

# MRI Harmonisation Manual RIN – Neuroimaging Network

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# Section 1 – MRI Technologists Instructions

## **1.1 – General Introduction to MRI Procedures**

- Prior to starting to scan subjects for the study, you must submit a 'Dummy' or test scan with pdf/txt files of each sequence to the WP2 working group for evaluation and acceptance (Section 2.2). Moreover, send back the present SOP to reteimaging@istituto-besta.it adding the changes specific of your site in the "Notes changes" column of each sequence and the required information about multi-band/compressed sensing options. The SOP must be renamed adding the name of your site after the version number. Example: ReteNeuroimaging\_SOP\_WP2\_2020\_v3\_Besta.
- 2 Perform the MRI scan using the agreed upon parameters for your scanner (Section 2.3 and 2.4). These parameters should be used for all study scans.
- 3 Anonymize dicom files as explained in Section 3.1. Dicom files must be saved, when it is possible, as **STANDARD DICOM** instead of enhanced dicom. If dicom files cannot be save in the standard format, please inform the **WP2 working group** sending a mail to reteimaging@istituto-besta.it. The image headers must include all scan parameters e.g.: TE, TR, FOV, image matrix. The information recorded should be consistent with the information provided to you by the WP2 working group.

## **Important resume**:

- save DICOM as **STANDARD DICOM**,
- when you anonymize the data before loading onto the platform, leave intact all the header fields that refer to the image acquisition,
- upload only DICOM files (.dcm/.IMA); delete all other files (example: DICOM/DIR, .sr files, PS/XX files, DWI reconstructions as FA, MD maps).
- 4 Make a second copy of the MRI scan to be retained at your site for possible future data access (e.g. Regulatory Authority Inspection or routine study monitoring).



## Section 2 – MRI scanning procedures

## 2.1 – General processes

Subject comfort during the scan is important. Please, <u>take care of adequate padding and neck support</u> to reduce head motion, in according to the standard practice at your institution.

Minimizing motion artefact is important for study scan quality. Use of standard Velcro head straps and foam wedges is recommended to immobilize the head. However, other methods of stabilizing the head which are used routinely at your institution are acceptable.

For brain scanning, the subject must be positioned appropriately so that the mid-line of the brain falls in the middle of the initial sagittal localizing sequence. Follow the routine procedures at your institution for your type of scanner for placing subject in the machine and general positioning.

*Attention*: Please refer back to the previous time point study scans, for study for each subject to enable exact repositioning between scans. This step is essential for the production of comparable scans.

The 32/64 channel coil should be used if available. The same coils should be used for all patients throughout the study. The information of MRI scanner and coil are the same provided in the initial Survey of the IRCCS advanced imaging Network (see Section 4).

*Attention*: In case of software or hardware updates of your scanner, send a communication with the module in Section 5 to Rete Imaging (<u>reteimaging@istituto-besta.it</u>).

## 2.2 – Dummy scan

Before each MRI center is accepted into the study, a test scan needs to be performed. This is referred to as the "Dummy Scan". This procedure enables the WP2 Working group to determine the following:

- scanner performance is within specification for entry into study
- the MRI site is able to produce and upload the electronic data required for the study.

When your dummy (or test) scan has been approved, you will be strongly advised that you store/save the approved scan protocol for the study on your scanner to avoid any mistakes being made when performing 'on study' MRI examinations.



## 2.3 – MRI scan protocol

#### 2.3.1 – Sequences

|    |                        | Table 1              |  |
|----|------------------------|----------------------|--|
| #  | Sequence               | Alignment            | Notes  |
| 1  | Localiser              |                      | Align the transverse slice to run parallel to<br>the anterior-posterior line of the corpus<br>callosum   |
| 2  | sT1W_3D                | Sagittal             | Align the slices parallel to the median line<br>(Fig. 3a,4a,5a) covering the entire brain (from<br>top of the scalp to cervical vertebra C3)           |
| 3  | FLAIR_3D               | Sagittal             | As above   |
| 4  | DWI_3b0_AP             | Axial (bicallosal) * | Align the slices parallel to the bicallosal line<br>(Fig. 3b,4b,5b) covering the entire brain<br>(from top of the scalp to the cerebellum) *           |
| 5  | DWI_2shell_7b0_PA      | Axial (bicallosal)   | As above   |
| 6  | QSM                    | Pure Axial           | Align the slice package using a <b>pure axial</b> (0 degree) orientation covering the entire brain (from top of the scalp to the cerebellum, included) |
| 7  | RS_fMRI_SE_AP          | Axial (bicallosal)   | As sequence DWI_3b0_AP   |
| 8  | RS_fMRI_SE_PA          | Axial (bicallosal)   | As above   |
| 9  | RS_fMRI_GE_AP          | Axial (bicallosal)   | As above   |
| 10 | RS_fMRI_200vol_vox3_PA | Axial (bicallosal)   | As above;<br><b>INSTRUCTION: Talk to the subject</b> and<br>ask to relax with <b>open eyes</b> during resting<br>state                                 |
| 10 | RS_fMRI_200vol_vox3_PA | Axial (bicallosal)   | ask to relax with open eyes during resting   |

Table 1

(\*) Attention! Put the subject inside the scanner so that bicallosal alignment and pure axial alignment correspond. Bicallosal plane: place the plane parallel to the anterior-posterior line of the corpus callosum (Figure 1).

Attention: on the same subject acquire the accelerated protocol with multiband and compressed sensing, if these options are available on the scanner of the site.



## 2.3.2 – Sequence details

The implementation of the sequences was carried out in the WP2 working group. A scheme has been defined for the different vendors.

The sequence parameters suggested for the study are summarized in the following tables.

#### Structural protocol

We will acquire a T1 3D and a FLAIR 3D scans as structural data. These images will have a resolution of  $1x1x1 \text{ mm}^3$  with a number of slices between 175 and 180, sagittally oriented. The total acquisition time should be  $\approx 12$  minutes.

#### Save the T1 3D as "sT1W\_3D" and the FLAIR 3D as "FLAIR\_3D".

| Table 2   |                       |                       |                       |                 |  |  |  |
|---|-----------------------|-----------------------|-----------------------|-----------------|--|--|--|
| Parameters  |                       | sT1V                  | V_3D                  |                 |  |  |  |
| Vendors   | Philips               | Siemens               | GE                    | NOTES - changes |  |  |  |
| Sequence type   | 3D FFE                | MP-RAGE               | 3D BRAVO              |                 |  |  |  |
| Slice orientation   | sagittal              | sagittal              | sagittal              |                 |  |  |  |
| FOV [mm]  | $240 \times 240$      | $256 \times 256$      | $256 \times 256$      |                 |  |  |  |
| Resolution [mm <sup>3</sup> ]   | $1 \times 1 \times 1$ | $1 \times 1 \times 1$ | $1 \times 1 \times 1$ |                 |  |  |  |
| Matrix (Base Resolution)  | $240 \times 240$      | 256 × 256             | $256 \times 256$      |                 |  |  |  |
| Slice thickness   | 1                     | 1                     | 1                     |                 |  |  |  |
| Slice gap (mm)  | -                     | _                     | -                     |                 |  |  |  |
| n. slices   | 175 – 180 (**)        | 175 – 180 (**)        | 175 – 180 (**)        |                 |  |  |  |
| Phase Encoding direction  | AP                    | AP                    | PA (non modif)        |                 |  |  |  |
| Slice order   | Interleaved           | Interleaved           | Interleaved           |                 |  |  |  |
| NSA/Averages/NEX  | 1                     | 1                     | 1                     |                 |  |  |  |
| TR [ms]   | shortest              | 2300                  | non modif             |                 |  |  |  |
| TE [ms]   | shortest              | 2.96                  | 3.2                   |                 |  |  |  |
| TI [ms]   | non modif (855)       | 900                   | 900                   |                 |  |  |  |
| Flip angle  | 8°                    | 9°                    | 9°                    |                 |  |  |  |
| Fat Suppression   | No                    | No                    | No                    |                 |  |  |  |
| k-space coverage<br>(Halfscan/Partial Fourier)  | No                    | No                    | No                    |                 |  |  |  |
| Acceleration factor   | $SENSE \leq 2.3$      | GRAPPA=2              | ARC=2                 |                 |  |  |  |
| Filter  | CLEAR on              | Prescan Normalize on  | PURE on               |                 |  |  |  |
| Bandwidth   | 191 Hz                | 240 Hz/Px             | 31.25 kHz             |                 |  |  |  |
| Duration [min]  | ≈ <b>5.30</b>         | ≈ <b>5.30</b>         | ≈ <b>5.30</b>         |                 |  |  |  |
| Compressed sensing (CS)<br>yes/no<br>model<br>CS factor<br>TR<br>TE<br>Duration<br>Other settings |                       |                       |                       |                 |  |  |  |



(\*\*) If 180 slices are not permitted, use the maximum value in the range 175-180 slices. Use the same number of slices for sT1w\_3D and FLAIR\_3D.

|  |                              | Table 3                      |                       |                          |
|--|------------------------------|------------------------------|-----------------------|--------------------------|
| Parameters   |                              | FLAI                         | R_3D                  |                          |
| Vendors  | Philips                      | Siemens                      | GE                    | NOTES - changes          |
| Sequence type  | T2-FLAIR TSE                 | TSE VFL                      | CUBE T2-FLAIR         |                          |
| Slice orientation                                    | sagittal                     | sagittal                     | sagittal              |                          |
| FOV [mm]   | $240 \times 240$             | 256 × 256                    | $256 \times 256$      |                          |
| Resolution [mm <sup>3</sup> ]                        | $1 \times 1 \times 1$        | $1 \times 1 \times 1$        | $1 \times 1 \times 1$ |                          |
| Matrix (Base Resolution)                             | $240 \times 240$             | 256 × 256                    | $256 \times 256$      |                          |
| Slice thickness                                      | 1                            | 1                            | 1                     |                          |
| Slice gap (mm)                                       | -                            | -                            | -                     |                          |
| n. slices  | 175 – 180 (**)               | 175 – 180 (**)               | 175 – 180 (**)        |                          |
| Phase Encoding direction                             | AP                           | AP                           | PA (non modif)        |                          |
| NSA/Averages/NEX                                     | 1-2                          | 1                            | 1-2                   |                          |
| TR [ms]  | 5000                         | 4500                         | 5000                  |                          |
| TE [ms]  | 300                          | 383                          | Max (119)             |                          |
| TI [ms]  | 1700                         | <b>1800 1480</b> Auto (1575) |                       | Modify from 1800 to 1480 |
| Fat Suppression                                      | SPIR                         | Fat sat (strong)             | classic               |                          |
| k-space coverage<br>(Halfscan/Partial Fourier)       | No                           | Allowed (grey)               | ZIP 2                 |                          |
| Slice k-space coverage<br>(Halfscan/Partial Fourier) | -                            | 7/8                          | -                     |                          |
| Acceleration factor                                  | SENSE=1.4                    | GRAPPA=2                     | ARC=2                 |                          |
| Filter   | CLEAR on                     | Prescan Normalize on         | PURE on               |                          |
| Bandwidth  | 1157.4 Hz<br>(WFS=0.375 pix) | 781 Hz/Px                    | 41.67 kHz             |                          |
| Duration [min]                                       | ≈ 5-7                        | ≈ 6.00                       | ≈ 5-7                 |                          |
| Compressed sensing (CS)                              |                              |                              |                       |                          |
| yes/no<br>model                                      |                              |                              |                       |                          |
| CS factor  |                              |                              |                       |                          |
| TR   |                              |                              |                       |                          |
| TE   |                              |                              |                       |                          |
| Duration   |                              |                              |                       |                          |
| Other settings                                       |                              |                              |                       |                          |

(\*\*) If 180 slices are not permitted, use the maximum value in the range 175-180 slices. Use the same number of slices for sT1w\_3D and FLAIR\_3D.

#### **NOTE FLAIR** (change June 2020):

Modificare TI da 1800 ms a 1480ms per una migliore soppressione del segnale in CSF.



## **DWI protocol**

For the DWI data, we will use a standard single shot echo planar imaging sequence (EPI) sequence with a resolution of  $2.5 \times 2.5 \times 2.5$  mm<sup>3</sup>, 30/32 (depending on the vendor) isotropically distributed diffusion weighted directions and two diffusion weightings of 1000 and 2000 s/mm<sup>2</sup>, with number of non-diffusion weighted (b = 0 s/mm<sup>2</sup>) images as shown in table 4, in addition to a b = 0 reversed blip acquisition. Use **same sequence preparation** between DWI\_3b0\_AP and DWI\_2shell\_7b0\_PA. The total acquisition time is  $\approx 10$  minutes.

#### Save them as "DWI\_3b0\_AP" and "DWI\_2shell\_7b0\_PA".

| Table 4   |                       |                                   |  |                       |  |   |                    |
|---|-----------------------|-----------------------------------|--|-----------------------|--|---|--------------------|
| Parameters  | L                     | OWI_3b0_A                         | Р  | DWI                   | [_2shell_7b(                             | _PA   |                    |
| Vendors   | Philips               | Siemens                           | GE   | Philips               | Siemens                                  | GE**  | NOTES -<br>changes |
| Sequence type                                     | Single shot SE<br>EPI | EPI SE 2D                         | 2D SE EPI  | Single shot SE<br>EPI | EPI SE 2D                                | 2D SE EPI   |                    |
| Slice orientation                                 | transversal           | transversal                       | oblique  | transversal           | transversal                              | oblique   |                    |
| FOV [mm]  | $240 \times 240$      | $240 \times 240$                  | $240 \times 240$   | $240 \times 240$      | 240 	imes 240                            | $240 \times 240$  |                    |
| Resolution [mm <sup>3</sup> ]                     | 2.5×2.5×2.5           | 2.5×2.5× 2.5                      | 2.5×2.5×2.5  | 2.5×2.5×2.5           | 2.5×2.5×2.5                              | 2.5×2.5×2.5   |                    |
| Matrix (Base<br>Resolution)                       | 96 × 96               | 96 × 96                           | 96 × 96 *<br>(rhimsize=96<br>rhrcxres=96<br>rhrcyres = 96) | 96 × 96               | 96 × 96                                  | 96 × 96 *<br>(rhimsize=96<br>rhrcxres =96<br>rhrcyres = 96) |                    |
| Slice thickness                                   | 2.5                   | 2.5                               | 2.5  | 2.5                   | 2.5                                      | 2.5   |                    |
| Slice gap [mm]                                    | 0                     | 0                                 | 0  | 0                     | 0  | 0   |                    |
| n. slices   | 60                    | 60                                | 60   | 60                    | 60                                       | 60  |                    |
| Phase Encoding direction                          | AP                    | AP***                             | AP *<br>(pepolar = 1)                                      | РА                    | PA***                                    | РА  |                    |
| Slice order                                       | interleaved           | interleaved                       | interleaved  | interleaved           | interleaved                              | interleaved   |                    |
| TR [ms]   | 8400                  | 8400                              | 8400   | 8400                  | 8400                                     | 8400  |                    |
| TE [ms]   | 85                    | 85                                | 85   | 85                    | 85                                       | 85  |                    |
| Flip angle  | 90°                   | 90°                               | 90°  | 90°                   | 90°                                      | 90°   |                    |
| Fat suppression                                   | yes                   | yes                               | yes  | yes                   | yes                                      | yes   |                    |
| k-space coverage<br>(Halfscan/Partial<br>Fourier) | 0.75                  | 6/8                               | -  | 0.75                  | 6/8                                      | -   |                    |
| Acceleration factor                               | SENSE≤2.3             | GRAPPA=2                          | ASSET=2  | SENSE≤2.3             | GRAPPA=2                                 | ASSET=2   |                    |
| Filter  | CLEAR on              | Prescan<br>Normalize on           | PURE on  | CLEAR on              | Prescan<br>Normalize on                  | PURE on   |                    |
| n. directions/ b0                                 | 3 b0                  | 3 b0                              | 3 b0   | 32 dir/7 b0           | 30 dir/7 b0                              | 32 dir/ 4 b0  |                    |
| b [s/mm <sup>2</sup> ]                            | 0                     | 0                                 | 10 ****  | 1000/2000             | 1000/2000                                | 1000/2000   |                    |
| Bandwidth   | 1040 Hz<br>(WFS=26)   | 1108 Hz/px                        | 250kHz   | 1040 Hz<br>(WFS=26)   | 1108 Hz/px                               | 250 kHz   |                    |
| EPI factor  | 47                    | 96                                |  | 47                    | 96                                       |   |                    |
| Specific settings                                 | -                     | Coil mode:<br>Adaptive<br>Combine | <b>Option on</b> :<br>EDR e Real<br>time field adj         | _                     | <b>Coil mode:</b><br>Adaptive<br>Combine | <b>Option on</b> :<br>EDR e Real<br>time field adj          |                    |
| Note  |                       |                                   |  | use same sequer       | nce preparation a                        | s DWI_3b0_AP  |                    |
|   |                       |                                   |  |                       |  |   |                    |

Table 4



| Duration [min] | ≈1 | ≈1 | ≈1 | <b>≈ 10</b> | ≈ <b>10</b> | <b>≈ 10</b> |  |
|----------------|----|----|----|-------------|-------------|-------------|--|
| Multiband (MB) |    |    |    |             |             |             |  |
| yes/no         |    |    |    |             |             |             |  |
| model          |    |    |    |             |             |             |  |
| MB factor      |    |    |    |             |             |             |  |
| TR             |    |    |    |             |             |             |  |
| TE             |    |    |    |             |             |             |  |
| Duration       |    |    |    |             |             |             |  |
| Other settings |    |    |    |             |             |             |  |

(\*) Acquisition in research mode, asterisk indicates CV that must be manually changed for GE scanner (highlighted in red).

(\*\*) Two separate sequences are acquired. All parameters are the same except for b-value that is b=1000 (first) and b=2000 (second), use **manual prescan**.

(\*\*\*) Siemens: each time the protocol is loaded, before starting the sequence, check that the **phase encoding direction** is correct **along the AP axis** (i.e. PA in DWI\_2shell\_7b0\_PA and AP in DWI\_3b0\_AP). Even if the initial protocol has been correctly set and saved, upon reopening the coding is reset along the RL axis and must be modified.

(\*\*\*\*) GE: to acquire 3b0, it is necessary to set here an additional b=10 s/mm<sup>2</sup>.



## Quantitative susceptibility mapping (QSM) protocol

For the QSM data, we will use a multi-echo gradient echo (GE) sequence with a resolution of  $1\times1\times1mm^3$ . Using different sequences on different vendors, standardizing echo-train and TE values is quite difficult. We aim to have uniform TE1 and average TE on all sites. The total acquisition time is  $\approx$ 8'-9' minutes. **Please, make sure to save both the magnitude and the phase of the signal, for each echo**. For **GE** site, we suggest to save, for each echo, magnitude, real part and imagery part of the signal. The sequence should generate n° of echoes × n° of slices × 2 images (n° of echoes × n° of slices × 3 images for GE).

#### Save it as "QSM".

|  |   | Table 5  |   |                  |  |  |  |  |
|--|---|--|---|------------------|--|--|--|--|
| Parameters   | QSM   |  |   |                  |  |  |  |  |
| Vendors  | Philips   | Siemens  | GE  | Notes - changes  |  |  |  |  |
| Sequence type  | 3D GR MULTIECHO<br>FFE-3D                                   | 3D GRE (swi3d8r)   | 3D SWAN   |                  |  |  |  |  |
| Slice orientation                                    | transversal   | transversal  | axial   |                  |  |  |  |  |
| FOV [mm]   | $224 \times 224$  | $224 \times 224$   | $224 \times 224$  |                  |  |  |  |  |
| Resolution [mm <sup>3</sup> ]                        | $1 \times 1 \times 1$                                       | $1 \times 1 \times 1$  | $1 \times 1 \times 1$   |                  |  |  |  |  |
| Matrix (Base Resolution)                             | 224 × 224   | 224 × 224  | 224 × 224 *<br>(rhimsize = 224<br>rhrcxres = 224<br>rhrcyres = 224)                       |                  |  |  |  |  |
| Slice thickness                                      | 1   | 1  | 1   |                  |  |  |  |  |
| Slice gap  | 0   | 0  | 0   |                  |  |  |  |  |
| n. slices  | 140   | 144  | 140-150   |                  |  |  |  |  |
| Phase Encoding direction                             | RL  | RL   | RL  |                  |  |  |  |  |
| NSA/Averages/NEX                                     | 1   | 1  | 1   |                  |  |  |  |  |
| FR [ms]  | 40  | 51   | 51  |                  |  |  |  |  |
| FE medio [ms]  | Close 26.2  | 25.2   | 28  |                  |  |  |  |  |
| First TE [ms]  | 5.4   | 5.6  | 5.6   |                  |  |  |  |  |
| n. echo [n]  | 7   | 8  | 7   |                  |  |  |  |  |
| A TE [ms]  | 5.2   | = first TE (5.6)   | ~ first TE<br>(not modif)   |                  |  |  |  |  |
| Flip angle   | 18  | 18   | 18  |                  |  |  |  |  |
| Flow compensation                                    | yes   | yes  | yes   |                  |  |  |  |  |
| k-space coverage<br>(Halfscan/Partial Fourier)       | no **   | 6/8  | 0.85  |                  |  |  |  |  |
| Slice k-space coverage<br>(Halfscan/Partial Fourier) | -   | 6/8  | -   |                  |  |  |  |  |
| Acceleration factor                                  | SENSE =2  | GRAPPA =2  | ASSET =2  |                  |  |  |  |  |
| Filter   | CLEAR on  | Prescan Normalize on   | none  |                  |  |  |  |  |
| Bandwidth  | 271 Hz (WFS=1.6)  | 340 Hz/px  | 31.25 kHz   |                  |  |  |  |  |
| Specific Settings                                    | Flyback=yes;<br>To save<br>Magnitude/Phase:<br>MIP/MPR=M, P | To save Magn/Phase:<br>SWI off, Coil Combine<br>Mode=Adapt Combine | To save all echoes:<br>rhfiesta = 0 *<br>To save<br>Magn/Real/Image<br>part: rhrcctrl=13* |                  |  |  |  |  |
| Duration [min]                                       | ≈ <b>8:11</b>   | ≈ <b>8:45</b>  | ≈ 8:01  |                  |  |  |  |  |
| Compressed sensing (CS)                              |   |  |   |                  |  |  |  |  |
| yes/no   |   |  |   |                  |  |  |  |  |
| model<br>Page 9                                      | DIN Neuroime  | ging Network Harn  |   | sion v 3 June 20 |  |  |  |  |



| CS factor      |  |  |
|----------------|--|--|
| TR             |  |  |
| TE             |  |  |
| Duration       |  |  |
| Other settings |  |  |

(\*) Acquisition in research mode, indicates CV that must be manually changed for GE scanner (highlighted in red).

(\*\*) Philips does not allow to enable the halfscan parameter and to save the images of Magnitude/Phase or Real/Imaginary parts.

#### **NOTE QSM: Siemens scanner** (change June 2020)

It has been observed that recent software package N4\_VE11C\_LATEST\_20170704\_P26 on MAGNETOM Prisma scanners might prevent acquisition due to predicted PNS threshold exceeding. If this happens, please allow the system software to automatically recalculate the gradient rise times and re-save the updated protocol.



## Resting state functional imaging (rs-fMRI) protocol

For the rs-fMRI data, we will use a standard gradient echo (GE) echo planar imaging sequence (EPI) sequence with a resolution of  $3\times3\times3$  mm<sup>3</sup>, repetition time of 2400 ms and echo time of 30 ms, in addition to a GE-EPI reversed blip acquisition. Two spin echo (SE) EPI images with reversed blip acquisitions will be acquired. The total acquisition time is  $\approx$ 10 minutes. **Please, talk to the subject** and ask to relax with **open eyes** during resting state RS\_fMRI\_200vol\_vox3\_PA. Use **same sequence preparation** between RS\_fMRI\_GE\_AP and RS\_fMRI\_200vol\_vox3\_PA.

#### Save the Spin Echo sequences as "RS\_fMRI\_SE\_PA" and "RS\_fMRI\_SE\_AP".

|  |                          |  | Table 6   |                          |                                   |  |                    |
|--|--------------------------|--|---|--------------------------|-----------------------------------|--|--------------------|
| Parameters   | RS_                      | _fMRI_SE_                                | AP  | RS                       | _fMRI_SE_                         | PA   |                    |
| Vendors  | Philips                  | Siemens                                  | GE  | Philips                  | Siemens                           | GE   | NOTES -<br>changes |
| Sequence type  | Single shot SE<br>EPI    | EPI SE 2D                                | 2D SE EPI   | Single shot SE<br>EPI    | EPI SE 2D                         | 2D SE EPI  | 8                  |
| Slice orientation                                    | transversal              | transversal                              | oblique   | transversal              | transversal                       | oblique  |                    |
| FOV [mm]   | $240 \times 240$         | $240 \times 240$                         | $240 \times 240$  | $240 \times 240$         | $240 \times 240$                  | $240 \times 240$   |                    |
| Resolution [mm <sup>3</sup> ]                        | 3.0×3.0×3.0              | 3.0×3.0×3.0                              | 3.0×3.0×3.0   | 3.0×3.0×3.0              | 3.0×3.0×3.0                       | 3.0×3.0×3.0  |                    |
| Matrix (Base<br>Resolution)                          | 80 × 80                  | 80 × 80                                  | 80 × 80 *<br>(rhimsize= 80<br>rhrcxres = 80<br>rhrcyres = 80) | 80 × 80                  | 80 × 80                           | $80 \times 80 *$<br>(rhimsize= 80<br>rhrcxres = 80<br>rhrcyres = 80) |                    |
| Slice thickness                                      | 3.0                      | 3.0                                      | 3.0   | 3.0                      | 3.0                               | 3.0  |                    |
| Slice gap [mm]                                       | 0.5                      | 0.5                                      | 0.5   | 0.5                      | 0.5                               | 0.5  |                    |
| n. slices  | 40                       | 40                                       | 40  | 40                       | 40                                | 40   |                    |
| Phase Encoding direction                             | AP                       | AP**                                     | AP *<br>(pepolar = 1)   | PA                       | PA **                             | PA   |                    |
| Slice order  | default                  | interleaved                              | interleaved   | default                  | interleaved                       | interleaved  |                    |
| TR [ms]  | 2400                     | 2400                                     | 2400  | 2400                     | 2400                              | 2400   |                    |
| TE [ms]  | 30                       | 32                                       | 30  | 30                       | 32                                | 30   |                    |
| Flip angle   | 80°                      | $80^{\circ}$                             | not modif   | 80°                      | 80°                               | not modif  |                    |
| Fat suppression                                      | yes                      | yes                                      | yes   | yes                      | yes                               | yes  |                    |
| k-space coverage<br>(Halfscan/Partial<br>Fourier)    | No                       | No                                       | No  | No                       | No                                | No   |                    |
| Acceleration<br>factor                               | SENSE= 2                 | GRAPPA=2                                 | ASSET=2   | SENSE=2                  | GRAPPA=2                          | ASSET=2  |                    |
| Filter   | CLEAR on                 | Prescan<br>Normalize on                  | PURE on   | CLEAR on                 | Prescan<br>Normalize on           | PURE on  |                    |
| Dynamic scans  | 1                        | 1  | 1   | 1                        | 1                                 | 1  |                    |
| Dummies scans  | 0                        | 0  | 0   | 0                        | 0                                 | 0  |                    |
| Bandwidth  | 3114.5 Hz<br>(WFS=10.47) | 2404 Hz/px                               | 250 kHz   | 3114.5 Hz<br>(WFS=10.47) | 2404 Hz/px                        | 250kHz   |                    |
| Specific settings                                    |                          | <b>Coil mode:</b><br>Adaptive<br>Combine |   |                          | Coil mode:<br>Adaptive<br>Combine |  |                    |
| Duration [min]                                       | ≈ <b>0:15</b>            | ≈ <b>0:15</b>                            | ≈ <b>0:15</b>   | ≈ <b>0:15</b>            | ≈ <b>0:15</b>                     | ≈ <b>0:15</b>  |                    |
| Multiband (MB)<br>yes/no<br>model<br>MB factor<br>TR |                          |  |   |                          |                                   |  |                    |
| TE<br>Data 11  |                          | TNT NI                                   |   |                          | · .· • •                          | 7  |                    |



Duration Other settings

(\*) Acquisition in **research mode**, indicates CV that must be manually changed for GE scanner (highlighted in red). (\*\*) Siemens: each time the protocol is loaded, before starting the sequence, check that the **phase encoding direction** is correct **along the AP axis** (i.e. PA in RS\_fMRI\_SE\_PA and AP in RS\_fMRI\_SE\_AP). Even if the initial protocol has been correctly set and saved, upon reopening the coding is reset along the RL axis and must be modified.

#### Save the Gradient Echo sequences as "RS\_fMRI\_GE\_AP" and "RS\_fMRI\_200vol\_vox3\_PA".

|   |                        |                                   | Table 7  |   |                                   |   |                    |
|---|------------------------|-----------------------------------|--|---|-----------------------------------|---|--------------------|
| Parameters  | RS_                    | _fMRI_GE_                         | AP   | RS_fMI  | RI_200vol_v                       | vox3_PA   |                    |
| Vendors   | Philips                | Siemens                           | GE   | Philips   | Siemens                           | GE  | Notes -<br>changes |
| Sequence type                                     | GE EPI                 | EPI FID 2D                        | GE EPI<br>Multi-Phase  | GE EPI  | EPI FID 2D                        | GE EPI<br>Multi-Phase   |                    |
| Slice orientation                                 | transversal            | transversal                       | oblique  | transversal                                       | transversal                       | oblique   |                    |
| FOV [mm]  | $240 \times 240$       | $240 \times 240$                  | $240 \times 240$   | $240 \times 240$                                  | $240 \times 240$                  | $240 \times 240$  |                    |
| Resolution [mm <sup>3</sup> ]                     | 3.0×3.0×3.0            | 3.0×3.0×3.0                       | 3.0×3.0×3.0  | 3.0×3.0×3.0                                       | 3.0×3.0×3.0                       | 3.0×3.0×3.0   |                    |
| Matrix (Base<br>Resolution)                       | 80 	imes 80            | 80 	imes 80                       | $80 \times 80 *$<br>(rhimsize= 80<br>rhrcxres = 80<br>rhrcyres = 80) | 80 	imes 80                                       | 80 	imes 80                       | 80 × 80 *<br>(rhimsize= 80<br>rhrcxres = 80<br>rhrcyres = 80) |                    |
| Slice thickness                                   | 3.0                    | 3.0                               | 3.0  | 3.0   | 3.0                               | 3.0   |                    |
| Slice gap [mm]                                    | 0.5                    | 0.5                               | 0.5  | 0.5   | 0.5                               | 0.5   |                    |
| n. slices   | 40                     | 40                                | 40   | 40  | 40                                | 40  |                    |
| Phase Encoding direction                          | AP                     | AP**                              | AP *<br>(pepolar = 1)  | PA  | PA**                              | РА  |                    |
| Slice order                                       | default                | interleaved descending            | interleaved  | default   | interleaved descending            | interleaved   |                    |
| TR [ms]   | 2400                   | 2400                              | 2400   | 2400  | 2400                              | 2400  |                    |
| TE [ms]   | 30                     | 30                                | 30   | 30  | 30                                | 30  |                    |
| Flip angle  | 80°                    | 80°                               | 80°  | 80°   | 80°                               | 80°   |                    |
| Fat suppression                                   | yes                    | yes                               | yes  | yes   | yes                               | yes   |                    |
| k-space coverage<br>(Halfscan/Partial<br>Fourier) | No                     | No                                | No   | No  | No                                | No  |                    |
| Acceleration<br>factor                            | SENSE= 2               | GRAPPA=2                          | ASSET=2  | SENSE= 2  | GRAPPA=2                          | ASSET=2   |                    |
| Filter  | CLEAR on               | Prescan<br>Normalize on           | PURE on  | CLEAR on  | Prescan<br>Normalize on           | PURE on   |                    |
| Dynamic scans<br>(phases)                         | 3                      | 3                                 | 3  | 200   | 200                               | 203<br>(multi-phase)  |                    |
| Dummies scans                                     | 0                      | 0                                 | 0  | 3   | -                                 | -   |                    |
| Bandwidth   | 2556 Hz<br>(WFS=14.07) | 2404 Hz/px                        | 250 kHz  | 2556 Hz<br>(WFS=14.07)                            | 2404 Hz/px                        | 250 kHz   |                    |
| EPI factor  | 39                     | 80                                |  | 39  | 80                                |   |                    |
| Specific settings                                 |                        | Coil mode:<br>Adaptive<br>Combine |  |   | Coil mode:<br>Adaptive<br>Combine |   |                    |
| Note  |                        |                                   |  | use same sequence preparation as<br>RS_fMRI_GE_AP |                                   |   |                    |
| Duration [min]                                    | ≈ <b>0:15</b>          | ≈ <b>0:15</b>                     | ≈ 0:15   | ≈ 8   | ≈8                                | ≈8  |                    |
| Multiband (MB)                                    |                        |                                   |  |   |                                   |   |                    |
| yes/no<br>model                                   |                        |                                   |  |   |                                   |   |                    |
| mouci   |                        |                                   |  |   |                                   |   |                    |

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| MB factor      |  |  |  |
|----------------|--|--|--|
| TR             |  |  |  |
| ТЕ             |  |  |  |
| dynamic scans  |  |  |  |
| Duration       |  |  |  |
| Other settings |  |  |  |

(\*) Acquisition in research mode, indicates CV that must be manually changed for GE scanner (highlighted in red).

(\*\*) Siemens: each time the protocol is loaded, before starting the sequence, check that the **phase encoding direction** is correct **along the AP axis** (i.e. PA in RS\_fMRI\_200vol\_vox3\_PA and AP in RS\_fMRI\_GE\_AP). Even if the initial protocol has been correctly set and saved, upon reopening the coding is reset along the RL axis and must be modified.



## 2.4 – Positioning of sequences packages

Plan your scans as follow, in order to standardize the positioning of the sequence packages between the different centers and to avoid introducing confounding effects.

#### Localiser

Position the subject and perform 'localiser' scans in order to align the transverse slices for all scans to run parallel to the inferior points of the corpus callosum (bicallosal plane).

*Attention*: Put attention to place the subject inside the scanner so that **bicallosal alignment** and pure axial alignment correspond. (see **Figure 1**).

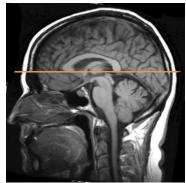


Figure 1

We recommend that you use axial, coronal and sagittal planning scans to optimally position the subject (example image showing positioning in all three planes given below).

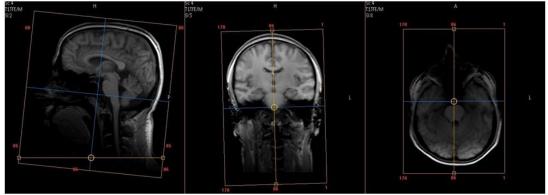


Figure 2

## Structural protocol (sT1W\_3D and FLAIR\_3D)

For the 3DT1w and FLAIR protocols, plan the scan to achieve adequate coverage of the entire brain, and also include the brainstem, and down to cervical cord level C3 if possible.

#### DWI and rs-fMRI protocols

For the axial DWI and fMRI acquisitions, plan the scan to achieve adequate coverage of the whole brain, including the scalp and cerebellum, using the anterior-posterior line of the corpus callosum (bicallosal plane) as reference. Try to put the subject inside the scanner so that this alignment correspond to the pure axial alignment (0 degree).

#### **QSM protocol**

For the QSM acquisition, plan the scan to achieve adequate coverage of the whole brain, including the scalp and cerebellum, using the pure axial alignment (0 degree).

For the detailed description and visual inspection of sequence alignment follow the subsequent figures for Philips, Siemens, and GE.



## 2.4.1 – Positioning using a 3T Philips Achieva scanner

| sT1W_3D<br>FLAIR_3D<br>(Figure 3a)   | First the scan. Include from scalp to cervical cord level C3 if possible.   |
|--|---|
| DWI_2shell_7b0_PA<br>RS_fMRI_3SE_PA<br>RS_fMRI_200vol_vox3_PA<br>(Figure 3b) | Orange arrow indicate the phase encoding direction. Include from scalp to cerebellum if possible.   |
| DWI_3b0_AP<br>RS_fMRI_3SE_AP<br>RS_fMRI_GE_AP<br>(Figure 3c)                 | $ f_{n} = 0 $ The phase encoding direction. The phase encoding direction is the phase encoding direction. The phase encoding direction is the phase encoding direction is the phase encoding direction. The phase encoding direction is the phase encoding di |
| QSM<br>(Figure 3d)   | Orange arrow indicate the phase encoding direction.     Image arrow indite the phase encoding direction. <  |



## 2.4.2 – Positioning using a 3T Siemens Skyra scanner

| sT1W_3D<br>FLAIR_3D<br>(Figure 4a)   |  |
|--|--|
|  | Yellow arrows indicate brain structures that must be included in the scan. |
| DWI_2shell_7b0_PA<br>RS_fMRI_3SE_PA<br>RS_fMRI_200vol_vox3_PA<br>(Figure 4b) |  |
|  | Orange arrow indicate the phase encoding direction.                        |
| DWI_3b0_AP<br>RS_fMRI_3SE_AP<br>RS_fMRI_GE_AP<br>(Figure 4c)                 | Orange arrow indicate the phase encoding direction.                        |
|  |  |
| QSM<br>(Figure 4d)   | Orange arrow indicate the phase encoding direction.                        |
|  | Cover the entire brain (white arrows)                                      |



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## 2.4.3 – Positioning using a 3T GE Discovery 750MR scanner

| sT1W_3D<br>FLAIR_3D<br>(Figure 5a)  | Yellow arrows indicate brain structures that must be included in the scan.                                      |
|---|---|
| DWI_1000shell<br>DWI_2000shell<br>RS_fMRI_3SE_PA<br>RS_fMRI_200vol_vox3_PA<br>(Figure 5b) | Orange arrow indicate the phase encoding direction.   |
| DWI_3b0_AP<br>RS_fMRI_3SE_AP<br>RS_fMRI_GE_AP<br>(Figure 5c)                              | Orange arrow indicate the phase encoding direction.   |
|   | orange arrow indicate the phase encoding direction.   |
| QSM<br>(Figure 5d)  | Orange arrow indicate the phase encoding direction.<br>Cover the entire brain with axial orientation (0 degree) |



## 2.5 – Clinical protocols

As defined in WP1 Working group on "Dementia patients", the basic clinical protocol includes:

| Sequence             | Slice<br>orientation | Phase<br>encoding | FOV range<br>[mm <sup>2</sup> ] or [mm <sup>3</sup> ] | ACQ Voxel range<br>[mm <sup>2</sup> ] or [mm <sup>3</sup> ] | Slice<br>thickness<br>[mm] | Slice gap<br>range<br>[mm] |
|----------------------|----------------------|-------------------|---|---|----------------------------|----------------------------|
| T1-3D                | Sagittal             | AP                | FH(240-256) x AP(240-256) x<br>RL(170-190)            | 1 x 1 x 1   | 1                          | -                          |
| T2-FLAIR-3D          | Sagittal             | AP                | FH(240-256) x AP(240-256) x<br>RL(170-190)            | 1 x 1 x 1   | 1                          | -                          |
| T2-2D FSE/TSE        | Axial                | RL                | AP(220-256) x RL(220-256)                             | (0.5-0.7) x (0.5-0.7)                                       | 4                          | 0-0.4                      |
| SWI-3D ^             | Axial                | RL                | AP(220-256) x RL(220-256) x<br>FH(120-180)            | (0.5-0.7) x (0.5-0.7)                                       | 1.5                        | -                          |
| or<br>SWI-2D ^<br>or | Axial                | RL                | AP(220-256) x RL(220-256)                             | (0.5-0.7) x (0.5-0.7)                                       | 1.5                        | 0-0.4                      |
| T2*-2D ^             | Axial                | RL                | AP(220-256) x RL(220-256)                             | (0.5-0.7) x (0.5-0.7)                                       | 4                          | 0-0.4                      |
| DWI                  | Axial                | AP/RL             | AP(240-256) x RL(240-256)                             | (1.5-2) x (1.5-2)   | 4                          | 0-0.4                      |

Only sequences in **red** need to be added to the harmonized protocol.



# Section 3 – MRI scanner: software and hardware update

| Site: | Site code: |
|-------|------------|
|-------|------------|

## MRI scanner information

Date of software/hardware intervention:

## □ Hardware interventions

Describe the type of hardware intervention:

|             | th (T):                  |
|-------------|--------------------------|
| Vendor:     |                          |
|             |                          |
|             | allation:                |
| Gradients   | Maximum Amplitude:       |
|             | Maximum Slew Rate:       |
|             |                          |
|             | □ Software interventions |
| Software ve | rsion:                   |

Name: \_\_\_\_\_

Signature: \_\_\_\_\_

Date: \_\_\_\_\_

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