of the the lesion
    a. The lesion should not be seen "peeking" out from behind the mask (undertracing)
    b. You should not see a line/border of white matter on the edge of mask (overtracing)

Main things to remember when determining if something is a lesion:

- Shape (*is it tubular or irregular?*)
- Location (*is this pathology normal to see in this area?*)
- Intensity (*is it very dark (hypointense), or only slightly dark?*)
- Border (*is there a gray halo?*)
- Symmetry (*is it occurring in similar areas in both hemispheres?*)
- Direction (*are all shapes 'moving' together, or do they simply 'touch' and then go in different directions/trajectories?)*

itk-SNAP Shortcuts

(http://www.itksnap.org/pmwiki/pmwiki.php?n=Documentation.KeyboardShortcuts)

S = show or hide the segmentation
Shift+**X** = show or hide crosshairs
Hold Right-Click + Drag = zoom in and out