**MESA Exam 6 Ancillary Study 253 Data Set Variable Guide**

Brain MRI – Microbleeds

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| --- | --- |
| **Data Set name :** | MESAe6as253\_BMRIMB\_20240116 |
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**MESA Ancillary study #253, Atrial Fibrillation Study**

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See ancillary study publications1-5 in the Reference list below for information on ancillary study methods and for examples of how to analyze the brain MRI data. Please acknowledge the Atrial Fibrillation Ancillary Study funding in all publications that use these brain MRI data, as follows:

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MESA participants from all six field centers who participated in the Atrial Fibrillation ancillary study4,5 at Exam 6 were invited to complete a 3T brain MRI a median 18 (IQR: 16, 20) months after the Exam 6 visit. This data set contains one record per ancillary study participant (n=1062) who completed a brain MRI in March 2018 through August 2019 as part of the Atrial Fibrillation ancillary study. We refer to the microbleeds as “brain microbleeds” (MBs) rather than the commonly used term “cerebral microbleeds” (CMBs), because in this project we quantify microbleeds throughout the brain (including brainstem and cerebellum), not just in the cerebrum.

Drs. Tanweer Rashid and Mohamad Habes at the University of Texas Health Science Center San Antonio provided this Microbleeds dataset of microbleed counts and volumes. All volumes are expressed in microliters (µl). Microbleeds were initially identified by a deep learning-based method that used T2-weighted, quantitative susceptibility mapping (QSM) and susceptibility-weighted imaging (SWI) to segment the lesions and differentiate microbleeds from iron deposits.6 Identified lesions were then reviewed by a radiologist (Jeffrey B. Ware) who made the final classification. Microbleed location was classified by mapping the 146 MUlti-atlas region Segmentation utilizing Ensembles (MUSE) based regions of interest7 to the Microbleed Anatomical Rating Scale (MARS) regions of interest8 and grouping them into three categories: lobar (frontal, parietal, temporal, occipital, and insula), deep (basal ganglia, thalamus, internal capsule, corpus callosum, and deep and periventricular white matter), and infratentorial (brainstem and cerebellum). More details on mapping the regions of interest from MUSE to MARS definitions are in the Supplemental Methods and Table at the end of this document.1

QC codes:

The variable qsm\_swi\_image\_quality contains information on quality control issues. The values and their explanations are as follows:

0 Images are clean/distortion-free

1 Images have minor noise/distortions

2 Images have moderate noise/distortions

3 Images have heavy noise/distortions

4 Cannot use

Exclusions:

Of the 1062 participants with brain MRI, 3 had no SWI sequence and therefore have no microbleed data. A total of 53+18 = 71 participants had inadequate image quality on the SWI sequence (qsm\_swi\_image\_quality = 3 or 4) and must also be excluded; all microbleed variables have been set to missing for those 3 + 71 = 74 participants. These exclusions leave 988 participants available for microbleeds analysis.

Recommended adjustments: All brain MRI analyses in MESA should be adjusted for field center.

Corrections to microbleed location mapping:

A small number of microbleeds was assigned to the following “ventricle” locations: deep ventricle, temporal ventricle, or infratentorial ventricle. Microbleeds are actually not located in the ventricles, but these microbleeds were mis-assigned to ventricular locations due mis-registration or over/under-segmentation of the brain structures. These “ventricle” microbleeds should be recategorized as follows:

deep\_ventricle --> deepperiventwm

temporal\_ventricles --> temporal

ignore infratentorialvent because there were no microbleeds categorized to that region

Abbreviations:

wm white matter

**References**

1. Jensen PN, Rashid T, Ware JB, Cui Y, Sitlani CM, Austin TR, Longstreth Jr WT, Bertoni AG, Marmourian E, Bryan RN, et al. Association of brain microbleeds with risk factors, cognition and MRI markers in MESA. *Alzheimers Dement*. 2023;Jun 8. doi: 10.1002/alz.13346

2. Austin TR, Nasrallah IM, Erus G, Desiderio LM, Chen LY, Greenland P, Harding BN, Hughes TM, Jensen PN, Longstreth WT, Jr., et al. Association of Brain Volumes and White Matter Injury With Race, Ethnicity, and Cardiovascular Risk Factors: The Multi-Ethnic Study of Atherosclerosis. *Journal of the American Heart Association*. 2022;11:e023159. doi: 10.1161/JAHA.121.023159

3. Austin TR, Jensen PN, Nasrallah IM, Habes M, Rashid T, Ware JB, Chen LY, Greenland P, Hughes TM, Post WS, et al. Left Atrial Function and Arrhythmias in Relation to Small Vessel Disease on Brain MRI: The Multi-Ethnic Study of Atherosclerosis. *Journal of the American Heart Association*. 2022;11:e026460. doi: 10.1161/JAHA.122.026460

4. Heckbert SR, Austin TR, Jensen PN, Floyd JS, Psaty BM, Soliman EZ, Kronmal RA. Yield and consistency of arrhythmia detection with patch electrocardiographic monitoring: The Multi-Ethnic Study of Atherosclerosis. *J Electrocardiol*. 2018;51:997-1002.

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7. Doshi J, Erus G, Ou Y, Resnick SM, Gur RC, Gur RE, Satterthwaite TD, Furth S, Davatzikos C, Alzheimer's Neuroimaging Initiative. MUSE: MUlti-atlas region Segmentation utilizing Ensembles of registration algorithms and parameters, and locally optimal atlas selection. *Neuroimage*. 2016;127:186-195. doi: 10.1016/j.neuroimage.2015.11.073

8. Gregoire SM, Chaudhary UJ, Brown MM, Yousry TA, Kallis C, Jager HR, Werring DJ. The Microbleed Anatomical Rating Scale (MARS): reliability of a tool to map brain microbleeds. *Neurology*. 2009;73:1759-1766. doi: 10.1212/WNL.0b013e3181c34a7d

| **Order** | **Variable** | **Variable Description** |
| --- | --- | --- |
| 1 | idno | MESA Participant ID  |
| 2 | agebrainmri6c | Age at exam 6 brain MRI  |
| 3 | brainmri\_tt6c | Time from baseline to exam 6 brain MRI (days)  |
| 4 | qsm\_swi\_image\_quality | QSM SWI Image Quality |
| 5 | mb\_exclude | 0 = Include in analysis of MB1 = Exclude from MB analysis |
| 6 | mb\_n\_total | # of MBs: TOTAL  |
| 7 | mb\_n\_lobar | # of MBs: LOBAR  |
| 8 | mb\_n\_deep | # of MBs: DEEP  |
| 9 | mb\_n\_infratentorial | # of MBs: INFRATENTORIAL  |
| 10 | mb\_n\_brainstem | # of MBs: BRAINSTEM  |
| 11 | mb\_n\_cerebellum | # of MBs: CEREBELLUM  |
| 12 | mb\_n\_ventral\_dc | # of MBs: VENTRAL DC  |
| 13 | mb\_n\_infratentorialvent | # of MBs: INFRATENTORIAL VENTRICLES  |
| 14 | mb\_n\_basal\_ganglia | # of MBs: BASAL GANGLIA  |
| 15 | mb\_n\_thalamus | # of MBs: THALAMUS  |
| 16 | mb\_n\_internal\_capsule | # of MBs: INTERNAL CAPSULE  |
| 17 | mb\_n\_corpus\_callosum | # of MBs: CORPUS CALLOSUM  |
| 18 | mb\_n\_deepperiventwm | # of MBs: DEEP PERIVENTRICULAR WM  |
| 19 | mb\_n\_deep\_ventricle | # of MBs: DEEP VENTRICLE  |
| 20 | mb\_n\_fornix | # of MBs: FORNIX  |
| 21 | mb\_n\_frontal | # of MBs: FRONTAL  |
| 22 | mb\_n\_parietal | # of MBs: PARIETAL  |
| 23 | mb\_n\_temporal | # of MBs: TEMPORAL  |
| 24 | mb\_n\_temporal\_ventricles | # of MBs: TEMPORAL VENTRICLES  |
| 25 | mb\_n\_occipital | # of MBs: OCCIPITAL  |
| 26 | mb\_n\_insula | # of MBs: INSULA  |
| 27 | mb\_v\_lobar | MB Volume: LOBAR  |
| 28 | mb\_v\_deep | MB Volume: DEEP  |
| 29 | mb\_v\_infratentorial | MB Volume: INFRATENTORIAL  |
| 30 | mb\_v\_brainstem | MB Volume: BRAINSTEM  |
| 31 | mb\_v\_cerebellum | MB Volume: CEREBELLUM  |
| 32 | mb\_v\_ventral\_dc | MB Volume: VENTRAL DC  |
| 33 | mb\_v\_infratentorialvent | MB Volume: INFRATENTORIAL VENTRICLES  |
| 34 | mb\_v\_basal\_ganglia | MB Volume: BASAL GANGLIA  |
| 35 | mb\_v\_thalamus | MB Volume: THALAMUS  |
| 36 | mb\_v\_internal\_capsule | MB Volume: INTERNAL CAPSULE  |
| 37 | mb\_v\_corpus\_callosum | MB Volume: CORPUS CALLOSUM  |
| 38 | mb\_v\_deepperiventwm | MB Volume: DEEP PERIVENTRICULAR WM  |
| 39 | mb\_v\_deep\_ventricle | MB Volume: DEEP VENTRICLE  |
| 40 | mb\_v\_fornix | MB Volume: FORNIX  |
| 41 | mb\_v\_frontal | MB Volume: FRONTAL  |
| 42 | mb\_v\_parietal | MB Volume: PARIETAL  |
| 43 | mb\_v\_temporal | MB Volume: TEMPORAL  |
| 44 | mb\_v\_temporal\_ventricles | MB Volume: TEMPORAL VENTRICLES  |
| 45 | mb\_v\_occipital | MB Volume: OCCIPITAL  |
| 46 | mb\_v\_insula | MB Volume: INSULA  |

**Supplemental Methods and Table**

*Regions of interest (ROI) for mapping microbleeds*

We mapped microbleeds to the regions described in the Microbleed Anatomical Rating Scale (MARS).8 We grouped the ROIs of the existing MUlti-atlas region Segmentation utilizing Ensembles (MUSE) segmentation2,7 into lobar, deep, and infratentorial regions to align as closely as possible with MARS definitions. The mapping between MUSE and MARS ROIs is shown in the Table below.

Periventricular white matter was not a part of the MUSE ROIs and had to be generated separately. The process involved creating a binary mask of the ventricles and then using a spherical structural element (size, 7 voxels) to perform morphological dilation of the ventricle masks. Finally, periventricular white matter is defined as the region resulting from the union of the dilated image and the surrounding MUSE ROIs.

**Table.** MUSE regions of interest (ROI) grouped according to MARS ROI definitions, and percent of lobar, deep, and infratentorial microbleeds in each MARS ROI

| **MUSE ROIs** | **MARS ROIs** |
| --- | --- |
| **Lobar Microbleeds** |
| Basal forebrain Frontal lobe white matter Anterior cingulate gyrus Anterior orbital gyrus Central operculum Frontal operculum Frontal pole Gyrus rectus Lateral orbital gyrus Middle cingulate gyrus Medial frontal cortex Middle frontal gyrus Medial orbital gyrus Precentral gyrus medial segment Superior frontal gyrus medial segment Opercular part of the inferior frontal gyrus Orbital part of the inferior frontal gyrus Parietal operculum Posterior orbital gyrus Precentral gyrus Subcallosal area Superior frontal gyrus Supplementary motor cortex Triangular part of the inferior frontal gyrus | Frontal (43% of lobar) |
| Parietal lobe white matter Angular gyrus Postcentral gyrus medial segment Posterior cingulate gyrus Precuneus Postcentral gyrus Supramarginal gyrus Superior parietal lobule | Parietal (20% of lobar) |
| Occipital lobe white matter Calcarine cortex Cuneus Inferior occipital gyrus Lingual gyrus Middle occipital gyrusOccipital pole Occipital fusiform gyrus Superior occipital gyrus  | Occipital (13% of lobar) |
| Amygdala Hippocampus Temporal lobe white matter Entorhinal area Fusiform gyrus Inferior temporal gyrus Middle temporal gyrus Parahippocampal gyrus Planum polare Planum temporale Superior temporal gyrus Temporal pole Transverse temporal gyrus | Temporal (23% of lobar) |
| Anterior insula Posterior insula  | Insula (2% of lobar) |
| **Deep Microbleeds** |
| Accumbens area Caudate Pallidum Putamen  | Basal ganglia (14% of deep) |
| Thalamus proper  | Thalamus (12% of deep) |
| Anterior limb of internal capsule Posterior limb of internal capsule including cerebral peduncle  | Internal capsule (1% of deep) |
| Corpus callosum  | Corpus callosum (1% of deep) |
| Periventricular white matter\*Fornix  | Deep and periventricular WM (73% of deep) |
| **Infratentorial Microbleeds** |
| BrainstemVentral diencephalon | Brainstem (32% of infratentorial) |
| Cerebellum exterior Cerebellum white matter Cerebellar Vermal Lobules I-V Cerebellar Vermal Lobules VI-VII Cerebellar Vermal Lobules VIII-X  | Cerebellum (68% of infratentorial) |

\* Region derived by additional image processing