High throughput lesion evaluation and quality control for incorporating quantitative imaging metrics into clinical practice

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DISCLOSURES

K.L. and A.K. are employees of **Octave Bioscience**, Inc.

M.I.'s contribution to this study was as a paid consultant, and was not part of his Stanford University duties or responsibilities.

Dr. Kinkel is a scientific consult and/or educational speaker for Alexion, Bristol Myers Squibb, Biogen, Sanofi/Genzyme and Roche/Genentech

GOAL

MRI quantitative lesion metrics in the clinic

- MS lesion counts and volumes are poised to be **salient clinical biomarkers of disease progression**
- Why don't we have widespread adoption?

Lesion Volume
Lesion Counts
Whole Brain
Atrophy
Spinal cord area
etc...

Roadblock to clinical use: Quality Control bottleneck

- Automated segmentation methods have error rate
  - Algorithmic variability
  - Image quality variability
  - Low expert agreement
- Visual quality control (QC) is required before a clinical decision can be made.
- **Visual QC is fundamentally *time consuming***
  - Especially if segmentation errors need to be edited

OBJECTIVE

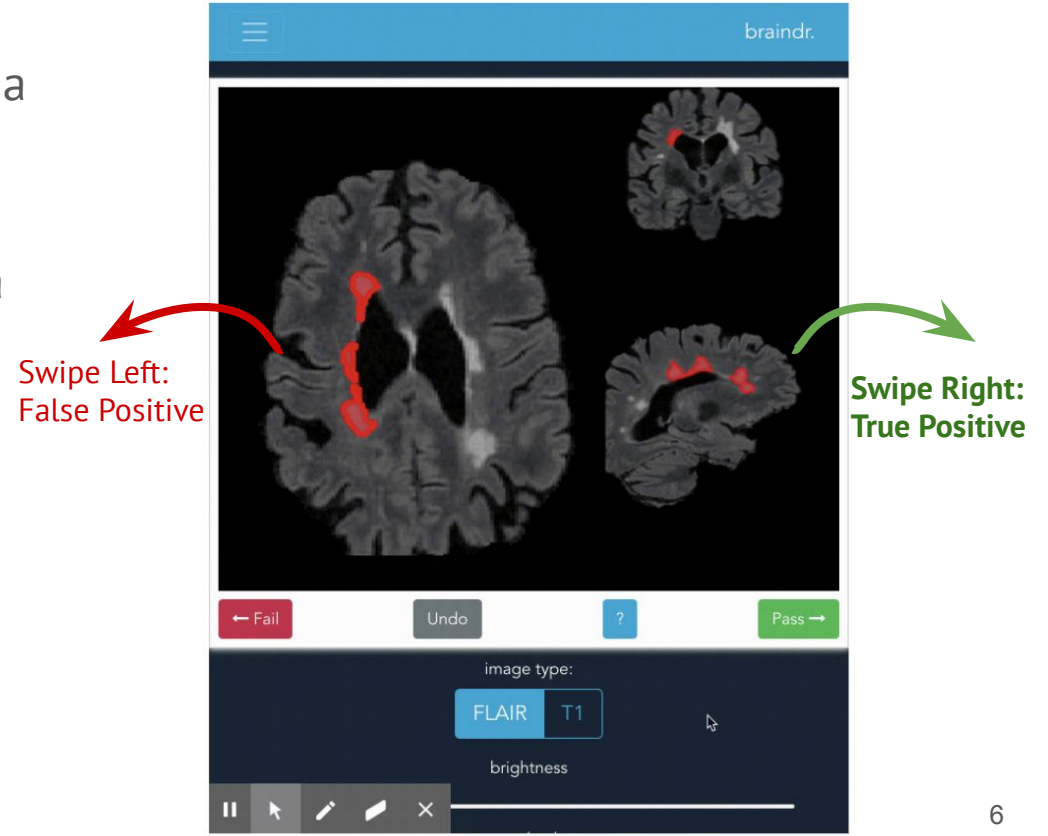
Time efficient QC and training

- Use an efficient web interface[1] to quickly:
    a. Evaluate experts and non-experts to understand and resolve disagreements
    b. QC the output of automated lesion segmentation methods.
- Evaluate feasibility
    a. number of lesions QC'd
    b. intra-rater reliability
    c. inter-rater reliability
    d. the types of lesions that are disagreed upon

[1] Keshavan A et al. *Frontiers in Neuroinformatics*, 2019

Braindr: App to quickly rate lesions

- Potential lesions (PLs) screened via binary “swipe” on app (right=pass, left=fail)
- 2D Triplanar view with lesion area blinking red → **quick decision making**
- Compatible with smartphones, tablets, and desktop
- Toggle between T2 FLAIR and T1 images
- Adjust brightness/contrast



Generate high volume of potential lesions to rate

- 3D T1 and T2 FLAIR images from 32 subjects were registered, N4 bias field corrected, and z-scored.
- Thresholded subtraction images (Z_FLAIR-Z_T1) at varying levels.
- Generated a triplanar image of each resulting segmentation (called a potential lesion, PL), resulting in over **80,000** individual PL's needing QC, which simulates a **high-throughput scenario with a high error rate**.
- Measured variability between and within raters by calculating the Intraclass correlation coefficients (ICC).

>14K images rated; reliable consensus

- Feasibility: **14,973** PLs were labelled by 5 raters.
- Inter-rater reliability for an average rating **ICC(2,k) = 0.92**, and individual ICC(2,1) = 0.74.
- Disagreements occurred more frequently on PL's in the **brainstem, cerebellum, hippocampus, and basal ganglia**.

Rater	ICC(1,1)
Neuroradiologist (MI)	0.97
Beginner (MB)	0.90
Tech 1 (AK)	0.87
Tech 2 (KL)	0.85
Neurologist (BD)	0.84

Intrarater Reliabilities

Feasible for high volume patient load in clinic

- We simultaneously evaluated raters, and QC'd lesions from an automated method using a quick, scalable, web application. This enables us to
  - 1) improve expert agreement on lesion identification
  - 2) develop better quality education materials for experts and non-experts alike
  - 3) train new raters quickly
  - 4) **ensure the quality of the measurements at scale**.

NEXT STEPS

Machine learning to triage lesion segmentation QC

- In a high-throughput scenario, we need a **triage system for segmentation QC**
- With the training dataset we've generated here, we can:
  - **Predict** which image segmentations will need more editing by raters
  - **Prioritize** the rating of potential lesions based on classification uncertainty to train models more quickly (Active Learning)
  - **Decide** which potential lesions should go to which raters (e.g. lesions in regions that are difficult to assess should go to more experienced raters)

Questions?

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