FFCM-MRF Manual

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1. Installation

- Download & Install **MATLAB R2017** or higher version.
- Download & Install **SPM12** (https://www.fil.ion.ucl.ac.uk/spm/), start MATLAB and add SPM12 to your path, either using *File* > *Set Path* > *Add Folder...* or typing the following in the MATLAB Command window:

  >> addpath path/to/spm12.
- Download **FFCM-MRF** from our github page: https://github.com/YueCui-Labs/FFCM-MRF. Download & Install **Python 3.8** or higher using Anaconda and enter the following command to install the necessary packages in the FFCM-MRF directory, Anaconda will tell you if additional packages are necessary.

  pip install -r requirements.txt.
- Start MATLAB and add FFCM-MRF to your path, either using *File* > *Set Path* > *Add Folder...* or typing the following in the MATLAB Command window:

  >> addpath path/to/FFCM-MRF.
- Launch **FFCM-MRF** by using the command

  >> FFCM-MRF.

2. Functions

List of functions include preprocessing, FFCM-MRF vascular segmentation and quantification:

- **Preprocessing**
  - **Skull stripping (brain extraction)**

    Use the skull stripping module to remove the brain skull and extract the brain tissues using HD-BET tool for humans (Isensee et al., 2019) and DeepBet for macaques (Wang et al., 2021).
  - **Denoising**

    Denoise by filtering out noise in the image using the scikit-image package (Van der Walt et al., 2014).
  - **Bias field correction:**

Correct bias field inhomogeneity artifacts using API of SPM12 toolkit (Ashburner et al., 2014).

- **FFCM-MRF vascular segmentation**
  - **Histogram matching**

    Transform a TOF-MRA so that its histogram matches a target histogram.
  - **Vessel enhancement**

    Enhance the response of vessel tissue while suppressing the response of non-vascular tissue using Jerman's method (Jerman et al., 2016).
  - **Vessel segmentation**

    Segment the intracranial cerebrovascular tissue using the FFCM-MRF algorithm.
- **Vascular quantification**
  - **Vessel quantification**

    Calculates various morphometric features, including vessel volume (density), vessel length (density), and vessel diameter (mean, maximum, minimum, and median) given a brain atlas.

3. Step-by-step processing

Type *FFCM-MRF* in Matlab command line to open the window shown in Figure 1.

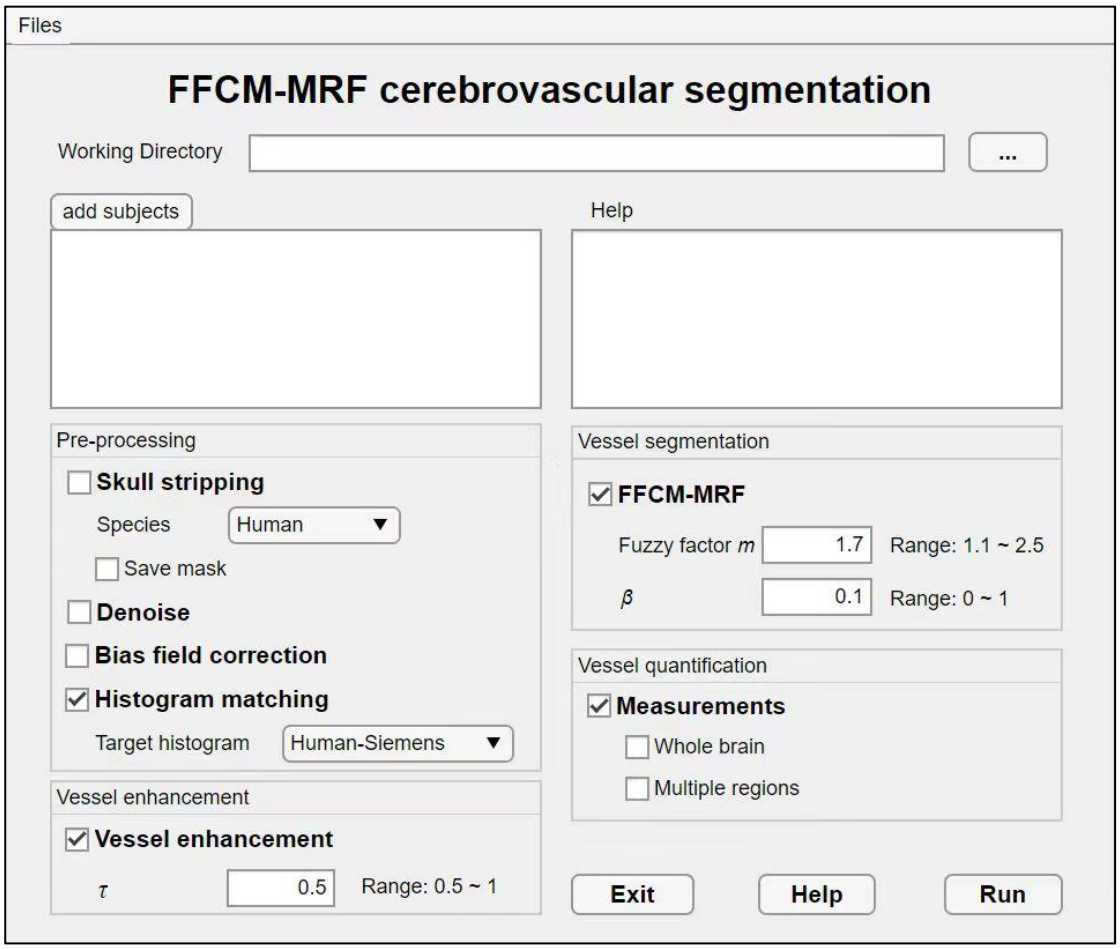

Figure 1. Graphical user interface and pipeline of FFCM-MRF.

3.1 File naming rules

The raw TOF-MRA image should be renamed *MRA.nii* or *MRA.nii.gz* in the folder with the name of the subject's ID. Load the subject's folder and the subject's ID will list in the left top rectangular blank box. The results of preprocessing, vascular segmentation and quantification will save in this subject folder with distinct suffixes.

3.2 Skull stripping

The skull stripping module includes integrated skull stripping tools for either human or macaque subjects. The solution for human and macaque skull stripping is provided by HD-BET (Isensee et al., 2019) and DeepBet (Wang et al., 2021) for humans and macaques, respectively.

To utilize this module, users should select the subject type (human or macaque) using the "species" drop-down box and check the "save mask" checkbox to save the mask of the brain tissue

after skull stripping. The “skull stripping” module automatically looks for *MRA.nii* or *MRA.nii.gz* as the input file and outputs *MRA_brain.nii.gz* and *MRA_brain_mask.nii.gz* (optional). The module's results are presented in Figures 2 and 3. It is strongly recommended to check skull stripped images slice by slice for each subject and to perform manual editing if necessary. Users can select other skull stripping tools as long as they follow the file naming rules.

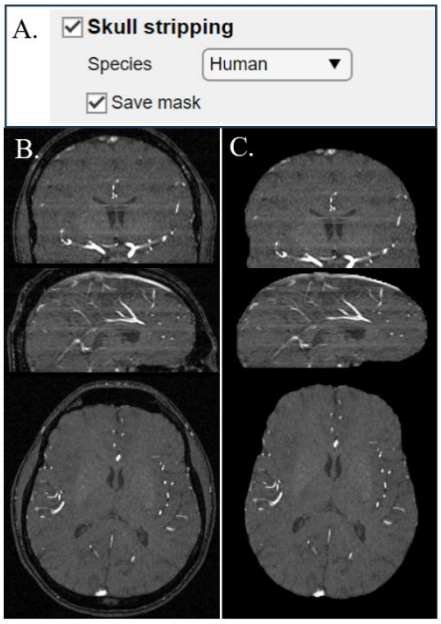

Figure 2. Skull stripping function. A, User interface; B, TOF-MRA image before skull stripping (*MRA.nii.gz*); C, TOF-MRA image after skull stripping (*MRA_brain.nii.gz*).

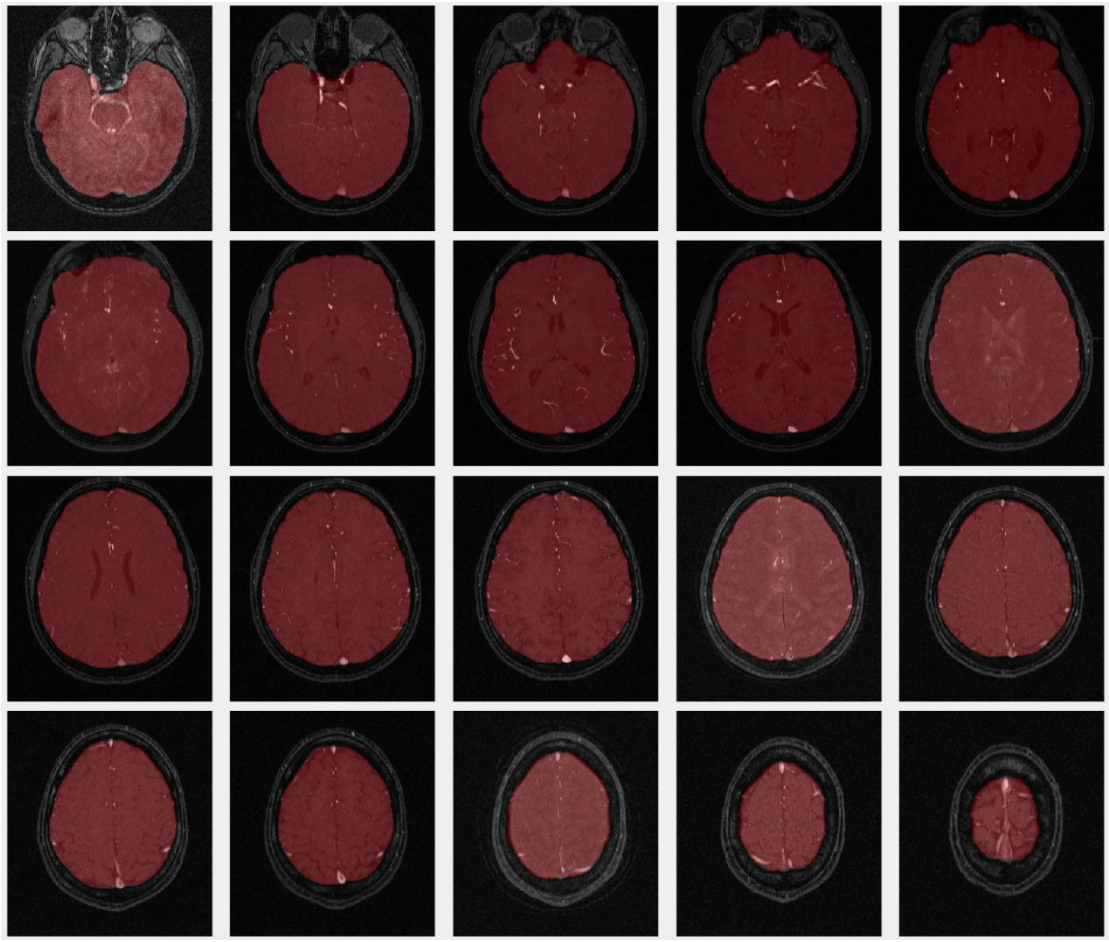

Figure 3. Visualization of a TOF-MRA image overlaid by an extracted brain mask, which is shown in red.

3.3 Denoising

The denoising module uses a non-local means filtering denoising algorithm (Buades et al., 2005) to remove noise from the input image. To utilize this module, users can simply check the “Denoise” checkbox. This module automatically looks for *MRA_brain.nii.gz* as the input file and outputs *MRA_brain_denoise.nii.gz*. This stage is optional as it may blur the image and affect the vascular segmentation results. Users can select other image denoising tools as long as they follow the file naming rules.

3.4 Bias field correction

The bias field correction module uses the bias field correction tool in the SPM12 toolkit to correct bias field inhomogeneity artifacts. To utilize this module, users can simply check the "Bias Field Correction" checkbox. This step is recommended.

This module automatically looks for *MRA_brain_denoise.nii.gz* or *MRA_brain.nii.gz* as the input file and outputs *MRA_brain_denoise.nii.gz*. The results of the “Denoising” and “Bias field correction” modules are presented in Figure 4.

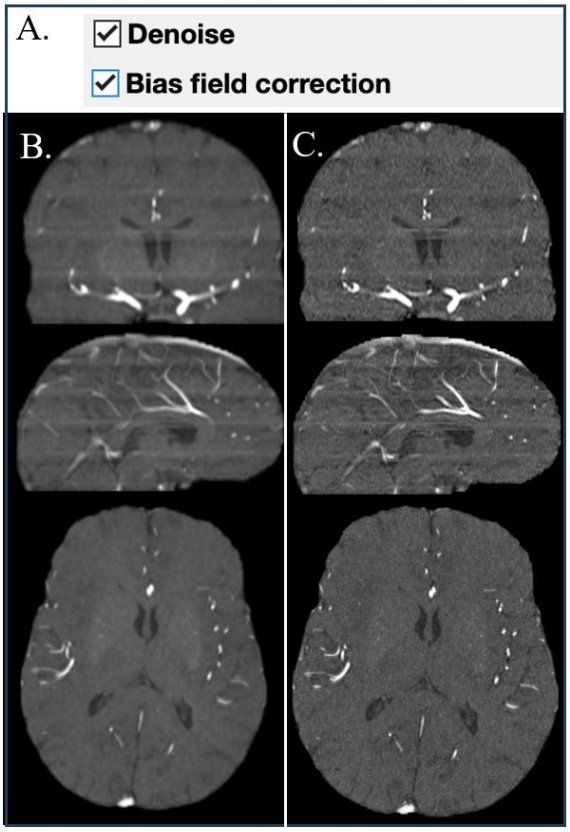

Figure 4. Denoising and bias field correction functions. A, User interface; B, TOF-MRA image after denoising (*MRA_brain_denoise.nii.gz)*; C, TOF-MRA image after bias field correction (*MRA_brain_biasfield_correct.nii.gz).*

3.5 Histogram matching

The histogram matching module uses a selected target histogram to normalize the TOF-MRA image. The software has integrated some target histograms for different MR vendors and species. To utilize this module, users should select a proper "Target histogram" based on the species of the subject and select the correct MR scanner from the drop-down box. This step is mandatory and is followed by vessel segmentation.

This module automatically looks for *MRA_brain_biasfield_correct.niii.gz* or *MRA_brain_denoise.nii.gz* or *MRA_brain.nii.gz* as the input file and outputs

MRA_brain_match.nii.gz. The results of this module are presented in Figure 5.

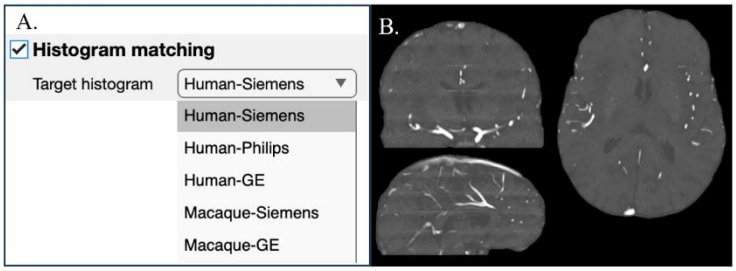

Figure 5. Histogram matching function. A, User interface with built-in target histograms; B, TOF-MRA image after histogram matching (*MRA_brain_match.nii.gz)*

3.6 Vessel enhancement

The vessel enhancement module enhances the response of vessel tissue while suppressing the response of non-vascular tissue. Parameter τ can be set by users within the range of 0.5 to 1, with a default value of 0.8. This step is mandatory and is followed by vessel segmentation.

This module automatically looks for *MRA_brain_biasfield_correct.niii.gz* or *MRA_brain_denoise.nii.gz* or *MRA_brain.nii.gz* as the input file and outputs *MRA_brain_enhance.nii.gz*. The results of this module are presented in Figure 6.

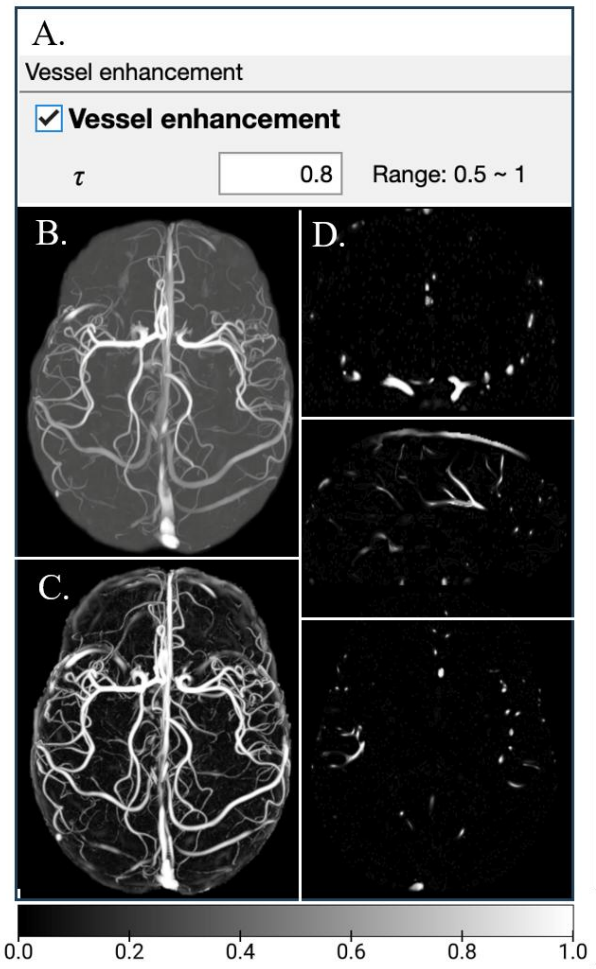

Figure 6. Vessel enhancement function. A, User interface; B, Maximum intensity projection (MIP) view of TOF-MRA image; C, MIP view of enhanced TOF-MRA image; D, 2D multi-planar views of enhanced TOF-MRA image (*MRA_brain_enhance.nii.gz)*.

3.7 Vessel segmentation

The FFCM-MRF vessel segmentation module consists of two main steps: FFCM and MRF. The FFCM algorithm performs a rudimentary vessel segmentation, and the MRF further refines the segmentation by integrating vessel shape priors and spatial constraints. Two parameters m and β can be adjusted by users. m can be set within the range of 1.1 to 2.5, with a default value of 1.7. The value of β can range from 0 to 1, with a default value of 0.1.

This module automatically looks for *MRA_brain_match.nii.gz* and *MRA_brain_enhance.nii.gz* as the input files and outputs *MRA_brain_vessel.nii.gz*. The visualization results for this module are presented in Figure 7.

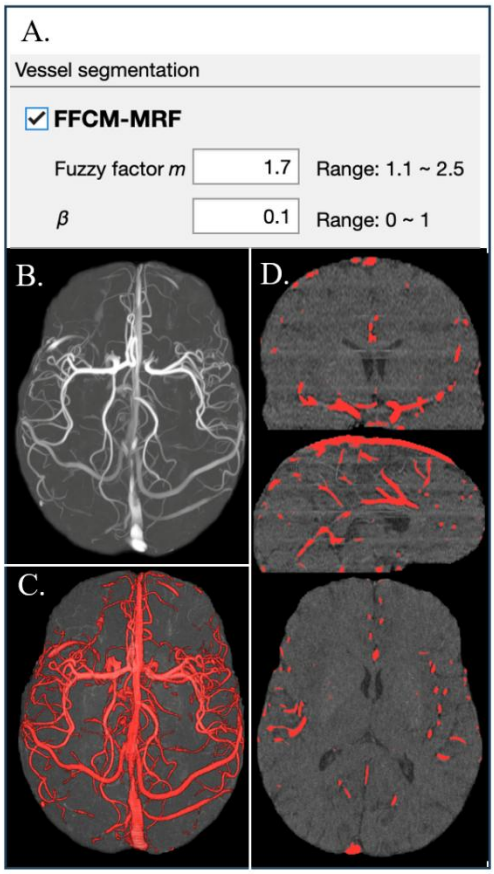

Figure 7. Vessel segmentation function. A, User interface; B, Maximum intensity projection (MIP) view of TOF-MRA image; C, 3D rendering of cerebrovascular segmentation (*MRA_brain_vessel.nii.gz*); D, 2D multi-planar views of segmentation overlaid on TOF-MRA image.

3.8 Vessel quantification

The vessel quantification module calculates morphometric features including vessel volume (density), vessel length (density), and vessel diameter (mean, maximum, minimum, and median) given a brain atlas. These features are calculated using the SimpleITK and nibabel libraries in Python. Additional features will be added in the future. Vascular morphometric features for the entire brain and/or specific brain regions can be calculated given a brain atlas in native space aligned with the individual TOF-MRA. The diameter is calculated based on resampling the vascular segmentation at equal intervals when the image is anisotropic. After the calculation is completed, a new folder named "stats" will be created in the subfolder of the selected subject. The files with "*vessel_resample.nii.gz*", "*centerline.nii.gz*" and "*diameter.nii.gz*" will also be saved in

the folder. Of these files, "*vessel_resample.nii.gz*" is the resampled file.

If users choose to calculate features at the whole brain level, the program will save an Excel file named "feature_summary.csv" with all the calculated features in the output folder. If users choose to perform calculations at multiple brain regions, the brain atlas in native space aligned with the individual TOF-MRA with the name of "atlas.nii.gz" must be in the folder where the input images are located. After the calculation finishes, an Excel file named "summary.csv" and five morphometric images will be saved in the output folder.

This module automatically looks for *MRA_brain_vessel.nii.gz* as the input file and outputs features files. The visualization results for this module are presented in Figure 8.

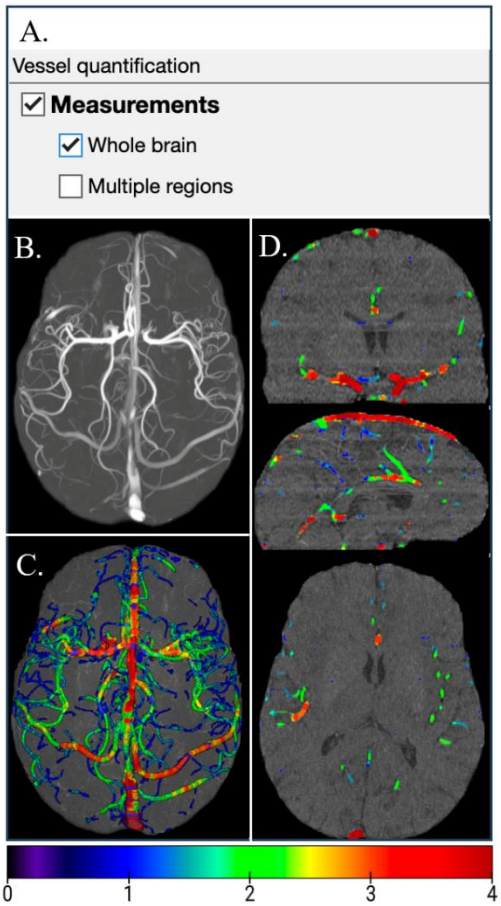

Figure 8. Vessel quantification function. A, User interface; B, Maximum intensity projection (MIP) view of TOF-MRA image; C, 3D rendering of cerebrovascular diameter map

(*diameter.nii.gz*); D, 2D multi-planar views of cerebrovascular diameter map overlaid on TOF-MRA image.

3.9 Visualization

When the FFCM-MRF vascular segmentation and quantification are completed, multi-planar views of the results will pop-up in a new window. This window includes the maximum intensity projection (MIP) view of the TOF-MRA image, cerebrovascular segmentation, and diameter map as shown in Figure 9.

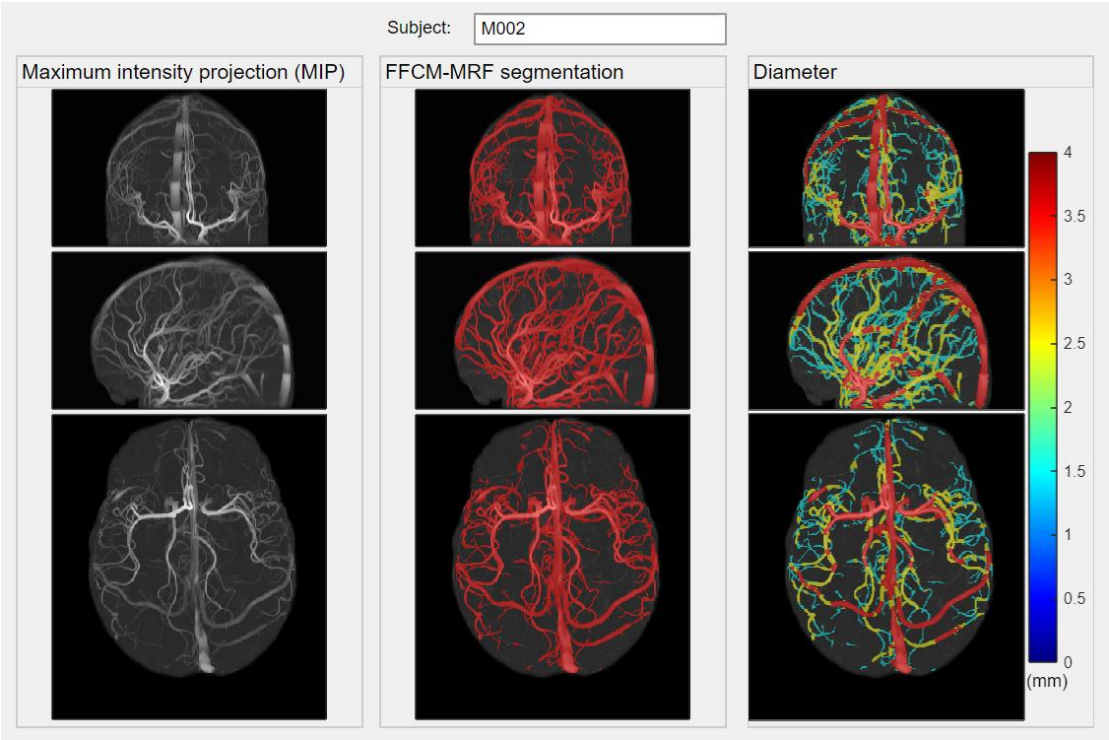

Figure 9. Visualization of the maximum intensity projection (MIP) view of a TOF-MRA image (left column), cerebrovascular segmentation results (middle column), and diameter map in mm (right column).

References

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