

Generalizable Automated Cerebral Microbleed Detection on SWI Using 3D Attention U-Net with External Cohort Validation

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BACKGROUND

- Cerebral microbleeds (CMBs) on susceptibility-weighted (SWI) MRI are key biomarkers linking small-vessel disease including cerebral amyloid angiopathy in Alzheimer's disease¹
- CMB burden informs risk stratification and anti-amyloid therapy eligibility because of its association with ARIA²⁻³
- Manual detection is labor-intensive with moderate inter-reader agreement and a tendency to miss small lesions⁴⁻⁶
- An automated SWI-based CMB detection pipeline was developed to address these clinical gaps

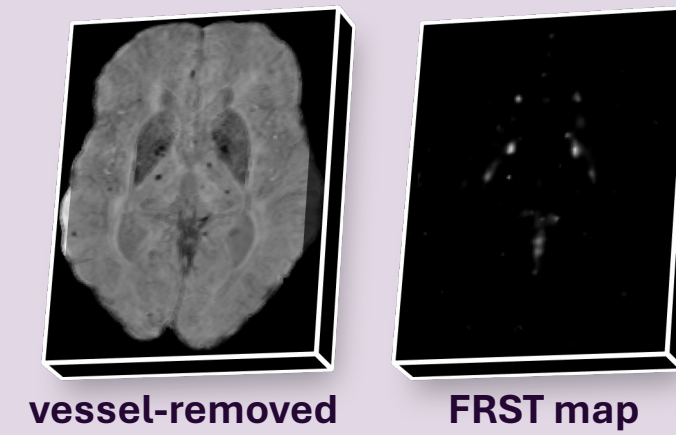
MATERIAL AND METHODS

1. Data

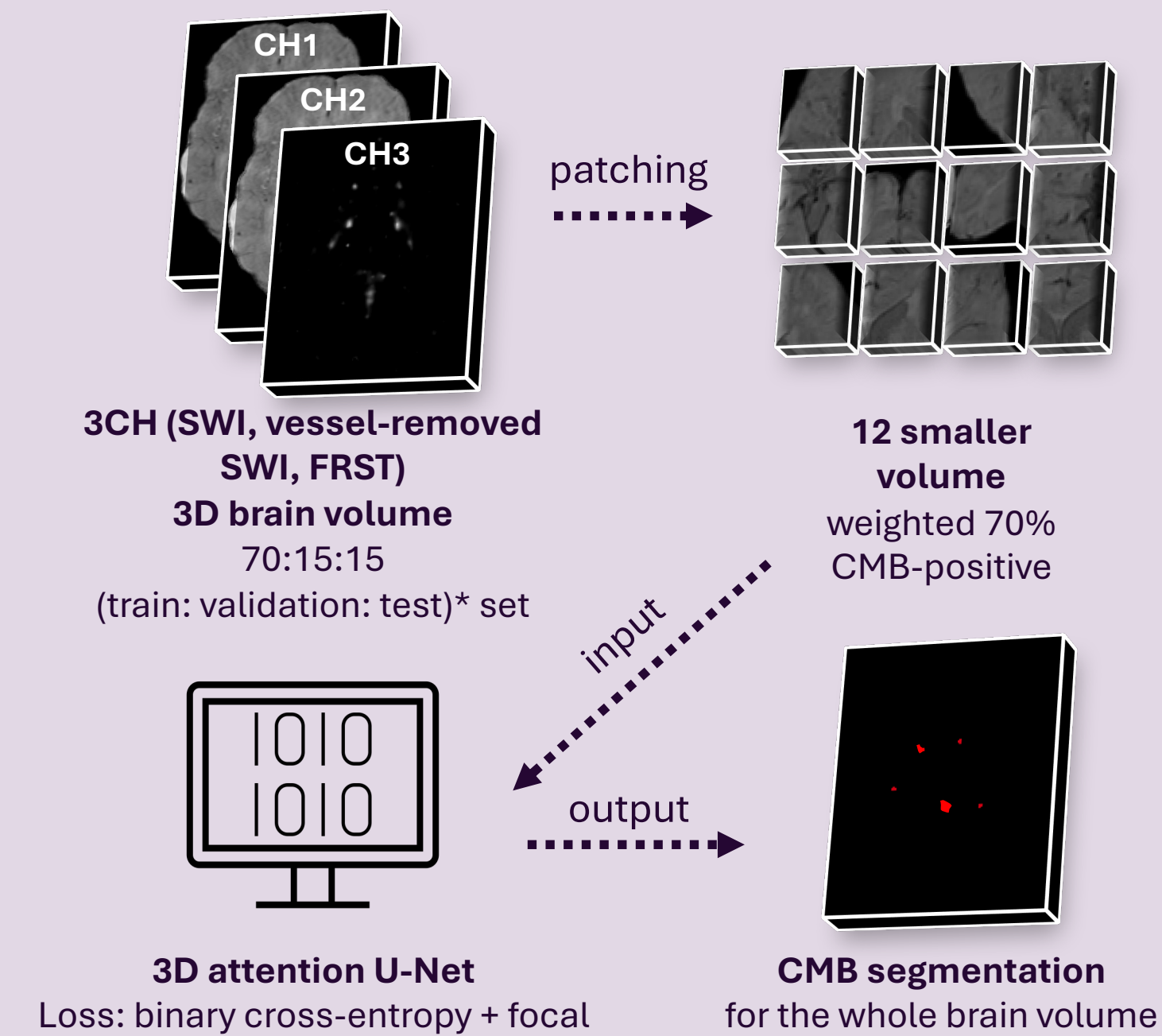
- Pooled 1,086 SWIs (41% positive-CMB) from ACTIVATION and AcT trial for training and testing. Annotated by 3 expert physicians
- Patients presenting with stroke or transient ischemic attack
- External validation set from FAVR for 191 SWIs (expert-rated CMB counts)

2. Preprocessing

- Skull stripping (FSL-BET)
- N4 bias correction
- Intensity normalization
- MNI registration
- Vessel-removed SWI (Frangi/Hessian filtering)
- FRST generation for CMB enhancement



3. Modeling



*All splits were stratified by present of CMB, number of CMB, and dataset

4. Evaluation

- Case-level** assessed how well the model classifies positive and negative cases (Sensitivity, Specificity, and MAE)
- External validation** was performed using the same case-level performance metrics as the internal evaluation. In addition, agreement in CMB burden categories (0, 1–4, 5–9, 10–19, and ≥ 20 CMBs) was assessed using Quadratic Weighted Kappa (QWK), with confusion matrices used to visualize category-wise classification performance.

RESULTS

- An internal test set total of 163 SWI (41% positive). CMBs in positive cases Median = 3 (IQR 1-7)
- An external test set total of 191 SWI (48% positive). CMBs in positive cases Median = 10 (IQR 2.5-43.5)

Table 1. The performance of the CMB detection algorithm for internal and external test set.

	%Sens (95%CI)	%Spec (95%CI)	MAE (95%CI)
Internal test set (ACTIVATION+AcT)	80.6 (69.1-89.2)	81.3 (72.0-88.5)	1.7 (1.0-2.3)
External test set (FAVR)	92.3 (85.0-96.2)	94.0 (87.5-97.2)	24.1 (11.6-36.7)

Quadratic weighted kappa (QWK) = 92.9%

External Validation Results on the FAVR Dataset

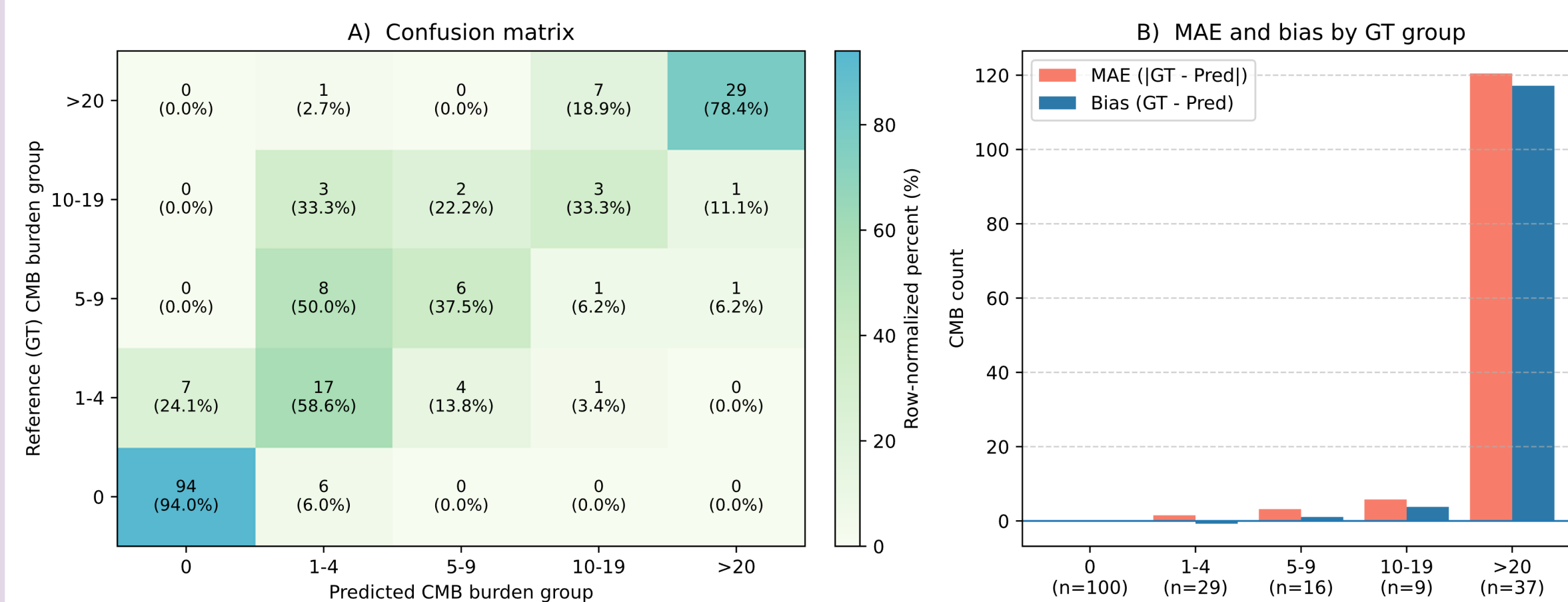


Figure 1. Performance of automated CMB detection on the external FAVR dataset. Panel A displays the ordinal confusion matrix with case counts and row-normalized percentages. Panel B illustrates group-wise mean absolute error (MAE) and bias, showing that larger errors are primarily driven by cases with very high CMB burden. GT refers to ground truth.

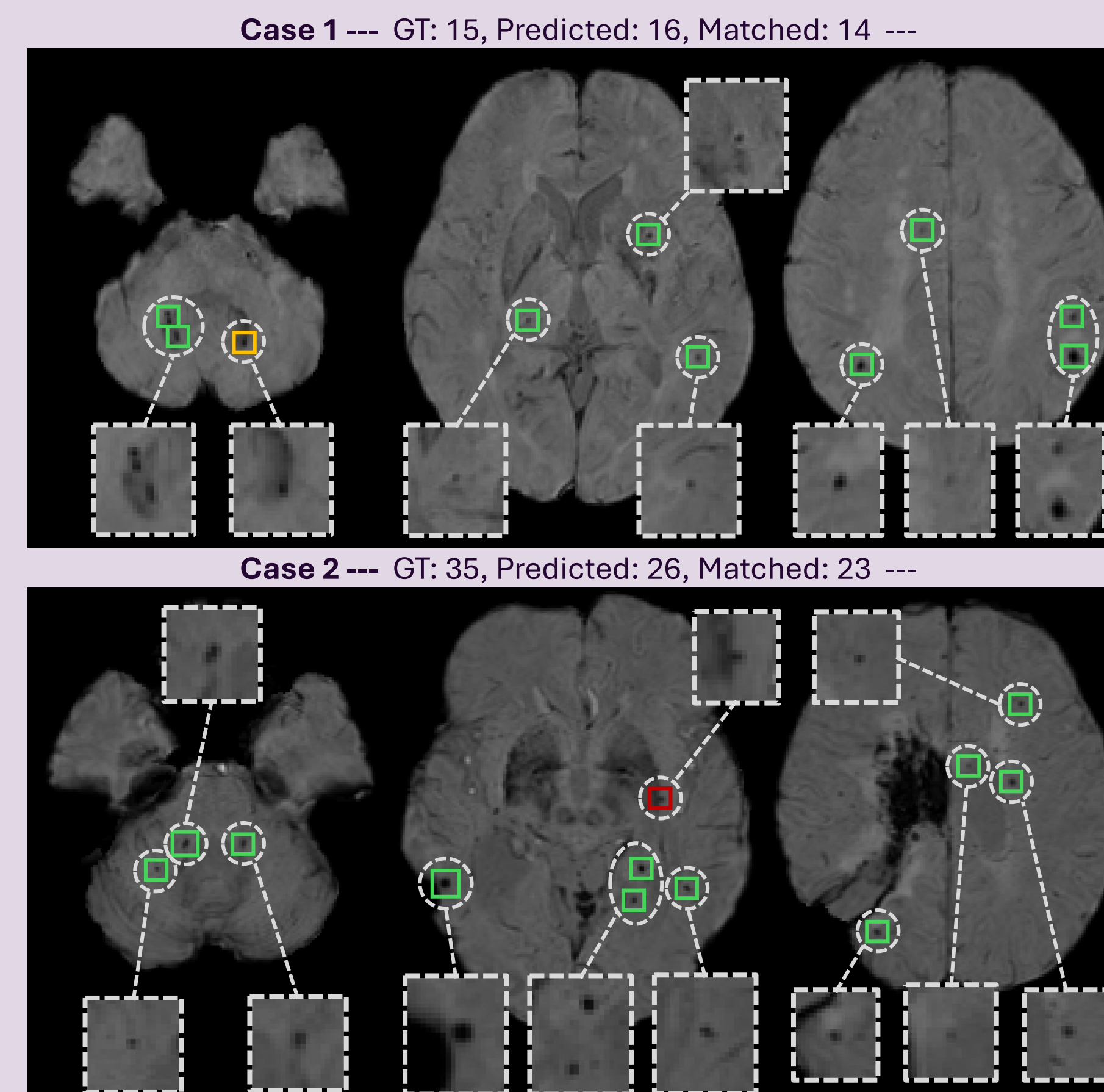


Figure 2. Representative cases with high CMB burden and false detections. Green squares indicate true positives, yellow indicates false positives, and red indicates false negatives. GT = ground truth.

DISCUSSION

- Strong generalizability across external datasets with consistently high case-level sensitivity and specificity despite differing CMB burden distributions.
- Robust ordinal burden classification (QWK=0.929), supporting reliable stratification of clinically relevant CMB severity.
- Underestimation in high-burden cases (>20 CMBs), likely reflecting a higher proportion of clustered CMB distributions in the external validation set compared with the training data.

CONCLUSION

A 3D Attention U-Net enabled robust and generalizable automated CMB detection on SWI, demonstrating strong case-level and ordinal count-level performance in external validation. This approach may facilitate scalable CMB assessment for neuroimaging research and therapy-related decision-making.

References

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