Intracranial hemorrhage localization: A CT imaging pipeline

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Introduction: Intracranial Hemorrhage affects are elderly

Intracerebral hemorrhage (ICH) is a form of stroke where a blood vessel ruptures in the brain.
In 2009, 66% of people hospitalized for stroke were ≥ 65 [5]. For every 10 years over 55 years of age, the risk of stroke doubles [7, 2]. For adults over age 65, the risk of dying from stroke is estimated to be 3 to 7 times that of the population [4, 3].

Goals and Demographics

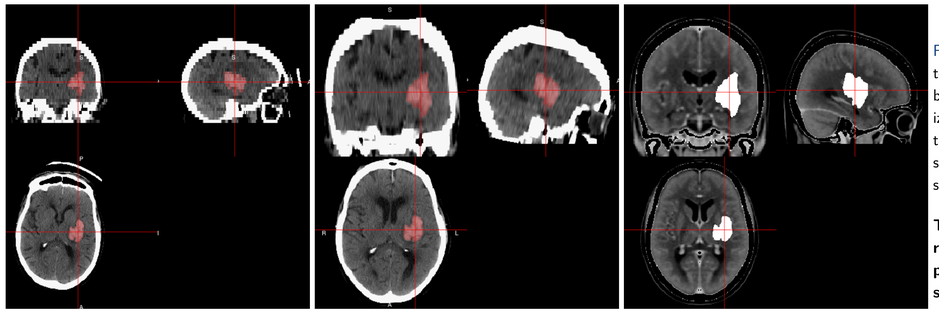
- Register patient CT scans to a common CT template
- Create a 3D density map of where ICH occurring in a population of patients
- Determine if differences in ICH location relate to the NIHSS score (voxel-wise)
- Generate a stroke region of interest (ROI) and associate it with health effects (NIHSS score)

This analysis included 111 patients from the MISTIE (N = 94) and ICES (N = 17) trials. In these trials, patients were randomized to standard of care medical management or an intervention. Patients were required to have a pre-randomization scan with ICH segmentations.

Variable (N = 111)	N (%) or Mean (SD)
Age in Years: Mean (SD)	60.8 (11.2)
NIHSS Score: Mean (SD)	22.1 (8.7)
Reader-Classified ICH Location	
Putamen	68 (61.3%)
Lobar	33 (29.7%)
Globus Palidus	6 (5.4%)
Thalamus	4 (3.6%)

Table 1: Descriptive statistics of the demographic information on the patients.

Image Processing



(a) **Original image** in native space (b) **Registered image** with ICH mask highlighted in pink. (c) **Template brain** with ICH mask overlaid.

Figure 1: Patient brains were registered to the template using the Clinical toolbox [6], using SPM8's unified normalizationsegmentation [1]. After registration, patient images are in the same space; information can be summarized spatially across patients.

Take Home Message: We can register people's brains to a template brain to compare across subjects.

Voxel-wise Regression on NIHSS Score

We did voxel-wise linear regressions on the NIHSS score for voxels that had > 10 patients with ICH at that location:

$$\text{NIHSS}_i = \beta_0 + \beta_1(v)\text{ICH}_i(v) + \varepsilon_{iv}, \quad \varepsilon_{iv} \sim N\left(0, \sigma_v^2\right) \tag{1}$$

where i is patient, v is voxel, and ε_{iv} are homoscedastic normal errors.

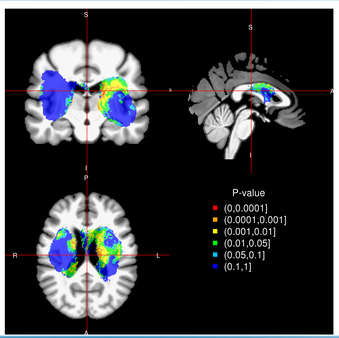


Figure 2: Voxels with the smallest p-values seem to be near the ventricles. No voxel survived a Bonferroni correction.
Take Home Message: We can do voxel-wise analyses with CT on scalar functional scores.

References

[1] John Ashburner and Karl J. Friston. "Unified segmentation". In: *NeuroImage* 26.3 (July 1, 2005), pp. 839–851.
[2] Robert D. Jr Brown et al. "Stroke Incidence, Prevalence, and Survival: Secular Trends in Rochester, Minnesota, Through 1989". In: *Stroke March 1996* 27.3 (1996), pp. 373–380.
[3] Antonio Di Carlo et al. "Stroke in an elderly population: incidence and impact on survival and daily function". In: *Cerebrovascular Diseases* 16.2 (2003), 141150.
[4] Edward Feldmann. *Intracerebral hemorrhage*. Futura Publishing Company, 1994.
[5] Margaret Jean Hall, Shaleah Levant, and Carol J. DeFrances. "Hospitalization for stroke in US hospitals, 19892009". In: *Diabetes* 18.23 (2012), p. 23.
[6] Christopher Rorden et al. "Age-specific CT and MRI templates for spatial normalization". In: *NeuroImage* 61.4 (July 16, 2012), pp. 957–965.
[7] Philip A. Wolf et al. "Secular trends in stroke incidence and mortality. The Framingham Study." In: *Stroke* 23.11 (1992), 15511555.

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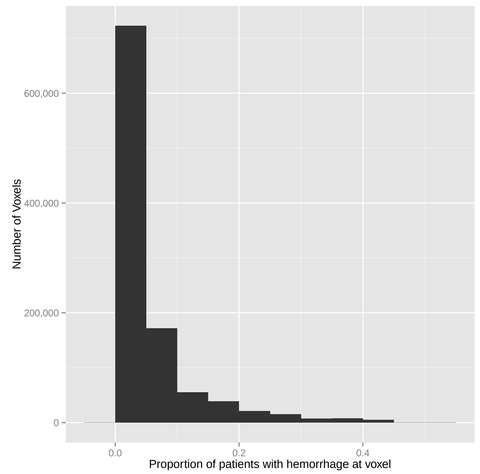
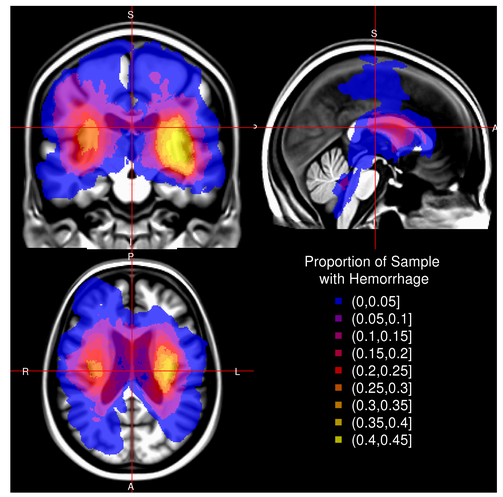
Creating a 3D Histogram of ICH Prevalence



(a) **Distribution** of proportion of patients with hemorrhage. All voxels with 0 proportion are excluded.



(b) **Template brain (MRI T1)** with proportion of hemorrhage overlaid

Figure 3: Most voxels have a low prevalence (median: 3%), but some voxels ($V = 5685$) have prevalence $> 40\%$. In the spatial map, hotter colors (yellow) indicate more people had ICH at this location. Most ICH occurs in the middle of the brain, predominantly on the left. **Take Home Message: We can create population-level metrics/maps of ICH in this framework.**

Region of Interest Analysis

We thresholded the p-values from model (1) at 0.01 (Figure 2) and created a ROI. We used other thresholds, and the results were similar as below, but this threshold performed best.

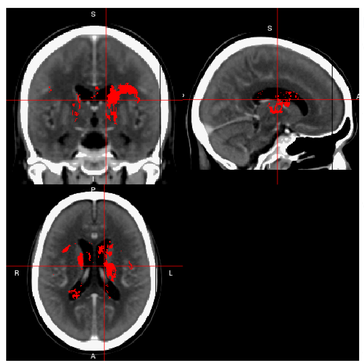


Figure 4: The areas colored in red correspond to voxels with a p-value < 0.01 in the unadjusted model. Of the voxels selected, we calculated a scan-level ROI coverage:

$$\text{Coverage} = \frac{\#\text{ Voxels classified ICH in ROI}}{\#\text{ Voxels in ROI}}$$

This coverage is then put into the following patient-level model:

$$\text{NIHSS}_i = \beta_0 + \beta_1 \text{Coverage}_i + \beta_2 \text{Age}_i + \beta_3 \text{Sex}_i + \beta_2 \text{Total ICH Volume}_i + \varepsilon_i, \quad \varepsilon_i \sim N\left(0, \sigma^2\right) \tag{4}$$

$$\text{NIHSS}_i = \beta_0 + \beta_{1j} \text{Location}_{ij} + \beta_2 \text{Age}_i + \beta_3 \text{Sex}_i + \beta_2 \text{Total ICH Volume}_i + \varepsilon_i, \quad \varepsilon_i \sim N\left(0, \sigma^2\right) \tag{5}$$

where Location_{ij} is an indicator that the ICH for patient i was classified as location j, i.e. putamen or caudate.

Model	P-value	Adjusted R^2	R^2	AIC	RMSE
Reader-Assessed ICH Location		0.129	0.178	18.60	8.116
ROI Coverage	0.0100	0.254	0.282	0.00	7.511

Table 3: Table of model-fit measures for NIHSS score model: reader-based location vs. CT voxel-based ROI coverage.

Take Home Message: CT-level location information may be a better predictor than reader-assessed.

Conclusions

- Registration to a template allows for summaries of population of patients with ICH previously not available, with potentially more information.
- We can also do similar voxel-wise analyses as seen in the MRI literature with CT imaging.
- CT-scan-level information of location better predicts NIHSS score better than reader-assessed categorization.

Limitations

We acknowledge the coverage has information about the outcome by the way the ROI was created. This analysis is more exploratory and proof of concept than inferential. We plan to do cross-validation as well as test the ROI performance in an independent set of individuals. The population has exclusion criteria which may limit generalizability and are from a clinical trial population.