

## Quantification and Analysis of Large Multimodal Clinical Image Studies: Application to Stroke



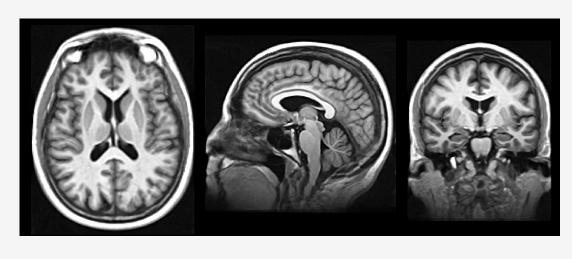
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#### Motivation

Clinical vs research quality imaging datasets

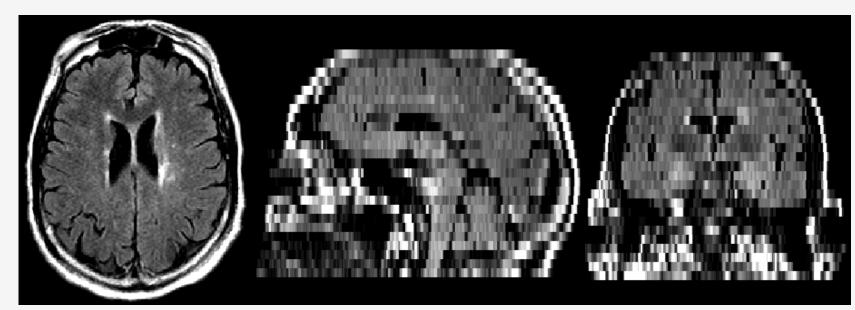
- Resolution, contrast, field of view
- Potential for analysis: many subjects, sites



Research scan (T1 MPRAGE)

#### Stroke dataset

- 1089 patients
  - 3000 more from international consortium
- Different sites, scanners, protocols
- T1, T2-FLAIR, DWI
- 5-7mm slice thickness, axial/sagittal acquisition
- Clinical indicator: vascular degeneration (WMH)



Stroke patient scan: T2-FLAIR, axial acquisition

#### Goal: Meaningful modeling and analysis of clinical image datasets

- Registration: align subjects for spatial analysis
- Segmentation: automatic WMH detection
- These enable population analysis of WMH growth in our cohort
- Tools for these steps exist, but must be tailored for clinical data

#### Registration

Want to align all modalities, all subjects into common space

- Rigid registration for within-subject multimodal registration
- *Nonrigid* registration for subject  $\longleftrightarrow$  atlas registration

#### Key insights that we apply

- Choice of metric is critical
  - If intensities match, correlation (CC) outperforms mutual information (MI) and SSD
  - If intensities differ, use MI, even within same modality
- Brain masking is critical, even if skull stripping fails

#### Initialize with rigid registration

• Use MI to compare images: variable acquisition  $\rightarrow$  intensities don't match

#### **Brain masking**

- Skull stripping algorithms remove too much/too little
- Use rigid registration to get rough brain mask from atlas



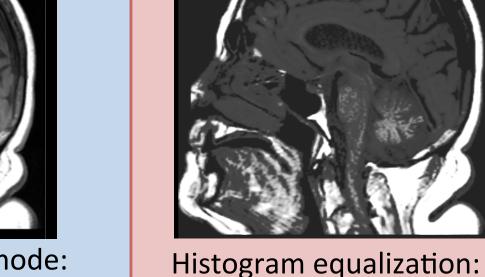


Skull strip from BET

#### **Intensity correction**

- Can't use histogram equalization: different histogram shapes
- Match mode of white matter intensity within mask: uniform global scaling

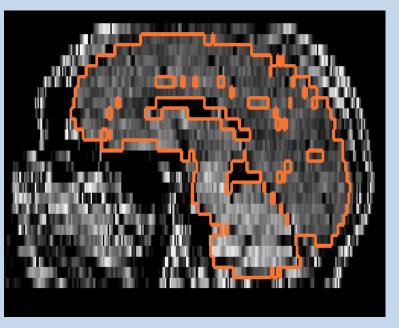




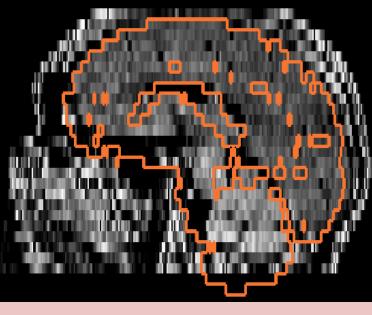
Matched intensity mode: maintains contrast

### Final nonrigid registration Compute metric on brain mask voxels only

- Use intensity-corrected image
- Use CC as metric



Segmentation overlay: Our pipeline



low brain contrast

Segmentation overlay: Simple registration

#### Registration quality

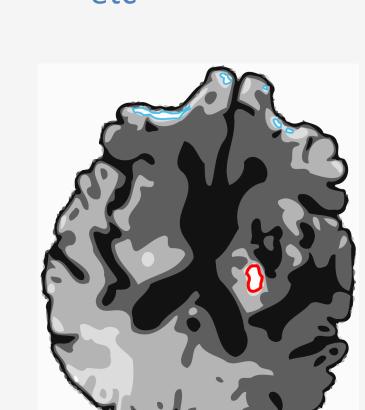
- Construct image of voxelwise median intensity in atlas space
- Remove outliers (distance to median)
  - Tukey fence threshold:
    3<sup>rd</sup> quartile + 1.5 x (interquartile range)

# 

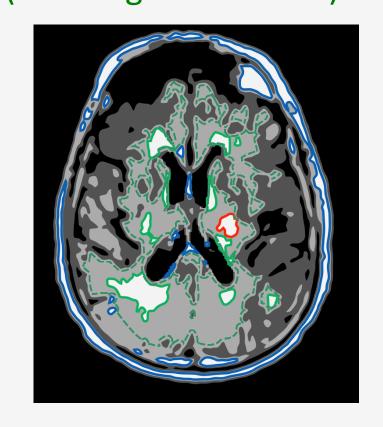
#### Segmentation

- White matter hyperintensity
  - Bright on FLAIR
  - Use expert-defined mask to constrain to relevant white matter regions
- Stroke tissue
- Bright on FLAIR and DWI

- DWI
- All bright regions outlined
- Red: Stroke
- Blue: irrelevant regions, artifacts, etc



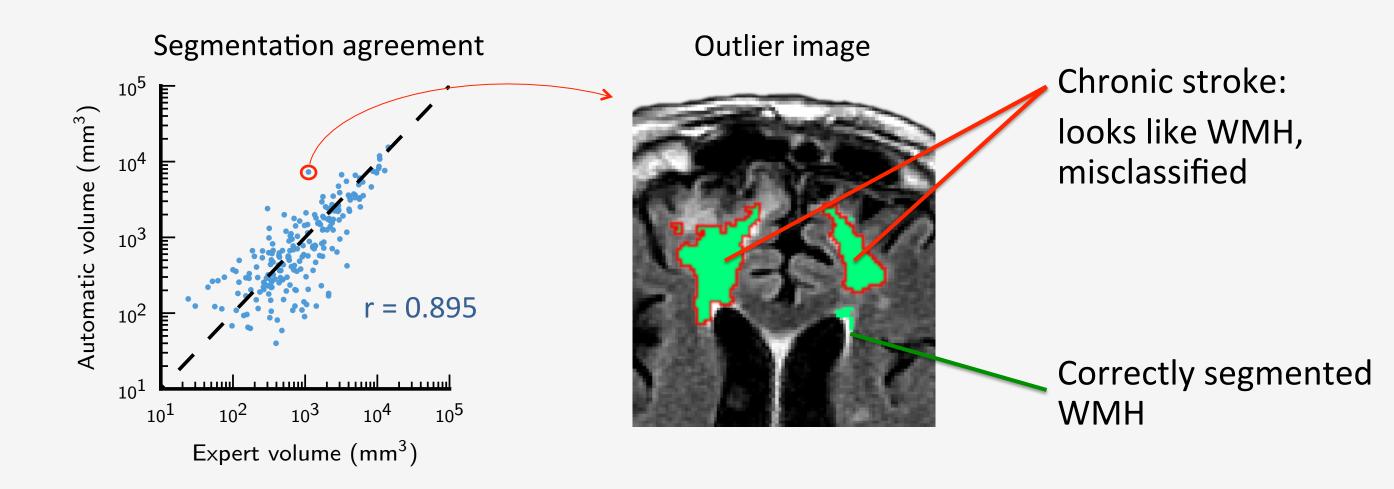
- T2-FLAIR
  - All bright regions outlined
  - Green: WMH
  - Red: Stroke
  - Blue: irrelevant regions, artifacts, etc
- Use expert-defined mask (dotted green outline)



- Automatic segmentation
  - Propagate expert-defined mask using registrations
  - Remove acute stroke from analysis using DWI
  - Predict label L (normal or pathology) from intensity I using MAP classification:

$$L = \arg\max_{L} p(L|I) = \arg\max_{L} p(I|L)p(I)$$

• Learn p(I|L) from 10 manually segmented patient images



#### Analysis

- Goal: understand WMH change with age
  - Overall volume change
- Change in spatial distribution
- Technique: regression mixture modeling
- Assume two clusters of patients
- Each has a different growth pattern of WMH volume as a function of time
- Use hard-assignment EM to jointly estimate cluster labels and regression coefficients
- Nadaraya-Watson kernel regression within each cluster

