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Athens Medical School

National and Kapodistrian
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Automated TTC image-based analysis of mouse brain lesions

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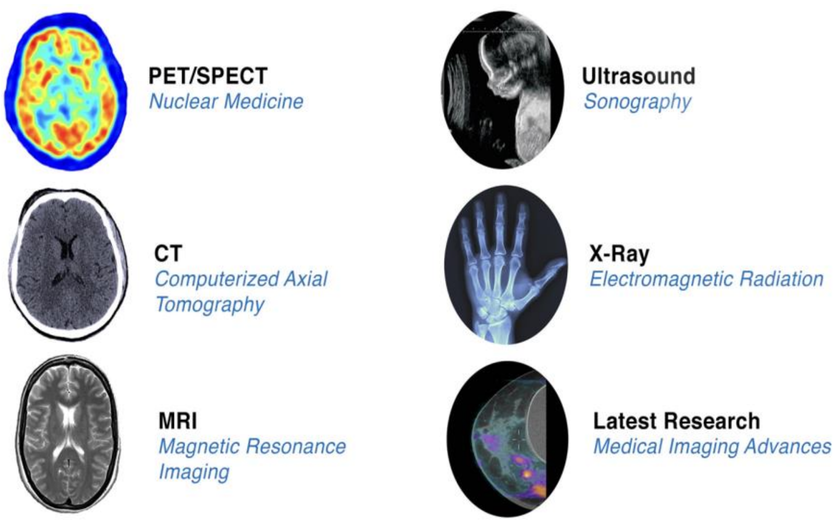
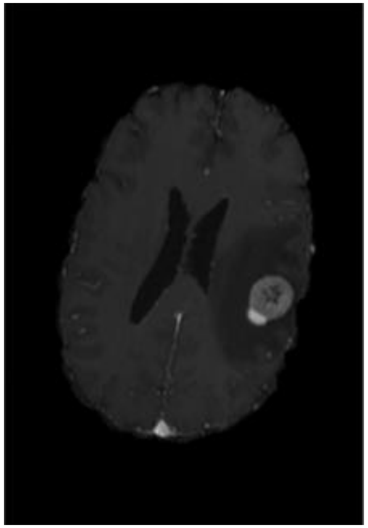
Medical Imaging

- **Medical Imaging Modalities (3D)**
  - MRI, CT, PET, etc.
- **Abnormality detection**
  - Based on intensity variations, spatial and other characteristics
  - Atlas Based
  - Combined techniques





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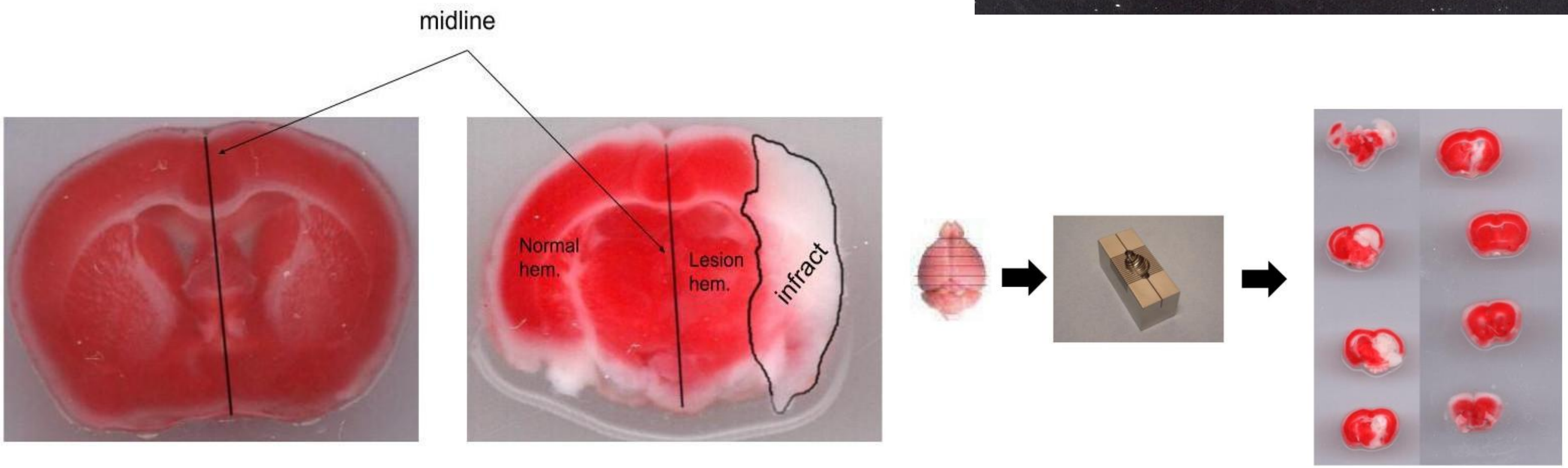
Lab Data

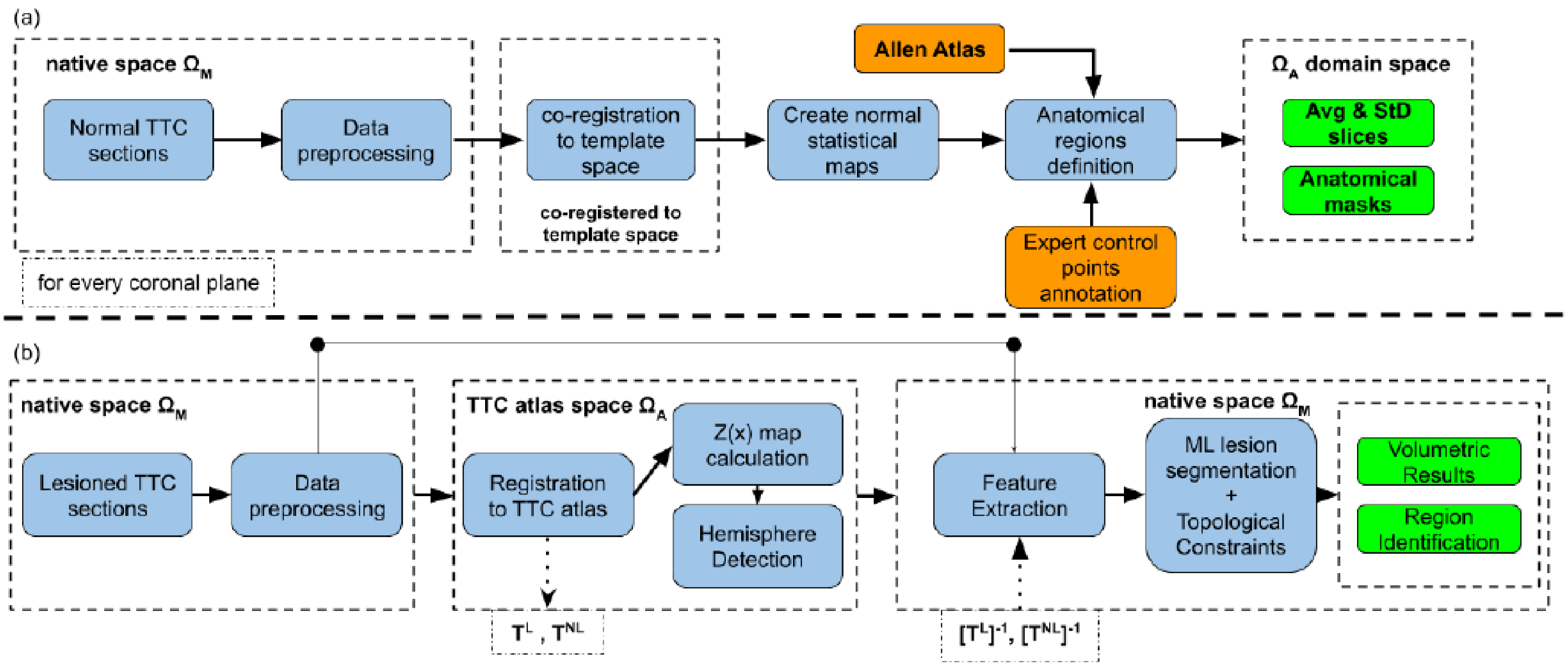
- TTC stained mouse brains.
- Coronal slices at 1mm distance taken within a direction of anterior to posterior (x-axis).
- Normal/abnormal ➡ (red/white).
- Pixel size at 0.021 mm.
- Unilateral lesions.



The problem: automated detection and analysis of brain lesions (strokes)

- **Our data**
  - TTC stained **2D slices**.
  - Red for normal and White for lesion regions.
  - **Detection** of lesioned regions.
  - **Identification** of lesioned regions.
- **Challenges**
  - Poor discriminative ability.
  - Staining Artifacts.
  - 2D and out of plane deformations.
  - Lack of comparative data sets/known base.
- **Contribution**
  - Construction of a **TTC mouse brain atlas**.
  - Design and implement a framework for **automated detection and analysis** of mouse brain lesions.

Pipeline

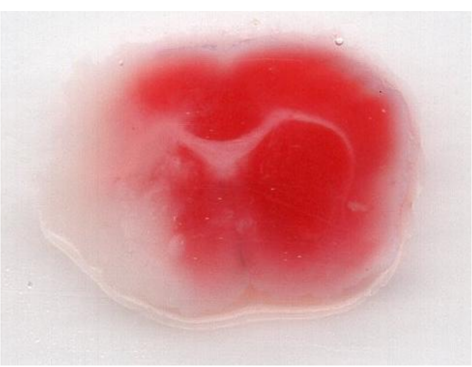


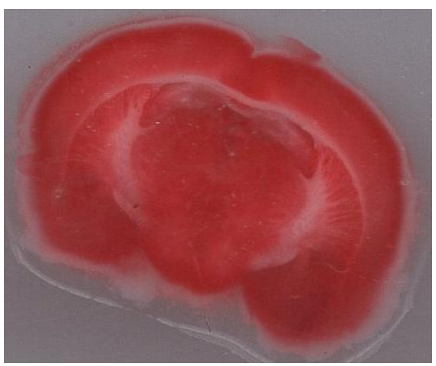
Methodology in a nutshell

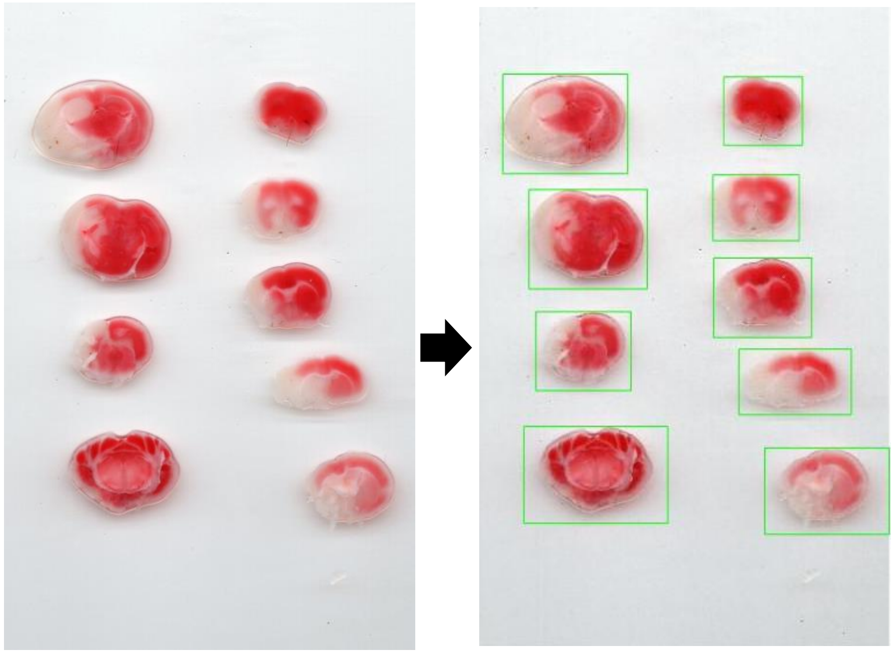
- Preprocessing of medical 2D images
- Create a representative TTC atlas.
- Register (common space) subject slices to corresponding TTC atlas slice.
- Create probability map of abnormal points (z-score image).
  - Use common space.
- Train and use a machine learning model to Predict Lesion Areas.
- Volumetry and affected regions identification.

Data Preprocessing (1)

- **Extract separate images.**
- **Purpose → Noisy data.**
  - Our data contains both tissue and **non tissue information** (background).
  - Without an accurate background segmentation the **registration process might fail.**
    - Loose boundaries, artifacts.
- **Data preprocessing in a nutshell:**
  - Background segmentation.
  - PCA alignment.

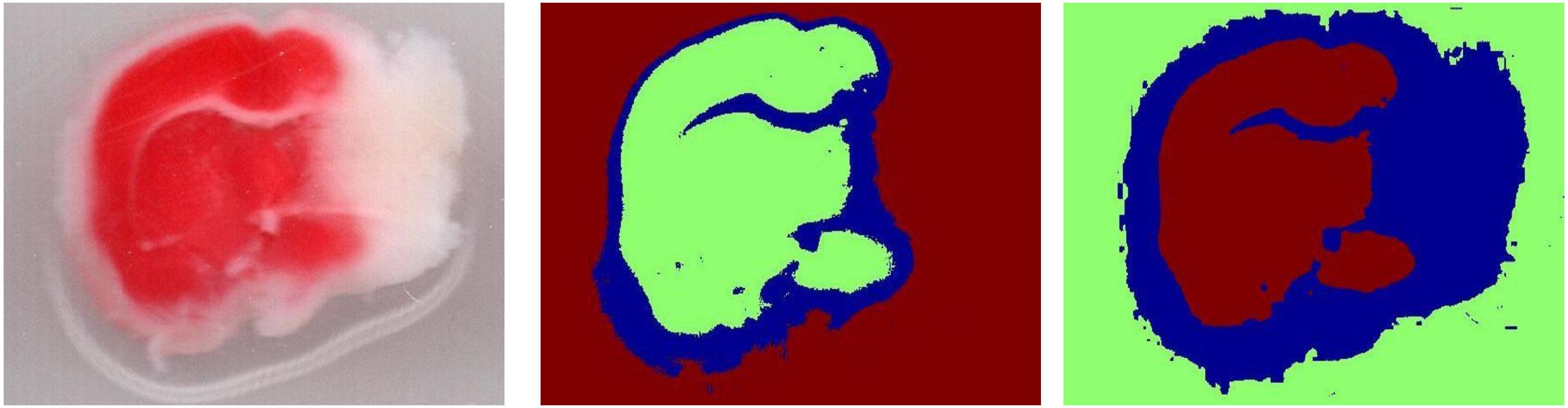






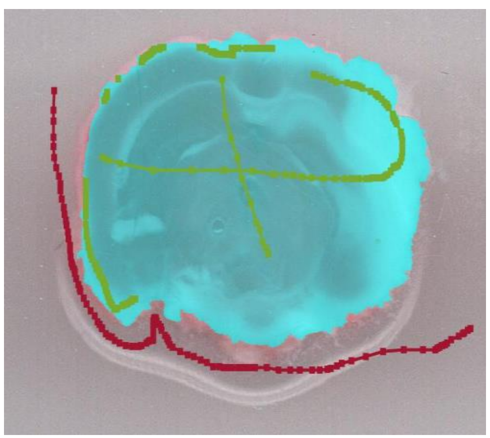
Data Preprocessing (2)

- **Background Segmentation**
  - **Superpixels & K-means clustering.**
    - Obtain background and foreground clusters. But, producing not ideal results.
  - **Markov Random Fields (MRF).**
    - Improve clustering accuracy.



Data Preprocessing (3)

- **Slice rotations.**
  - During the cutting procedure brain slices will **differ in terms of their orientation with the horizontal axis.**
  - Such rotations might exceed registration algorithm search bound.
- **Principal Component Analysis (PCA) rotation.**



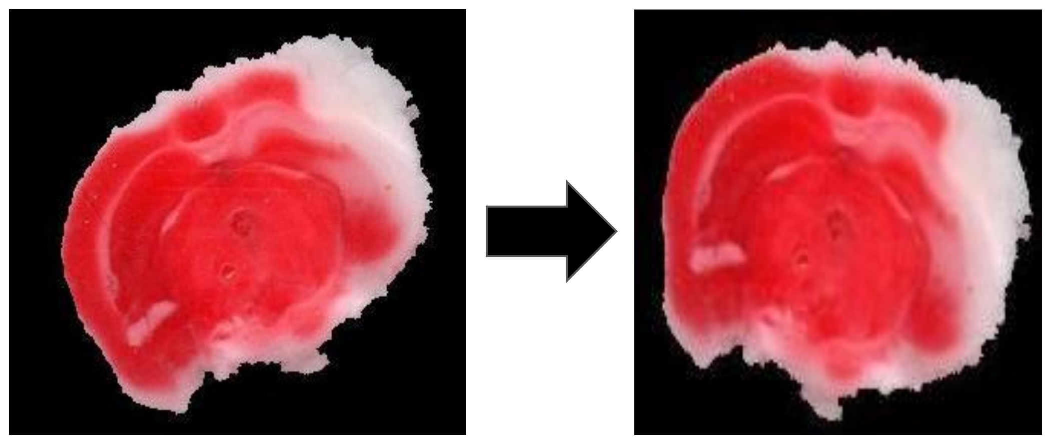
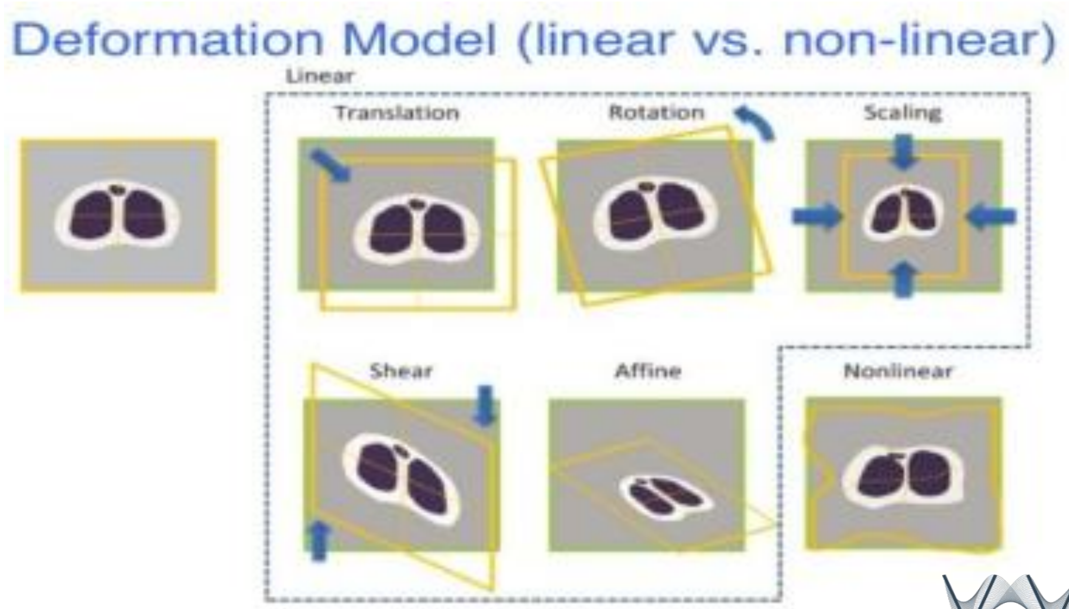


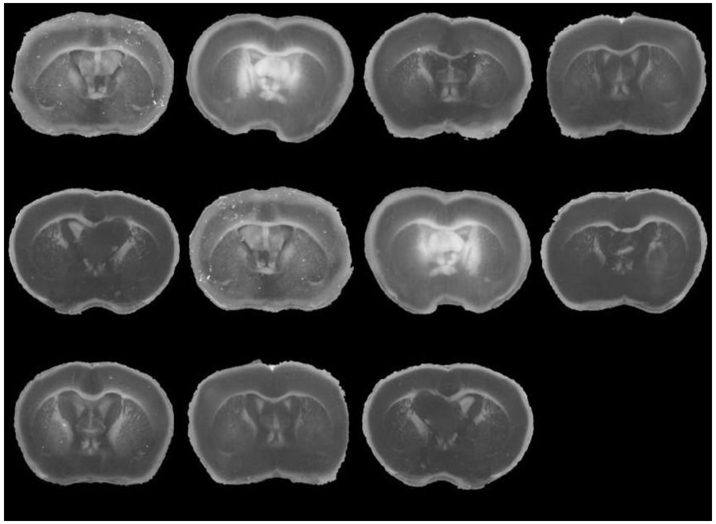
Image Registration

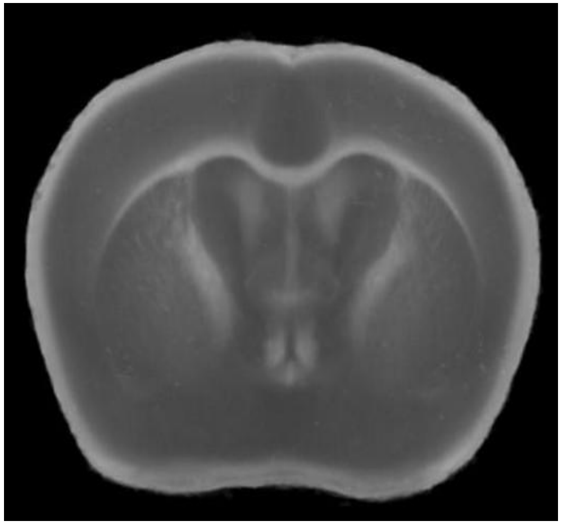
- **Purpose:** Apply registration to **compare images** and fill-in missing information by utilizing registered information (such as anatomical areas).
- Typically, Image registration refers to the process of **transforming** an image in order to fit into a given space (a.k.a., Atlas) s.t. the error is minimized.
- Practically, we project the **moving** image to the **reference** image (image in Atlas) and try to minimize a given **error function**.
  - In this particular problem **target space is the TTC Atlas space.**
- Registration steps:
  - **Linear**
  - **Deformable**

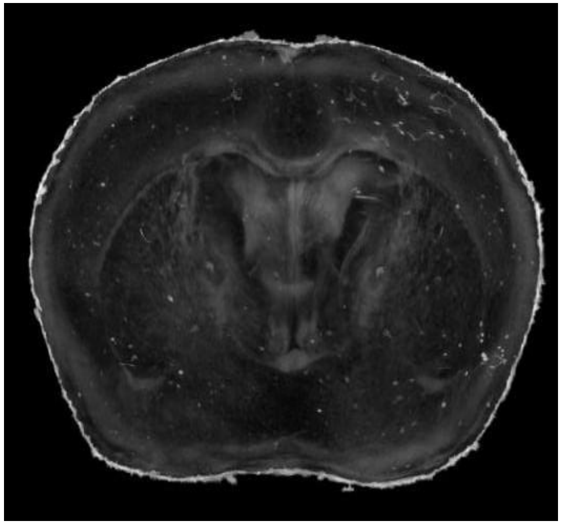


TTC Atlas (1)

- **Need of a TTC atlas:**
  - **Data must be comparable** i.e. reference and subject slice under the same protocol.
- **No TTC atlas is available (to the best of our knowledge).**
  - Solution: Create a representative one.
- **Each x-index position is represented by an average slice & a standard deviation image.**
  - Create an average slice using multiple samples (healthy subjects).
  - **Image registration** is a prerequisite.







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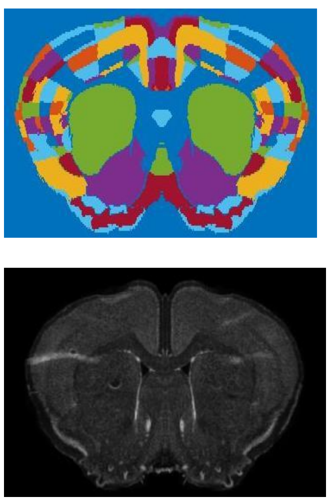
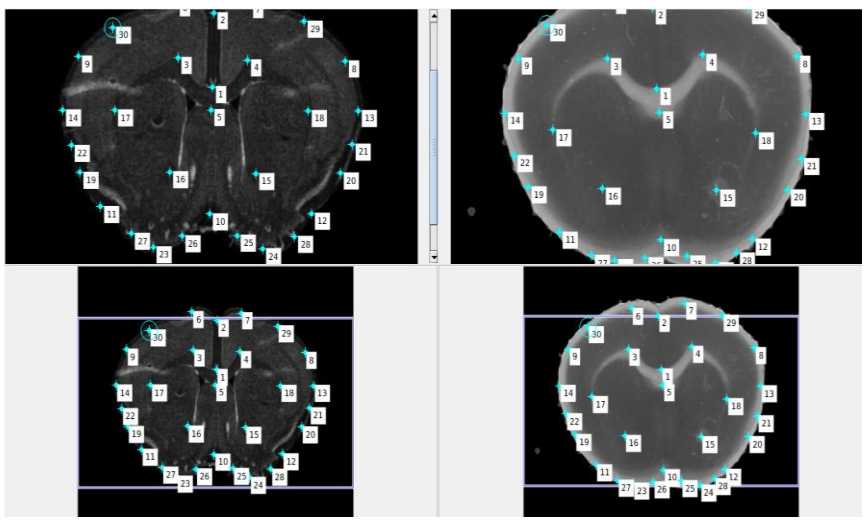
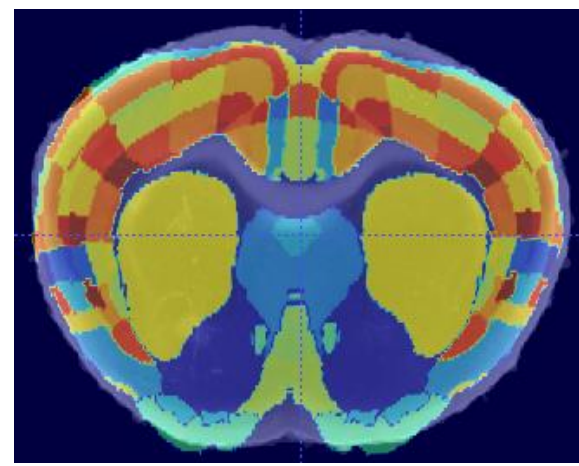
TTC Atlas (2)

- **Handling lack of spatial anatomical information at TTC atlas.**
  - Finding it through projecting Allen slices to TTC Atlas (semi-automated).
    - Set control points (control points are describing the same area at fixed and moving image).
    - Polynomial fitting or Local Weighted Mean Transformation.
    - Experts’ intervention is required.
  - **Use obtained transformation to “project” Allen anatomical Masks to TTC Atlas.**

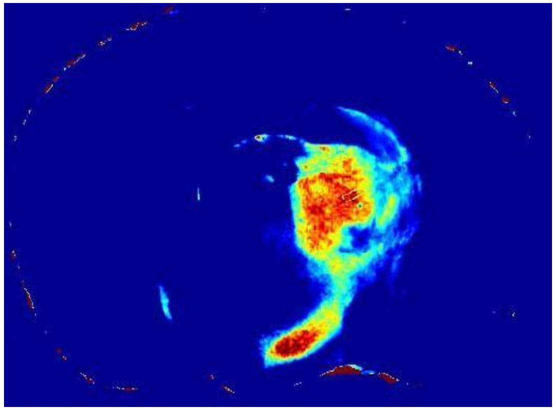






Automated Lesion Detection (1)

- **Register subject slice to corresponding atlas slice.**
  - Registration process (linear and deformable) between a subject slice and its corresponding atlas slice.
  - Subject slice and reference slice (atlas slice) co-registered at TTC Atlas space i.e. **data can be comparable**.
  - **Z-score image calculation**
    - A value at this probability map indicates deviation from the reference slice value i.e deviation from normality.
  - **Decide lesion hemisphere.**
    - Choose a **threshold** to distinguish normal from abnormal points.
    - Detect **midline** and choose lesion hemisphere based on abnormal points.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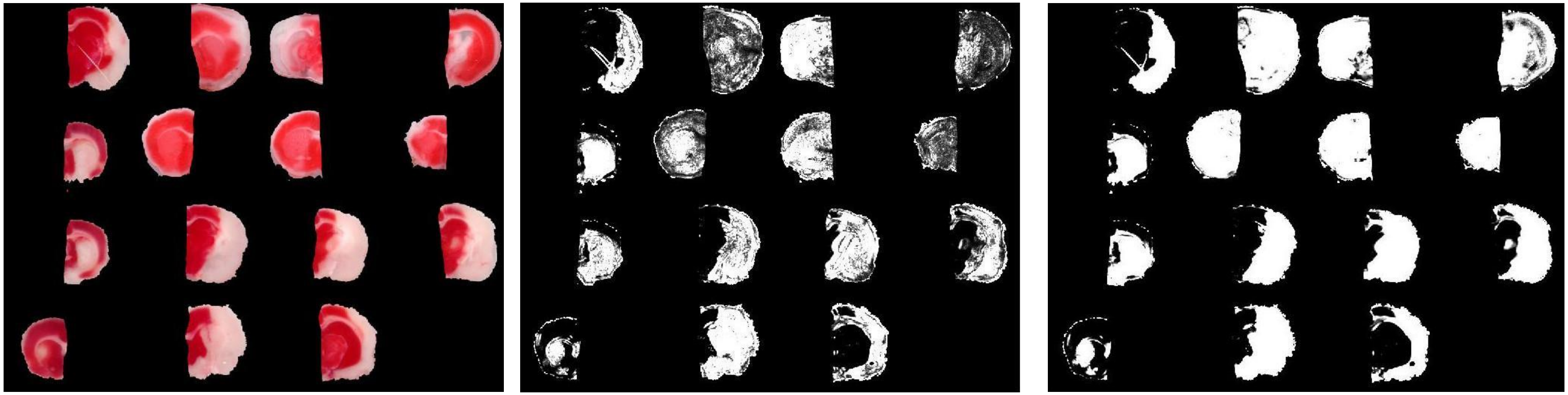
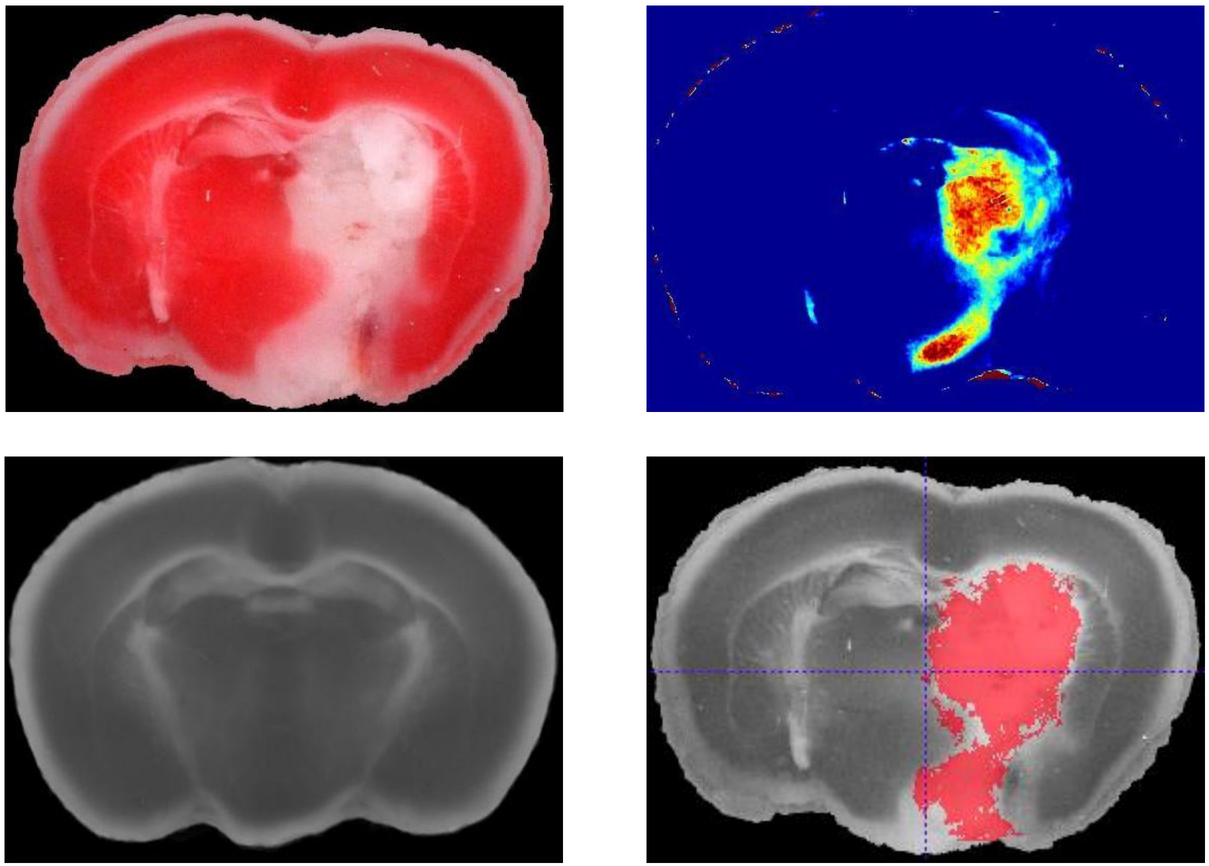
Automated Lesion Detection (2)

- **Train a machine learning model to predict lesion points on subject slices.**
  - **Random Forest model**.
  - Train the model using 5 stroke slices (lack of data for a deep learning approach)..
  - Expert annotation masks.
  - **13 features were used for this model.**
    - Features based on intensity values, z-score features, **hemisphere difference based features** etc.



Automated Lesion Detection (3)

- **Use ML model to predict final lesion values.**
  - Final lesion prediction (lesion mask).



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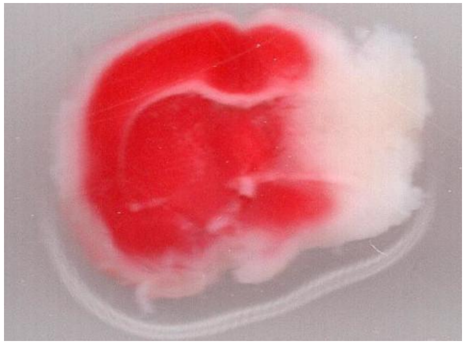
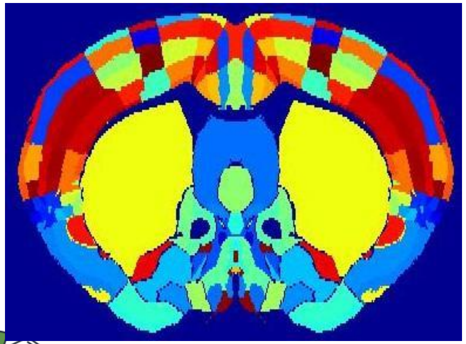
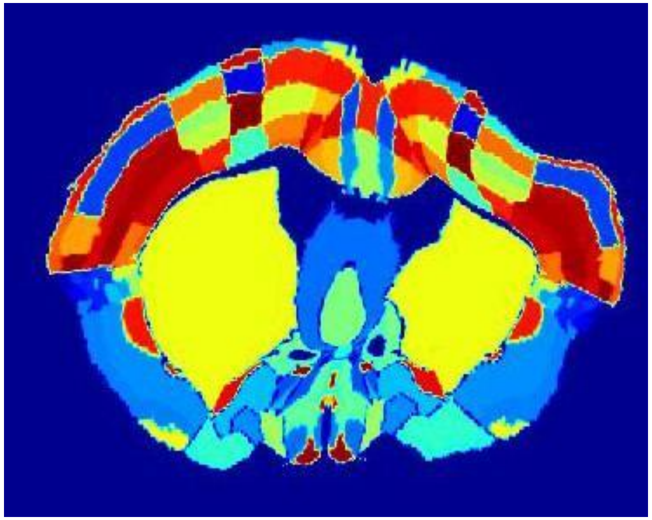
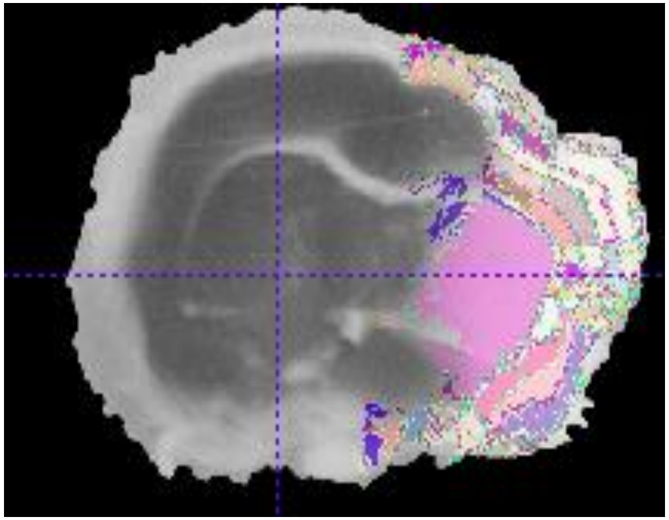
Automated Lesion Detection (4)

- **Project masks at subject space.**
  - Inverse transformations and apply to each mask.
    - Obtain mask at subject space (native space).
  - Overlay masks to subject slice. **Access accuracy**.
  - Compute Area of each mask.
    - Area = number_of_pixels * pixel_area.
  - Extract affected anatomical regions & percentage of coverage.









Damigos, Gerasimos, et al. "**Machine learning based analysis of stroke lesions on mouse tissue sections.**" *Journal of Cerebral Blood Flow & Metabolism* (2022): 0271678X221083387.

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Thank you for your time!!

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