

# Detecting and classifying CMBs (Cerebral Microbleeds) using MRI

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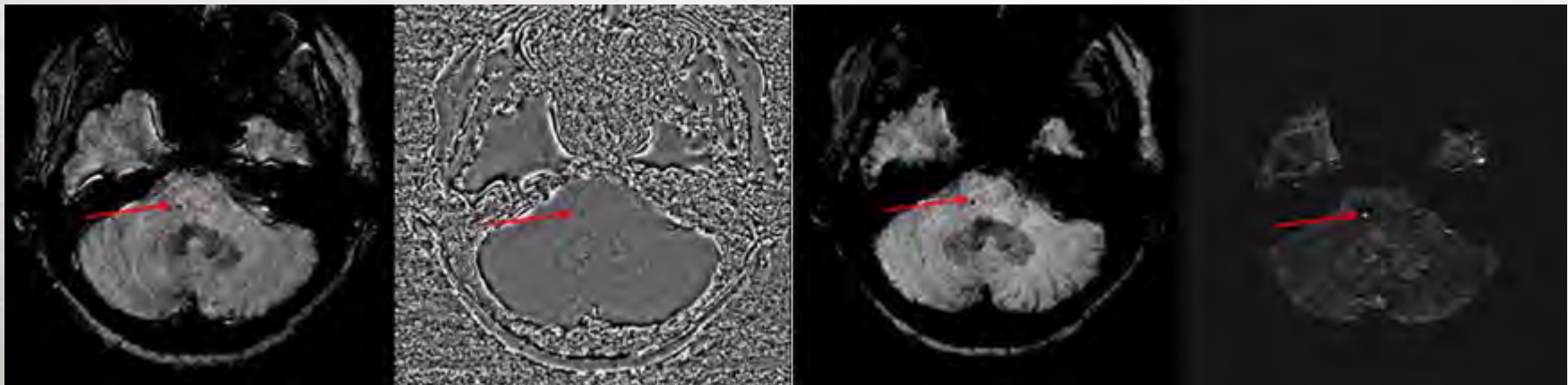
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# What are Cerebral Microbleeds?

- Chronic, focal deposits of hemosiderin.
- Appear as focal hypo-intense lesions on T2\* weighted gradient echo images
- CMBs are associated with dementia, stroke and TBI.
- CMBs are also associated with neurologically healthy elderly individuals.

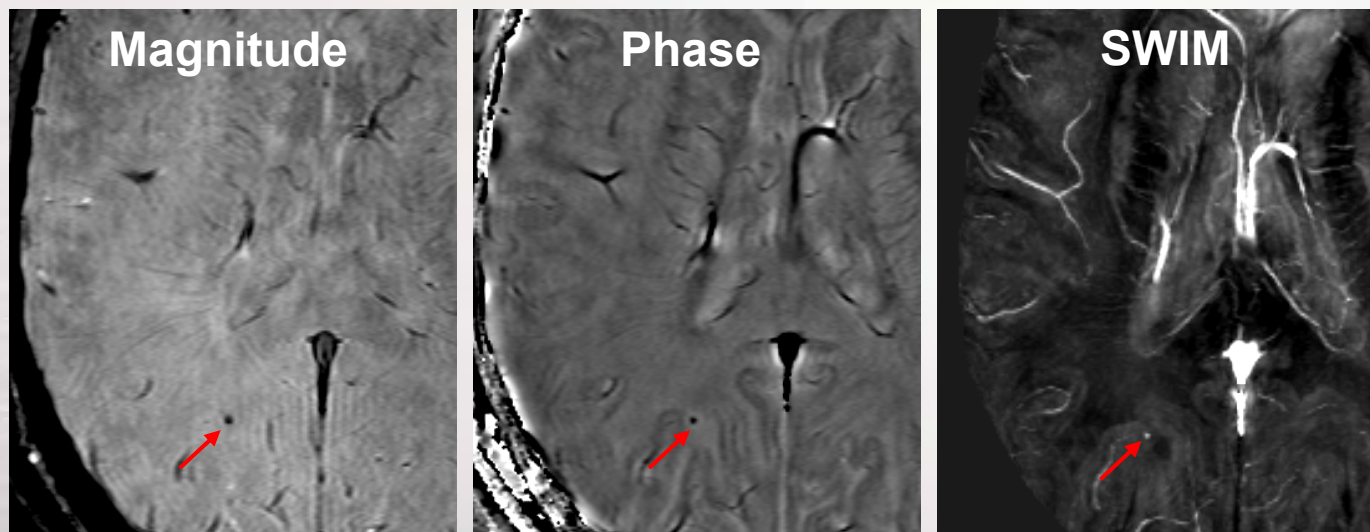


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# Detecting CMBs with MRI

- Susceptibility weighted imaging (SWI) and quantitative susceptibility mapping (SWIM) offer sensitive methods to detect CMBs.



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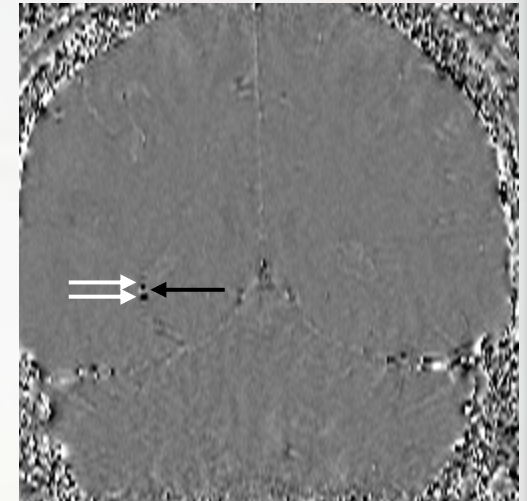
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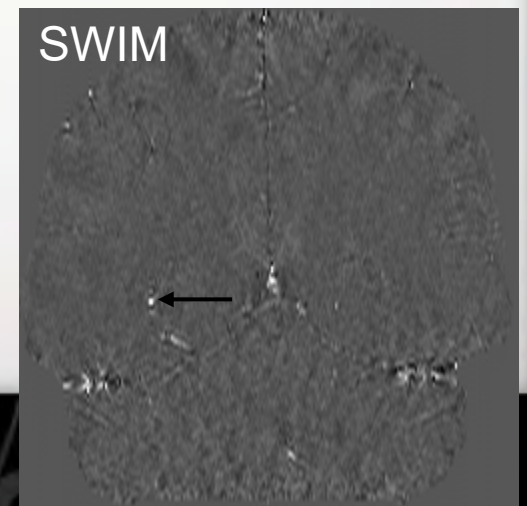
# CMB Detection Criteria

- Round or ovoid in plane and through plane.
- Black on T2\*W MRI with blooming
- Dipole effect in SWI phase
- Bright on SWIM (no remaining dipole effect)
- Isolated from veins
- Not continuous with venous structures
- At least half surrounded by brain parenchyma or CSF and not air
- Distinct from other potential mimics
- CMB diameter < 5mm (or 10 pixels)
- View the data on MIPs
- View the data from different orientations

SWI – Phase



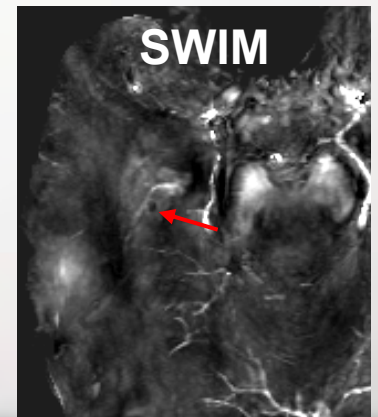
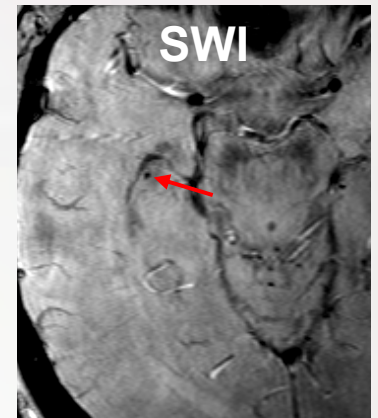
SWIM



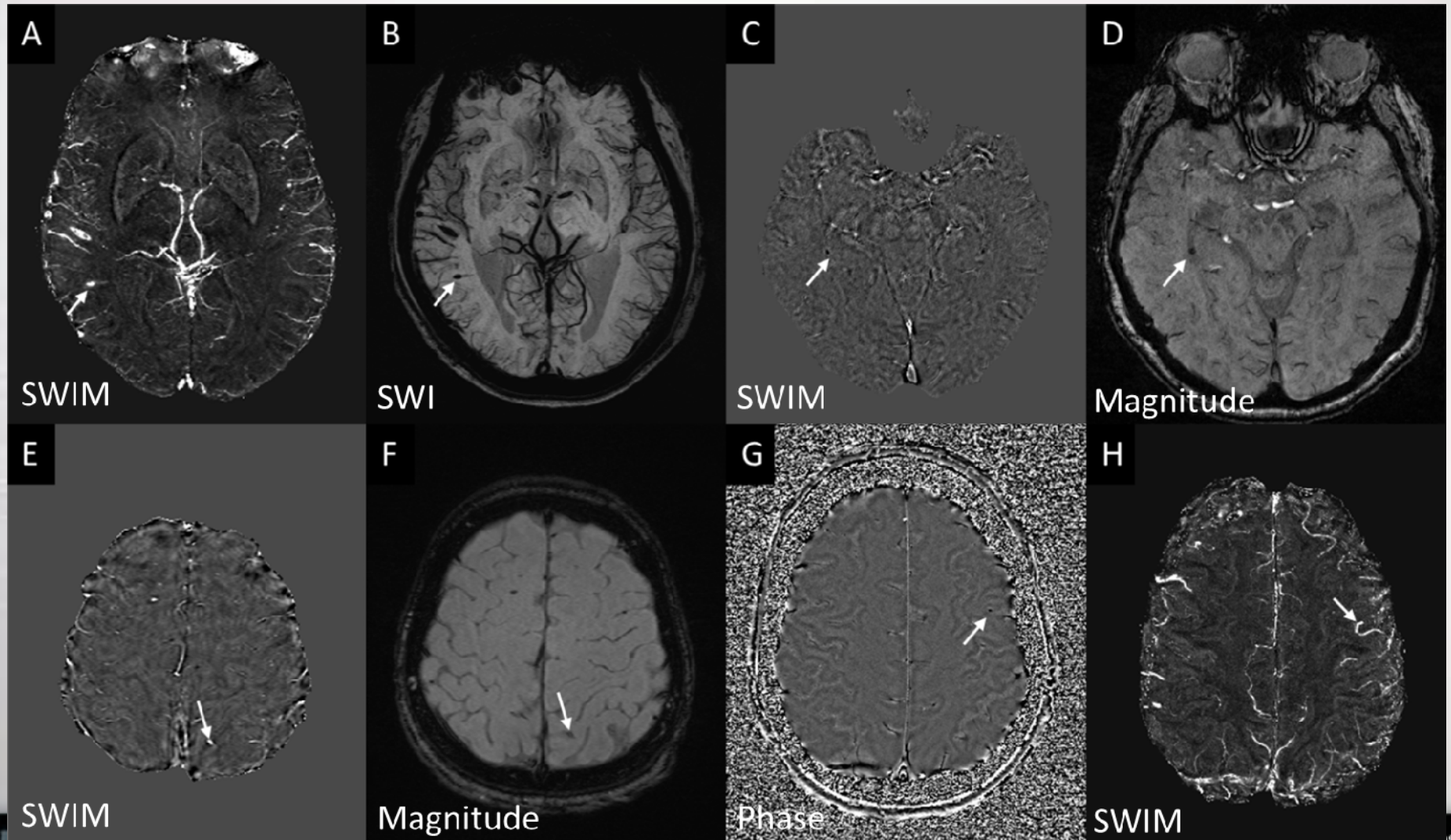
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# Calcification Mimic

- Both Calcium and Hemosiderin appear hypo-intense in SWI.
- The phase behavior of calcium shows diamagnetism while hemosiderin shows paramagnetism.
- SWIM reconstructs calcifications as negative (dark) susceptibilities while hemosiderin is positive (bright), allowing for simple discrimination.



# Mimics



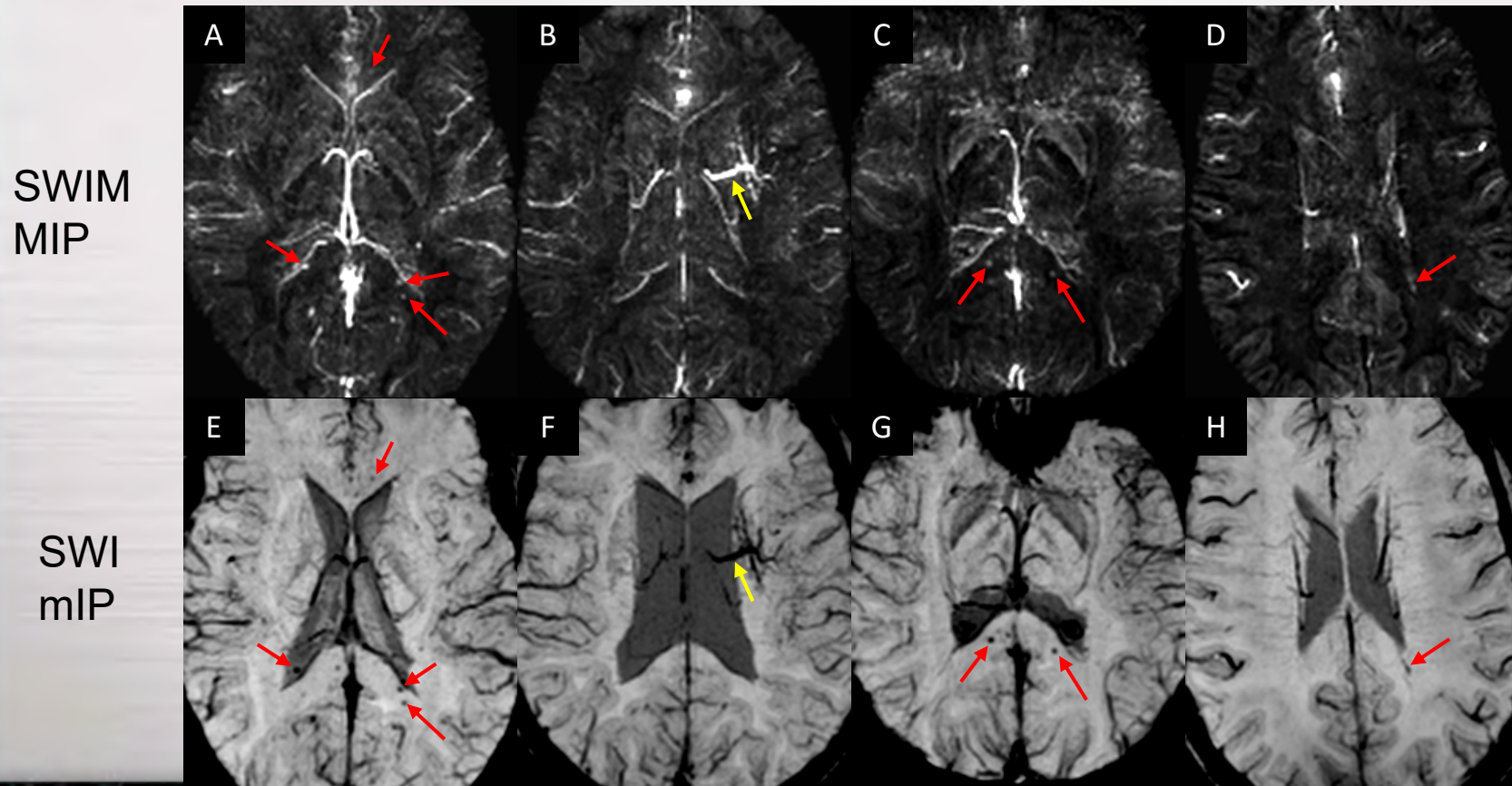
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# TBI Corpus Callosum (CC) CMBs

- Concussive mild TBI shows multiple CMBs in genu and splenium of CC (red).
- Venous anomaly with high susceptibility is shown (yellow).

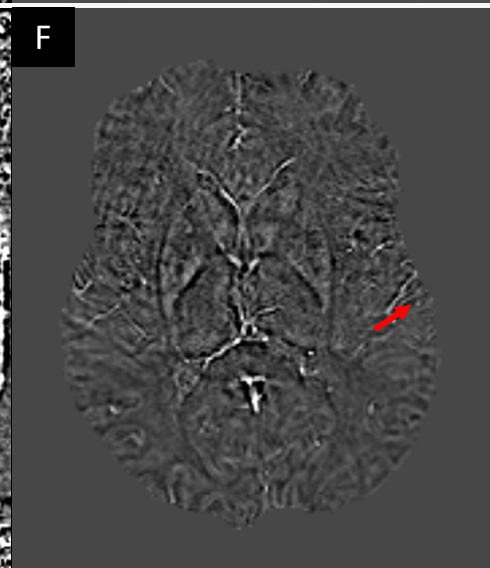
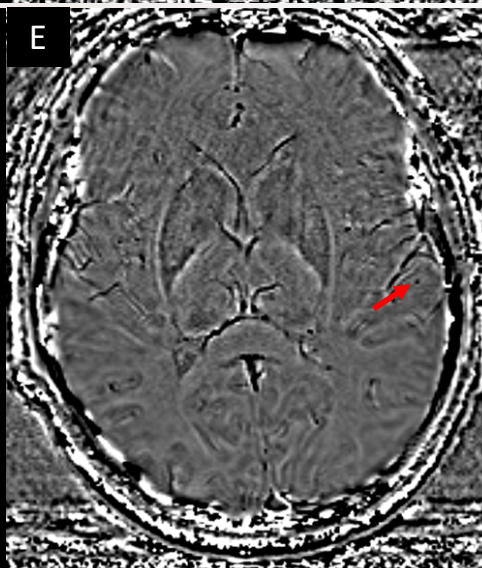
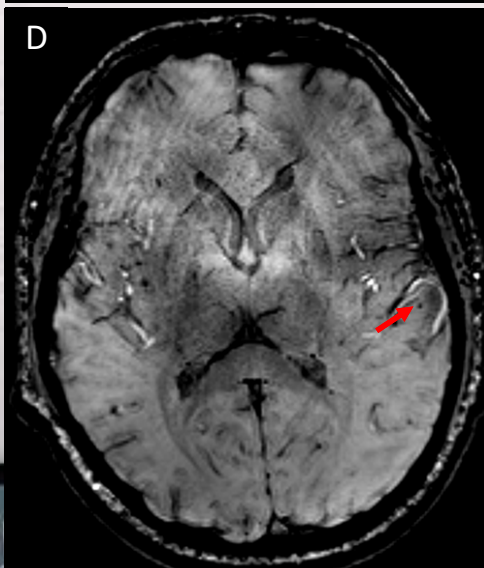
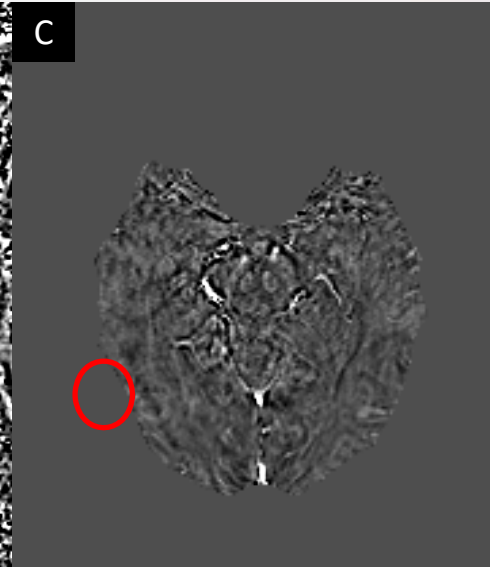
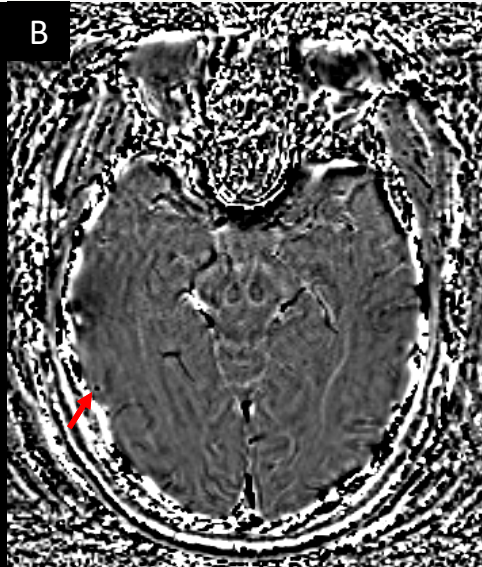
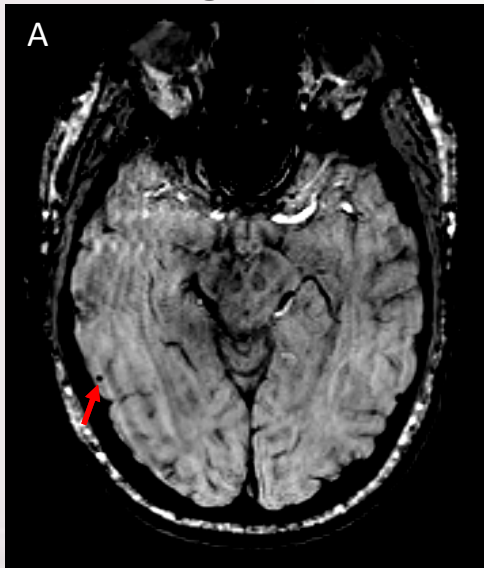


# CMBs Near The Edge of Brain

Magnitude

Phase

SWIM



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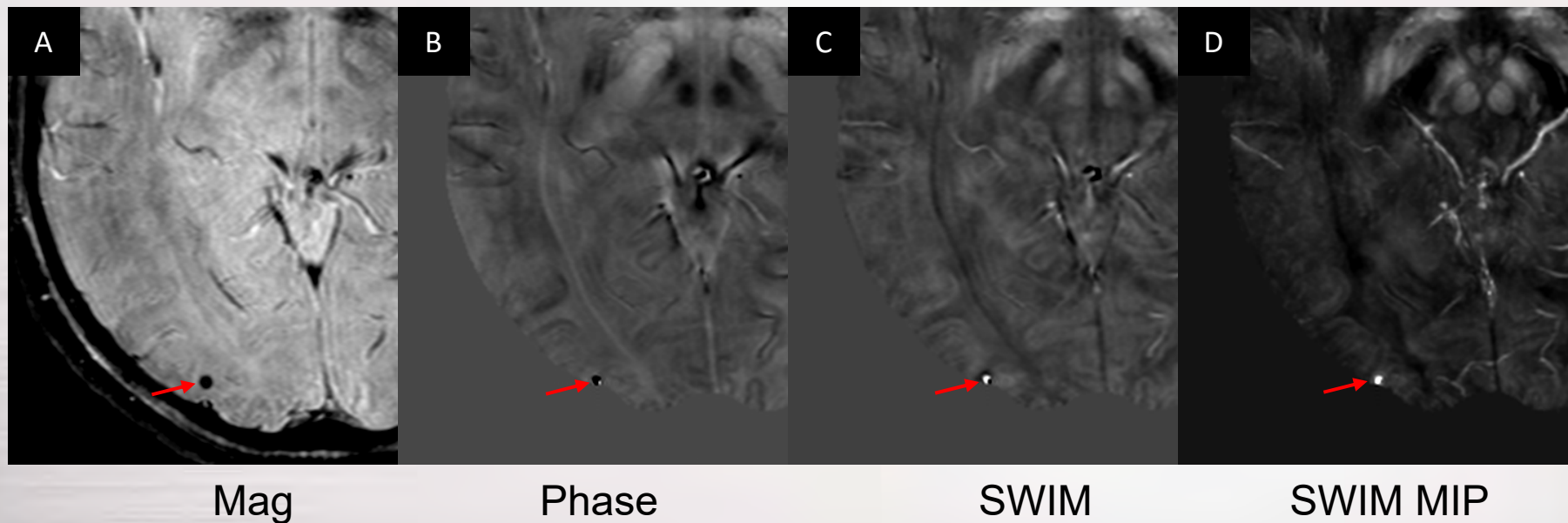
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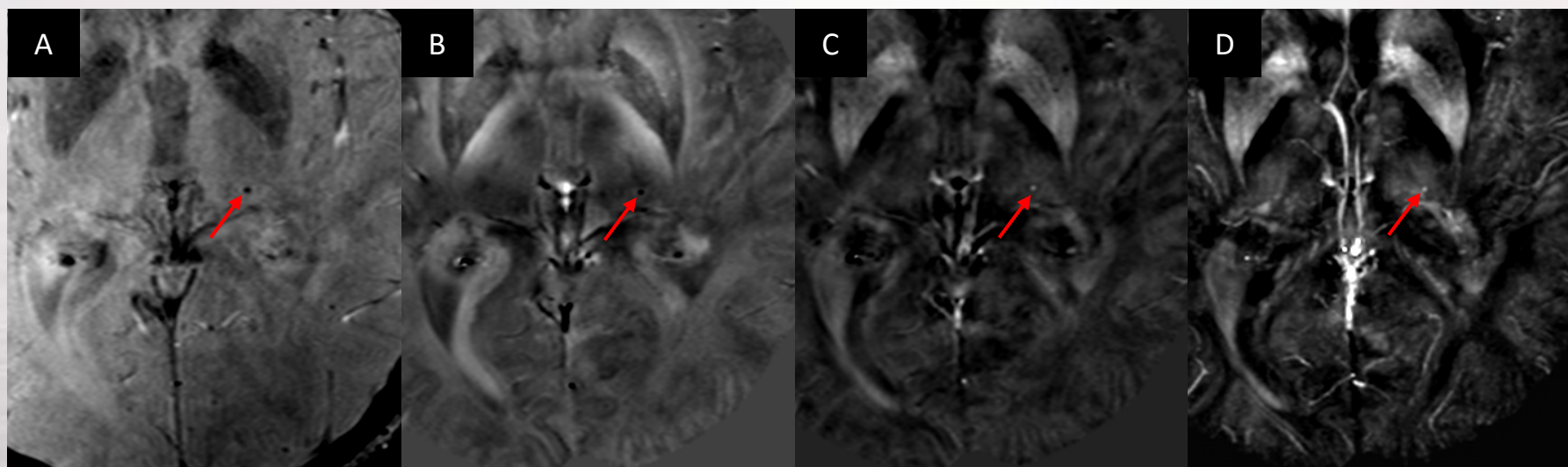
# CMBs Near The Edge of Brain



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# Thalamus CMB (common in hypertension)



Mag

Phase

SWIM

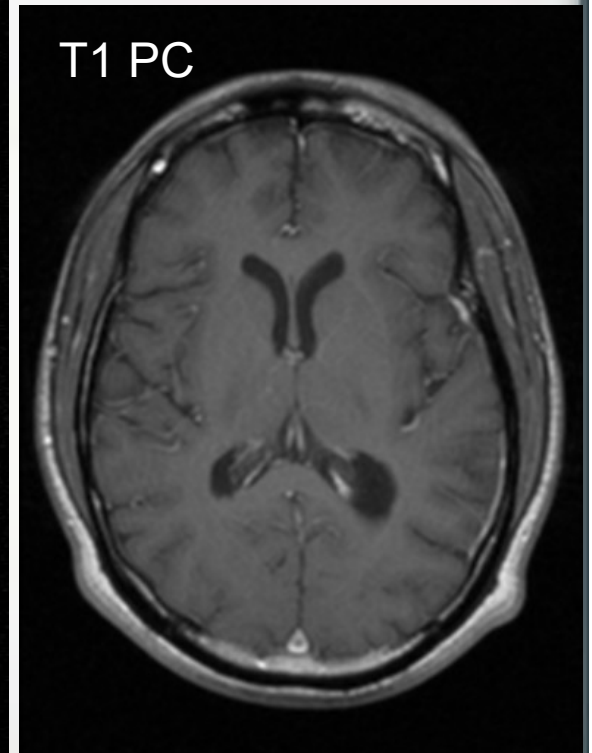
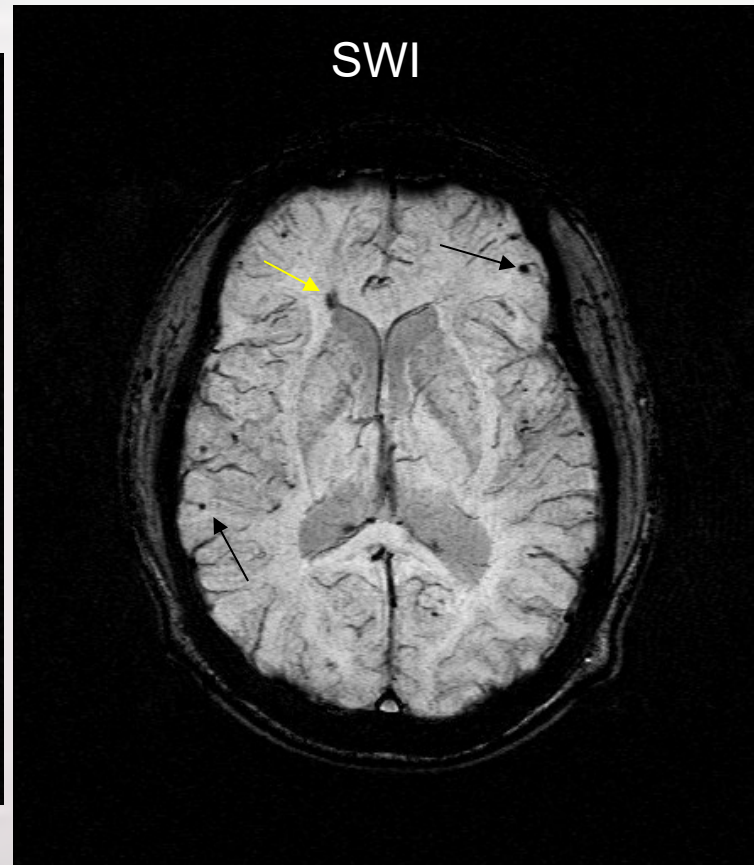
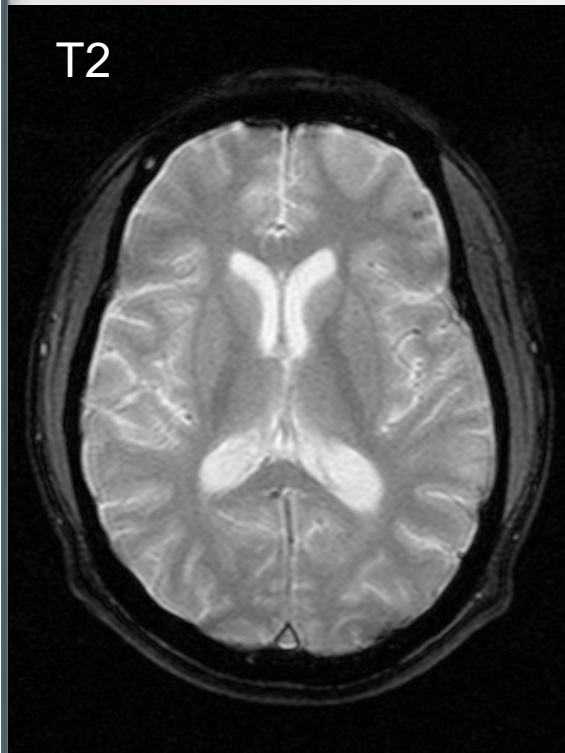
SWIM MIP



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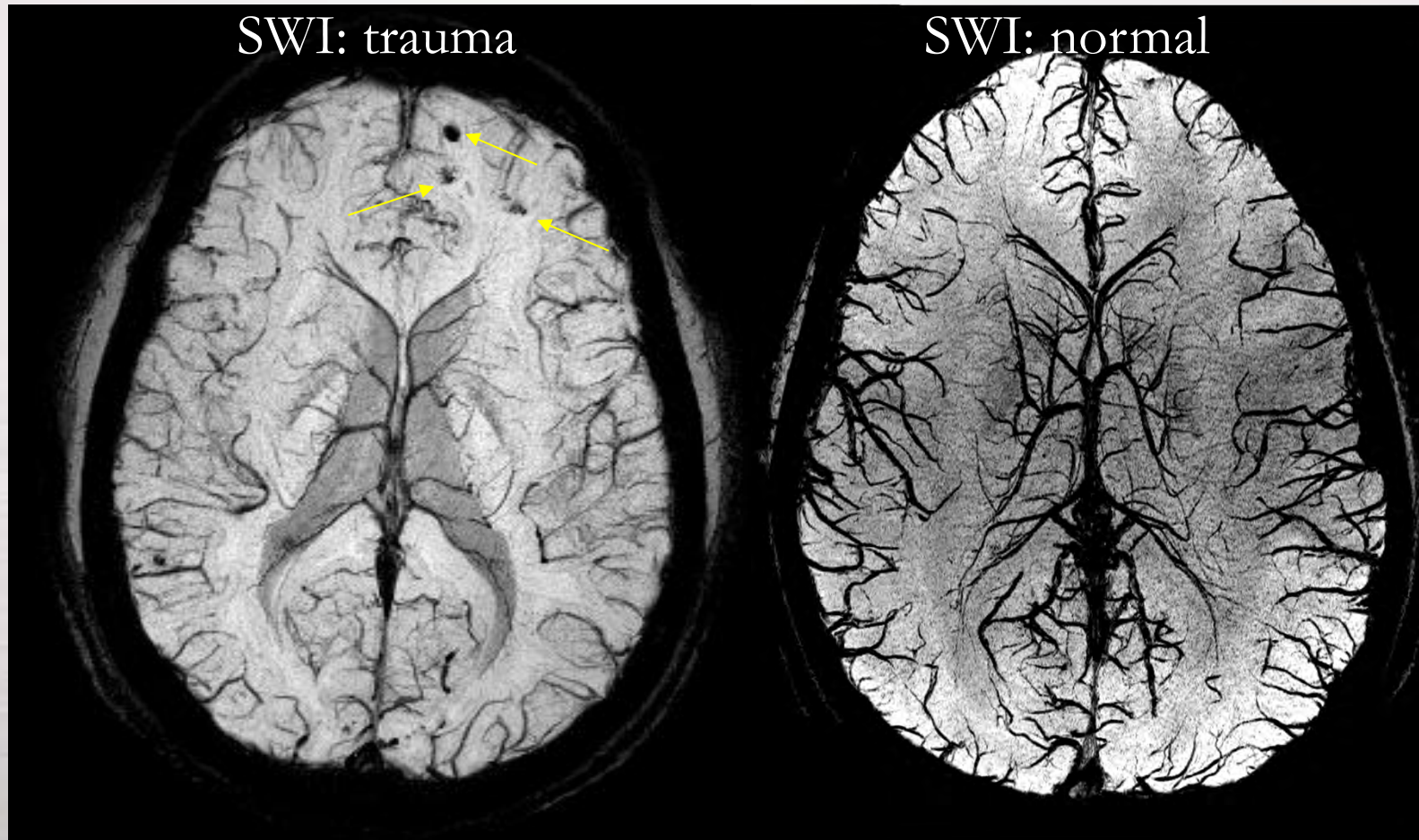
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# Motorcycle trauma: medullary vein involvement with shearing and tadpole effect

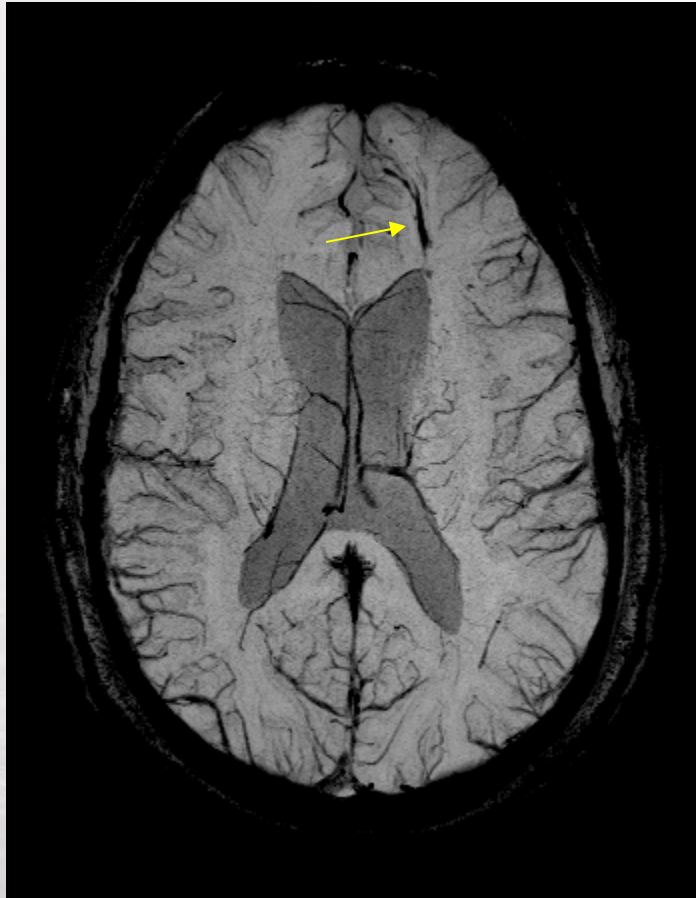




# Frontal white matter damage



# Frontal white matter damage



We have now seen this type of venous vascular damage (likely venous thrombosis) in 35 out of 100 cases of mild, moderate and severe TBI.

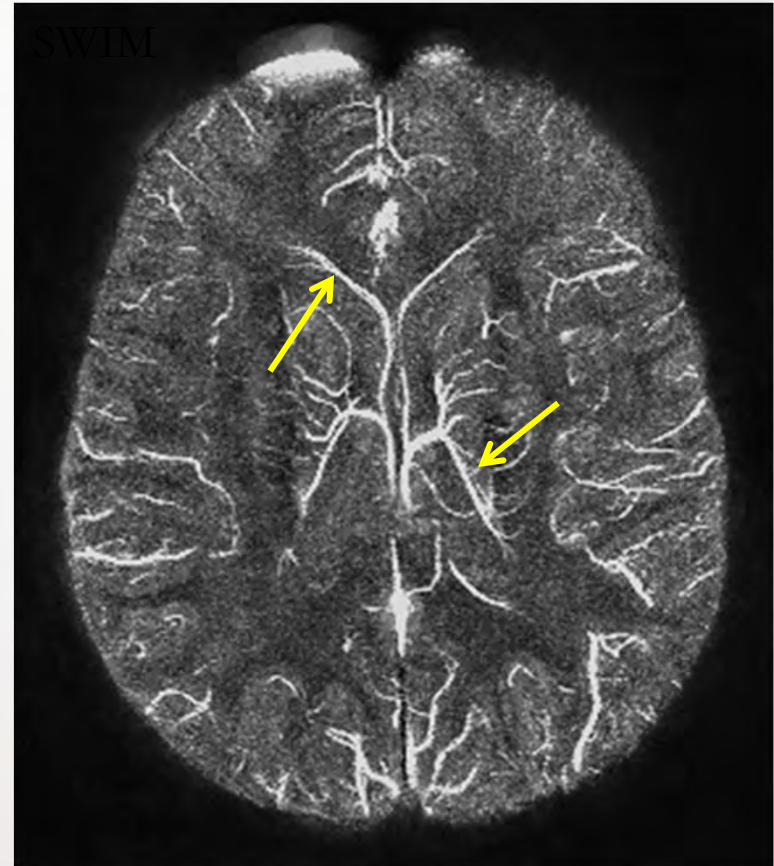


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# SWI VS. SWIM



➤SWI enhances the presence of ferritin, hemosiderin and deoxy-Hb; provides exquisite images to diagnose microbleeds and abnormal oxygenation levels



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# A longitudinal study in MS: Objectives

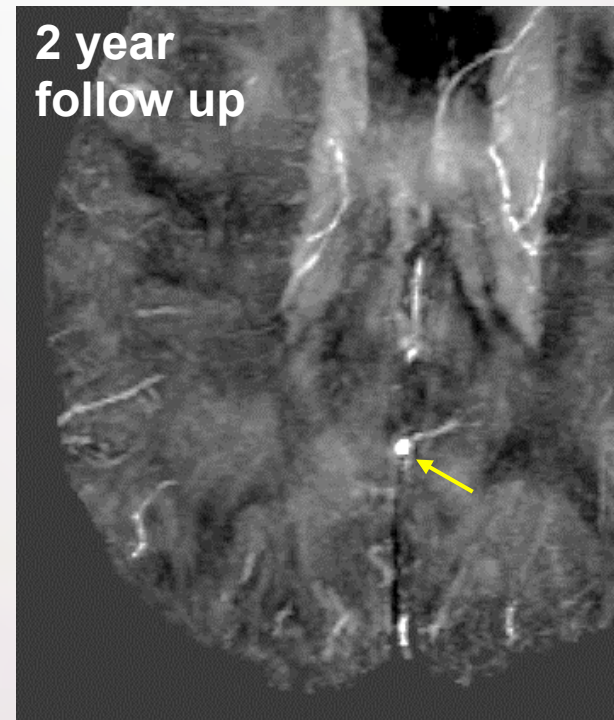
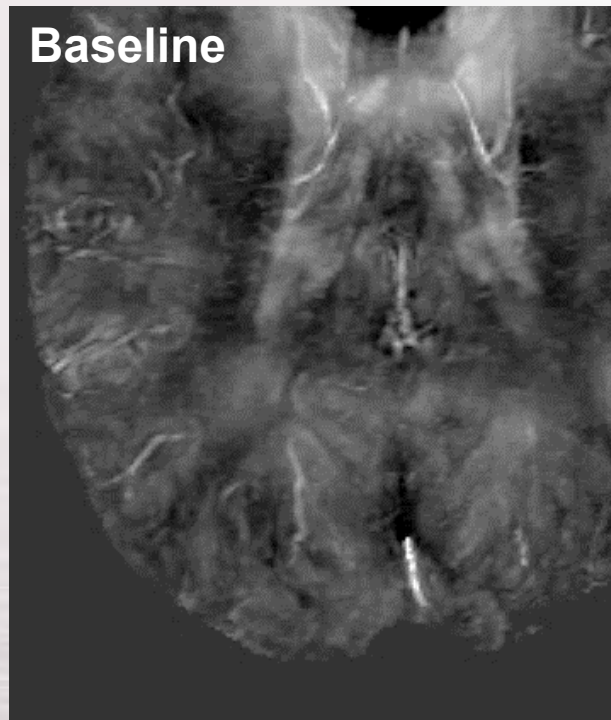
- The prevalence of CMBs in Multiple Sclerosis (MS) patients is sought to better understand neurovascular complications in this disease.
- Using SWI and SWIM, we study CMBs longitudinally in a cohort of MS patients.
- How rapidly to patients with CMBs develop more?



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# A longitudinal study in MS: Objectives

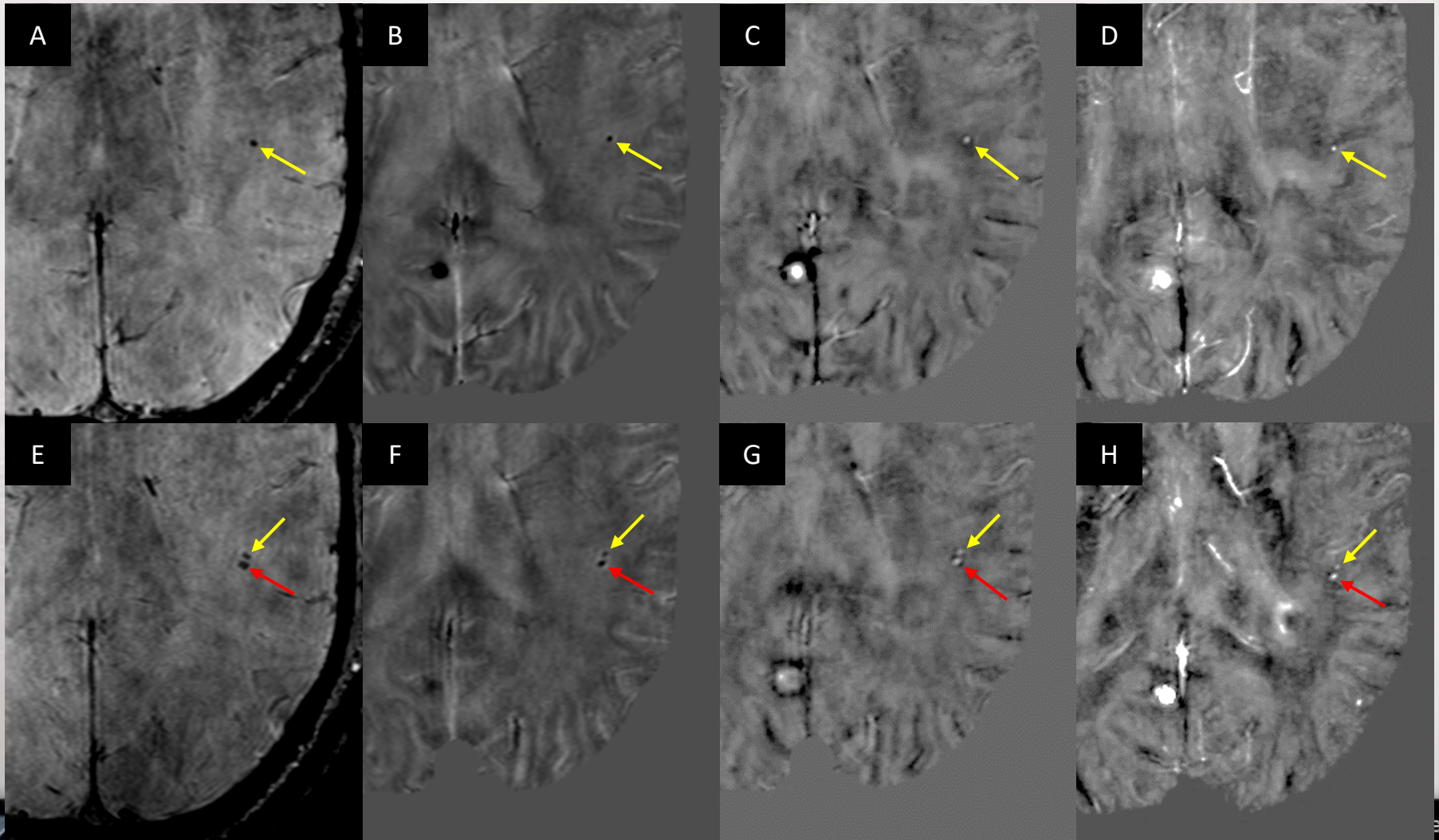


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# Longitudinal CMB Imaging – New CMB

Scan 1





# Methods

- 50 MS subjects imaged on a GE 3T scanner at baseline and at 2-year follow-up.
  - 40 RR, 8 SP, 2 PP
  - 19 male, 31 female
  - Disease duration was 12.9+/-9 years
  - EDSS was 3.0+/-2 for baseline
  - EDSS was 3.1+/-2 for follow-up



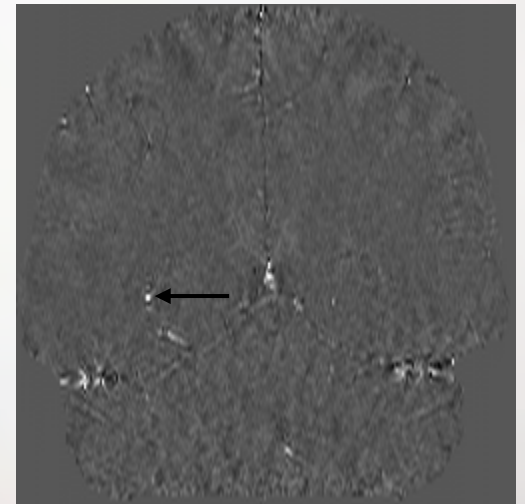
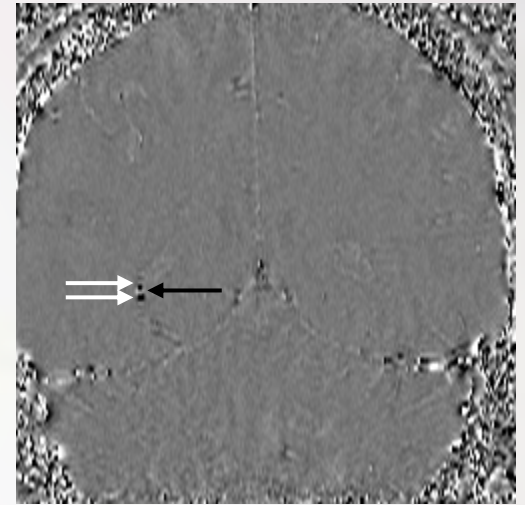
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# Methods

- SWI collected on all subjects.
  - TR=40ms
  - TE=21ms
  - Resolution=  $0.5 \times 0.5 \times 2.0 \text{ mm}^3$
- SWIM was generated.

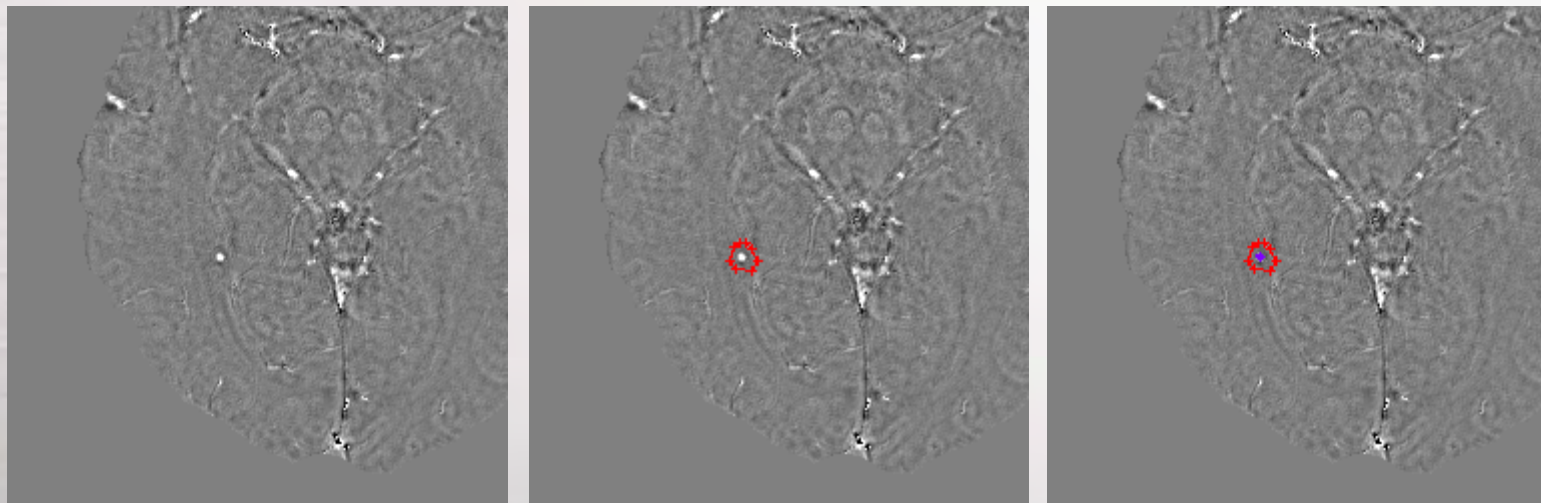
SWI – Phase



SWIM

# CMB Quantification

- In SWIM, the CMB were included in ROI and thresholds of 50ppb were applied to determine the CMB's volume and susceptibility.
- 50ppb was chosen since it is around  $2\sigma$  above the mean of white matter





# Blinded Assessment of 50 RRMS cases

- Five separated and randomized groups of images were assessed by 2 raters
  1. Short echo SWI magnitude
  2. Long echo SWI magnitude
  3. SWI composite
  4. SWI phase & SWIM
  5. Gold Standard : All images reviewed simultaneously



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# Blinded Assessment of 50 RRMS cases

- One false positive was found by 1 rater in long echo SWI magnitude and SWI composite.
- One false negative was found in long echo SWI magnitude by both raters.
- Rater 1 had 5 false negatives and rater 2 had 2 false negatives for short echo magnitude.
- SWIM/phase had no false negatives or positives.



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# Inter-rater Reliability Test

- IRR test includes 15 subjects.
  - 10 MS
    - 3 CMB total
      - 2 subjects with 1 CMB each
      - 1 subject with 2 CMB
  - 5 TBI
    - 9 CMB total
      - 4 subjects with 1 CMB each
      - 1 subject with 5 CMB
- ***SWI count and MARS location tested***
- SWI volume and mean  $\chi$  tested
- T2 FLAIR lesion volumes tested
- ICC2 > 0.9 was achieved by all 3 original raters for all measurements
- Only one Rater missed 1 CMB on subject with 5 CMB



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# MARS Rating Form

## Definite

R

L

Brainstem (B)

Cerebellum (C)

Basal Ganglia (Bg)

Thalamus (Th)

Internal Capsule (Ic)

External Capsule (Ec)

Corpus Callosum (Cc)

Deep and periventricular WM (DPWM)

Frontal (F)

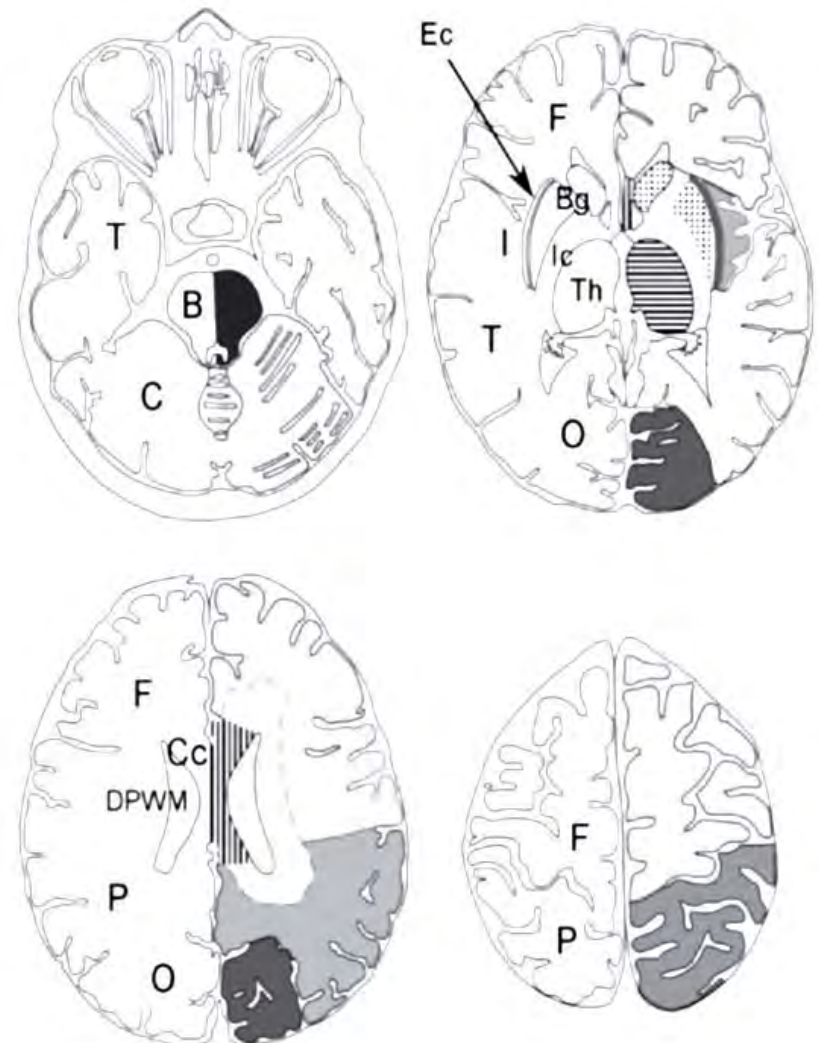
Parietal (P)

Temporal (T)

Occipital (O)

Insula (I)

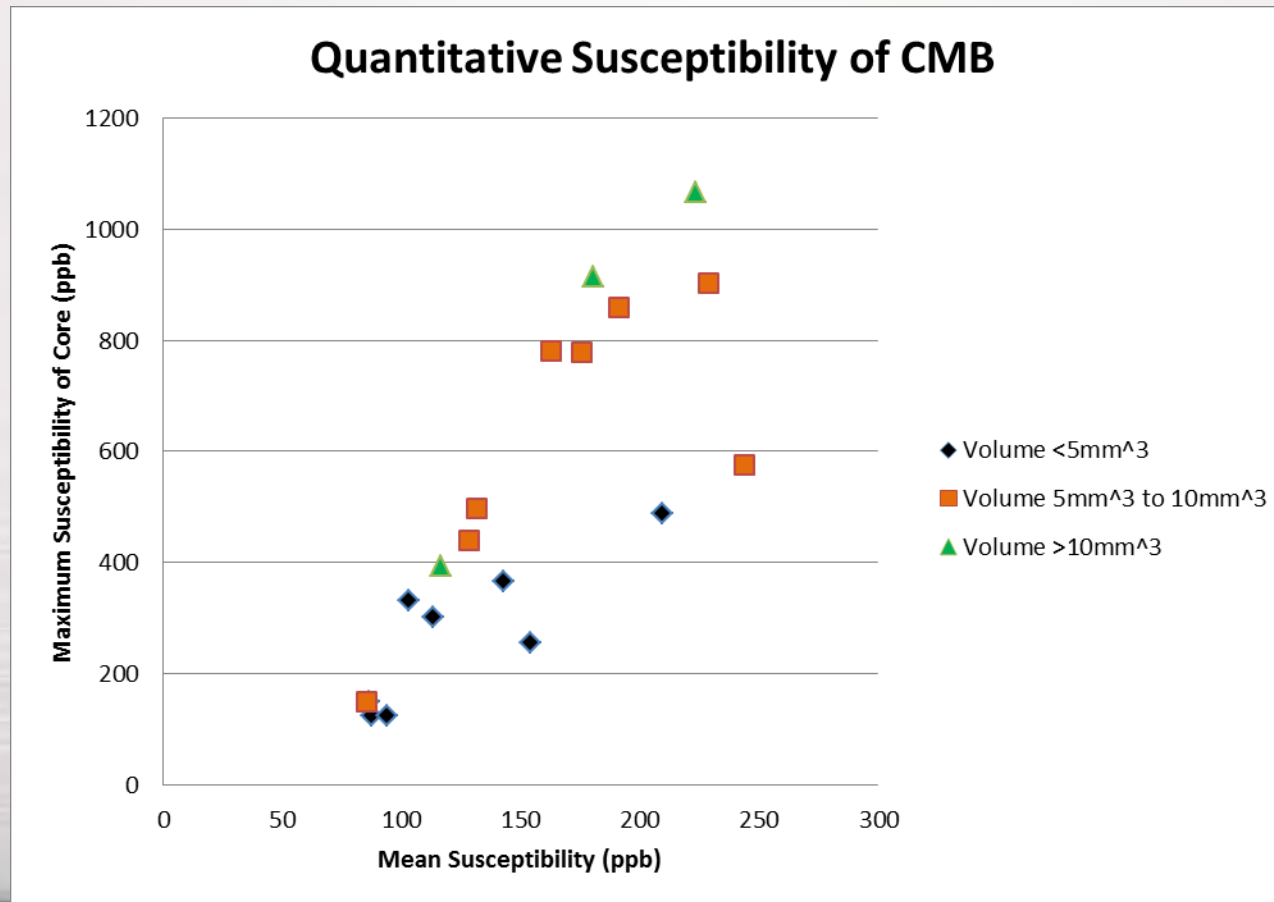
Sub Totals



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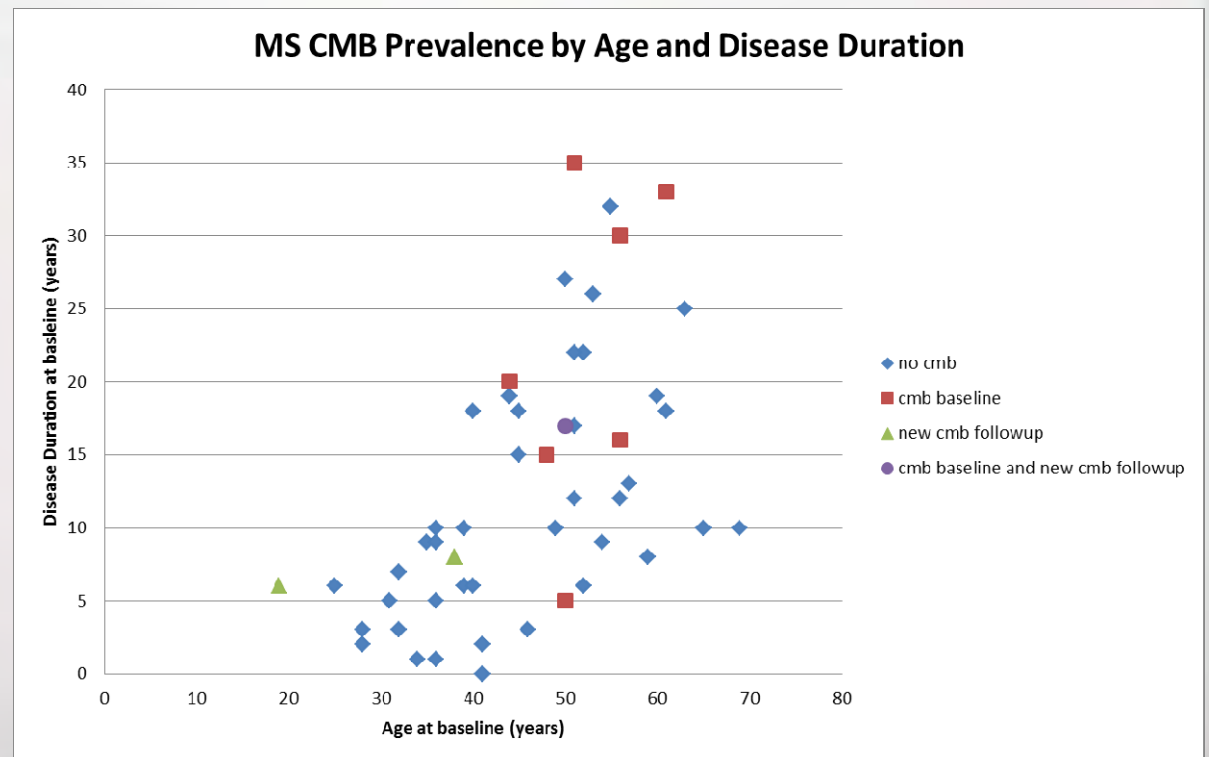
# Quantification of CMB from Phases 1 and 2



# Results for Phase I

- Nine subjects (18%) had CMB at baseline.
- Two subjects with no CMB at baseline had a new CMB at the two year follow up.
- Two subjects had 2 and 3 CMBs at baseline and had 3 and 5 CMBs at follow up.

Note that the longer the duration of the disease the higher the likelihood of having a CMB.



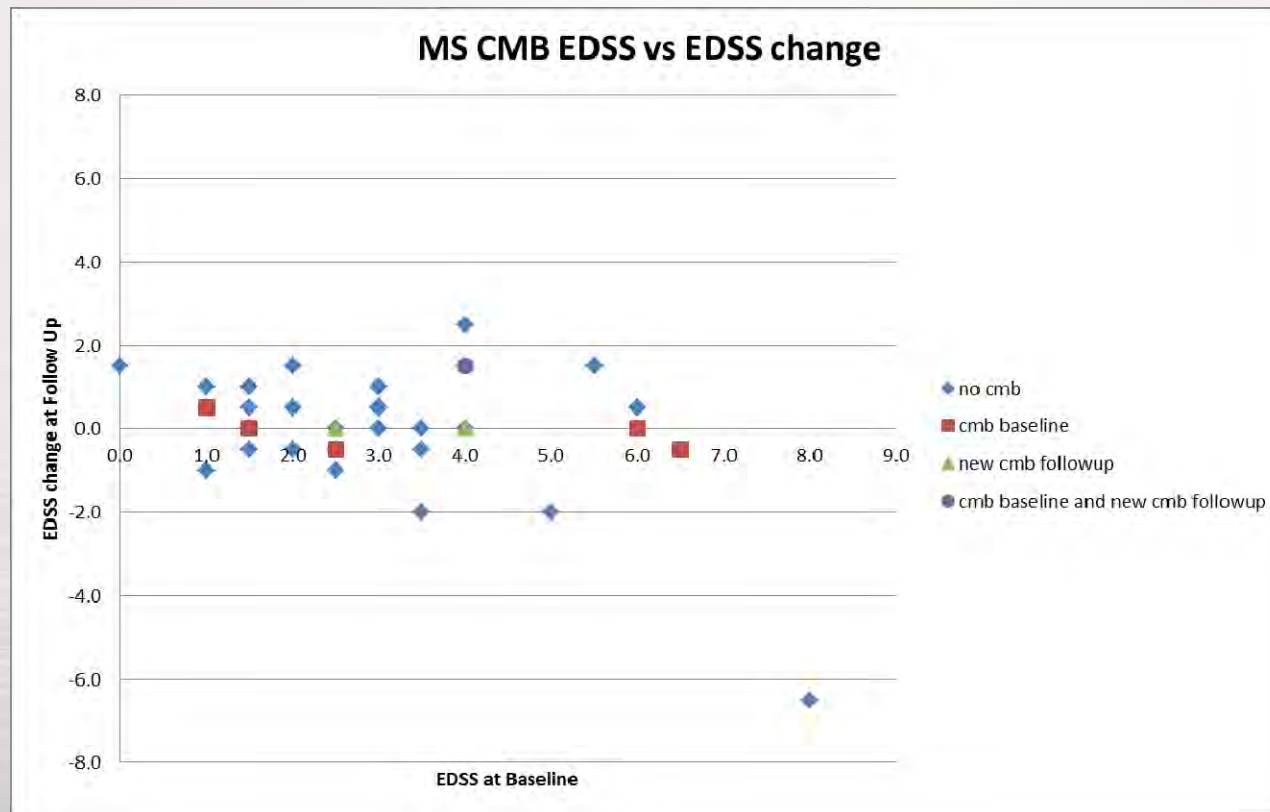
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# Results for Phase I

- Change in EDSS did not correlate with CMB prevalence or development of CMBs.
- 15% of subjects younger than 50 years old had CMB at follow up
- 30% of subjects older than 50 years old had CMB at follow up



# CMB Detection and Quantification

## Phase 1

- 18% percent of RRMS in this study have CMBs
- Age and disease duration were not factors in CMB
  - 7 Female had 1 CMB each
  - 2 Male had 2 CMB each
- Average CMB volume =  $9.3 \pm 7 \text{ mm}^3$
- Average CMB  $\chi$  of  $171.2 \pm 66 \text{ ppb}$
- Maximum CMB core  $\chi$  ranged from 124 to 1066ppb
- CMBs were not located in T2 FLAIR or T1WI lesions



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# Combined Phase 1 and 2

- Is there a higher CMB prevalence in MS population?
  - This study 14% (14/100)
    - Phase 1 – 18% (9/50)
    - Phase 2 – 10% (5/50)
  - Casson et al. 2014 Sports Health
    - NFL players – 9% ages 30 to 60 (45 sample size)
  - Cordonnier et al. 2006 Neurology
    - 17% of all patients exhibited one CMB (772 sample size) increased with age
    - 10% of patients with subjective complaints
    - 18% in Alzheimers
    - 20% in mild cognitive impairment
  - Ham et al. 2014 J Neurol
    - 15% PD patients with normal cognitive function average age 69 (123 sample size)
    - 12% healthy controls average age 70 (49 sample size)
  - Yang et al. 2015 Neurological research
    - 14.6% of stroke outpatients (1289 sample size)
    - <50: 1.3%    50-59: 10.7%    60-69: 17.6%    ≥70: 23.6%



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# Conclusions

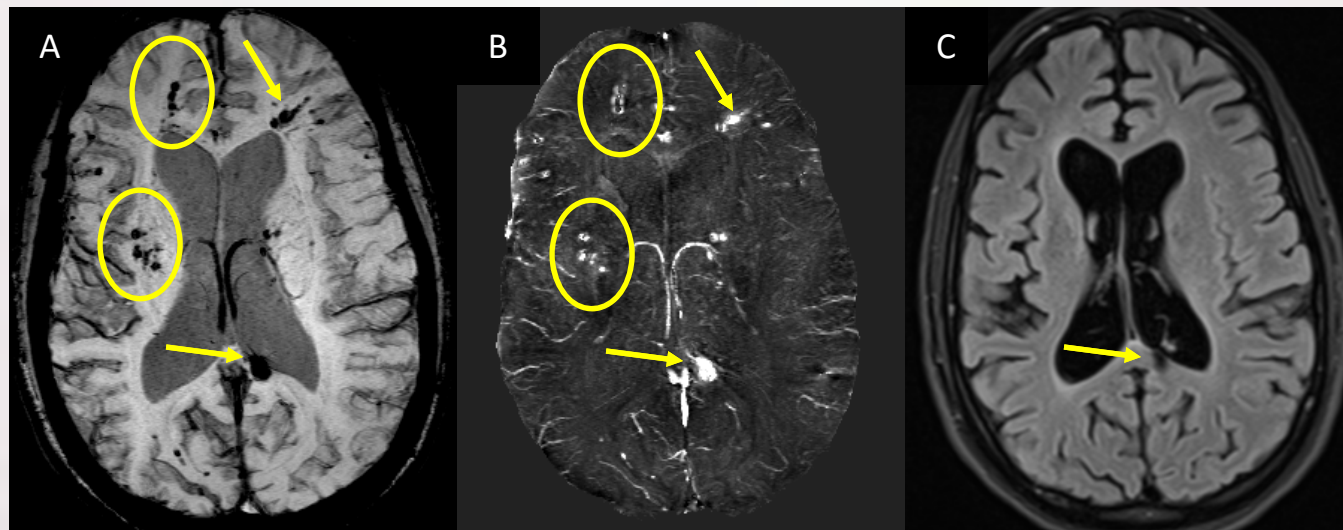
- Literature suggests a low prevalence of CMBs in the healthy population younger than 50 years old (less than about 5%).
- This prevalence increases with each decade over 50 years old.
- This study suggests that MS patients may have a higher prevalence of CMBs compared to Healthy Controls.



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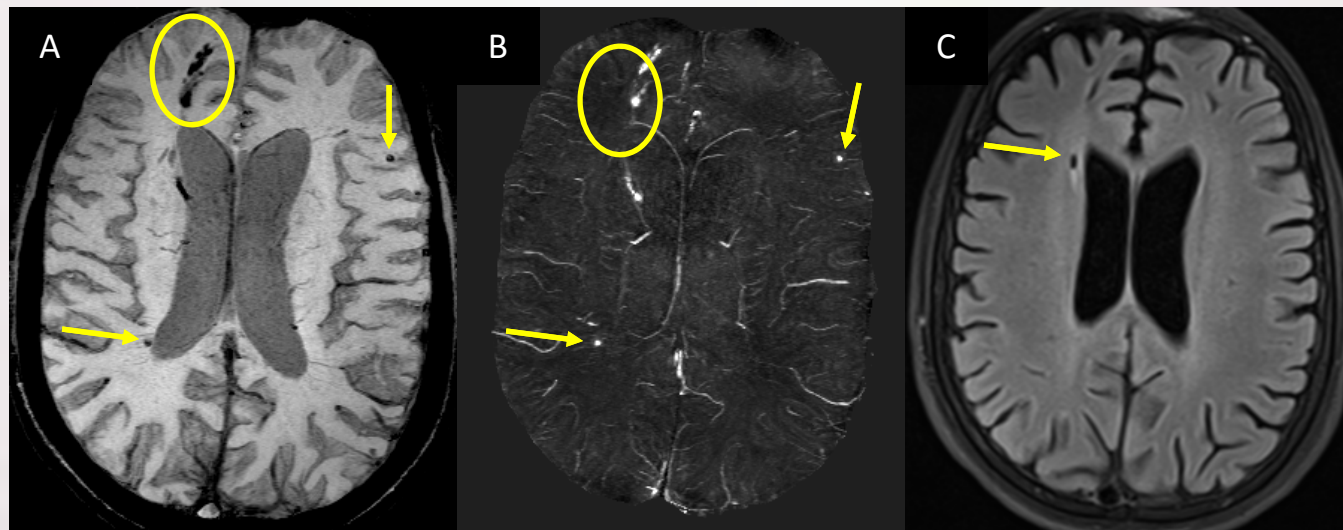
**Figure Legend:**

A: SWI mIP, B: SWIM MIP, C: FLAIR



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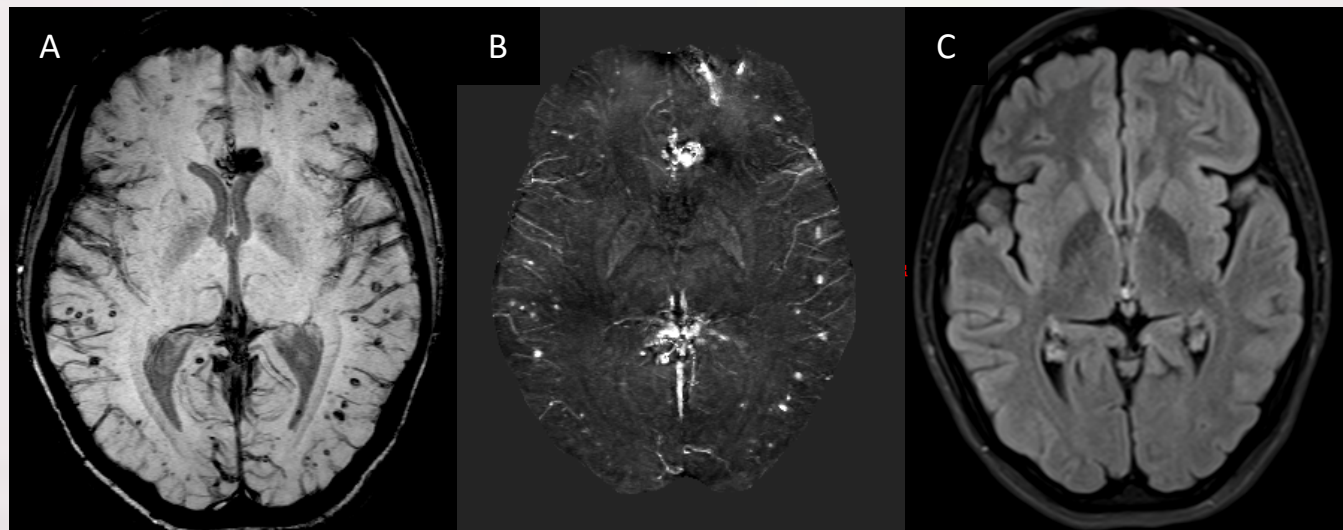
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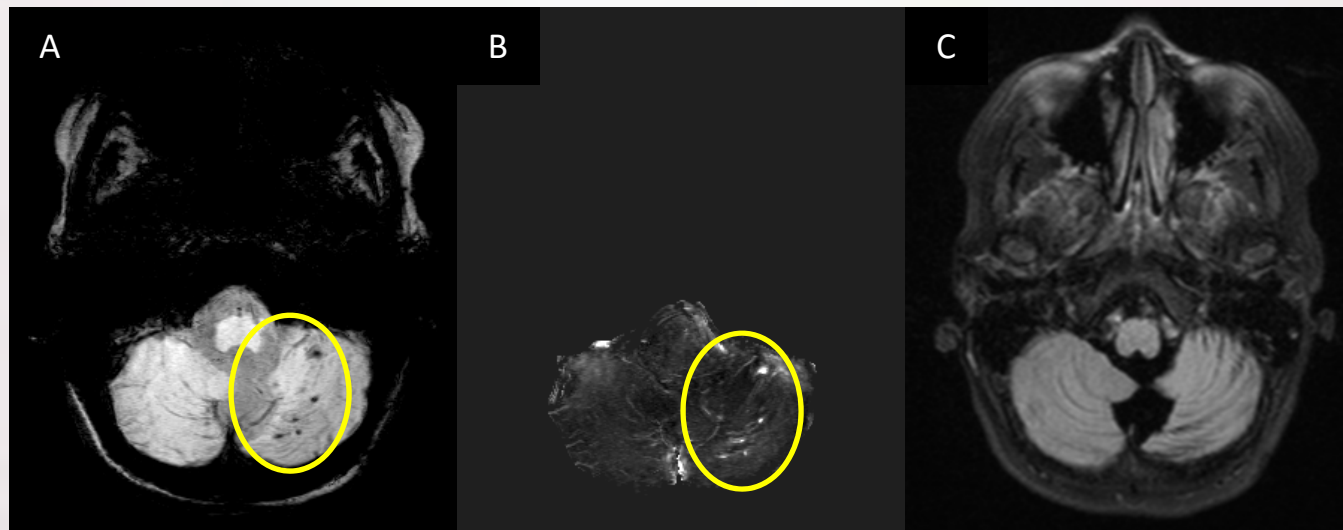
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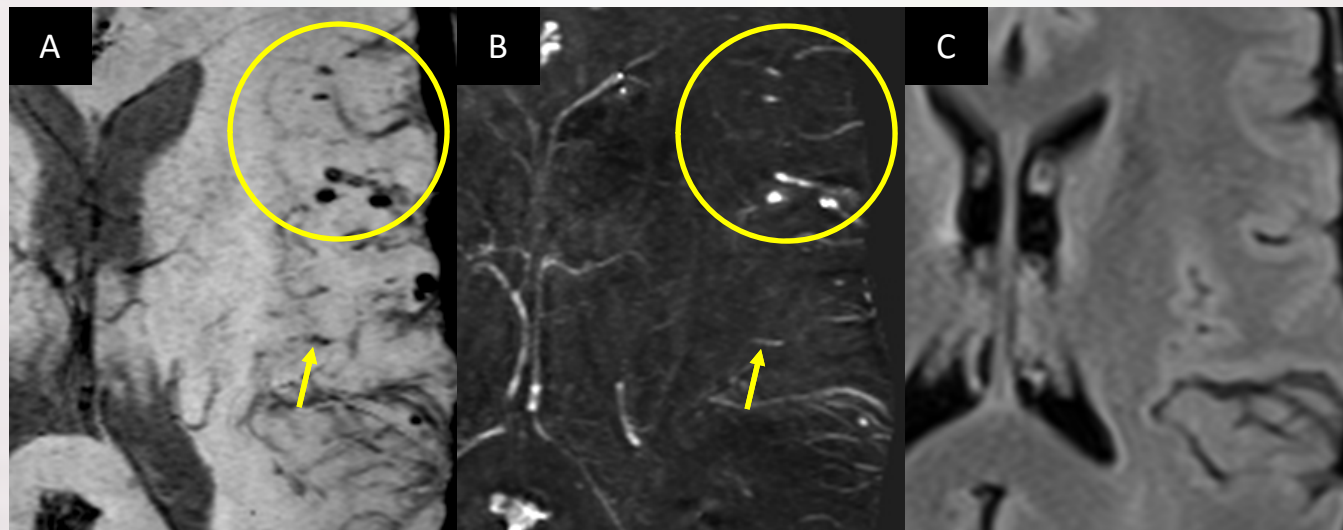
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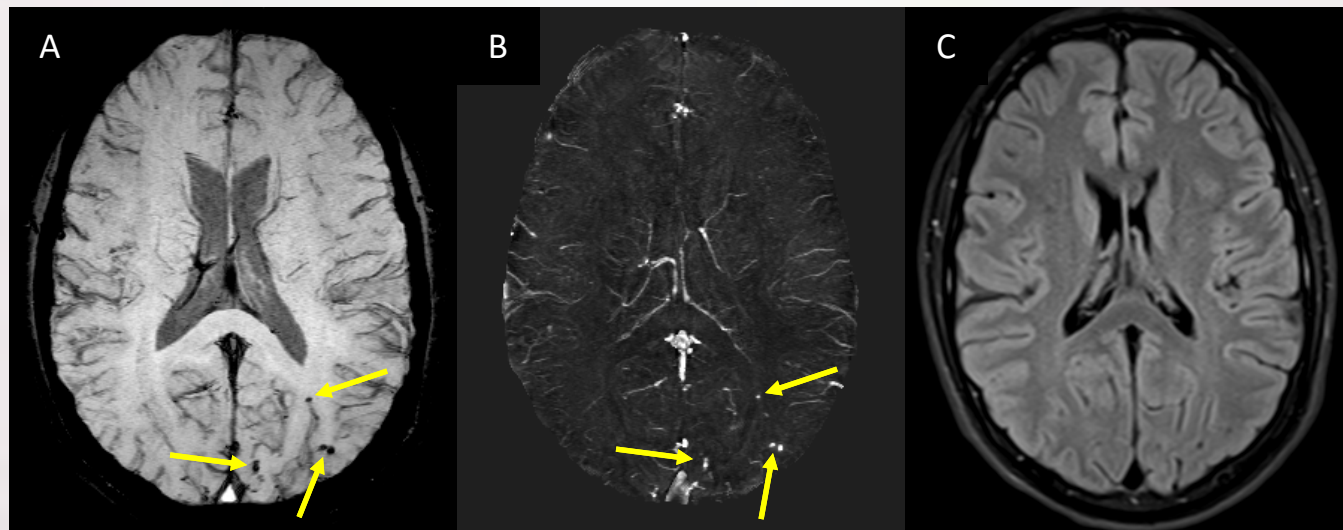
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**Figure Legend:**

A: SWI mIP, B: SWIM MIP, C: FLAIR





**Figure Legend:**

A: SWI mIP, B: SWIM MIP, C: FLAIR

# Summary

- CMB detection and quantification
  - Detection guidelines using SWI/phase/SWIM
  - Inter-rater reliability test
  - Sensitivity and Specificity of SWI modalities
  - Protocol for CMB quantification
  - ***Can we detect them automatically?***
- CMB simulations
  - What is the proposed limit of CMB detection for a given resolution?
  - What other factors affect CMB detection sensitivity and specificity?
- CMBs
  - Have been validated histologically



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