Virtual High Energy Monochromatic (190keV) CT ASPECTS Predicts Malignant Cerebral Edema after Large Hemispheric Infarction

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Introduction

- Imaging biomarkers of malignant cerebral edema (MCE) after large hemispheric infarct (LHI) are understudied.
- We hypothesize that acute virtual high-energy monochromatic (190keV) CT imaging (VMI) enables earlier detection of secondary injury from MCE.

Methods

Figure 1.

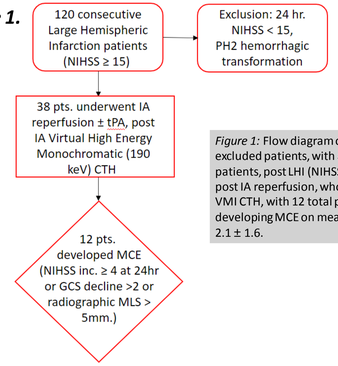

Figure 1: Flow diagram of included and excluded patients, with a total of 38 patients, post LHI (NIHSS ≥ 15), status post IA reperfusion, who underwent a VMI CTH, with 12 total patients developing MCE on mean post stroke day 2.1 ± 1.6.

Design:

- Retrospective, pilot study of novel VMI variables
  - *VMI Alberta Stroke Program Early CT Score (ASPECTS)*
  - *CT-HARM (hyperacute reperfusion markers)*
    - Iodine density (ID) of coinciding ASPECTS locations
    - Triplane average maximum ID
- Fisher's exact test and Wilcoxon Rank Sum test were used for univariate analysis, and outcomes were analyzed by logistic regression model.

Definitions:

- Malignant cerebral edema (MCE):
  - Early neurological decline (END): increase in NIHSS ≥ 4 in 1st 24 hrs. or GCS decline > 2 in first 48 hours, not related to fever, sedation, or seizure or
  - Radiographic evidence of herniation (midline shift > 5mm).

Outcomes:

- Primary outcome was MCE.
- Secondary outcomes included hemorrhagic transformation, need for decompressive craniectomy (DC), and increased intracranial pressure (ICP) treatment.

Results

Table 1: Baseline Characteristics

Characteristic	All Patients (n = 38)
Women (%)	17 (44.7)
Age, years	66.8 ± 15.3
Race (SD)	
White	15 (39.5)
African American	23 (60.5)
Past Medical History (%)	
HTN	27 (71.0)
CHF	12 (31.6)
Prior Stroke/TIA	8 (21.1)
DM	11 (30.0)
CAD	9 (23.7)
Tobacco Use	18 (47.4)
Clinical Syndrome	
R MCA	15 (39.5)
L MCA	16 (42.1)
R ICA/MCA	1 (2.6)
L ICA/MCA	6 (15.8)
Admission Glucose (mg/dL)	128.5 [106.0,149.0]
Stress Glucose Ratio	1.1 ± 0.3
Admission CTH ASPECTS	9.0 [7.0,10.0]
DECT ASPECTS	4.6 ± 2.3
Delta ASPECTS (Admission ASPECTS – DECT ASPECTS)	3.9 ± 2.6
NIHSS Admission	21.5 [18,25]
NIHSS 24 hours	20.5 [16,23]
GCS Admission	9.9 ± 3.6
GCS 24 hours	9.4 ± 2.6
GCS 48 hours	9.6 ± 3.2
TPA administration	11 (36.7)
TICI Score	
0	4 (10.5)
1	0 (0)
2a	1 (2.6)
2b	11 (28.9)
2c	13 (34.2)
3	9 (23.7)
Number of passes	1.5 [1.0,2.0]
Malignant cerebral edema	12 (31.6)
Hemorrhagic transformation	14 (36.8)
ICP treatment	6 (15.8)
Early Neurological Decline (NIHSS increase ≥ 4 in 1st 24hrs.)	3 (7.9)
GCS decline > 2 in 1st 48 hours	12 (31.6)
Hemicraniectomy	4 (10.5)
Maximum Iodine density (ID)	0.81 [0.55,1.73]

Figure 2. **Index Patient**

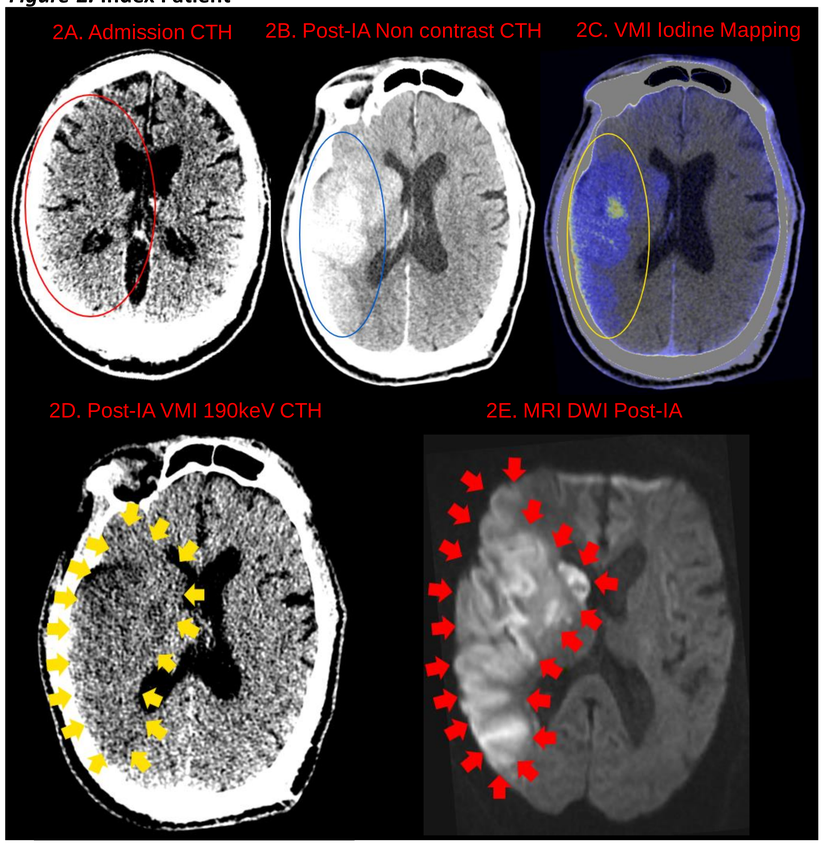

Figure 2: Index patient: 66-year-old male with initial NIHSS 19 found to have R MCA occlusion, obtained TICI 2c reperfusion, with 24hr NIHSS 19. Reperfusion obtained 6 hrs. after last known well. *Figure 2A*: Admission non-contrast CTH (Window length (WL) 30:30) ASPECTS 10. *Figure 2B*: Post-IA reperfusion, non-contrasted CTH (WL 70:30) ASPECTS 4. *Figure 2C*: VMI brain hemorrhage sequence demonstrating iodine mapping. *Figure 2D*: VMI monoenergetic 190 keV CTH (WL 30:30) *ASPECTS 2* demonstrating early infarct burden, sequence obtained 6 hours post reperfusion. *Figure 2E*: MRI DWI sequence demonstrating infarct distribution correlating with VMI 190 keV sequence early ischemic changes.

Results

Figure 3.

Multivariate Logistic Regression				
Outcome: Malignant Cerebral Edema	Regression Coefficient	Chi-Square	P-value	Odds Ratio (95% CI)
Intercept	7.9178	4.1765	0.041	-
Age	-0.0452	1.9973	0.1576	0.957 (0.898-1.018)
Sex	-0.1245	0.0161	0.899	0.833 (0.129-6.038)
NIHSS Admission	-0.1212	0.8919	0.345	0.886 (0.689-1.139)
Initial Glucose	0.0024	0.1974	0.6568	1.002 (0.992-1.013)
TPA administration	-0.1912	0.0342	0.8533	0.826 (0.109-6.267)
VMI ASPECT	**-0.8084**	**8.615**	**0.0033**	**0.446 (0.26-0.764)**

Figure 4.

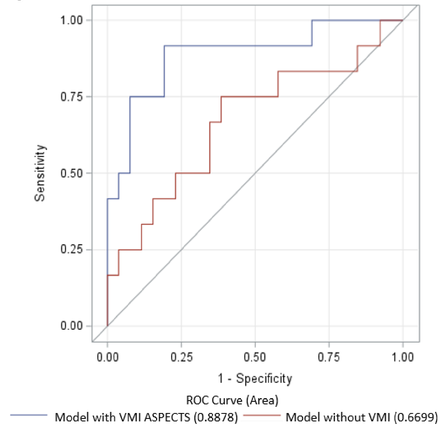

Figure 3: In a logistic regression analysis, VMI ASPECTS was a predictor of MCE (aOR, 0.45; 95% CI: [0.6, 0.76]; p = 0.0033) after adjusting for age, sex, initial NIHSS, admission glucose, and tPA, with a mean AUROC (*Figure 4*) of 0.888; 95% CI [0.7635, 1.0000] compared to 0.6699; 95 % CI [0.4698, 0.8699] without VMI ASPECTS.

Figure 5: **Siemens Healthcare (syngo.via)**

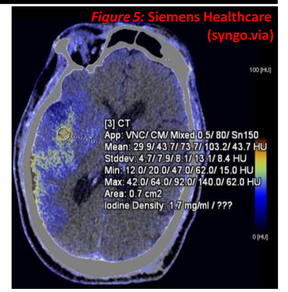

Figure 5: Siemens Healthcare modified brain hemorrhage application (syngo.via) demonstrating quantification of maximum iodinated contrast density (ID) in mg/mL averaged in 3 planes, ROI (white circle) showing max ID 1.7 mg/mL.

Figure 6: **Philips Intellispace Portal (ISP)**

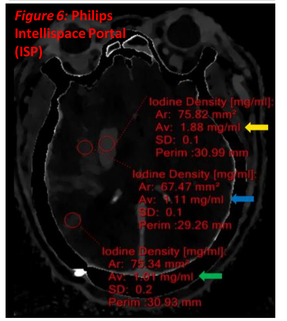

Figure 6: Philips Intellispace Portal (ISP) software demonstrating quantification of ID in individual ASPECTS locations, Ex. lentiform (1.88 mg/mL, yellow), insula (1.11 mg/mL, blue), & M3 (1.01 mg/mL, green). In a univariate analysis, ASPECTS insular, M1, M5, & M6 ID were associated with MCE, though max ID was not.

Discussion

- Acute VMI ASPECTS predicts MCE after LHI and may improve models predicting secondary brain injury after stroke.
- CT HARM/iodine extravasation may be a marker of BBB disruption and cytotoxic edema, with future investigations aimed at quantifying hemispheric total iodine content/volumetrics and total infarct volume as a predictor of MCE.