

## MORPHOMETRY PROTOCOLS (January 2009)

The following protocols are recommended for use with FreeSurfer. They have been tested on Siemens 1.5 T and 3 T MRI scanners (Sonata, Avanto, Allegra, Trio, TIM Trio). The 32-channel coil is recommended if available, otherwise the sequences will work with the 12-channel head matrix coil (also with 2x acceleration). 1 mm<sup>3</sup> isotropic resolution is recommended but 1.3 x 1 x 1.3 mm<sup>3</sup> is acceptable and can be used to save time or improve SNR.

### MPRAGE

The following MPRAGE protocol was developed for good contrast between gray matter, white matter and CSF per unit of acquisition time. CSF appears dark and gray matter intensity is somewhere between CSF and white matter. Since the MPRAGE is not a steady-state sequence, different spatial frequencies have different contrasts, and gray matter intensity is not exactly midway between white matter and CSF for all spatial frequencies.

This protocol evolved together with FreeSurfer and is the basic acquisition protocol for brain morphometry studies. In cases where cortical thickness is the main interest, or cortical thickness and segmentation of other brain structures is required but time is limited, the MPRAGE should be used. If more time is available, the multiecho FLASH protocol is the preferred protocol for whole-brain segmentation. Listed below is the multiecho MPRAGE (MEMPR) protocol which has better B1 distortion properties than the single echo MPRAGE (as described in the section below on bandwidth matched imaging). The multiecho MPRAGE also contains T2\* information that can be used to distinguish dura from cortical gray matter, adjacent tissues that are isointense in the standard MPRAGE protocol. If the MEMPRAGE sequence is not available, a single echo with a lower bandwidth of around 195 Hz/px is recommended.

*Sequence:* tfl\_mgh\_multiecho or tfl

*Acquisition time:* 6:03

*Voxel size:* 1.0 x 1.0 x 1.0 mm<sup>3</sup>

*Geometry:* FoV 256 mm (256 x 256 matrix), 176 sagittal slices, slice thickness 1 mm, phase encoding anterior-posterior (readout superior-inferior) (3D encoding)

*Timing:* TR 2530 ms (3T)/2730 ms (1.5T), TI 1100 ms (3T)/1000 ms (1.5T), TE 1.64/3.5/5.36/7.22 ms, bandwidth 651 Hz/px for all echoes (bipolar readout trajectory)

*RF:* Non-selective IR, non-selective excitation at 7°

*Acceleration:* 2x GRAPPA (32 ref. lines)

(fast RF and gradient mode, no oversampling, no partial Fourier encoding, no fat suppression, no partial phase encoding, use "Prescan Normalize" but no other filters and avoid regular "Normalize", use "Adaptive Combine", increase image intensity (Fourier) scaling factor to 4.0 if possible, enable RMS averaging for MEMPR if available)

*Exceptions:* if multiple echo sequence is not available, choose bandwidth of 195 Hz/px and TE will be 3.31 ms. If acceleration is disabled and resolution is 1 mm<sup>3</sup> isotropic, increase TI to 1200 ms.

### FLASH

The FLASH protocol is preferred for whole-brain segmentation where all brain structures are labeled by FreeSurfer. The acquisition requires more time – at least two separate acquisitions at two different flip angles are needed. However, the acquisition provides the data needed to calculate true quantitative T1 tissue parameters (measured in units of time) rather than the arbitrary T1-weighting that the MPRAGE provides. Proton density can also be calculated using two or more FLASH acquisitions. Listed below is the multiecho FLASH (MEF) protocol which delivers less distortion due to B0 inhomogeneities than single echo FLASH (as described in more detail in the following section). The multiecho FLASH sequence also provides T2\* information, albeit quite noisy given the short TR. If this sequence is not available, a single echo with a lower bandwidth such as 130 Hz/px can be used.

*Sequence:* gre\_mgh\_multiecho or gre

*Acquisition time:* 8:28

*Voxel size:* 1.0 x 1.0 x 1.0 mm<sup>3</sup>

*Geometry:* FoV 256 mm (256 x 256 matrix), 176 sagittal slices, slice thickness 1 mm, phase encoding anterior-posterior (readout superior-inferior) (3D encoding)

*Timing:* TR 20 ms, TE 1.85+n2.0 ms ( $n = 0, \dots, 7$ ), bandwidth 651 Hz/px for all echoes (bipolar readout trajectory)

*RF:* non-selective excitation at 30° and 5° (then 20°, then 3°)

*Acceleration:* 2x GRAPPA (32 ref. lines)

(fast RF and gradient mode, no oversampling, no partial Fourier encoding, no fat suppression, no partial phase encoding, no flow compensation, use "Prescan Normalize" but no other filters and avoid regular "Normalize", use "Adaptive Combine", increase image intensity (Fourier) scaling factor to 4.0 if possible)

*Exceptions:* if multiple echo sequence is not available, choose bandwidth of 130 Hz/px to 200 Hz/px and minimize TE.

### **Bandwidth matched imaging**

For multispectral morphometry (where more than one contrast is used to assess structures), it is important that the images align properly so that voxels match across images of different contrasts. Although the amount of B0 related distortion is small, differences between structural scans with different bandwidths are nevertheless sufficient that the borders of structures and the cortical ribbon may not be properly aligned everywhere especially in areas of higher susceptibility change.

To solve the differential distortion problem, we assembled a set of high bandwidth protocols. The higher bandwidth results in lower SNR but the SNR is recovered by acquiring and combining the multiple echoes. The chosen bandwidth of 651 Hz/px is also convenient for the T2-SPACE (T2 weighted) sequence, therefore all of these sequences can be matched to a high bandwidth and residual distortions are matched.

Listed below is the T2-SPACE protocol to accompany the above-listed protocol. Together with the MEMPR and MEF, this protocol provides a T1-weighted volume, T2-weighted volume and the data needed to estimate quantitative PD, T1 and approximate T2\*.

*Sequence:* tse\_vfl

*Acquisition time:* 5:00

*Voxel size:* 1.0 x 1.0 x 1.0 mm<sup>3</sup>

*Geometry:* FoV 256 mm (256 x 256 matrix), FoV phase 79.7%, 176 sagittal slices, slice thickness 1 mm, phase encoding anterior-posterior (readout superior-inferior) (3D encoding)

*Timing:* TR 3390 ms, TE 388 ms, bandwidth 651 Hz/px, turbo factor 115, slice turbo factor 2, echo train duration 769, echo spacing will be 3.36 ms

*RF:* non-selective excitation (flip angle mode "T2 var")

*Acceleration:* 2x GRAPPA (24 ref. lines)

(normal RF and fast gradient mode, no oversampling, no partial Fourier encoding, no partial phase encoding, no flow compensation, use "Prescan Normalize" and avoid regular "Normalize", use "Adaptive Combine", different Siemens software baselines may vary w.r.t. timing parameters and exact FoV phase)

For 1.3 x 1 x 1.3 mm<sup>3</sup> resolution, change "Phase resolution" to 75%, slice thickness to 1.33 mm and number of slices to 128 for all of the above sequences (for T2-SPACE the phase resolution may not be exactly 75%). Since this decreases acquisition time, parallel acceleration may be switched off to further increase SNR.

Custom multiecho sequences for Siemens scanners are available from the Martinos Center. The sequences and protocols are provided for free, but an indemnification document must be signed.