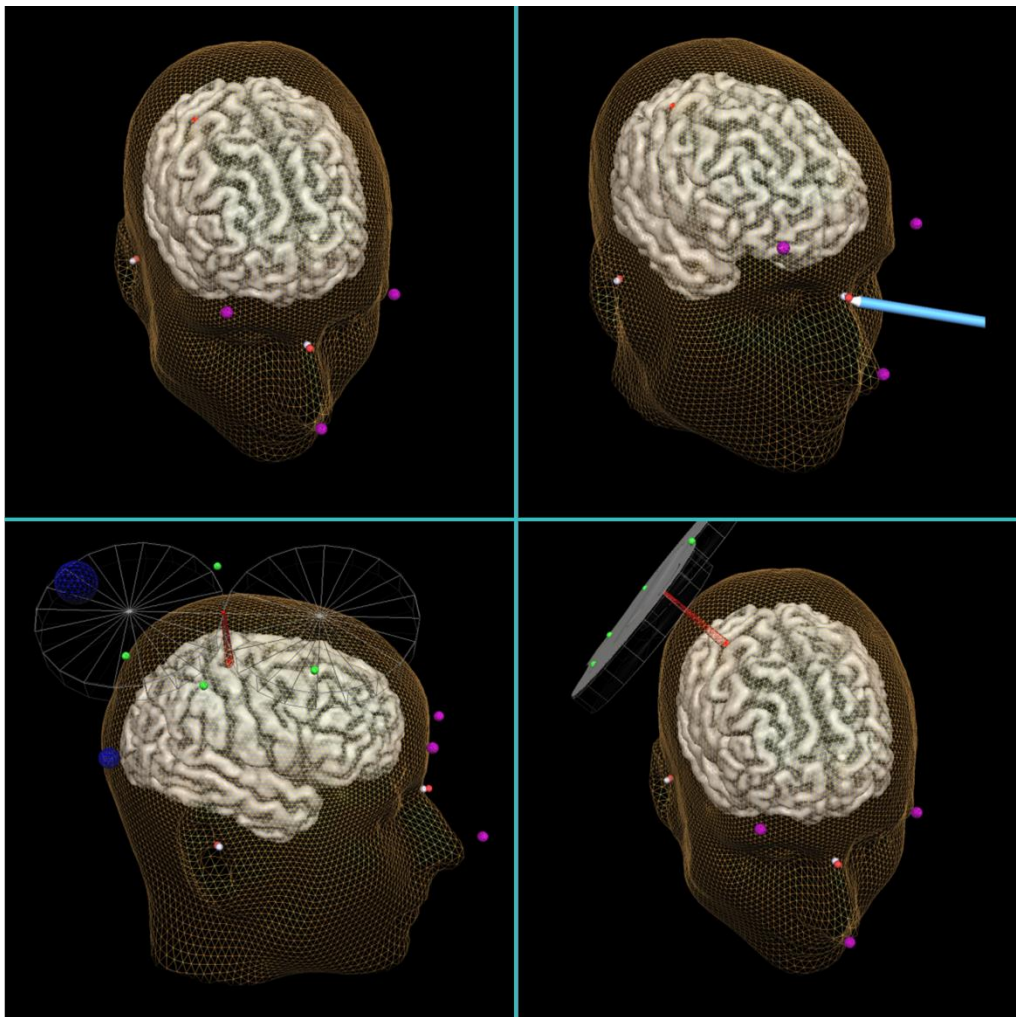

TMS NEURONAVIGATOR (ZEBRIS)



Getting Started Guide

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About This Document

Preface

Welcome to the Getting Started Guide for the TMS Neuronavigator! While TMS neuronavigation has been part of the widely used multi-modal neuroimaging software package BrainVoyager QX, the TMS Neuronavigator is a standalone neuronavigation-focused software package. With a simplified application-focused user interface, this new software makes neuronavigation easier. The TMS Neuronavigator uses the same file formats as BrainVoyager QX. Jointly used, both software packages offer powerful application and analysis options.

This guide can be used as a self-study tutorial and describes the essential features of the software and the complementary hardware components.

Explanation of symbols used in this tutorial

| | | | | | |
|---|---|---|---|---|---|
|  |  |  |  |  |  |
| setup | information | click | type | save | stop |

Hardware and Software Requirements

The TMS Neuronavigator runs on Windows Vista/7/8, both 32-bit and 64-bit versions. Please take the following hardware requirements into account:

| | |
|-----------------------|--|
| CPU: | multi-core processor |
| Memory: | 4+ GB |
| Graphics: | NVIDIA GeForce or Quadro, ATI Radeon or equivalent with 512+ MB dedicated memory |
| USB 2.0 or 3.0 Ports: | minimum 4 |
| Monitor: | diagonal: minimum 20" |
| Primary Storage: | 500+ GB hard drive, maybe also an external second hard drive (1 TB) |

Contact

Brain Innovation bv

Visiting and Mail Address:
Oxfordlaan 55
6229 EV Maastricht
The Netherlands

www.brainvoyager.com
support.brainvoyager.com
Phone: +31 (0)43 2100120
Fax: +31 (0)43 2100121

Please contact our Sales team for questions regarding Sales/Licensing/Repair:

sales@brainvoyager.com

Provide license ID, computer system specifications, and describe the faulty part or malfunction of the system. Please also contact the sales team for legal terms and conditions (document available).

Please contact our support team for questions regarding the integration of new TMS coil models in the software, the usage of the software and in case you encounter an error in this document or in the software:

support@brainvoyager.com

We are happy to answer your questions to the best of our knowledge.

For more general TMS or Neuronavigation questions you are welcome to contact Prof. dr. Alexander Sack:

a.sack@maastrichtuniversity.nl

Zebris Medical GmbH

Visiting address:
Max-Eyth-Weg 42
88316 Isny, Germany

Contact via:
URL: www.zebris.de
Phone: +49 (0)7562 9726 0
Fax: +49 (0)7562 9726 50

Please contact Zebris Medical for questions concerning the CMS20 system and its related hardware components.

Tutorial Data

Scanning Session Information

MRI Scanner: Siemens 3T MAGNETOM Prisma
RF Coil: 64-Ch Head-Neck Coil

Intra-Session Anatomical 3D Scan (MPRAGE)

Voxel Resolution: 1.0 x 1.0 x 1.0 mm³
Number Of Slices: 192
TR: 2250.0 ms
TE: 2.21 ms
Matrix: 256 x 256
Orientation: Sagittal
First Image: miclue_140514_GSG -0002-0001-00001.dcm

Experiment

Conditions:

Finger Tapping

Fixation
Right Index Finger
Left Index Finger

Stimulation Protocol

1 run, block design

Number of Slices: 37
Slice Thickness: 3.0 mm
Gap Thickness 0.0 mm
FoV: 196 mm x 196 mm
Matrix: 98 x 98
Number of Volumes: 290
TR: 2000.0 ms
TE: 25.0 ms

First Image: miclue_140514_GSG
-0010-0001-00001.dcm

| Volume Number | Condition Name |
|---------------|--------------------|
| 1 - 10 | Rest |
| 11 - 20 | Left Index Finger |
| 21 - 30 | Rest |
| 31 - 40 | Right Index Finger |
| 41 - 50 | Rest |
| 51 - 60 | Left Index Finger |
| 61 - 70 | Rest |
| 71 - 80 | Right Index Finger |
| 81 - 90 | Rest |
| 91 - 100 | Right Index Finger |
| 101 - 110 | Rest |
| 111 - 120 | Right Index Finger |
| 121 - 130 | Rest |
| 131 - 140 | Right Index Finger |
| 141 - 150 | Rest |
| 151 - 160 | Left Index Finger |
| 161 - 170 | Rest |
| 171 - 180 | Right Index Finger |
| 181 - 190 | Rest |
| 191 - 200 | Left Index Finger |
| 201 - 210 | Rest |
| 211 - 220 | Right Index Finger |
| 221 - 230 | Rest |
| 231 - 240 | Left Index Finger |
| 241 - 250 | Rest |
| 251 - 260 | Left Index Finger |
| 261 - 270 | Rest |
| 271 - 280 | Left Index Finger |
| 281 - 290 | Rest |

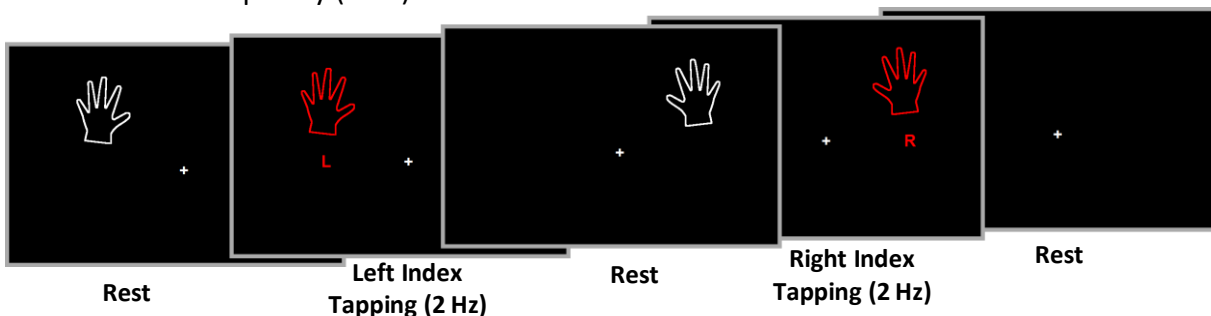
Experimental Design

Stimuli were presented with StimulGL, a free and open-source stimulus presentation framework (<https://sites.google.com/site/stimulgl/home>). The finger tapping experiment described in this document is made available as an example tutorial by the StimulGL installer. Please contact Sven Gijzen (sven.gijzen@maastrichtuniversity.nl) for more details.

The participant was presented with alternating blocks of rest and task.

During rest a white fixation cross was presented in the center of the screen together with a drawing of a hand left or right to the cross- depending on the subsequent task block (tapping with left or right index finger). This ensured that the participant knew in advance which type of finger tapping would follow next.

During task blocks the participant viewed a fixation cross with a flickering red image of a hand and the letter “L” left or the letter “R” right to the cross. The participant was instructed to perform finger tapping with the index finger of the same side as indicated on the screen and with the same frequency (2 Hz).



Part I Parts and Setup

1. Components of the Neuronavigation System

The **TMS Neuronavigator** consists of the TMS Neuronavigator software (Brain Innovation BV, The Netherlands) and an ultrasound-based position and motion measuring system CMS20 (Zebris Medical GmbH, Germany). Please check whether you have all items described below readily available.

1. The TMS Neuronavigator software (TMS NN) (including the license information)
2. The CMS20 position and motion measuring system with the following components:

2.1. The CMS20 Basic Unit

connecting the ultrasound transmitters, the ultrasound microphones and the computer running the TMS NN



2.2. The Power Adapter for the Basic Unit

Input: 100-240V, Output 18V/840mA



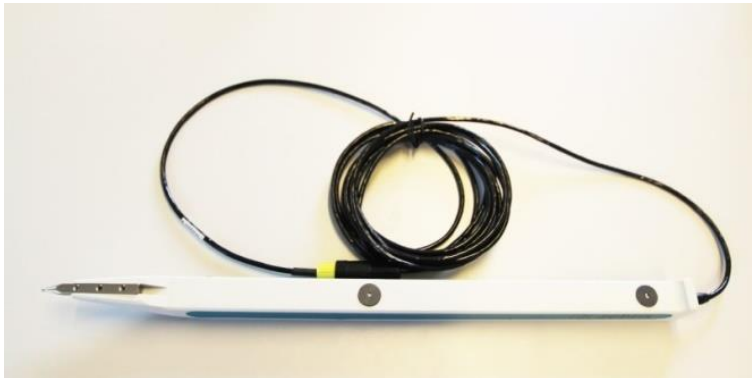
2.3. **A USB Cable**

connecting the Basic Unit with the computer running the TMS NN



2.4. **The Digitizer Stick (or Pointer)**

with two ultrasound transmitters, used for the coregistration of the head mesh and TMS coil mesh with the real head and TMS coil



2.5. **Three Single Ultrasound Transmitters (Head Marker 1 -3)**

which will be attached to the participant's forehead and nose, providing real-time information about the head position



2.6. **One TMS coil holder**

can be attached to most TMS coil handles (diameter: 25 – 30 mm)



- 2.7. **One Triple Ultrasound Transmitter (Coil Marker 1- 3)**
screwed to the TMS coil holder, provides information about the TMS coil position



- 2.8. **The Measuring Unit MA-XX 2 with the Floor Stand**
including three ultrasound microphones, receiving ultrasound signals from the transmitters (head markers, triple coil marker, Digitizer Stick)



- 2.9. **Adhesive Stickers**
to attach the three single ultrasound markers to the participant's face



All Hardware Components



2. Setup Instructions

- i** The CMS20 basic unit is the heart of the system and connects all components required for TMS neuronavigation.

Please note that the best measurement conditions exist in large rooms due to reduced sound reflection.

Simple measures for sound absorption may be taken to improve the measurement conditions:

- 1) Avoid, if possible, smooth metallic and glass surfaces, as well as parquet flooring or tiles.
- 2) Put up curtains and use a carpet if possible.

1. Start the setup of the neuronavigation system by connecting all ultrasound markers as well as the measuring unit to the correct plug-positions of the basic unit.
 The connectors have to be turned such that the painted arrows are on top before plugging them into the same-colored plug positions of the basic unit.



Grey: Measuring unit

Blue: Single head markers

Yellow: Digitizer Stick



LED: indicating connection with computer and power socket

Red: Triple coil marker



Afterwards turn the basic unit around and attach the power adapter and the USB cable.

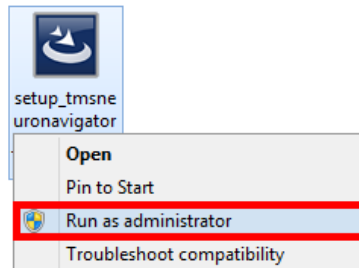


!!! Do not connect the USB cable to the computer yet !!!

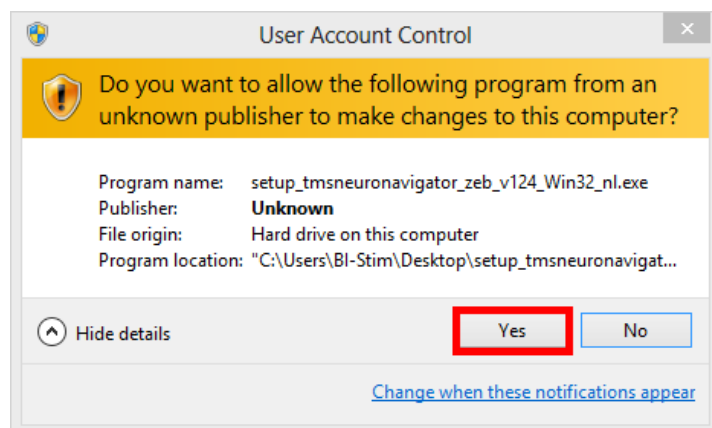


3. Installation of the Software

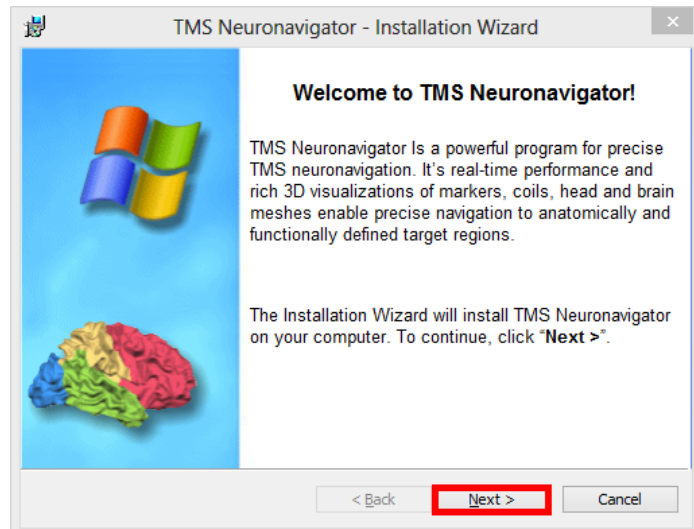
1. Place the TMS Neuronavigator installation CD into the CD/DVD drive of your computer, copy the installer to the desktop and run the installer as administrator:
[setup_tmsneuronavigator_zeb_v14_Win32.exe](#)



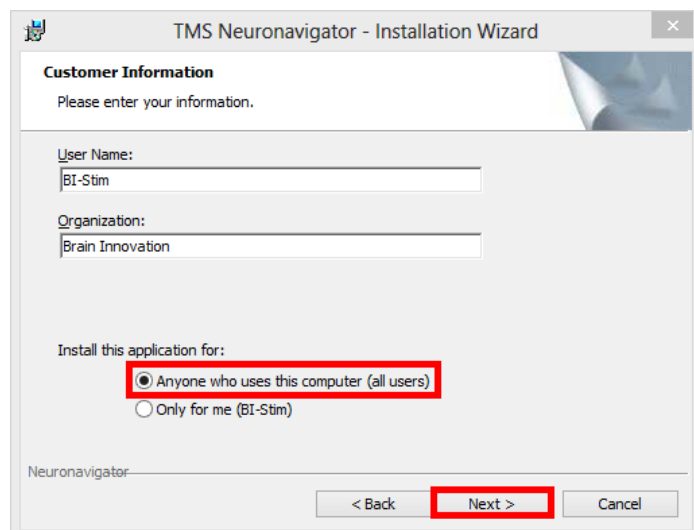
2. Ignore the Windows User Account Control Warning and click on “Yes”.



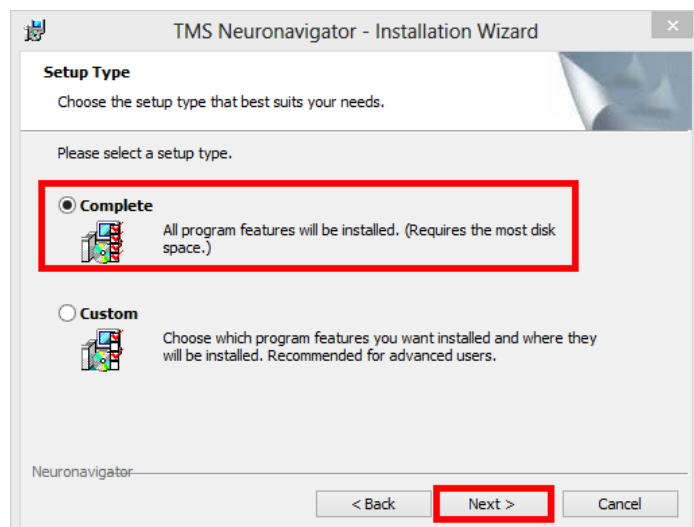
3. Follow the instructions of the installer.



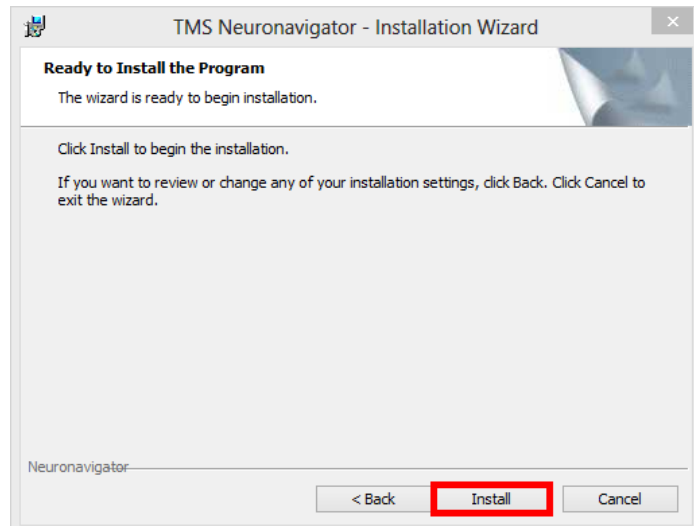
4. Make sure the TMS Neuronavigator is installed for all user accounts on the computer.



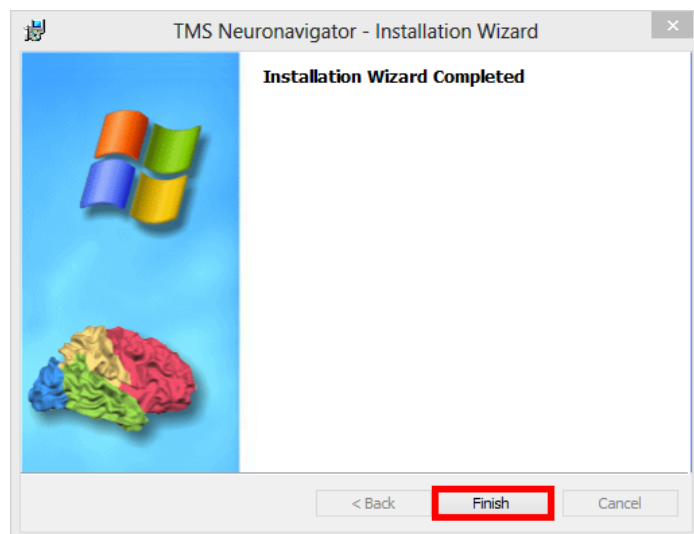
5. Keep the default choice "Complete" and confirm with "Next".



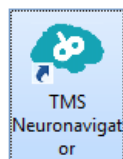
6. Install the TMS Neuronavigator by clicking on “Install”




7. Finish the installation.



8. Start the TMS Neuronavigator by double clicking on the “TMS Neuronavigator” icon on the desktop.

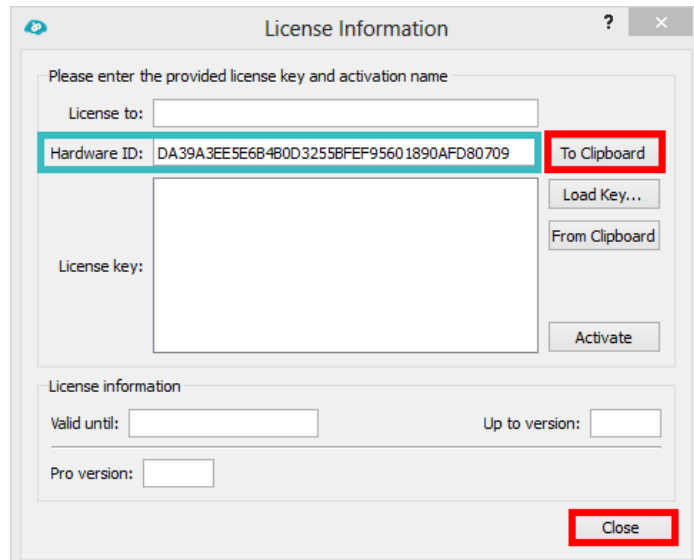


9.  A new window will open for software license specifications.

Please copy the hardware ID to the clipboard via the “To Clipboard” button and paste it in an email to:

support@brainvoyager.com

Please also provide the name, email address and postal address of the license owner.



License Information

Please enter the provided license key and activation name

License to:


Hardware ID: DA39A3EE5E6B4B0D3255BF95601890AFD80709


License key:

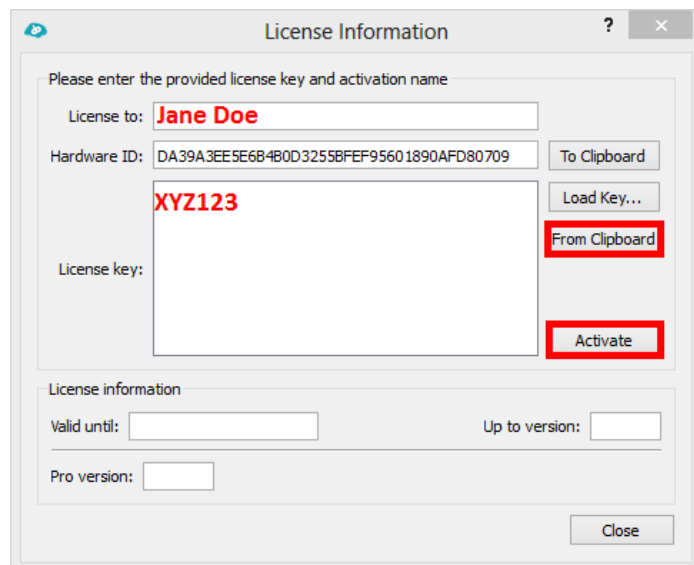
License information

Valid until: Up to version:

Pro version:

10.  The Brain Innovation support team will generate a license key for you and send it via email to the license owner.

11.  Open the TMS Neuronavigator via the icon on the desktop. In the appearing window specify the field “License to”: use the name of the license owner that you sent to Brain Innovation. Copy and paste the license key in the field “License key:” by clicking on “From Clipboard” and “Activate” the license.



License Information

Please enter the provided license key and activation name

License to: Jane Doe

Hardware ID: DA39A3EE5E6B4B0D3255BF95601890AFD80709


License key: XYZ123

License information

Valid until: Up to version:

Pro version:

4. Installation of the Zebris CMS20 Driver

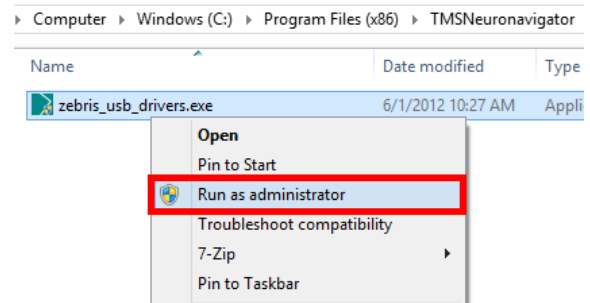
1.  After installing the software, the hardware driver for the position measuring CMS20 system has to be installed. If you have access to the internet, simply connect the CMS20 Basic Unit to the computer via the USB cable. Windows will automatically detect the new hardware and install the correct driver.

If you do not have access to the internet, please follow the instructions below:

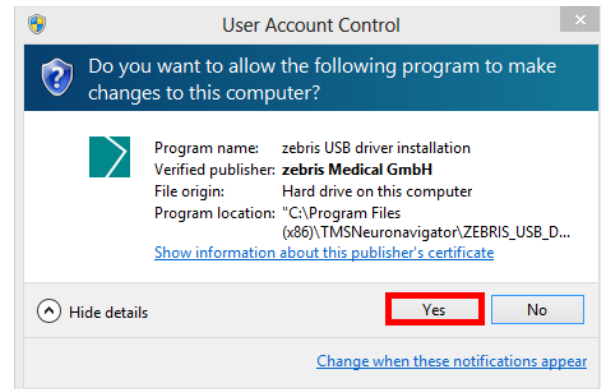
Preparation of Data


2. You can find the installer for the latest driver in the following directory:
C:\Program Files
(x86)\TMSNeuronavigator\
ZEBRIS_USB_DRIVER


Please launch the installer with administrator rights.




3. Ignore the Windows User Account Control Warning and click on "Yes".



 Note: The driver will be installed in the background.


4.  In order to see whether the driver installation has been successful, attach the USB cable from the CMS20 Basic Unit to the computer.

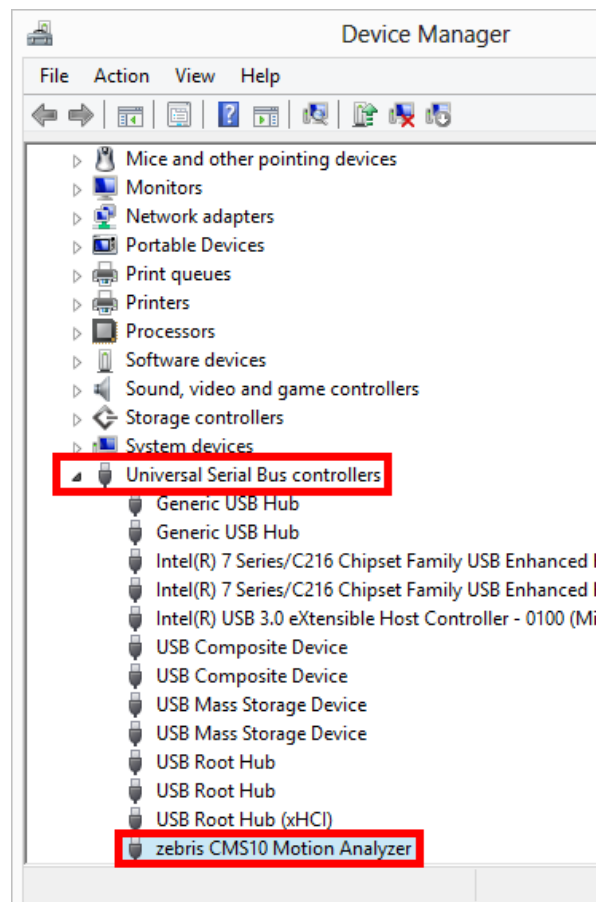
 Open the Windows Device Manager:

Windows 8: Go to Settings -> Control Panel -> System and Security -> Device Manager (in System category)

Windows 7: Start button -> Control Panel -> System and Security -> Device Manager

Windows Vista: Start button -> Control Panel -> System and Maintenance -> Device Manager

 If you see an entry in the Universal Serial Bus controllers that looks like the one on the right, the driver installation has been successful and the CMS20 system should work properly.





Part II Preparation of Data

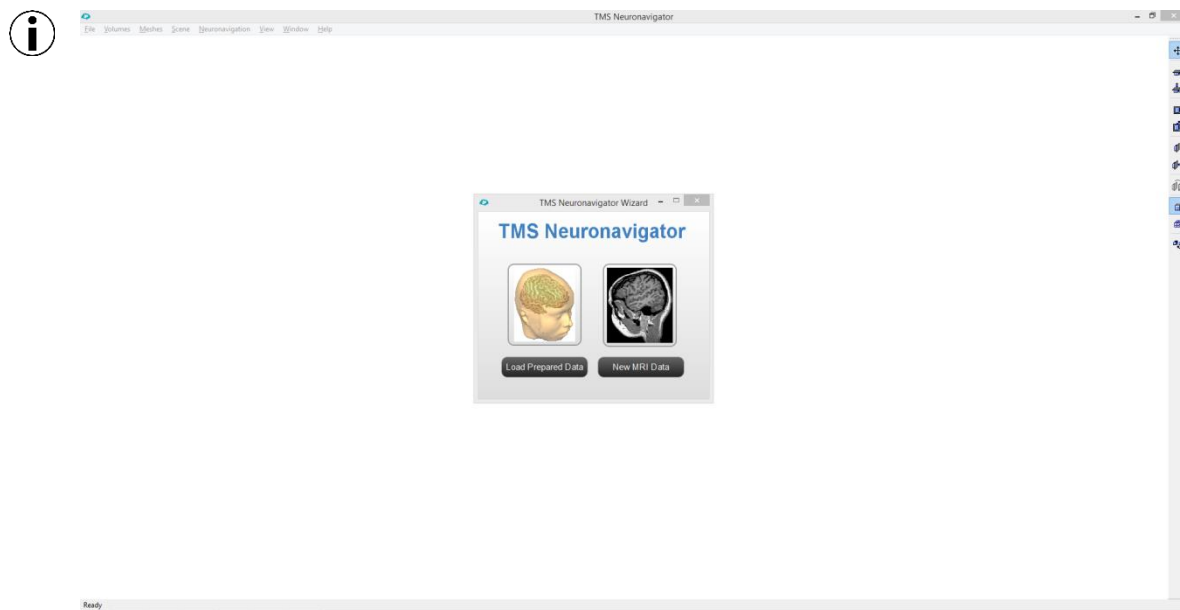
In order to use the TMS Neuronavigator it is necessary to acquire a single high-resolution T1-weighted structural MRI dataset for each participant and prepare it for neuronavigation.

The data preparation pipeline is a mainly automatic process and requires a minimum of user input and control. The following section describes the single steps involved in the preparation of an anatomical data set for neuronavigation.

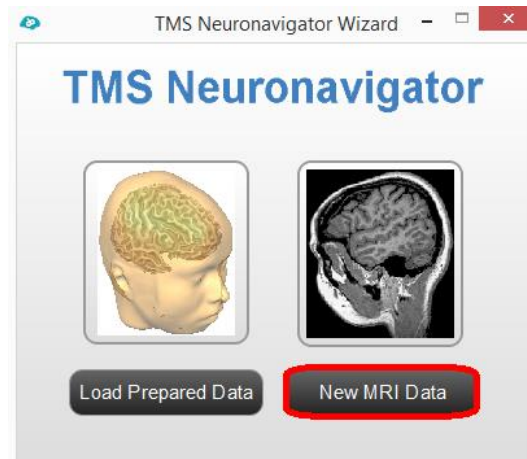
Some of the steps described in Part II can be started manually if necessary. Please see the Appendix of this tutorial for details.

1. Creation of a 3D Anatomical Project

1. As a first step open the TMS Neuronavigator. 
 The dialog that will open automatically is the so-called 'Wizard'. This wizard gives you the option to either load an already prepared data set of a participant ('Load Prepared Data') or to create a new data set for a subject ('New MRI Data').



2. When you start data preparation by choosing “New MRI Data”, the TMS Neuronavigator will import the original MRI data and guide you step by step through the creation of all files required for TMS Neuronavigation.

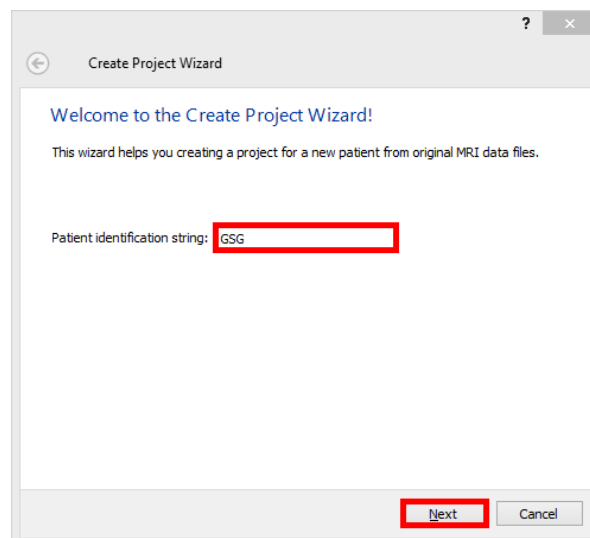


3. First you need to specify an identifier for the patient data set you’re about to import.

i You can use any string, but it is important that the identifier is unique.

The names of all subsequently created files will start with the same patient identifier, followed by an underscore to separate it from the remainder of the filename, i.e. “GSG_...”.

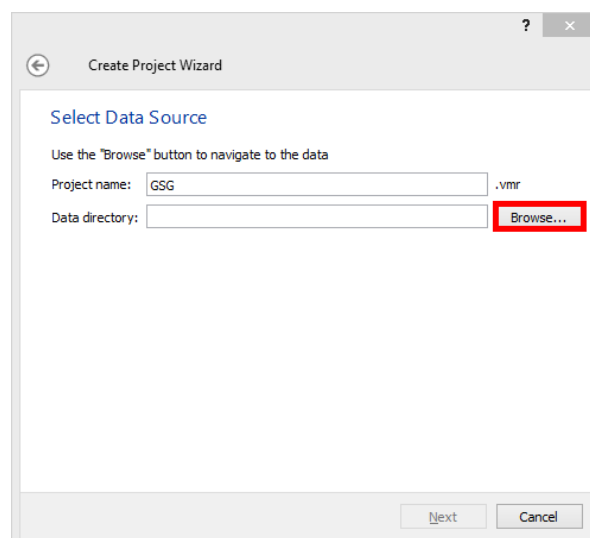
i Click “Next” to continue.





4. The next window displays the resulting project name (GSG.vmr). VMR stands for *Volume Magnetic Resonance* and describes a project type that stores the data belonging to a high-resolution T1-weighted anatomical 3D scan of the brain.

i Use the “Browse” button to locate the directory with the raw files on your hard disk.

i The TMS Neuronavigator requires raw files in a specific format, namely DICOM or .dcm/.ima files. Please make sure to export your raw files as DICOMs from the scanner. In case this is not possible please contact support@brainvoyager.com




Preparation of Data

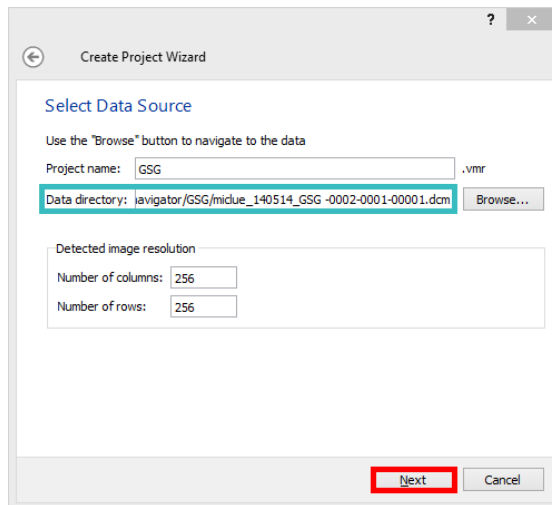
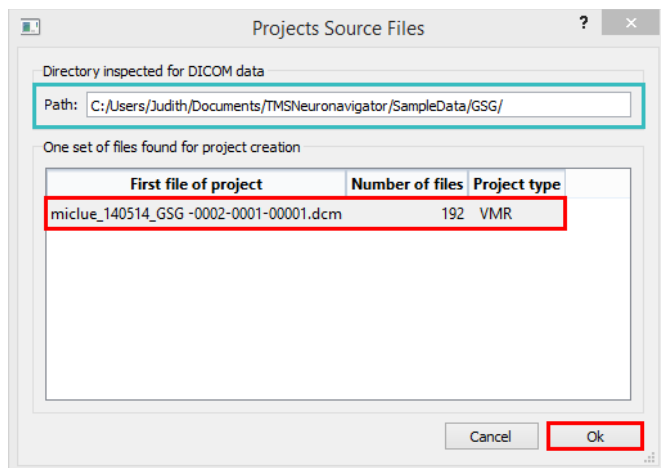
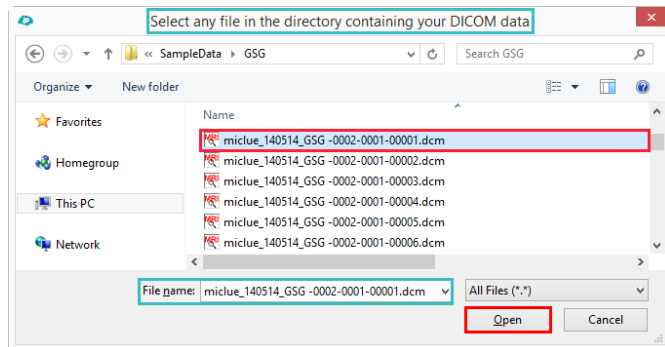
5. After navigating to the correct directory location, select any raw file and click on “Open”.

 It is possible that a new dialog appears asking you to rename the DICOM files. If this is the case, please confirm with YES.

In the current example the renaming step is not necessary.

6. The “Projects Source Files” window shows you how many different sets of DICOM files are located in the chosen directory. In this example there is just one, an anatomical data set (VMR). Select this data set and note that 192 DICOM files belong to that structural scan. Now close the window by clicking “OK”.

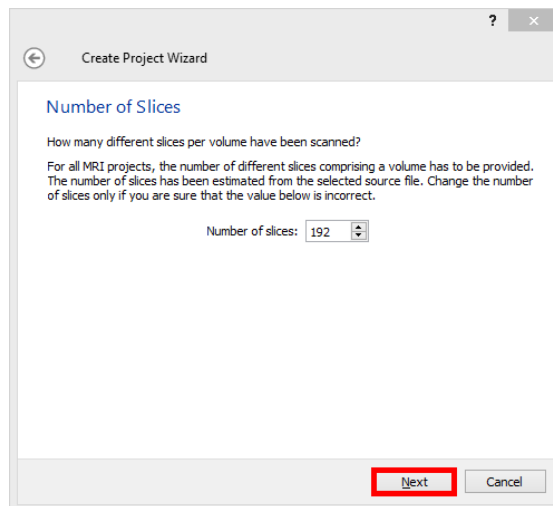
7. Now the data directory field contains the link to the first DICOM file of the MRI scan.

-  Click “Next” to continue to the next step.



8. This window displays the number of slices in the data set, which equals the number of source files in the current example.

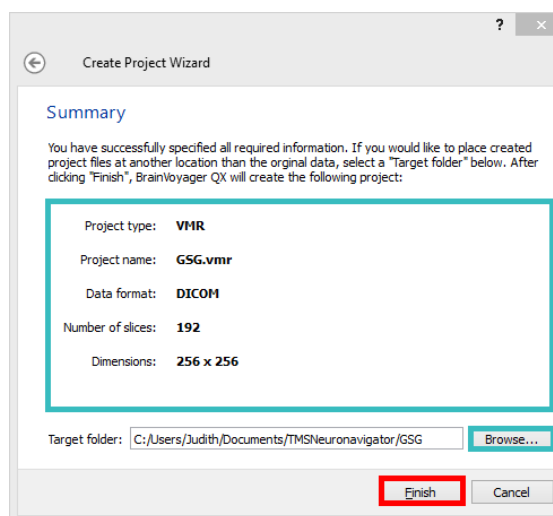
Continue to the next window via “Next”.



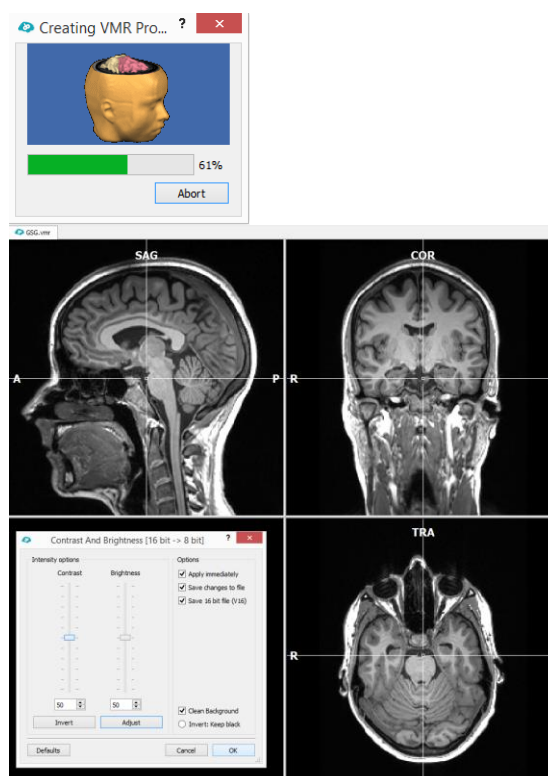
9. The last window presents a summary of the most relevant information specified in the previous windows.

You also have the option to specify a different target folder by clicking on “Browse”.

After verifying that the information is correct, click on “Finish” to build the project.



- i** The output of the project creation is a file called GSG.vmr.



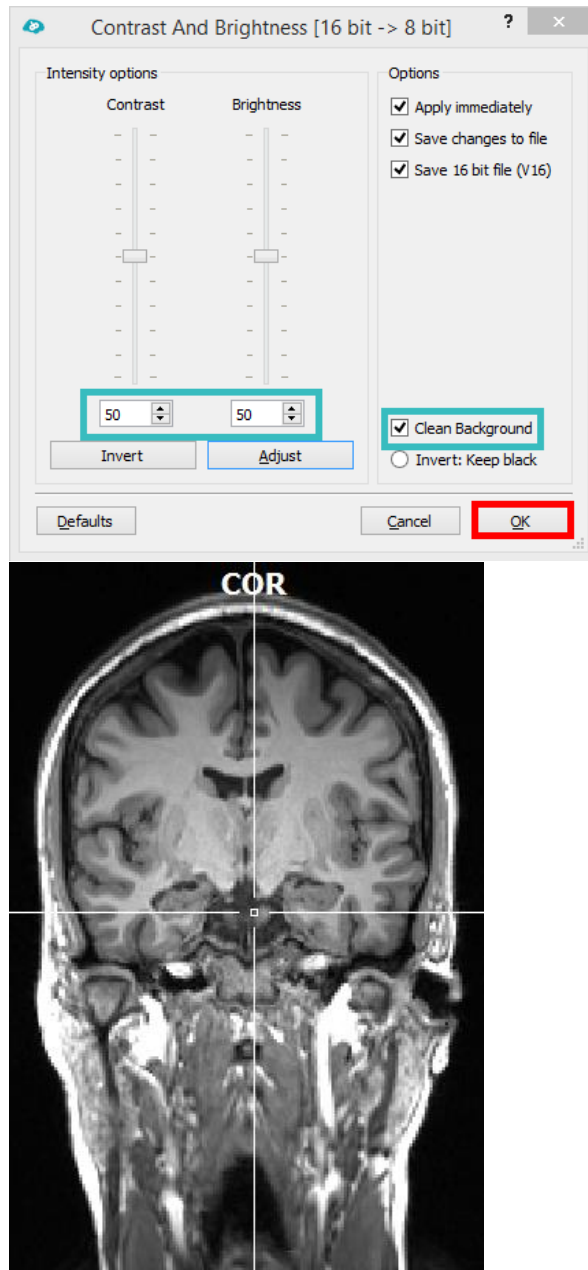
- After the process is finished, you will be asked to adapt the contrast and brightness of the data set in the “Contrast and Brightness” dialog. Please use the spin boxes as shown on the right.

In the optimal data set the white matter (WM) has intensity values around 160 and the grey matter (GM) around 100.

Note: The maximum intensity is white with an intensity of 225, while the minimum intensity is black, coded with 0.

The optimal intensity distribution cannot be easily checked in the current display.

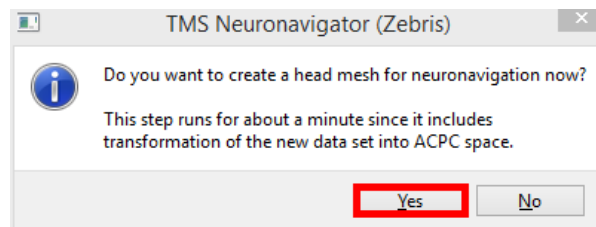
However, something that you can easily check is whether there is a clear difference between GM and WM voxels. If this is the case, close the dialog by clicking on “OK”.



2. Automatic ACPC Transformation

- The next step starts automatically with the dialog presented on the right.

Confirm with “Yes”



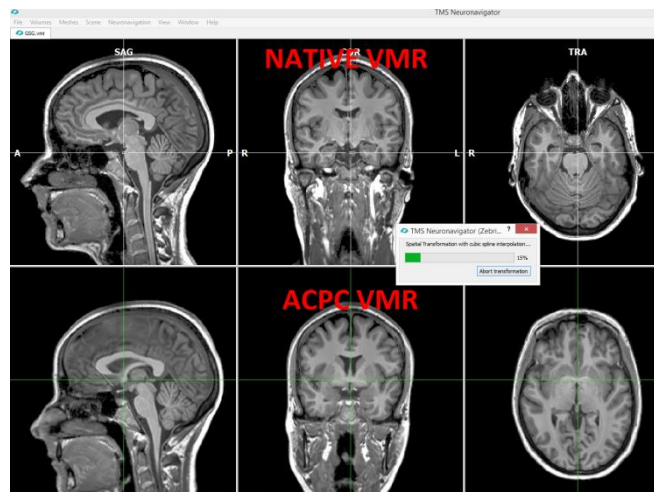
- For TMS Neuronavigation it is advised to **avoid any nonlinear anatomical data normalization** (i.e. Talairach or MNI normalization), as the size of the brain is changed during the normalization procedure. As a consequence precise neuronavigation based on the anatomical MRI data is not possible anymore, as the relationship between the physical world and the navigated model world is lost.

- ⓘ However, it is advised to bring the cerebrum into a **normalized orientation** by translating and rotating the 3D anatomical data set. This re-orientation procedure is called **ACPC transformation (AC = anterior commissure, PC = posterior commissure)** and is automatically performed by the TMS Neuronavigator. Note that this is a rigid transformation, i.e. the dimensions and hence the size of the subject's head and brain do not change.

The following steps are included:

First the AC point is determined and the brain is translated so that AC becomes the origin (center) of the data set. Afterwards, the brain is rotated around the AC point, such that the AC and PC are on the same axial plane. Furthermore, the brain is rotated around the AC-PC axis until the vertical axis separates the left and right hemisphere. The x axis runs from the left to the right hemisphere through the AC. The y-axis connects the AC and PC and runs from anterior to posterior. The z axis runs through the AC from inferior to superior.

- ⓘ During this procedure three new files are created:
- 1) GSG_aACPC.vmr
(this file is used for the surface reconstruction of the subject's head and is linked in the Patient Data Base)
 - 2) GSG_ToMSP.trf,
GSG_aACPC.trf
(these files contain the transformation parameters to bring the data set from native to ACPC space, TRF = Transformation)

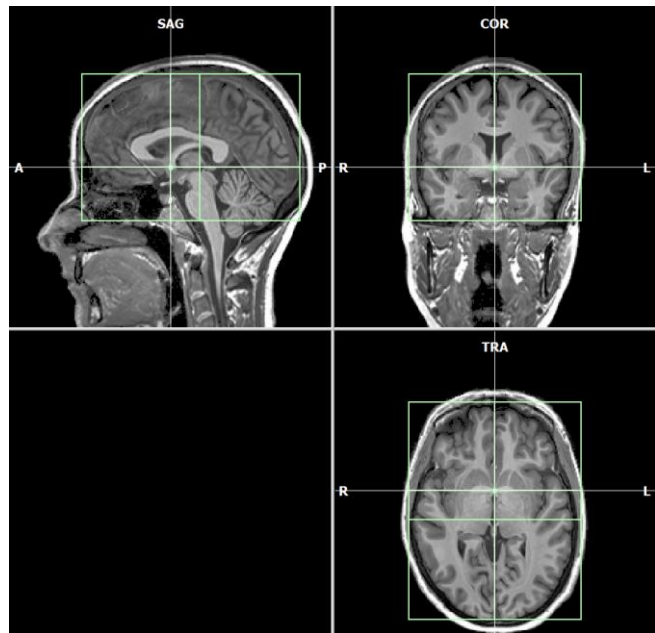


The resulting GSG_aACPC.vmr is shown on the right

- ⓘ In a second automatic step, eight reference points of the subject's cerebrum are defined which are usually used for Talairach transformation. Here, however, these individual reference points – the so called **Talairach landmarks** – are only specified to provide the option to the user to define TMS target points based on standard Talairach coordinates.
- The individual Talairach landmarks are then used to back-project the standard Talairach coordinate of the TMS target point to the individual brain. **NO Talairach transformation of the data set is performed, rather a back-transformation of the Talairach coordinate to the individual ACPC space is performed!**

- i** The result of this step is a transformation file (GSG_aACPC.tal) with the coordinates of the individual Talairach landmarks of that participant:

- 1) Anterior Commissure (AC)
 - 2) Posterior Commisure (PC)
- The border points of the cerebrum:
- 3) Most Anterior Point (AP)
 - 4) Most Posterior Point (PP)
 - 5) Most Superior Point (SP)
 - 6) Most Inferior Point (IP)
 - 7) Most Right Point (RP)
 - 8) MostLeft Point (LP)

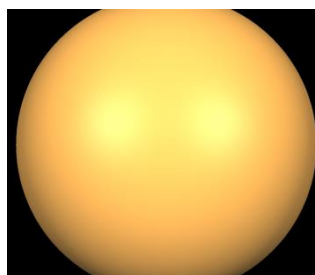


The green box in the image on the right represents the individual Talairach landmarks for the example subject.

3. Surface Reconstruction of the Head

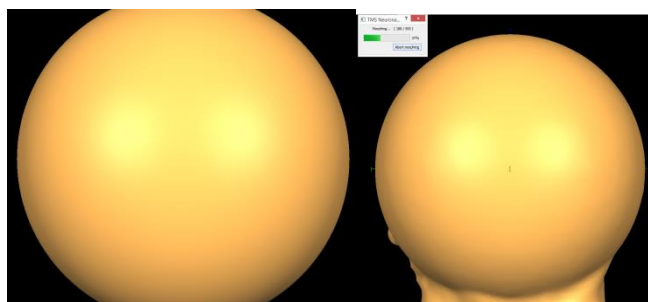
- i** In the next step a surface reconstruction of the head is created, the so-called head mesh. In general, a mesh is a collection of vertices, edges and faces that represent the shape of an object. The head mesh creation is part of the automatic data preparation pipeline.

- i** In order to generate a head mesh, a spherical mesh is created first.



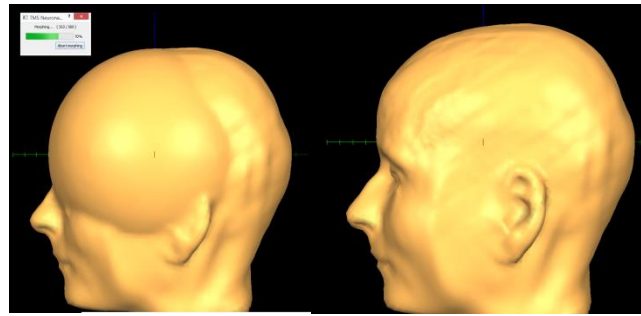
- i** An iterative morphing procedure is used to generate a head mesh out of the sphere mesh, i.e. the sphere will shrink continuously – only stopping when it finds non-background (i.e. high-intensity) values.

The images on the right show different stages of the morphing process.




The result of the head mesh creation are two files:

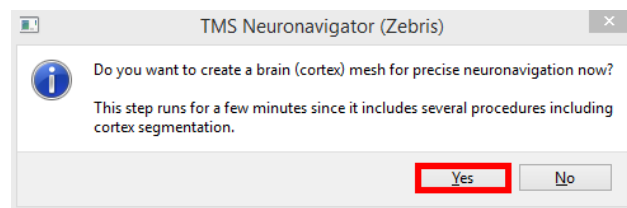
- 1) GSG_aACPC_Head.srf
- 2) GSG_aACPC_Head.vwp



- i** All mesh or surface files end with the file extension .srf for surface. For each generated surface file, a viewpoint (.vwp) file with an identical file name is saved to disk. This file defines the default orientation/viewpoint of the 3D surface file when opening it with the TMS Neuronavigator.
- All Mesh files are automatically opened in a separate surface window of the TMS Neuronavigator and can only be loaded when an anatomical data set, i.e. a VMR project is open already.

4. Automatic Cortex Segmentation

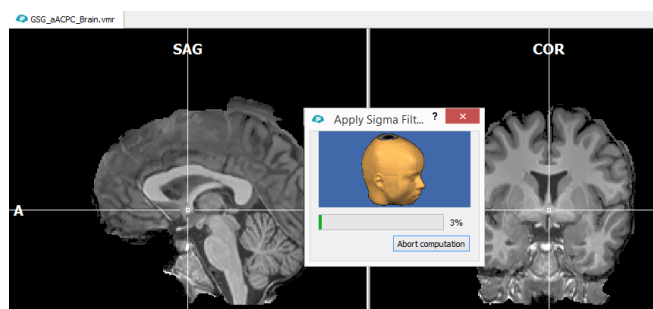
1.  The cortex segmentation starts automatically after the head mesh creation is finished. Please confirm the dialog with “Yes”.



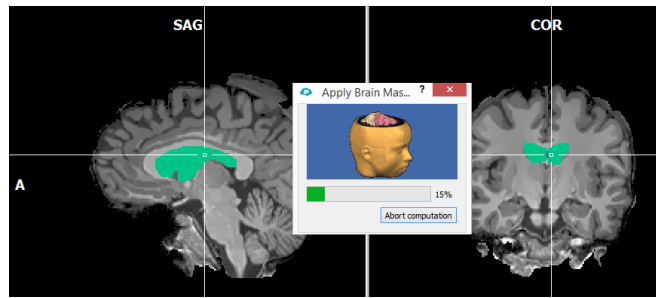
- i** This part of the procedure can take several minutes, as several steps are involved in the reconstruction of a high-quality cortex mesh.
- i** First, the data needs to be optimally prepared for cortex reconstruction, including the removal of non-brain tissue.



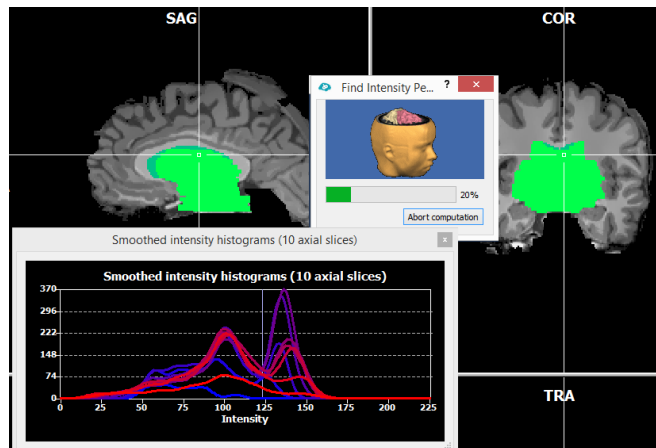
- i** Afterwards, a sigma filter is applied that smooths within the grey matter and within the white matter but keeps the boundary unblurred. This procedure increases the contrast between white and grey matter.



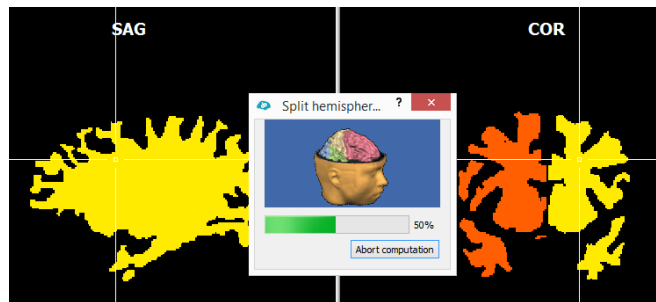
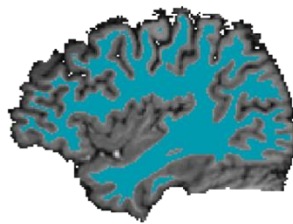
- i** In the next step the ventricles are filled and a default brain mask is applied to segment the brain from the surrounding head tissue and the cerebellum.



- i** In order to determine a threshold separating white from grey matter, the intensity values of the data are analyzed.



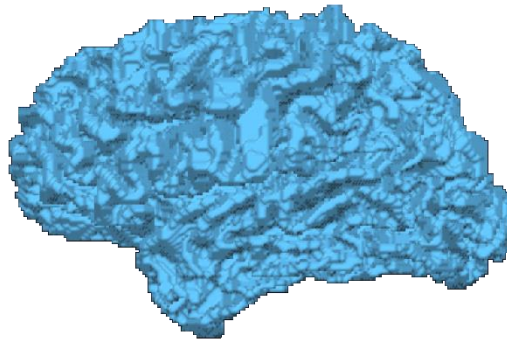
- i** Based on the estimates of the white and grey matter intensity peaks in the previous step, a white matter region growing process is performed to label white matter voxels. The outer boundary of this labelling process results in an initial representation of the cortical sheet. Several correction steps are performed to improve the quality of the segmented boundary. As a last preparation step, the left and right hemisphere (LH, RH) are disconnected.



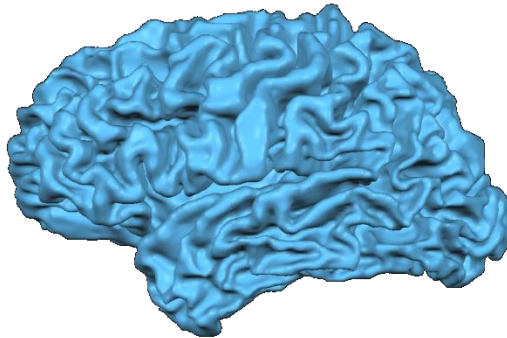
- i** During the cortical surface reconstruction, the yellow border will be used to create a mesh of the cortical sheet. Presented on the right is an image of the reconstructed border between the white matter and grey matter of the left hemisphere: "GSG_aCPC_Brain_LH_WM.vmr" The same file is created for the right hemisphere.



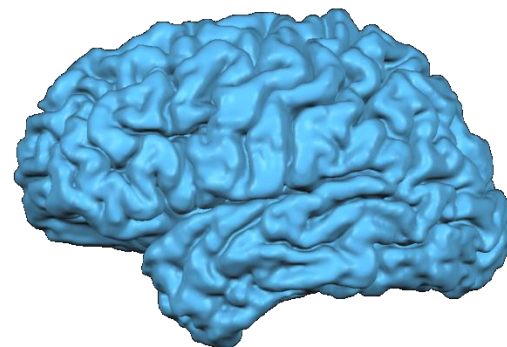
- ① These segmented images are used for the creation of the polygon meshes in the next step. First a non-smoothed reconstruction of the white matter – grey matter border (WM-GM) is created for both hemispheres:
 GSG_aACPC_Brain_LH_RECO.srf
 GSG_aACPC_Brain_RH_RECO.srf



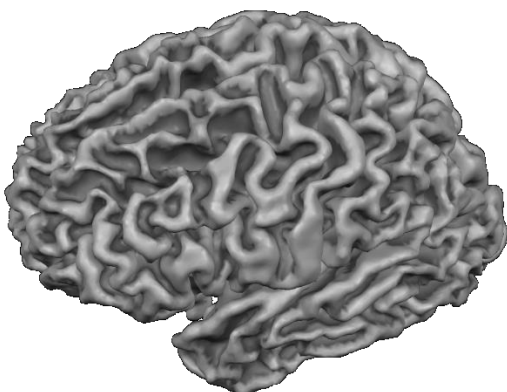
- ① In a next step the meshes are smoothed, following a slightly dilated version of the white/grey matter boundary:
 GSG_aACPC_Brain_LH_RECOSM.srf
 GSG_aACPC_Brain_RH_RECOSM.srf



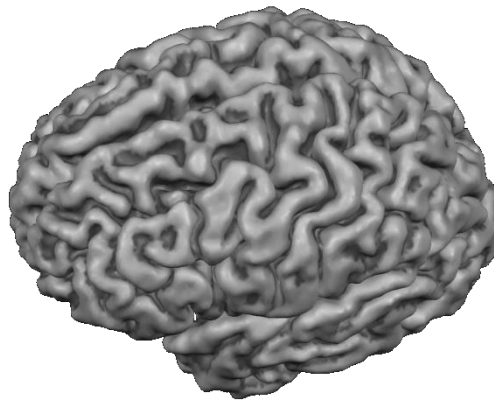
- ① The same procedure as described above is used for the creation of cortex meshes that follow the boundary of the outer grey matter: between the grey matter and the pial surface. These are the resulting files:
 GSG_aACPC_Brain_LH_GM.vmr
 GSG_aACPC_Brain_RH_GM.vmr
 GSG_aACPC_Brain_LH_GM.srf
 GSG_aACPC_Brain_RH_GM.srf



- ① In a last step the corresponding surface files of the left and right hemisphere are merged and re-colored according to the cortical folding pattern, with dark grey colors representing sulci and light grey colors representing gyri. These are the final merged cortex meshes:
 GSG_aACPC_Brain.srf



(representing the inner border of the grey matter)
GSG_aACPC_Brain_GM.srf
(representing the outer border of the grey matter – this file is used by default for neuronavigation)



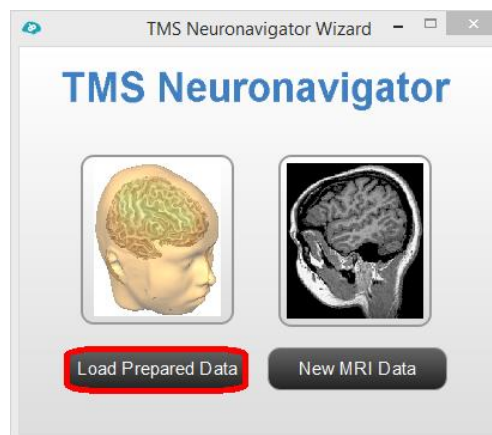
- i** This was the last step of the automatic data preparation for neuronavigation. The TMS Neuronavigator has automatically created a new entry in the Patient Data Base linking the necessary files of the participant for neuronavigation. The next section explains how these files can be loaded.

5. Loading Prepared Data via the TMS Neuronavigator Wizard

1. If you have closed the TMS Neuronavigator, re-open it now.

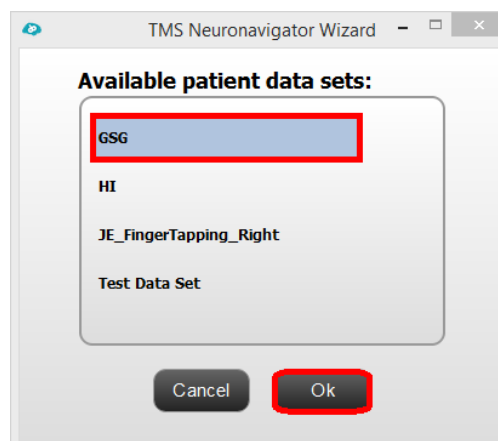


2. In the appearing wizard click on “Load Prepared Data”.



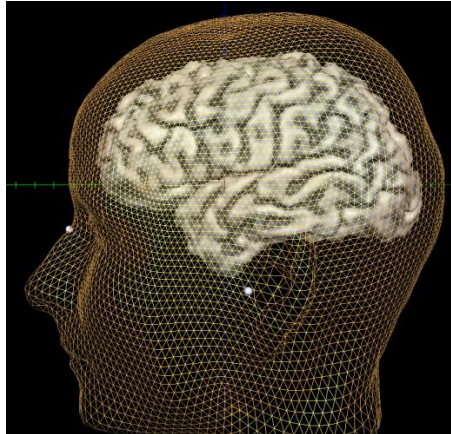
3. You will see a list of all participants for whom prepared data sets for TMS neuronavigation are available.

Select the patient identifier of the data set you would like to open, i.e. “GSG” and confirm your selection with “OK”.



- i** This will invoke all files of a patient which are linked to a single patient identifier in the “Patient Data Base”.

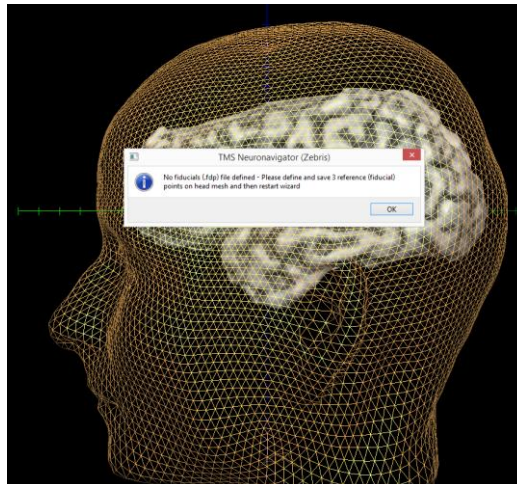
Part II, Section 9 describes how the files linked to a specific patient identifier can be changed.



6. Navigation in the Surface Module Window

- 1.** Open the TMS Neuronavigator and load the GSG data set using the wizard.

The program now displays the surface reconstructions of the head and brain created in the previous step.



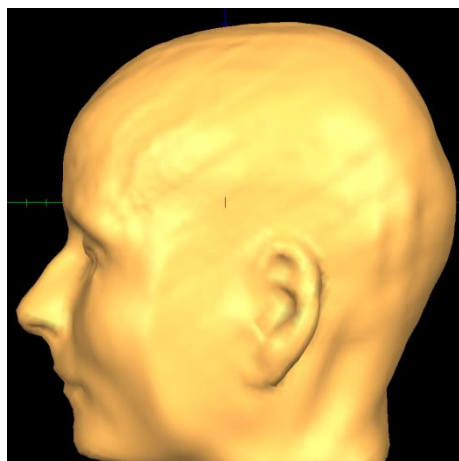
- i** Please note that you will see the following warning message at this point: “No fiducials (.fdp) file defined – Please define and save 3 reference (fiducial) points on head mesh and then restart wizard”

You will learn how to define the head mesh fiducials in step 8 of this guide. For now we will ignore this message.

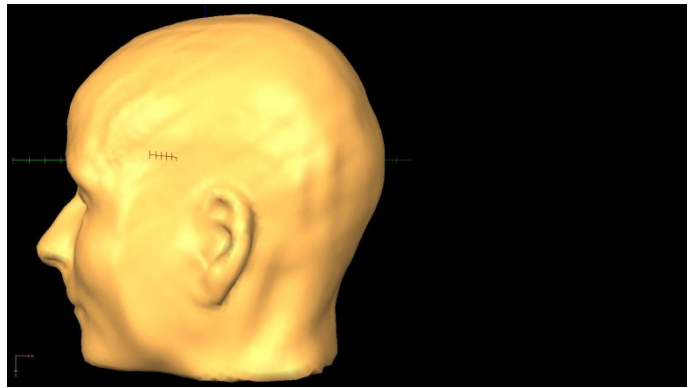
- 1.** Please click on the cross in the upper right corner of the dialog to close it. Please also close the appearing “Head Mesh Fiducials” dialog by using the “Close” button.

- i** When the head mesh fiducials are not defined yet, the TMS Neuronavigator shows the head surface in a shaded non-transparent way, therefore hiding the additionally loaded brain mesh.

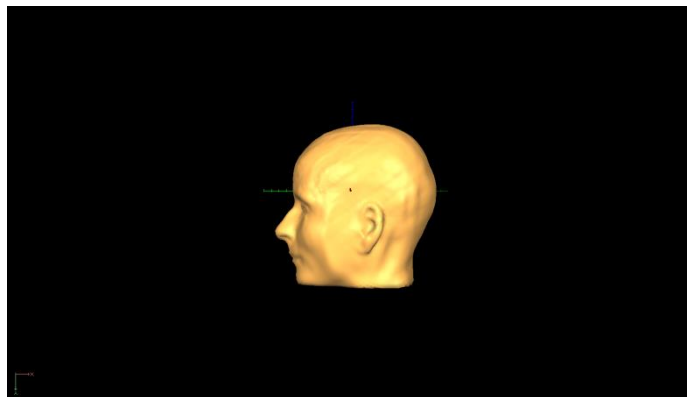
Now you will learn how to navigate the camera position of the 3D scene, also called the viewpoint.



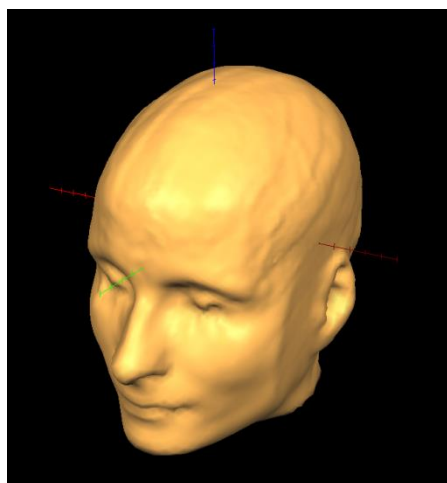
2. Click the right mouse button at an arbitrary point in the surface module window, hold it down and move the mouse. You will see that the mesh moves left-right and up-down as the mouse is moved left-right and up-down. Hence, with the **right mouse button** you can perform **translation movements in the y-direction** (left – right) and in the **z-direction** (up – down).



3. You can also move the viewpoint in the **x-direction** by holding down the **left and right mouse button** at the same time and by moving the mouse up and down. This movement of the viewpoint resembles “**zooming**” because the viewpoint is moved towards / away from the mesh. Alternatively use **Shift+Ctrl+ left click-dragging** for zooming.

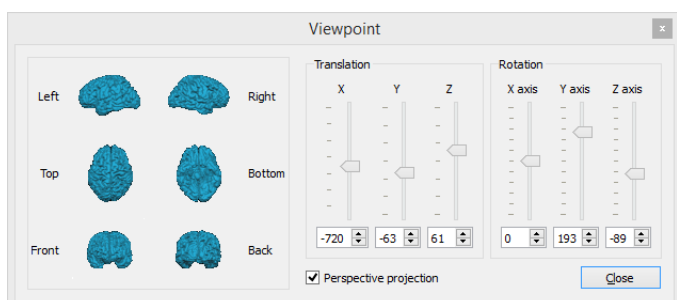


4. You can also rotate the viewpoint around the center of the scene by holding down the left mouse button and by moving the mouse left / right and up / down. This will rotate around two from three possible axes. While navigating, the status bar will show the current viewpoint position as well as angles as shown on the right.



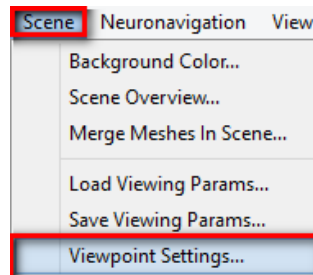
Viewpoint: x = -729.0 y = -30.0 z = 9.0 rot_x = 0.0 rot_y = 202.0 rot_z = -61.0

5. A helpful tool to navigate in the surface module window is the “Viewpoint Settings” dialog. Press the “**V**” key to invoke the “Viewpoint Settings” dialog. This dialog offers 6 sliders that allow changing the three translation and rotation parameters just described.



In addition it offers six standard viewpoints, which you can apply by clicking on the respective brain icons (“Left”, “Right”, “Top” etc.).

You can load the “Viewpoint” dialog also via “Scene -> Viewpoint Settings...”.



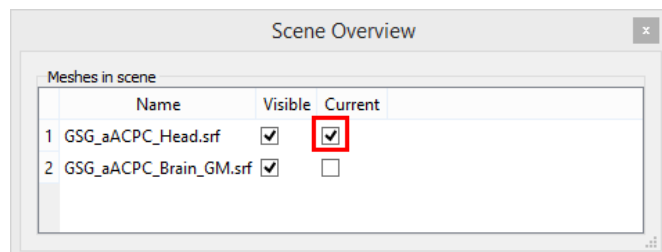
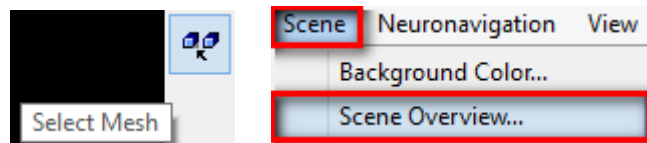
- i** You might have noticed the taskbar to the right of the surface window. This taskbar will be explained in detail in the next section. However, some of the icons will be mentioned already in this section, as they are crucial for handling meshes in the surface window of the TMS Neuronavigator.

6. The “Select Mesh” icon opens the “Scene Overview” dialog.



This dialog displays

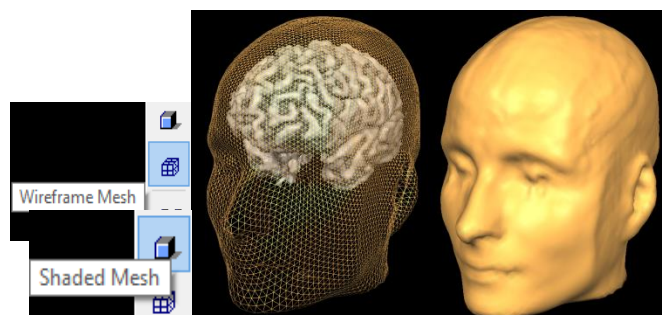
- 1) which mesh files are currently loaded in the surface module window (first column – “Name”)
- 2) which of these meshes are visible in the window (second column – “Visible”)
- 3) and which mesh is the mesh currently in focus in the surface window (third column – “Current”)



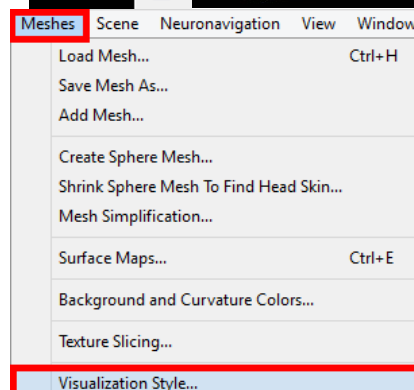
- i** In particular the last column is important, as **only properties of the mesh currently in focus can be changed**.

This means that we can only change the properties of the head mesh at the moment.

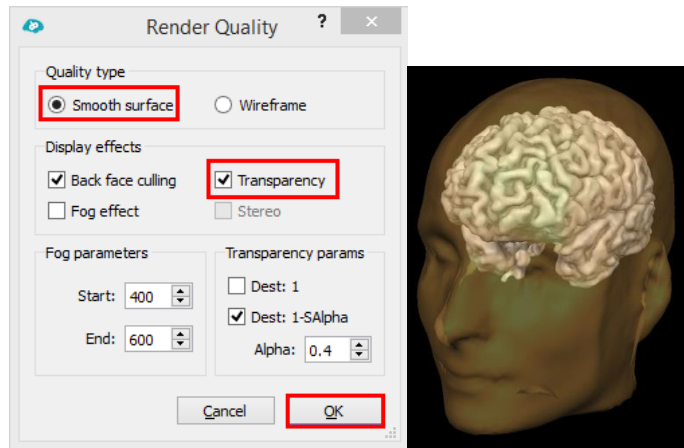
7. The mesh visualization icons change the visualization of the current mesh from a “Wireframe Mesh” to a “Shaded Mesh” and vice versa.



8. You can find more visualization options in the “Render Quality” dialog. Please go to “Meshes” and select the menu entry “Visualization Style...”



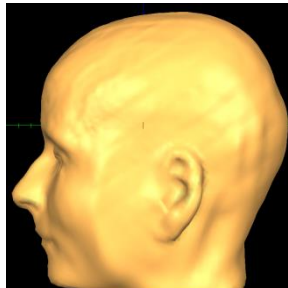
- In the appearing dialog you can change for example the transparency of the current mesh. Make sure that the “Smooth surface” option is selected, check “Transparency” and click “OK”.



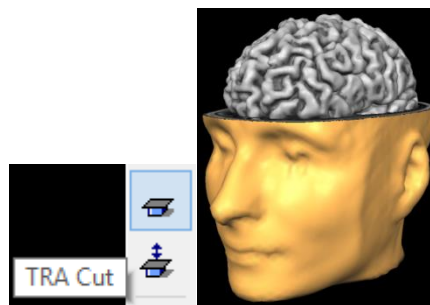
7. Slicing a Polygon Mesh

- In this step, you will see how to slice a polygon mesh. Sliced views of the head or brain mesh provide useful information about the spatial relation of 3D renderings (the mesh file) and the VMR files from which they have been built or to create different views for Neuronavigation.

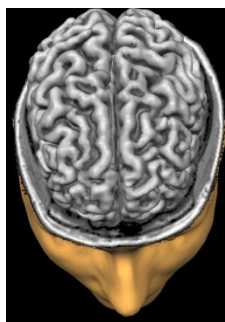
- Open the TMS Neuronavigator and load the GSG data set as described in the last step. The program now displays a surface module window as shown on the right.




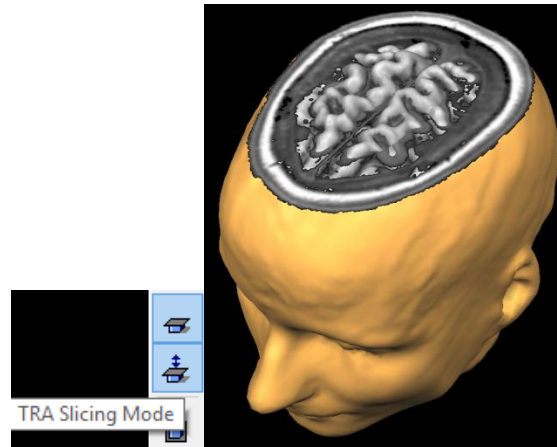
- Click the “TRA cut” icon in the taskbar. You will see an image similar to the one on the right showing a cut plane.




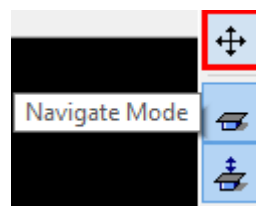
- Rotate the head to see the cut plane from above.




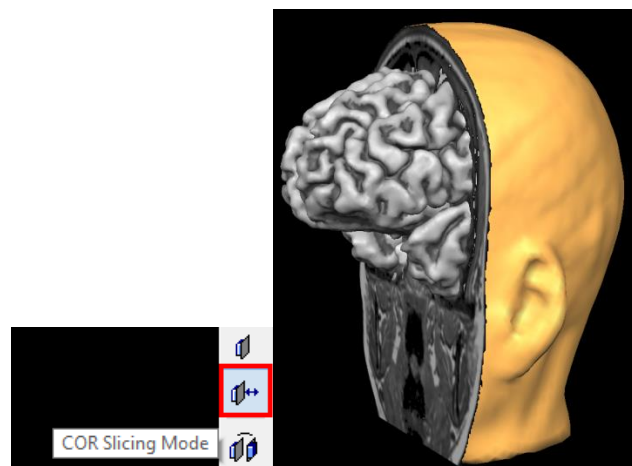
4.  Now change the cut plane. The “TRA Slicing Mode” mode is automatically enabled when the “TRA Cut” mode is selected. Now click with the left mouse button at any point in the surface module window, **hold down the mouse button, press the ALT key and move the mouse up and down.** You will see that the cut plane moves upward or downward, respectively.




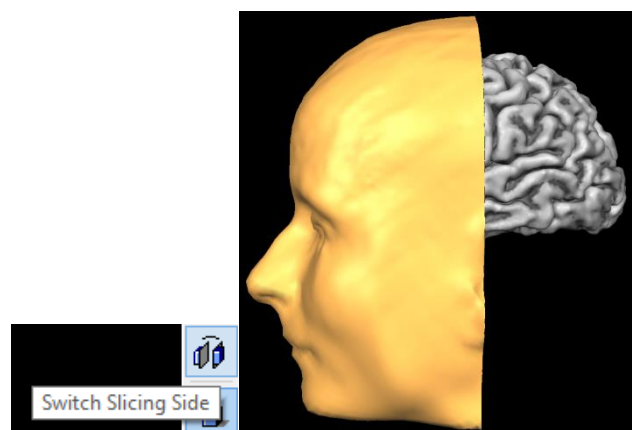
5.  In slicing mode, you can still use the mouse and keyboard for navigation. You may, however, stop the slicing mode and re-enter the pure navigation mode by clicking the “Navigation mode” icon.



6.  Besides transversal slicing, you can select sagittal and coronal slicing. Click the “COR Slicing Mode” icon. You will see a view as shown on the right.



7.  A cut shows one of two possible halves of the sliced object. You can also show the other half of the sliced object. Click the “Switch Slicing Side” icon. You now see a scene similar to the one on the right revealing the half of the object on the other side of the selected slice. You can do this with any of the three cut planes after having selected the respective slicing mode icon.



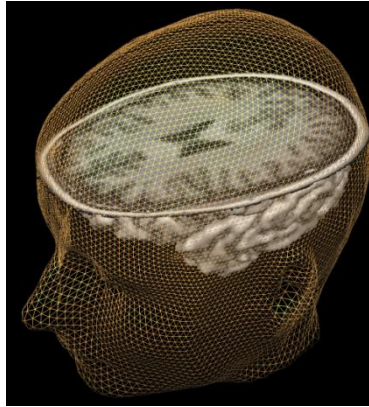
8. You can also slice the brain mesh.



In order to do that:


- 1) de-select the cut mode in the task bar,
- 2) change the head mesh presentation to “Wireframe Mesh”,
- 3) and select the brain mesh as the current mesh in the “Scene Overview” dialog

Now use the “TRA Slicing Mode” to replicate the image on the right.

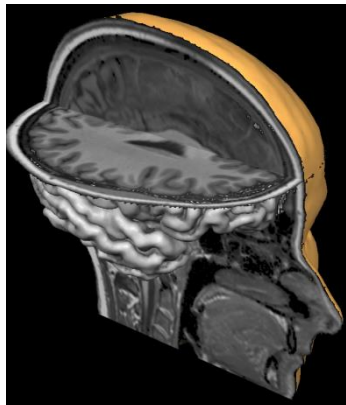


9. You can even slice multiple meshes after each other. Try to replicate the image on the right.




 It is important to realize that the slicing mode visualizes the underlying VMR data.

Hence, it is crucial that the meshes are loaded on the correct VMR file which was used for mesh creation.



This is automatically the case when the automatic data preparation pipeline was used in the TMS Neuronavigator and none of the files of the corresponding patient data set have been changed in the Patient Data Base.

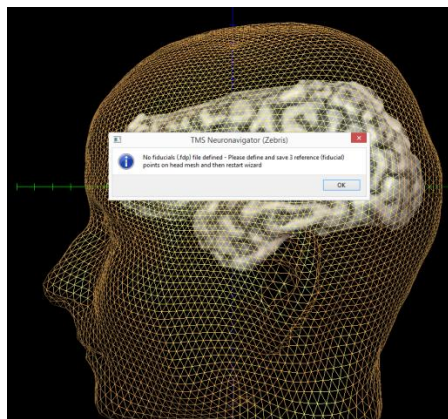
8. Definition of Coregistration Points on the Head Mesh (or short Head Mesh Fiducials)

 One detail that is still missing before you can start the neuronavigation are three reference points on the subject’s head which can be used for the coregistration of the head mesh in the program with the participant’s head in the external world. These points are also called head mesh fiducials.

1. Open the TMS Neuronavigator and load the “GSG” data set via the “Load Prepared Data” option of the TMS Neuronavigator wizard.



Close the warning message by using the “OK” button.

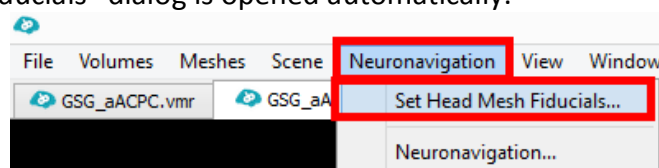
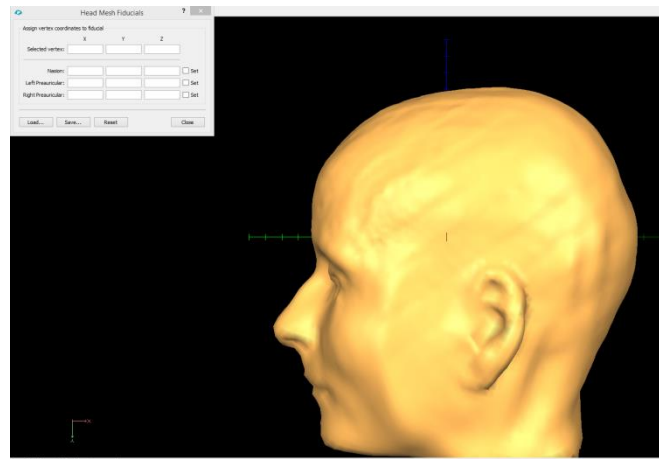


- It is easier to define reference points on the head mesh when the head is non-transparent and not in wireframe mode. Therefore the visualization style of the head mesh is set to shaded when no head mesh fiducials can be found for the data set.

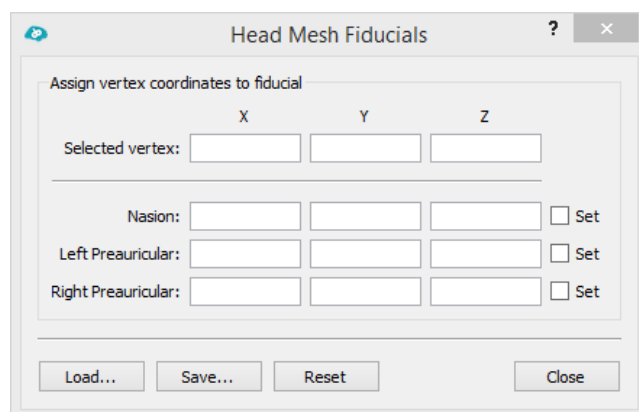
In the current program view two different surface files are loaded: the GSG_aACPC_Brain_GM.srf and the GSG_aACPC_Head.srf.

Since the head mesh is used to define the fiducials, the head mesh is selected as the current mesh and the “Head Mesh Fiducials” dialog is opened automatically.

- You can open the dialog manually via “Neuronavigation -> Set Head Mesh Fiducials...”.

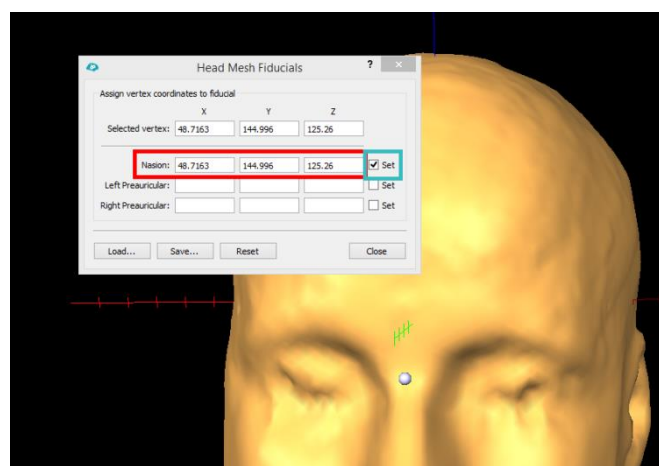


- In the “Head Mesh Fiducials” dialog you will find four different entries: The coordinates of the currently selected vertex and three reference points that need to be specified. The first point is the nasion and the other two points are the left and right preauricular points.



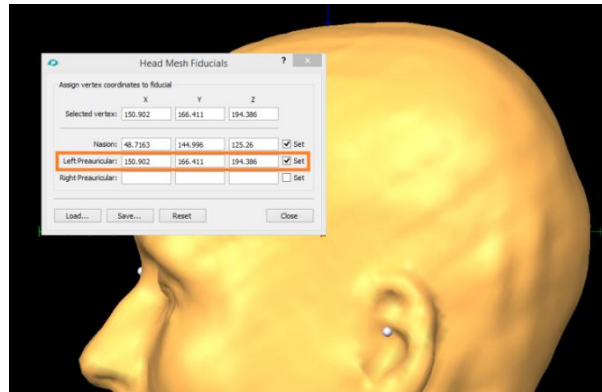
- It's not important that you select the exact same points suggested in the dialog. However, you should use fiducials in the vicinity of these suggested points that are easily identifiable on the head mesh in the software as well as on the real head of the subject.

- You need to start with the definition of the nasion. Please note that the order of the defined fiducials is important. Select a vertex on the head mesh using CTRL + Left-Mouse Button. This will automatically copy the selected vertex coordinate to the “Nasion” field and select the “Set” checkmark.



i If you want to correct the defined vertex for the nasion reference point, de-select the “Set” field next to the Nasion entry and you can select a new vertex with your mouse.

3. After checking the correct location of the nasion reference point on the head mesh, you can continue with defining a point close to the left ear that can be easily identified. Select the vertex by using again CTRL + Left Mouse Button.

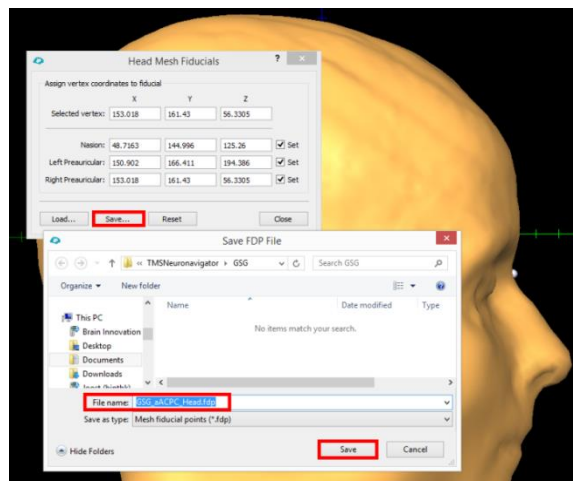


4. Finish the fiducial definition with selecting a reference point close to the right ear.

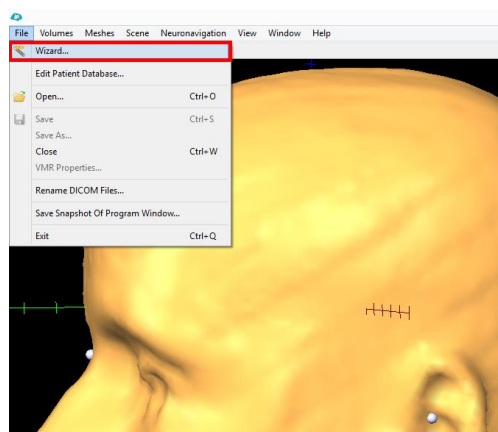


5. Save the defined head mesh fiducials to disk by clicking on “Save”. Accept the proposed file name: GSG_aACPC_Head.fdp

The coregistration points or head mesh fiducial points (.fdp) are automatically linked to the correct patient identifier. Next time the data set is loaded, the head mesh fiducials are automatically displayed on the head mesh.



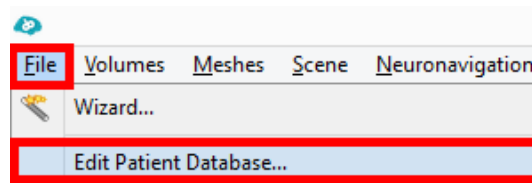
6. Close the “Head Mesh Fiducials” dialog and reload the data set via the wizard.



9. Editing the Patient Database

i The Patient Database lists all required files for neuronavigation.

1. To edit the links of files to a specific patient identifier, open the Patient Database via “File -> Edit Patient Database...”.



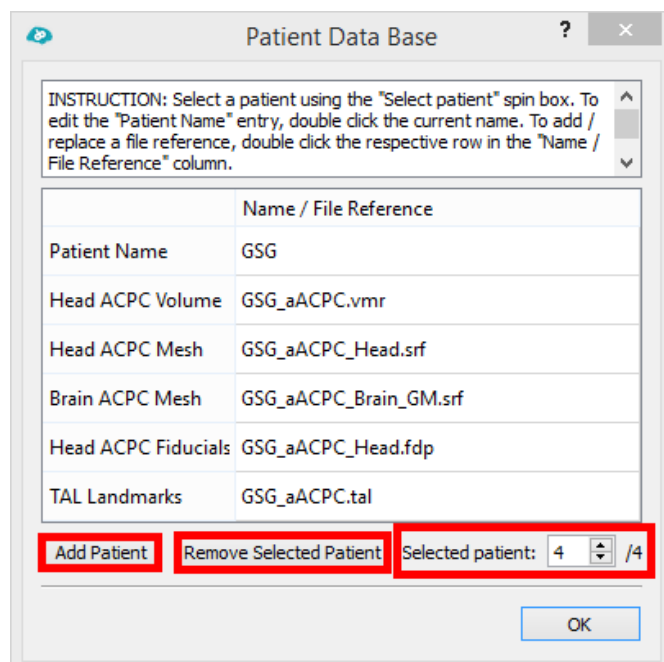
i In the left column you can see which files are required for neuronavigation and in the right column you can see the patient-specific filenames.

In the lower right corner you can see how many data sets are available. In this case 4 different patient data sets were prepared on this computer and are available in the Patient Data Base.

You can use the spin buttons next to the “Selected patient:” field to browse to a different data set.

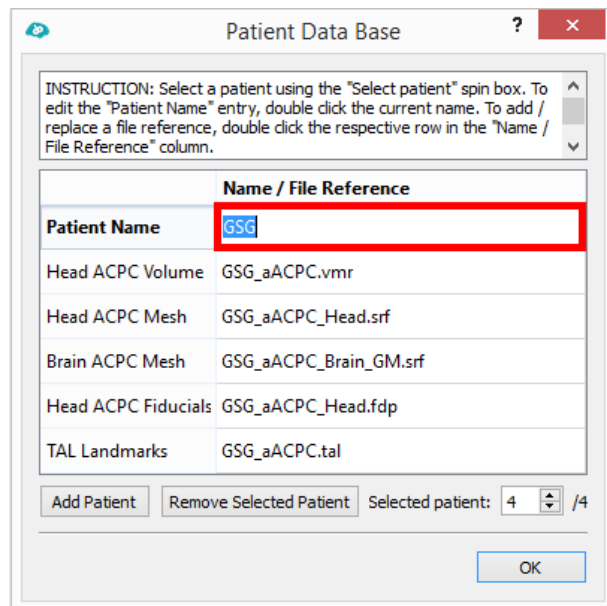
You can also add a new “empty” data set by clicking on “Add Patient”.

Furthermore, you can remove a specific data set from the Patient Data Base by clicking on “Remove Selected Patient”. Please note that no files will be deleted from your hard disk, only the links to the files will be removed from the Patient Data Base.



i If you want to change the patient identifier, please double click in the name field next to the “Patient Name”.

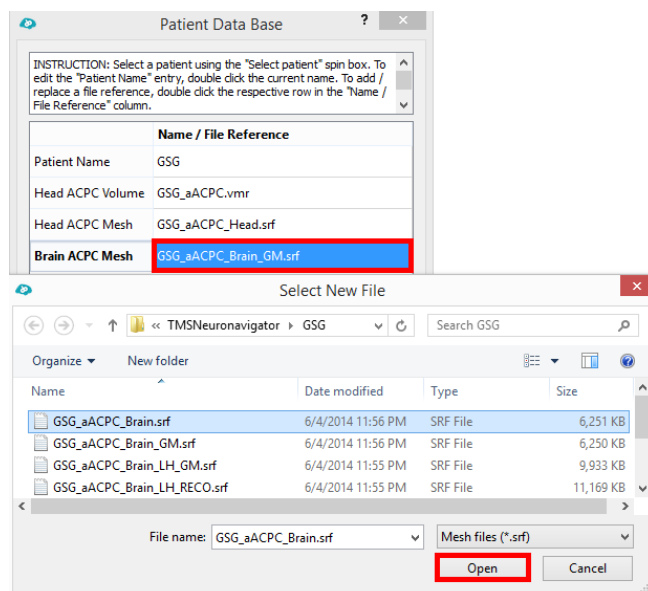
This will change the name displayed in the TMS Neuronavigator wizard after selecting “Load Prepared Data”.



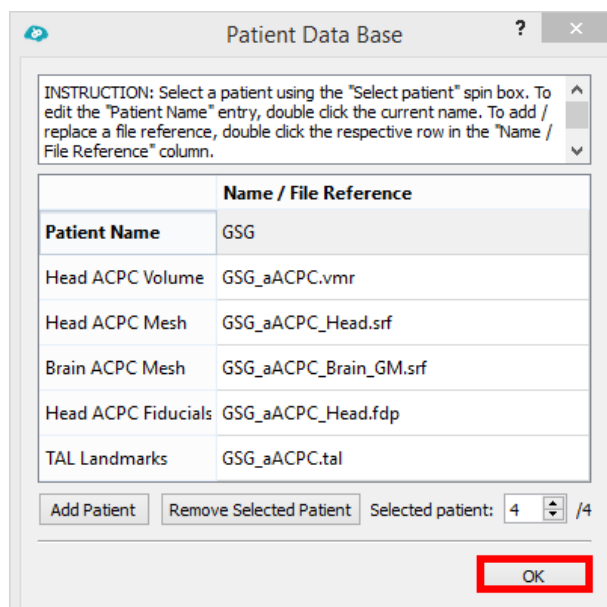
i In order to change a file or the path information of a file referenced in the Patient Data Base, double click on any file name in the right column and select the file you would like to link to the specific patient.

In the example on the right, the Grey Matter Mesh is exchanged with the Reconstructed and Smoothed Cortex Mesh of that same participant.

All files of a single data set should be located in the same folder.




i Close the Patient Data base by clicking on “OK”.

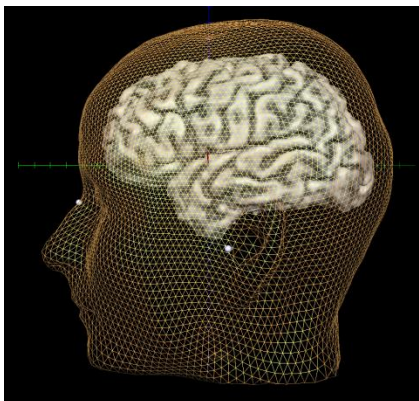



10. Definition of a TMS Target Point Based on Anatomical Landmarks

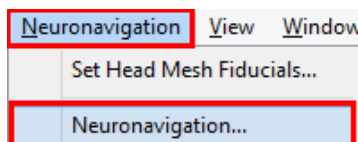
i The goal of the TMS neuronavigation is to deliver a TMS pulse to a predefined location on the cortex. This location can be specified via a so-called target point in the TMS Neuronavigator. The followings steps will show you how to define such a target point.

1.  Open the TMS Neuronavigator and load the GSG data set using the wizard.

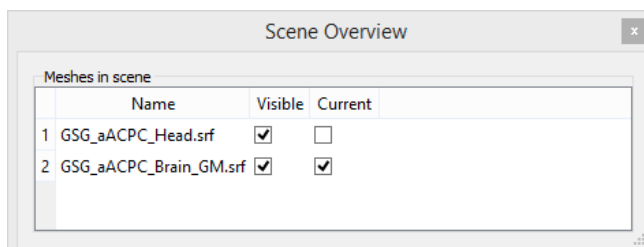
The program now displays a surface module window as shown on the right.



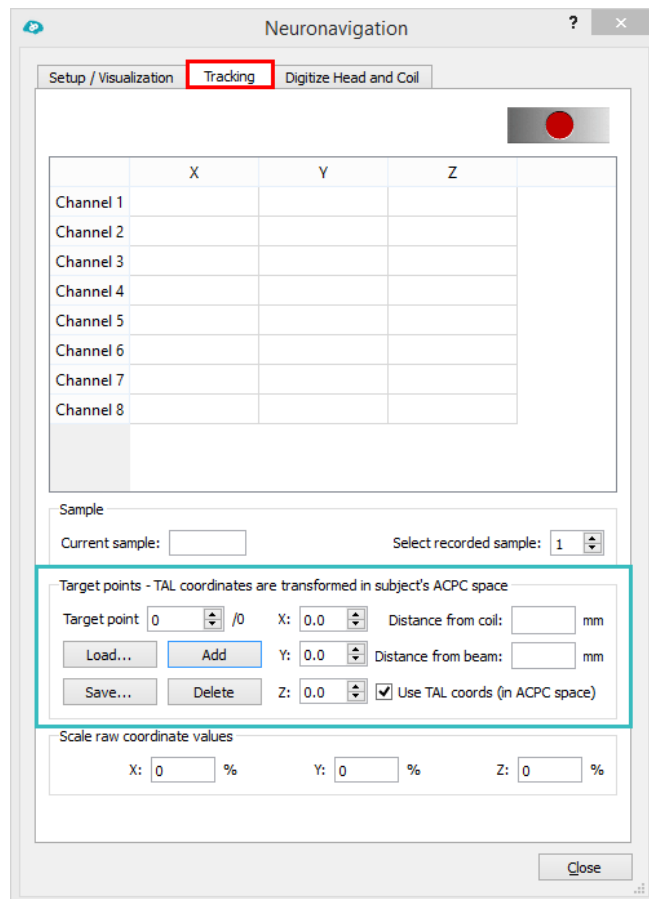
2.  The target point can be defined via the “Neuronavigation” dialog. Go to “Neuronavigation -> Neuronavigation..”.



i Note: When opening the “Neuronavigation” dialog, the “Scene Overview” window is automatically loaded. This allows you to switch between the head mesh and the brain mesh focus during neuronavigation.



i The “Neuronavigation” dialog contains three different tabs, which are important for different steps of the neuronavigation procedure. These tabs will be explained in detail in “Part III Neuronavigation” of this tutorial. For now we focus on the “Target points” field in the “Tracking” tab.

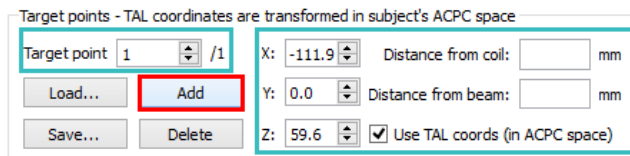


In this tutorial we will define a similar target point in three different ways:

- 1) Based on an anatomical landmark
- 2) Based on a Talairach coordinate from the literature
- 3) Based on a statistical map (functional MRI data)

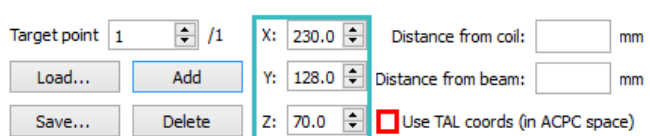
For all three options the target point should be located in the motor cortex of the right hemisphere (left hand). In the current step we will focus on the first option.

3. First, we need to add a target point to our data set by clicking on “Add” in the “Target points” field. This will automatically place a target point in the vicinity of the brain mesh.

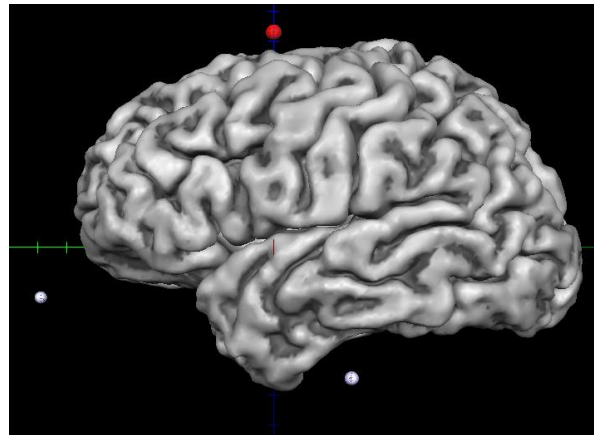


i At the same time the “Target point” spin box shows that there is now one target point available. The x, y and z fields show the calculated Talairach coordinate of the current target point, given a .tal file was created for that participant and the “Use TAL coords (in ACPC space)” option is checked.

i If one of the latter two is not true, system coordinates are displayed, which cannot be used to report the target position in a publication, as these coordinates are not standardized.



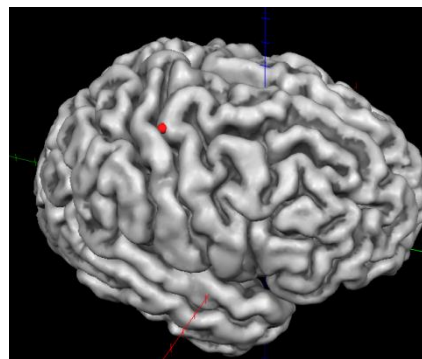
- i** Note: When the “Add” button in the “Target points” field is used, the head mesh is automatically hidden from view and the brain mesh is selected as the current mesh in focus.



You should see a similar image as presented on the right. The white points represent the head mesh fiducials, while the red point represents the new target point which has to be placed at the correct cortex location next.

- i** We want to place the target point on the hand area of the right motor cortex. A well-known anatomical landmark, described by Yousry et al., (1997), is a knob-like structure on the precentral gyrus.

4. Use CTRL + left click at the chosen position of the brain mesh and the target point is automatically moved to the same location.



- i** At the same time the coordinate fields are updated to the correct coordinate.

| | | | |
|----------|--|--|----|
| X: 38.1 | Distance from coil: | | mm |
| Y: -19.6 | Distance from beam: | | mm |
| Z: 58.0 | <input checked="" type="checkbox"/> Use TAL coords (in ACPC space) | | |

5. Save the target point to disk, by clicking on “Save”.



Choose a name that indicates:

- 1) on which data set the target point was defined, i.e. GSG_Brain_GM
- 2) which procedure was used, i.e. AL for anatomical landmark:
- 3) and which target points are included in the file, i.e. M1 for motor cortex

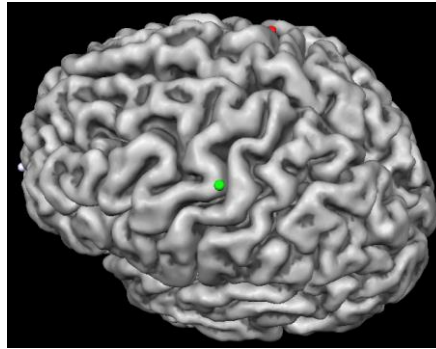
GSG_Brain_GM_AL_M1.tgp

The file extension tgp stands for target point.

Target points - TAL coordinates are transformed in

| | | |
|--|---------------------------------------|----------|
| Target point | 1 / 1 | X: 38.1 |
| <input type="button" value="Load..."/> | <input type="button" value="Add"/> | Y: -19.6 |
| <input type="button" value="Save..."/> | <input type="button" value="Delete"/> | Z: 58.0 |

6. You can define and save up to 10 target points in a single file, by using the procedure described above (click on “Add” and define location by CTRL+ left mouse button).
 Test this feature by defining a second target point for the hand area of the left motor cortex and saving both target points to the same .tgp file.



Target points - TAL coordinates are transformed in :

| | | | |
|--------------|--------|----|-------|
| Target point | 2 /2 | X: | -45.6 |
| Load... | Add | Y: | -22.9 |
| Save... | Delete | Z: | 52.4 |

- Both target points can be loaded during neuronavigation using the “Load” button in the “Target points” field. The “Target point” spin box indicates which target point is currently in focus for neuronavigation.

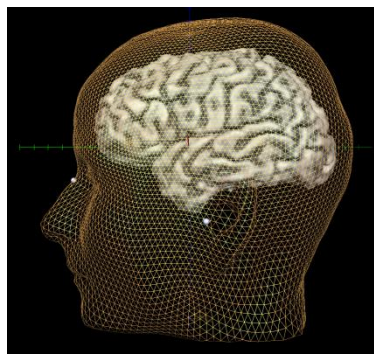
Target points - TAL coordinates are transformed in :

| | | | |
|--------------|--------|----|-------|
| Target point | 1 /2 | X: | 38.1 |
| Load... | Add | Y: | -19.6 |
| Save... | Delete | Z: | 58.0 |

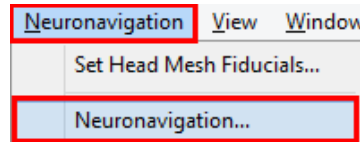
11. Definition of a TMS Target Point Based on Talairach Coordinates

- A second option to define target points for TMS neuronavigation is the definition based on Talairach coordinates reported in the literature. Be aware that this procedure is sub-optimal for individual target point specification, as standard Talairach coordinates can only represent an approximation of the targeted brain region. Talairach normalization is a volume normalization technique which does not account for the macro-anatomical variability across subjects. Nonetheless, in some rare cases it might be necessary to define target points in this way.

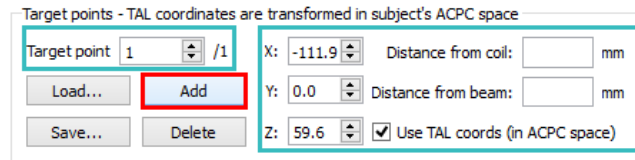
1. Open the TMS Neuronavigator and load the GSG data set using the wizard. The program now displays a surface module window as shown on the right.



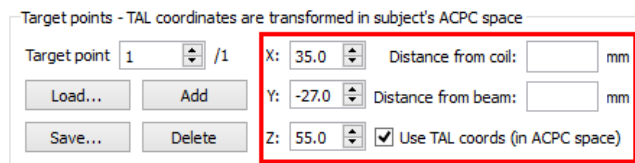
2. Open the “Neuronavigation” dialog via “Neuronavigation -> Neuronavigation..”.



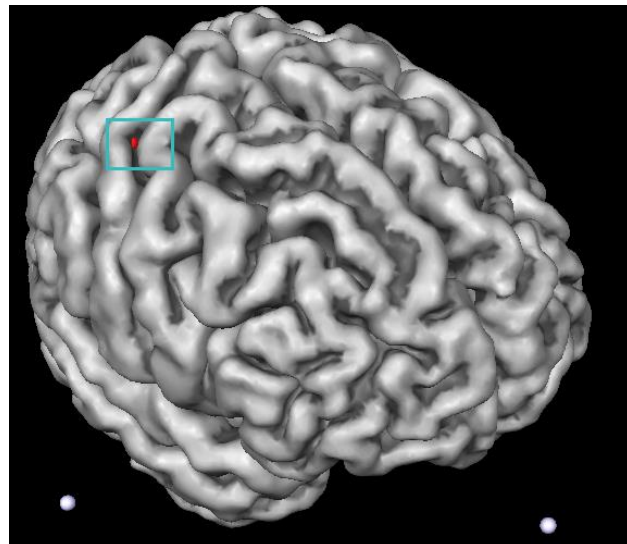
3. First, we need to add a target point to our data set by clicking on “Add” in the “Target points” field. This will automatically place a target point in the vicinity of the brain mesh.



4. Using the Talairach approach, we specify the target point location on the brain by entering a mean Talairach coordinate that we derived from a finger tapping experiment in the literature: $x = 35$, $y = -27$, $z = 55$ (Cramer et al., 1999).



- i** Please note that the target point is located at the anterior wall of the postcentral gyrus when using the mean Talairach coordinate. Hence, with the Talairach coordinate approach the TMS target point is located slightly posterior to the target point defined based on the individual anatomical landmark.



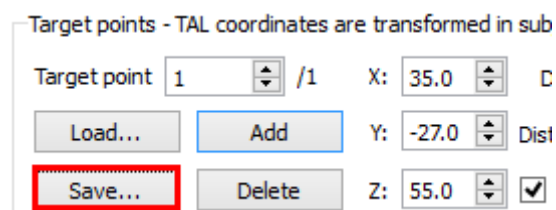
5. Save the target point to disk, by clicking on “Save”.



Choose a name that indicates:

- 1) on which data set the target point was defined, i.e. GSG_Brain_GM
- 2) which procedure was used, i.e. TAL for Talairach coordinate:
- 3) and which target points are included in the file, i.e. M1 for motor cortex

GSG_Brain_GM_TAL_M1.tgp




12. Definition of a TMS Target Point Based on Functional Data

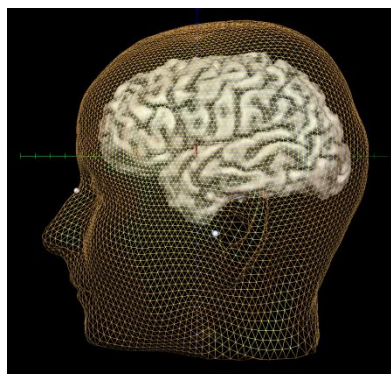
- i** The third option to define target points in the TMS Neuronavigator is the specification based on functional MRI data, e.g. a functional localizer of a specific brain region. This is particularly interesting for regions that are primarily defined by the function and show high inter-individual variability in the anatomical location. Hence, for regions with great variability in structural–functional correspondence, as for example language areas or the fusiform face area (Frost & Goebel, 2012).

- i** In order to use functional data for target point definition, you need to analyze your functional MRI data with BrainVoyager QX (Brain Innovation, The Netherlands) and import the resulting statistical volume maps (VMPs) in the TMS Neuronavigator. Details on how to perform standard fMRI data analysis (including project creation, preprocessing and coregistration of the functional and anatomical data) can be found in the BrainVoyager Getting Started Guide (<http://www.brainvoyager.com/bvresources/documentation/documentation.html>)

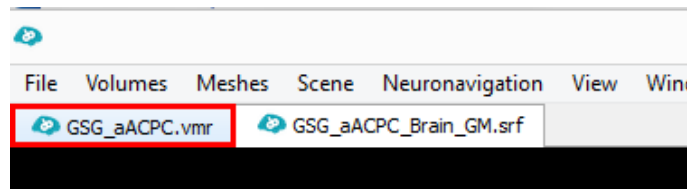
- i** For the current example, we analyzed the fMRI data of the finger tapping experiment (blocks of left and right index finger tapping) with BrainVoyager QX. Preprocessing of the functional data included: slice scan time correction, motion correction to detect and correct for small head movements, temporal filtering removing linear trends and non-linear temporal frequencies of 2 or less cycles per run. After preprocessing, the functional images were co-registered to the anatomical volume (GSG.vmr) and transformed into ACPC space (GSG_aACPC.trf). The whole brain analysis was performed using a standard univariate general linear model (GLM), with two predictors: one modelling right finger tapping and the other one modelling left finger tapping. In order to identify the hand region of the right motor cortex (tapping with the left index finger), we computed a simple contrast of the left finger tapping predictor versus baseline. This contrast was corrected for multiple comparisons using Bonferroni correction. The result was saved in a statistical volume map (VMP), containing one statistical value for each voxel.

In the following section you will see how this statistical map can be imported and used for target point definition in the TMS Neuronavigator.

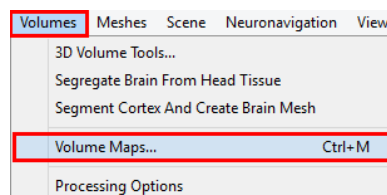
- 1.**  Open the TMS Neuronavigator and load the GSG data set using the wizard. The program now displays a surface module window as shown on the right.



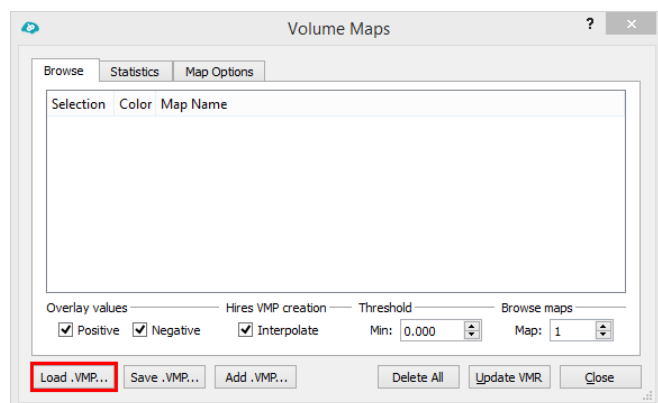
2. Now switch to the anatomical data set in ACPC space, by clicking on the “GSG_aACPC.vmr” tab in the main TMS Neuronavigator window.



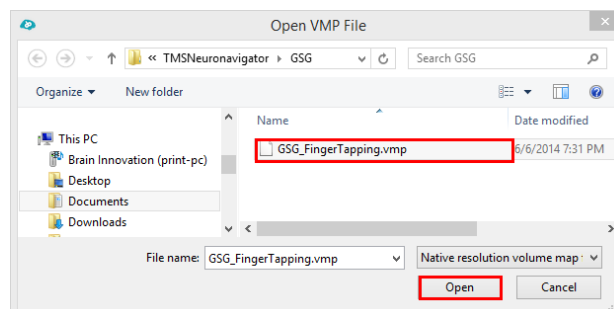
3. You can overlay the statistical map on the VMR via the “Volume Maps” dialog. Go to “Volumes -> Volume Maps ...”.




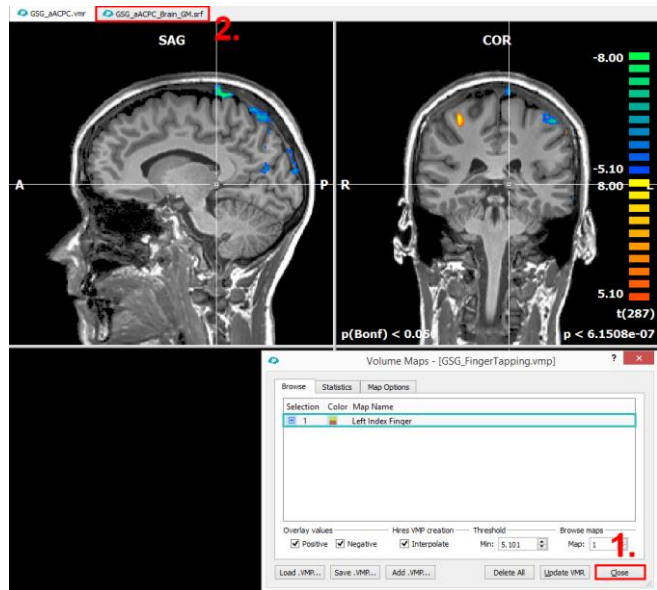
4. In the appearing dialog load the statistical map, via the button “Load .VMP...”




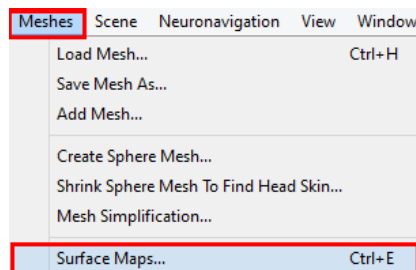
5. Select the correct .VMP file, in this example: GSG_FingerTapping.vmp and confirm your selection with “Open”.




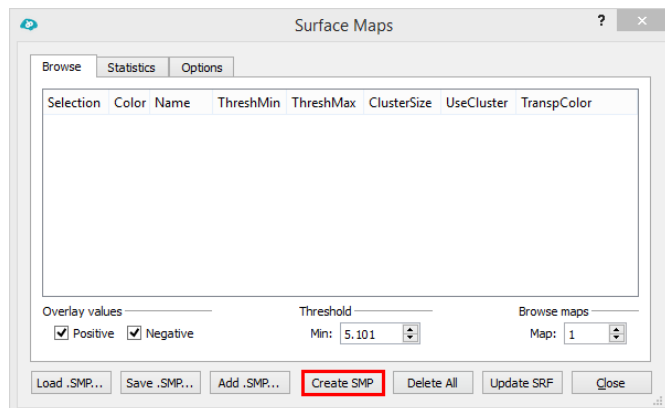
6.  The loaded statistical volume map can now be projected to the brain mesh. Close the “Volume Maps” dialog and switch back to the surface window by clicking on the GSG_aACPC_Brain_GM.srf tab of the main TMS Neuronavigator window.




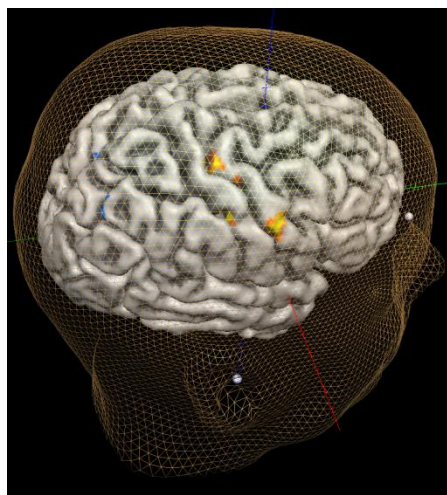
7.  In the surface window open the “Surface Maps” dialog via “Meshes -> Surface Maps”.



8.  Check in the “Scene Overview” dialog whether the correct mesh is currently in focus: GSG_aACPC_Brain_GM.srf. If this is the case, click on “Create SMP” in the “Surface Maps” dialog.



-  This step will project the selected VMP in Volume Space on to the currently selected surface mesh in Surface Space, creating a “Surface Map” = SMP.

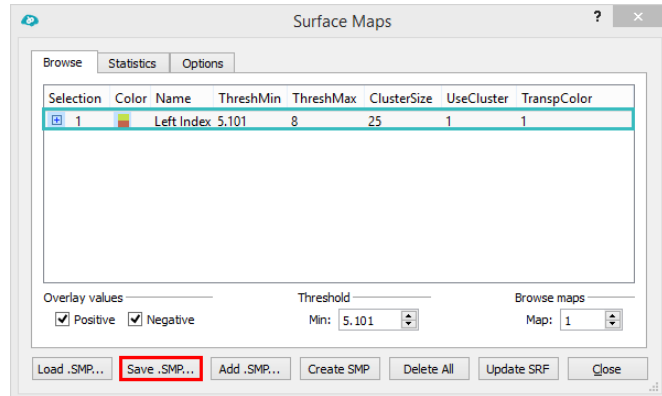


9. Save the created statistical surface map to disk by selecting “Save .SMP..”.

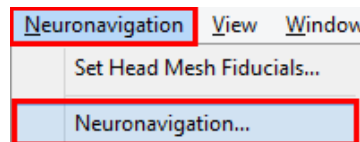


Choose a file name that indicates which mesh was used for the projection of the statistical map to surface space, as this SMP file is specific to the GSG_aACPC_Brain_GM.srf, e.g. GSG_FingerTapping_Brain_GM.smp.

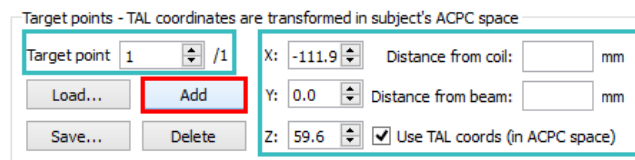
You can close the “Surface Maps” dialog via the button “Close”.



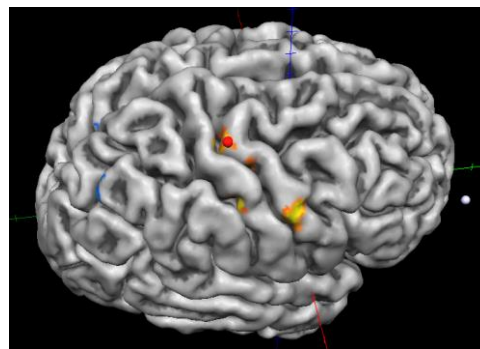
10. In order to specify a target point based on this functional map, open the “Neuronavigation” dialog.



11. Add a target point to the data set by clicking on “Add” in the “Target points” field. This will automatically place a target point in the vicinity of the brain mesh.



12. Use CTRL + left mouse button to place the target point at the hand region of the right motor cortex.



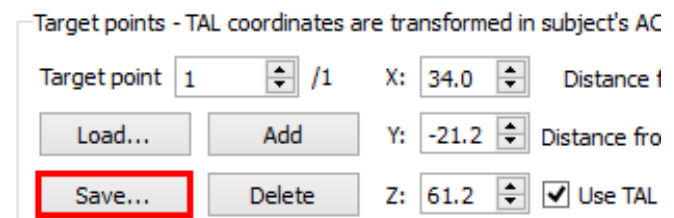
13. Finish the target point definition by saving the TGP file.



Choose a name that indicates:

- 1) on which data set the target point was defined, i.e. GSG_Brain_GM,
- 2) which procedure was used, i.e. FL for functional localizer,
- 3) and which target points are included in the file, i.e. M1 for motor cortex

GSG_Brain_GM_FL_M1.tgp

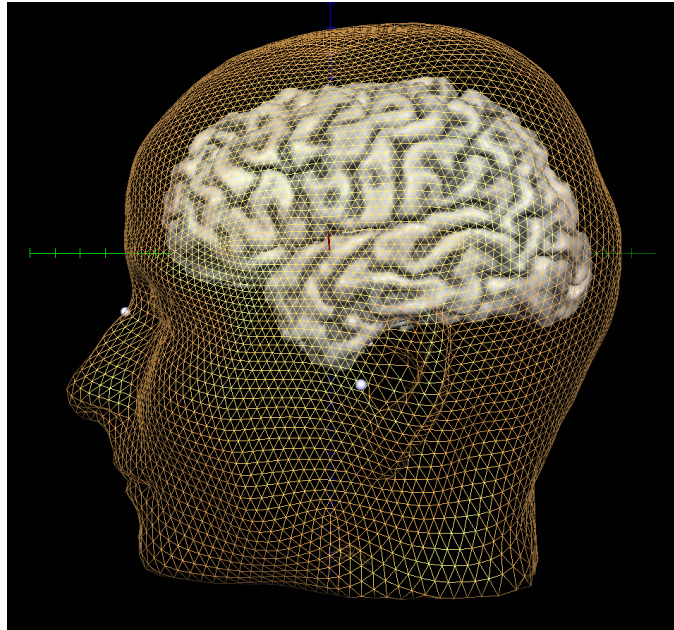


Part III Neuronavigation

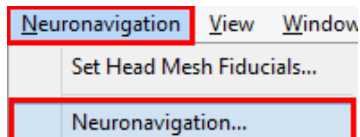
1. Explanation of the Neuronavigation Dialog

i After the data preparation is completed and a target point has been selected for TMS neuronavigation, we can start with the first steps of the neuronavigation process. We will start by explaining the “Setup/Visualization” tab of the Neuronavigation dialog.

1. Open the TMS Neuronavigator and load the GSG data set using the wizard.
The program now displays a surface module window as shown on the right.



2. Open the “Neuronavigation” dialog via “Neuronavigation -> Neuronavigation..”.

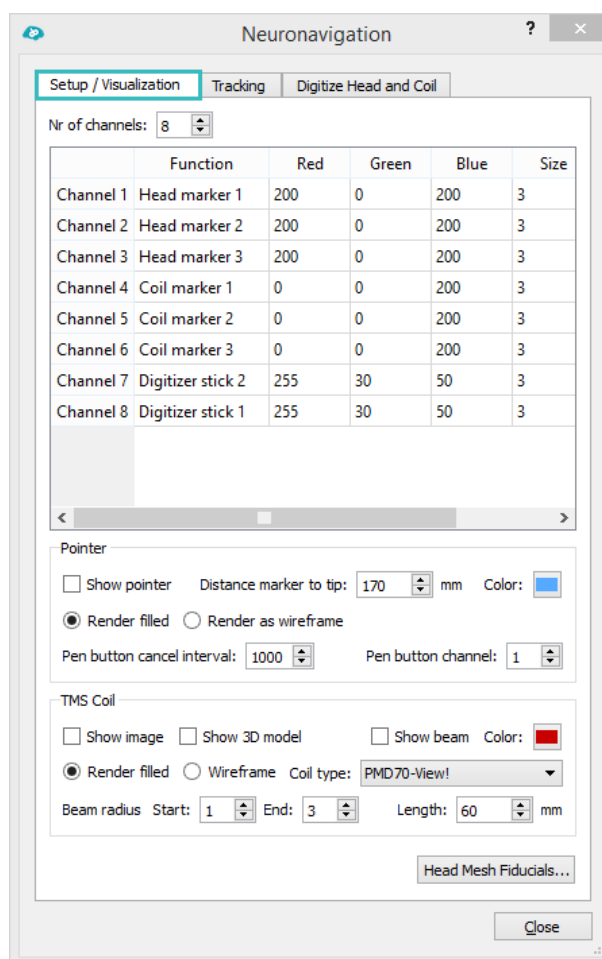


- i** Switch to the “Setup / Visualization” tab.

In the upper part of the window you can see that there are 8 different channels defined. Each channel represents an ultrasound transmitter used for the coregistration of the surface space to the external world.

In the middle part of the dialog the visualization of the Digitizer Stick is defined and can be changed if necessary.

The lower part of the window allows you to select the TMS coil as well as to change the visualization parameters of the coil. For the current tutorial we select the PMD70-View! Coil.



- i** The first three channels are the single ultrasound markers that will be attached to the subjects head.

After the CMS20 system has been started, you will see these single head markers as purple spheres (see RGB values next to the marker entries) floating close to the head mesh in the program. This is however only the case as long as the ultrasound signal from the transmitters is registered by the microphones in the measuring unit MA-XX2.

The next three channels represent the ultrasound transmitters from the triple TMS coil marker. These channels will be visualized as blue spheres floating close to a 3D model of the selected TMS coil in the program.

The last two channels in the list belong to the ultrasound transmitters of the Digitizer Stick and will be visible as red spheres in the surface window (as long as the ultrasound signal from these markers is picked up by the measuring unit of the CMS20 system).

Nr of channels: 8


| | Function | Red | Green | Blue | Size |
|-----------|-------------------|-----|-------|------|------|
| Channel 1 | Head marker 1 | 200 | 0 | 200 | 3 |
| Channel 2 | Head marker 2 | 200 | 0 | 200 | 3 |
| Channel 3 | Head marker 3 | 200 | 0 | 200 | 3 |
| Channel 4 | Coil marker 1 | 0 | 0 | 200 | 3 |
| Channel 5 | Coil marker 2 | 0 | 0 | 200 | 3 |
| Channel 6 | Coil marker 3 | 0 | 0 | 200 | 3 |
| Channel 7 | Digitizer stick 2 | 255 | 30 | 50 | 3 |
| Channel 8 | Digitizer stick 1 | 255 | 30 | 50 | 3 |

2. Coregister Head

i As a first step in the TMS neuronavigation process the head mesh in the surface window of the program has to be coregistered to the head of the participant in the external world. This will be explained in detail in the following section.

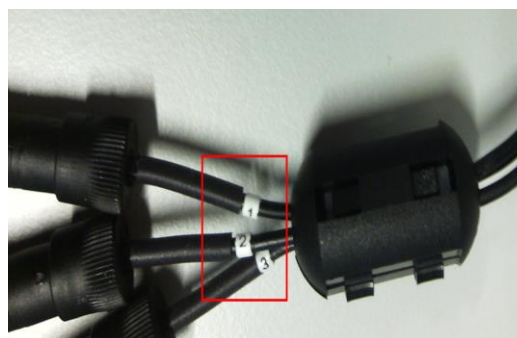
i Before we start, make sure that all hardware components are connected and working as described in Part 1 of this tutorial.



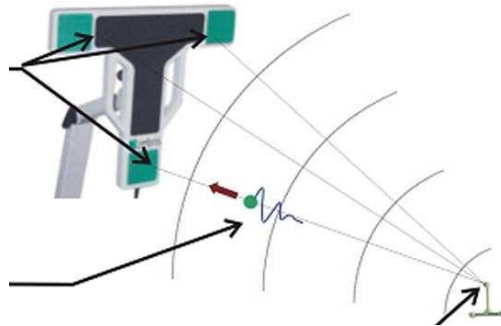
1.  As a next step, the single ultrasound markers will be attached to the subject's head. This can be achieved with adhesive stickers. It is very important that each marker is attached at the appropriate location. The marker labeled with "1" has to be attached to the left side of the participant's forehead, while marker "2" will be attached to the right side. The third marker will be attached to the tip of the subject's nose.



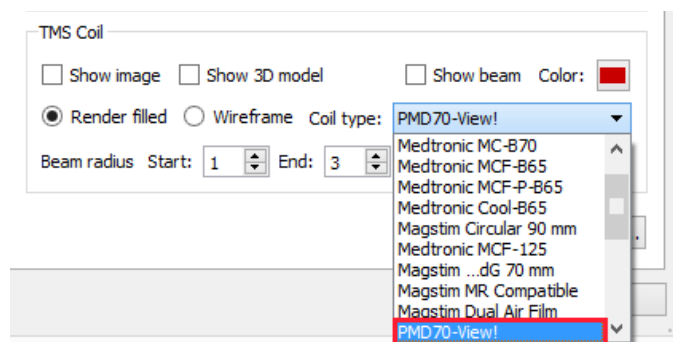
In case a transmitter falls off during the recording, you will have to attach this transmitter again and redo the complete coregistration procedure.



- i** It is important that the measuring system receives the ultrasound signal from all transmitters during the neuronavigation. Please ask the subject to directly face the measurement unit and do not exceed the distance of 2 meters between the measurement unit and the ultrasound transmitters.



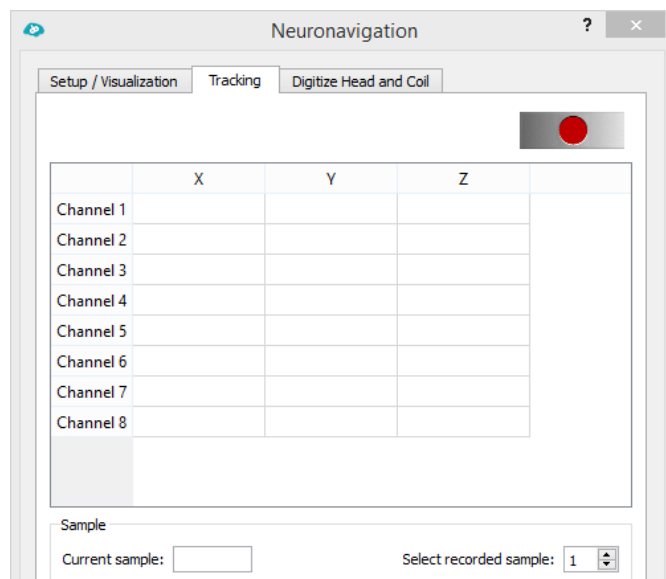
- i** The TMS Neuronavigator supports TMS coils from different vendors. Before you can start the CMS20 system make sure that the correct TMS coil is selected in the “Setup / Visualization” tab of the Neuronavigator dialog.



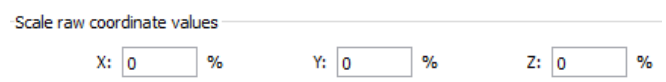
2. Now switch to the “Tracking” tab of the Neuronavigation dialog.



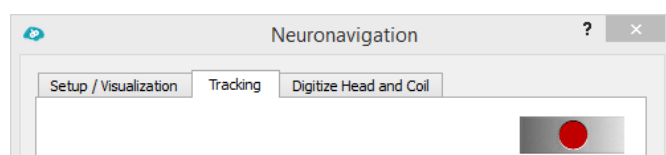
This tab displays the channel information of the 8 ultrasound transmitters as soon as the CMS20 system has been started.



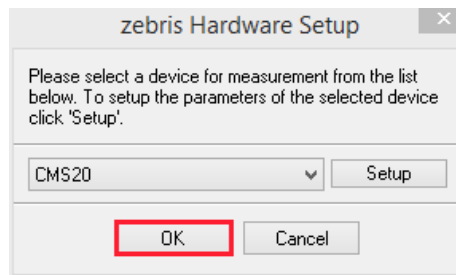
- i** In the lower part of the dialog you can scale the raw coordinate values. This might be useful if you expect for example distortions of your MRI data, e.g. due to gradient nonlinearities.



3. Start the tracking of the channels by using the record button.

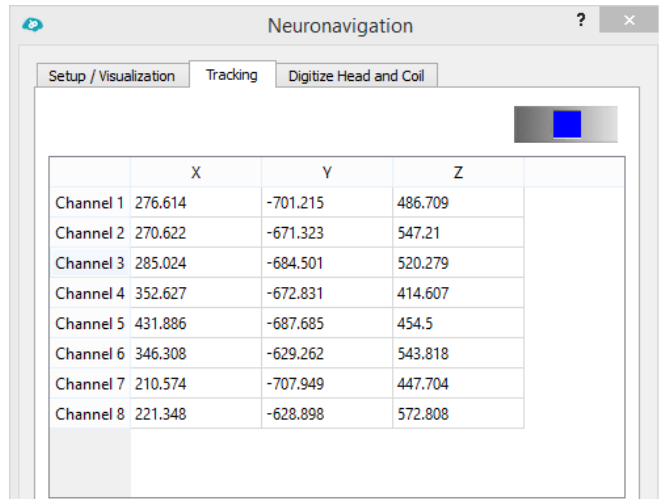


This will invoke the “Zebris Hardware Setup” dialog. If the system is correctly attached to the computer and the driver is running, the correct hardware will be selected by default – confirm with “OK”.



i As soon as the system starts measuring, you will see continuously updated channel coordinates in the tracking tab.

It is very important that all channels are visible; no obstacle should hide the transmitters (which would be indicated by “nan” in the x, y, and z coordinate field of the respective channel).



4. Once you have confirmed the visibility of all channels, you can switch to the “Digitize Head and Coil tab” and start with the coregistration of the participant’s head.

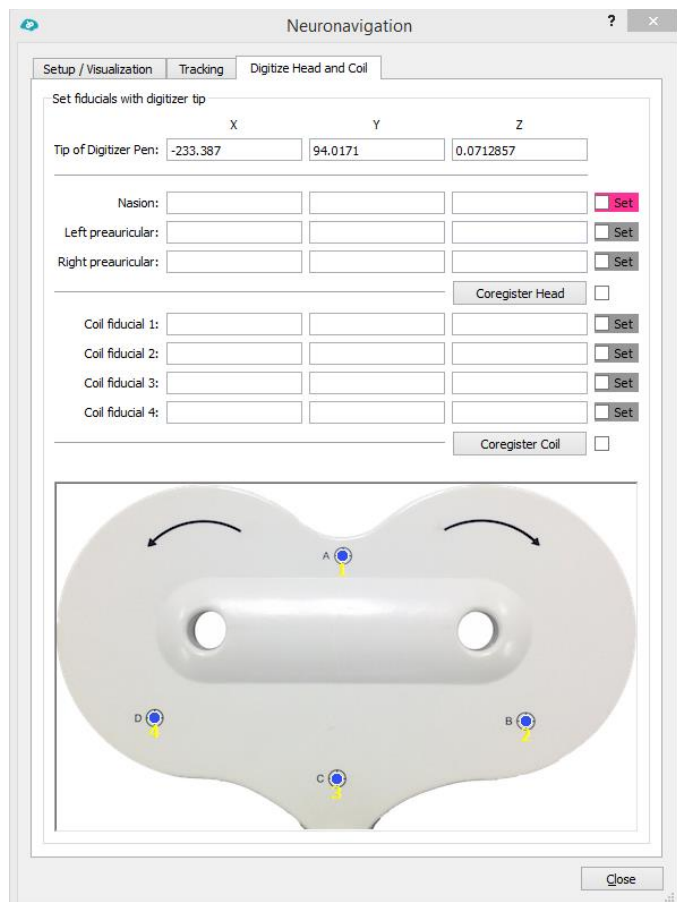



In the coregistration or Digitizer window several points need to be coregistered:

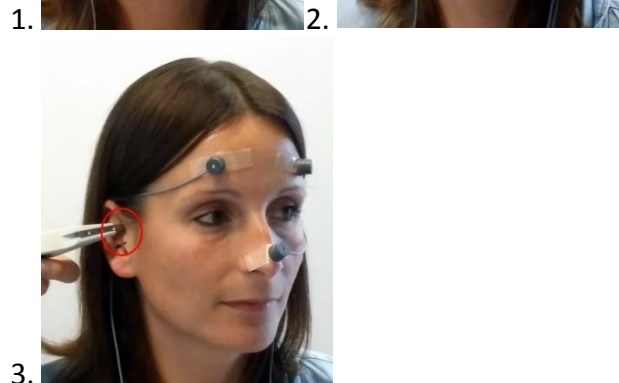
Three points which have been defined as reference points on the head mesh of the participant (the head mesh fiducials).

As well as multiple reference points on the TMS coil (the coil fiducials). The number of coil fiducials depends on the coil type, but never exceed 5.


Another important entry in this window is the coordinates of the Digitizer Pen (first row). The Digitizer Stick is used to perform the coregistration of the head and coil.

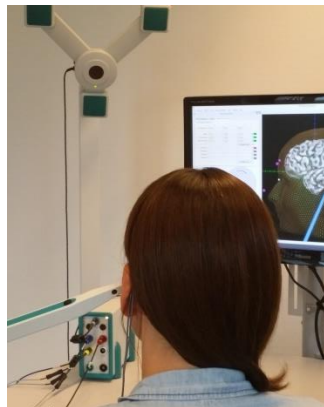



5.  Use the Digitizer Stick to identify the previously defined anatomical landmarks on the participant's real head. Define the points in the same order as indicated in the dialog, i.e. first the nasion, second the point close to the left ear and last the point close to the right ear.

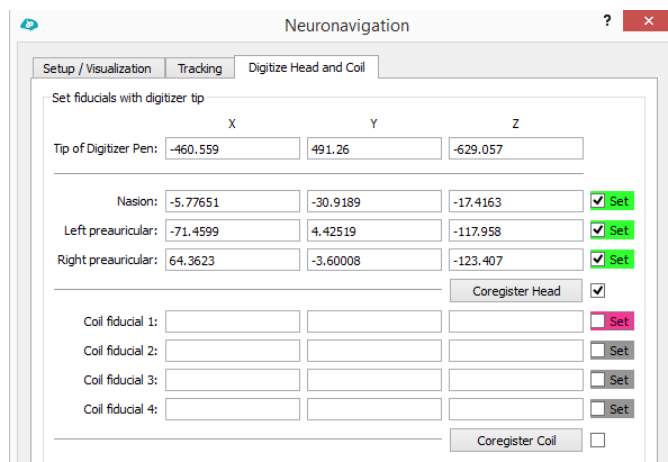



Touch with the tip of the stick the corresponding head location and confirm the correct position by pressing the button on the side of the Digitizer Stick. A short press will define the coordinate of this reference point and a longer button press will delete the coordinate of the last defined reference point again.


-  Make sure that the ultrasound transmitters of the Digitizer Stick as well as the single markers attached to the participant's head face the measuring unit when confirming the reference point location by pressing the button on the pointer.



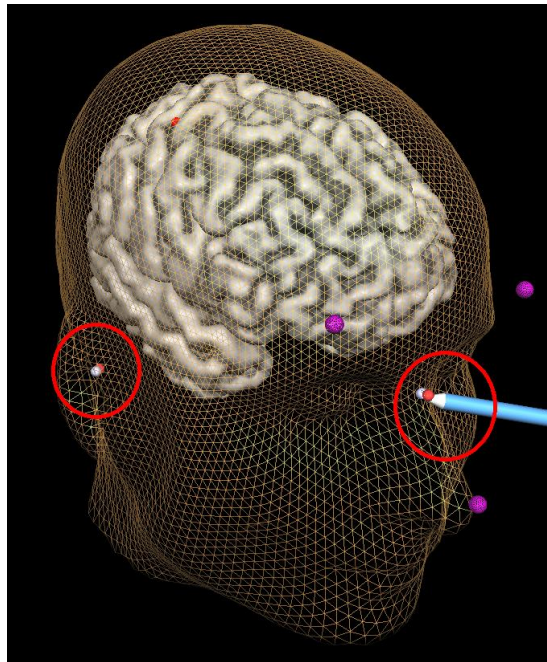
6.  Once you have defined a point the coordinates will appear in the respective field of the "Digitize Head and Coil" tab and the "Set" checkmark will appear next to the coordinate indicating that the point definition was successful. After defining all three head points, the coregistration of the head mesh and the participant's head in the external world will be performed automatically, as indicated by the "Coregister Head" checkmark.




7.  If the coregistration was successful, the red points – defined by the Digitizer Stick – should overlap with the white points - defined on the head mesh (see image on the right).


-  Additionally, check the quality of the coregistration procedure by touching the participant's head with the tip of the Digitizer Stick. This gesture should be displayed at the same location in the surface window.

Furthermore, three purple spheres appeared which indicate the location of the single ultrasound markers.



-  You can continue with the coregistration of the TMS coil.

3. Coregister TMS Coil


-  Before we can start with the coregistration of the TMS coil in the TMS Neuronavigator, the triple marker has to be attached to the TMS coil. For that purpose a TMS coil holder was delivered which can be screwed to different TMS coil handles and can be used to attach the triple ultrasound marker.

During navigation the triple marker transmitting information about the current position of the TMS coil in real-time must face the microphones to complete the coregistration. If it is temporary “off-view”, the display will freeze. Then the position will be recalculated in real-time and the display will be updated.


Be aware that you cannot change the triple marker/ coil holder configuration during navigation.

The setup must stay fixed after the coil coordinate system is linked with the head coordinate system. Planning on how to mount the marker is essential for a smooth coregistration and neuronavigation procedure.

Furthermore, check again whether the correct TMS coil has been selected. This can be easily done in the “Digitize Head and Coil” tab, as the image of the TMS coil displayed in the lower part of the window changes with the selected TMS coil in the Setup tab.


1.  For the coregistration procedure place the TMS coil in a stable position, e.g. on a table or in a holding device. This is done to ensure a fixed position of the coil during the reference point coregistration.



-  Define the points in the same order as shown in the “Digitize Head and Coil” tab. Make sure that the coordinates of the tip of the Digitizer Stick are always displayed in the neuronavigation window. If they are not displayed, the transmitters of the Digitizer Stick or the Coil Triple Marker do not face the measuring device and the coregistration device cannot be performed.

| | X | Y | Z | |
|--|----------------------|----------------------|----------------------|---|
| Tip of Digitizer Pen: | -460.559 | 491.26 | -629.057 | |
| Coil fiducial 1: | <input type="text"/> | <input type="text"/> | <input type="text"/> | <input checked="" type="checkbox"/> Set |
| Coil fiducial 2: | <input type="text"/> | <input type="text"/> | <input type="text"/> | <input type="checkbox"/> Set |
| Coil fiducial 3: | <input type="text"/> | <input type="text"/> | <input type="text"/> | <input type="checkbox"/> Set |
| Coil fiducial 4: | <input type="text"/> | <input type="text"/> | <input type="text"/> | <input type="checkbox"/> Set |
| <input type="button" value="Coregister Coil"/> | | | | <input type="checkbox"/> |

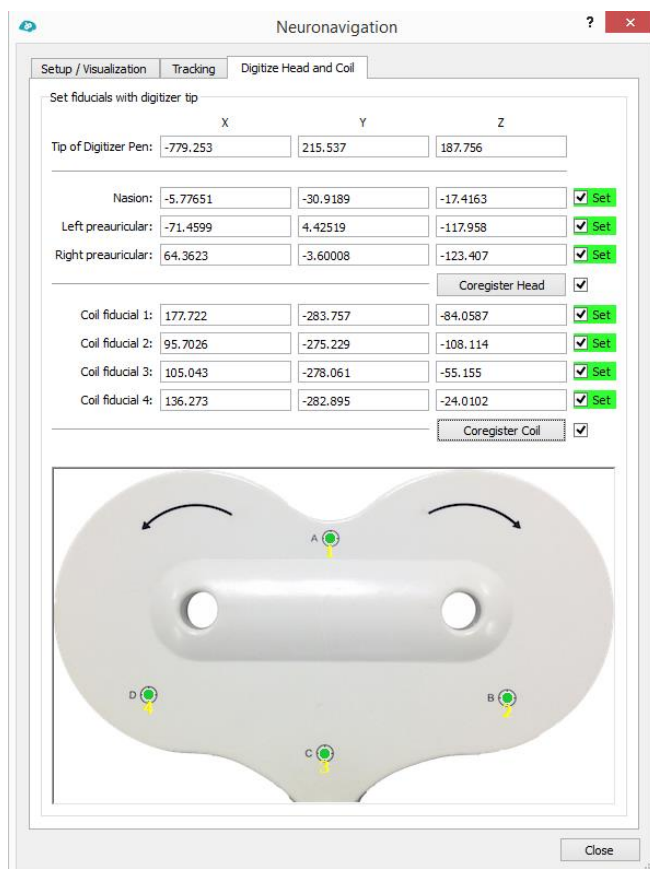


2.  Once you have located the first point, click the Digitizer button and the spatial coordinates of this point are saved. This is indicated by the “Set” checkmark to the right of the coordinate.

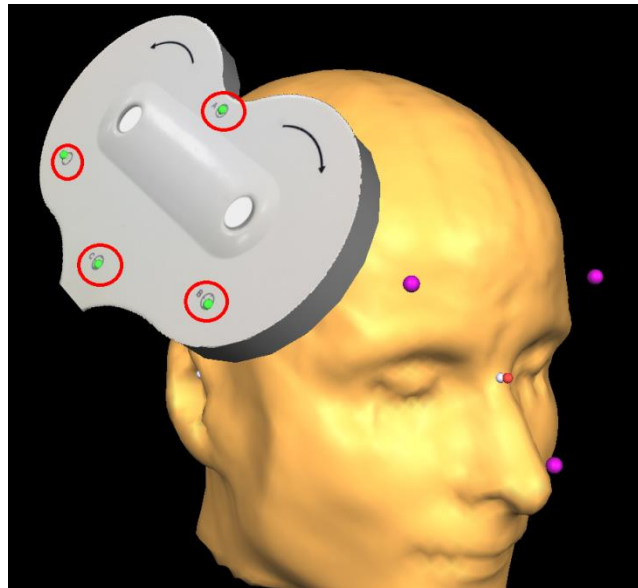
Repeat this step for the remaining three coil fiducials.



At the end, the coil coordinate system will be automatically coregistered to the head coordinate system, allowing for precise neuronavigation of the TMS coil.



- i** Inspect the quality of the coil coregistration by checking the locations of the green spheres displayed on the coil image in the surface module.



We can now start with the real-time TMS neuronavigation.

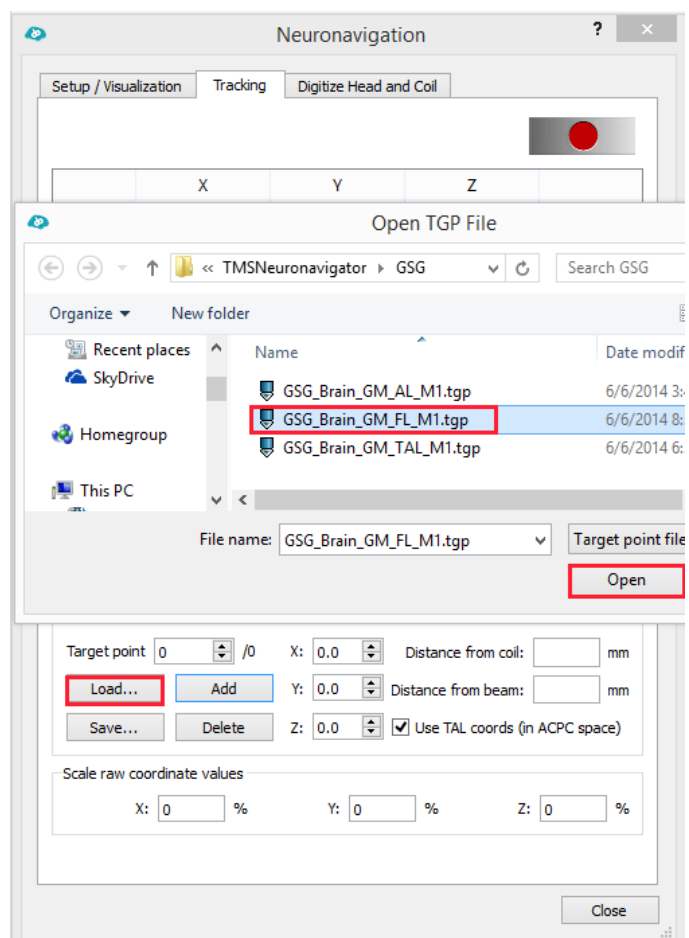
4. Real-Time Neuronavigation

- i** Using real-time neuronavigation, we want to focus the TMS coil on a certain target point on the cortex.

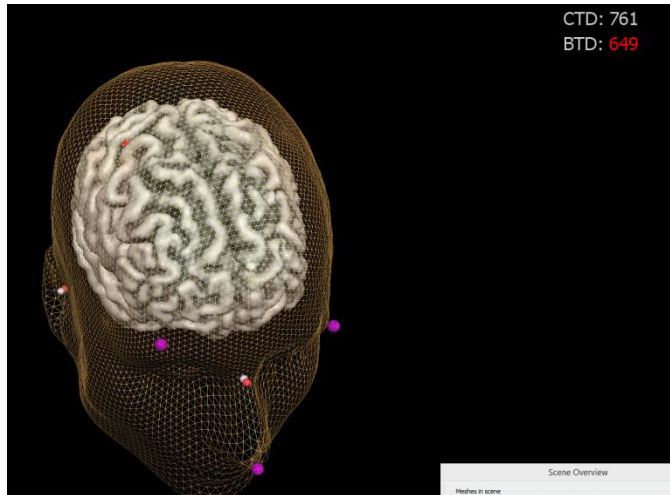
1. Load the functionally defined target point (GSG_Brain_GM_FL_M1.tgp) via the “Load...” button in the “Target points” field of the “Tracking” tab in the Neuronavigation window.

Three things will change:

- 1) The target point will be displayed on the head mesh.
- 2) The target point field in the “Tracking” tab will show the corresponding coordinates.



- 3) A coil-to-target-distance (CTD) and a beam-to-target-distance (BTD) value will appear in the upper right corner of the surface window. These values are only valid for the currently selected target point in the "Target point" spin box of the "Tracking" dialog (in case multiple target points have been defined).



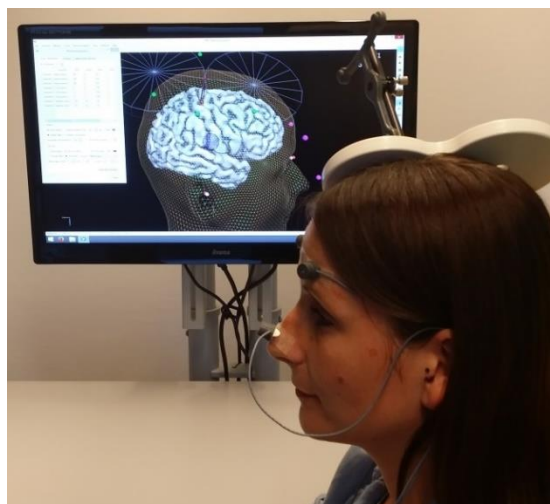
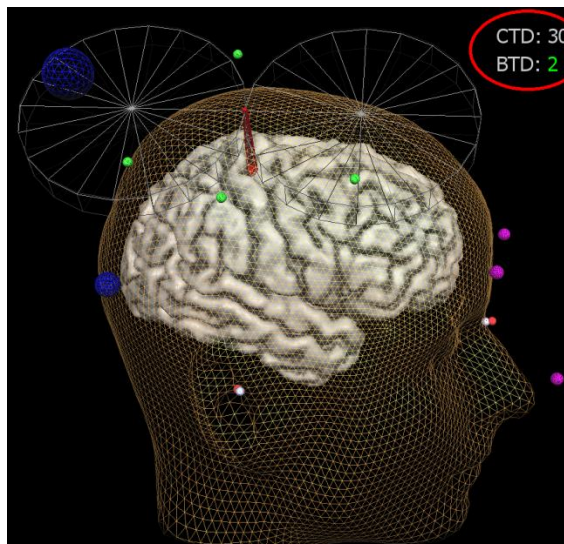
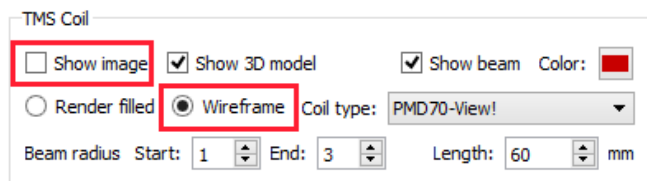
2. Now navigate the coil to the target.



When the TMS coil is visualized with an image, the image can block the view during the navigation.

In order to improve the visibility of the target point and the cortex, deselect the image of the TMS coil, which is required for the coregistration of the coil, and change the coil visualization to wireframe mode.

Once the BTD approaches values close to zero, the color will change to green and the TMS coil can be fixated for the TMS experiment.



Part IV Appendix

Manual Data Preparation

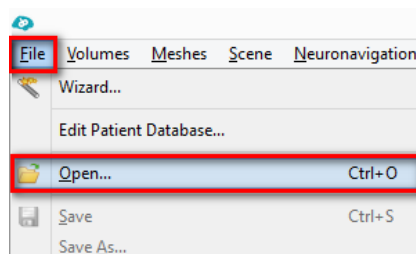
Step 2: Manual ACPC Transformation

- i** For some non-standard datasets (e.g., lesion data, data sets from children or elderly), it might be advised to perform the ACPC transformation manually. Furthermore, even in some standard adult data sets the automatic transformation to ACPC space fails. If this is the case, the ACPC transformation and the definition of the Talairach landmarks can be performed manually.

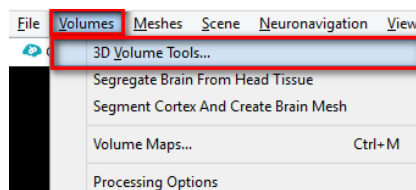
1. Open the TMS Neuronavigator and close the TMS Neuronavigator Wizard.



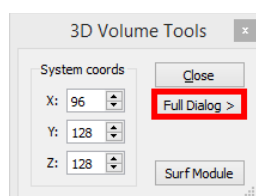
2. Go to “File -> Open” and select the GSG.vmr.



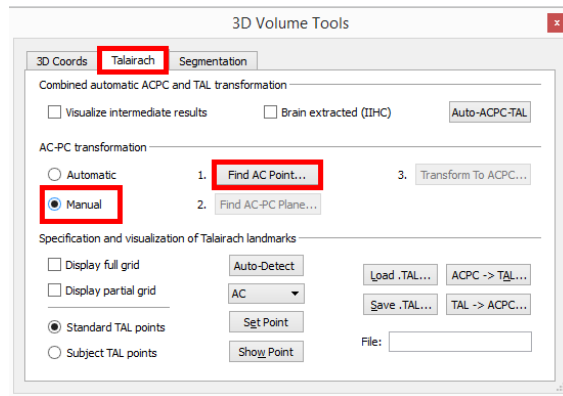
3. The “3D Volume Tools” dialog should be open in the right upper corner of the main program window. If this is not the case open the dialog via “Volumes -> 3D Volume Tools”.



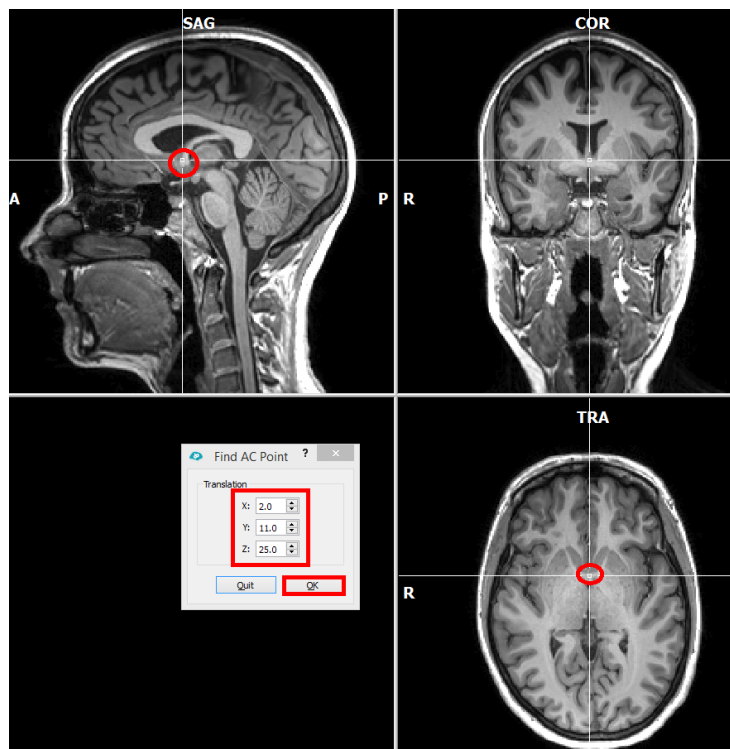
4. Expand the dialog as shown on the right.



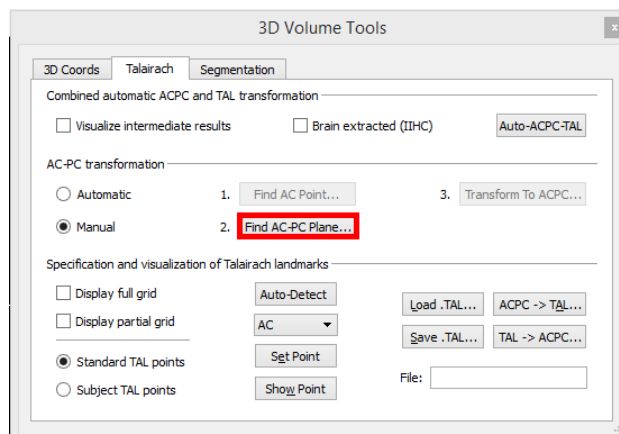
5. Move to the “Talairach” tab, choose the radio button “Manual” and click on “Find AC Point”.



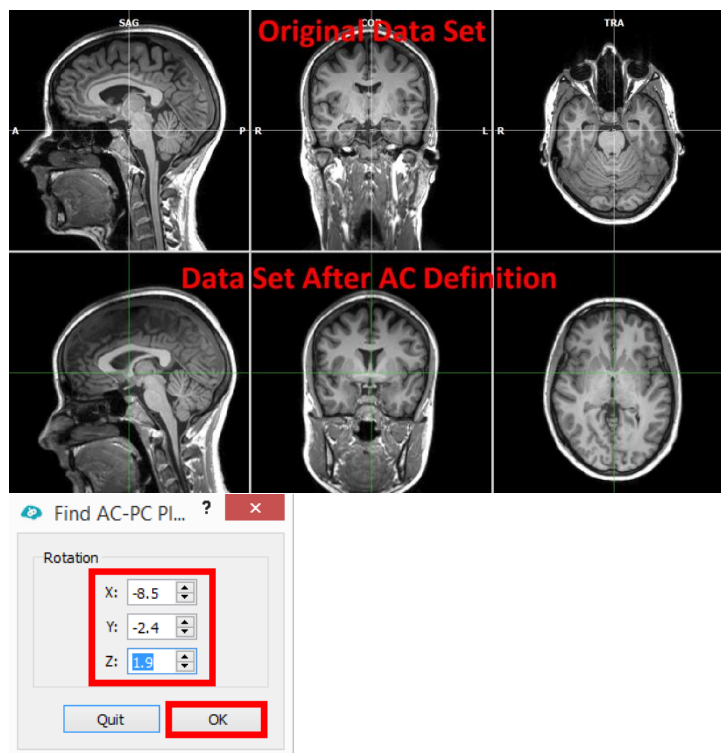
6. Use the spin boxes in the appearing “Find AC Point” dialog to identify the Anterior Commissure in the data set. Confirm your selection with “OK”.



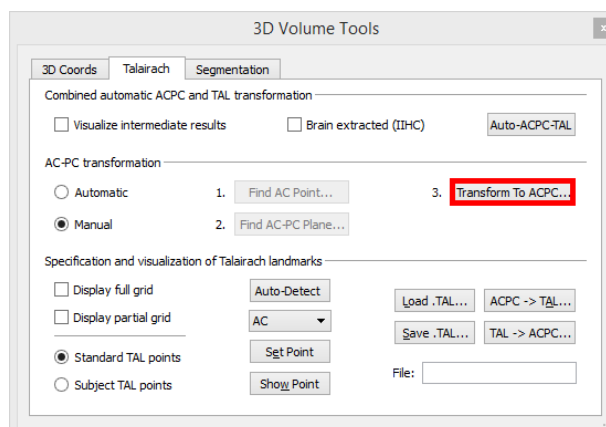
7. In order to define the AC-PC Plane, click next on “Find AC-PC Plane ...”



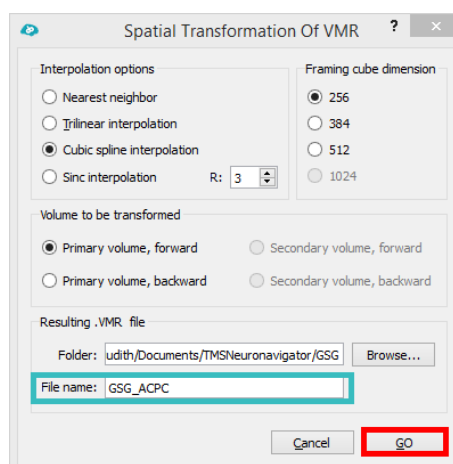
8. Use the “x” spin control in the “Rotation” field to rotate the dataset in the lower row until the view shows the posterior commissure. The rotation is executed around the position of the green cross. Since the cross is located at the anterior commissure, it will remain visible in the coregistration window despite rotation. The green cross can be used to adjust two additional angles, if necessary. Change the “y” and “z” angle to rotate the dataset in the coregistration window so that the green cross runs through the middle of the brain. Now click the “OK” button in the “Find AC-PC Plane” dialog.



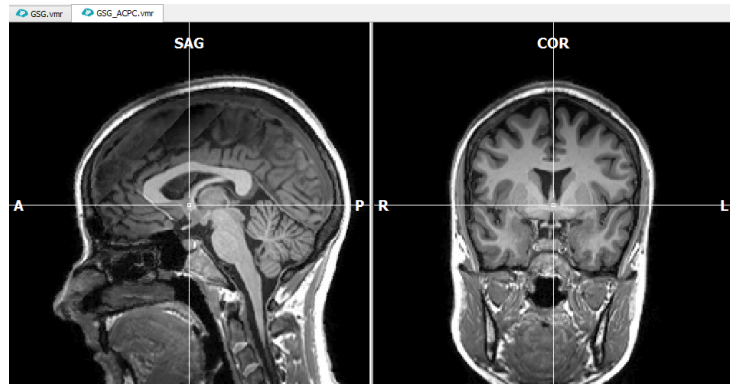
9. After having specified the AC-PC plane the “Transform to ACPC..” is enabled. In order to save the specified transformation (translation and rotation values) and to apply them to the 3D data set, click the “Transform to ACPC...” button.



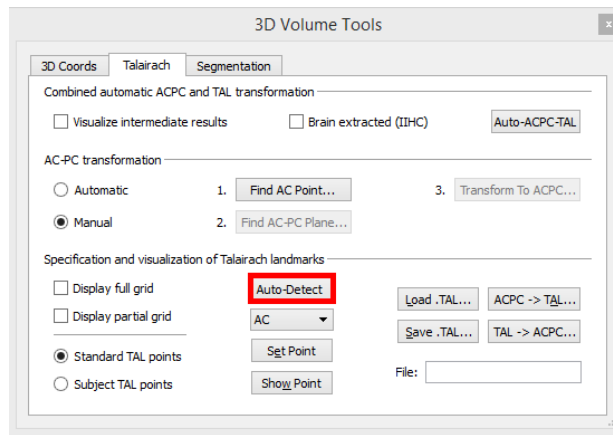
10. A “Spatial Transformation of VMR” dialog opens automatically. The TMS Neuronavigator will suggest the filename: “GSG_ACPC”, which is used to name both the spatial transformation (TRF) file as well as the resulting VMR file. Click the “GO” button to start the ACPC transformation.



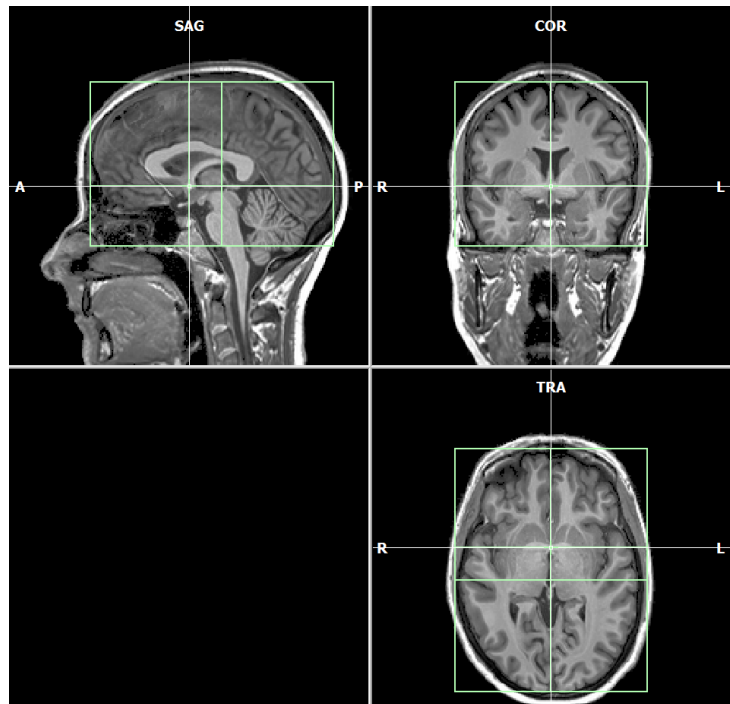
i The specified spatial transformation is now applied to the data set. After a few seconds the resulting new 3D volume has been computed and saved to disk. In addition, the new VMR is also shown automatically in a new window. The center of the new data set is the AC point and the brain is located in the AC-PC plane.



11. **m** In the second step, eight reference points have to be specified within the AC-PC transformed data set: AC, PC, AP, PP, SP, IP, RP and LP. Click on “Auto-Detect” in the “Specification and visualization of Talairach landmarks” field. The TMS Neuronavigator will identify all landmarks automatically.



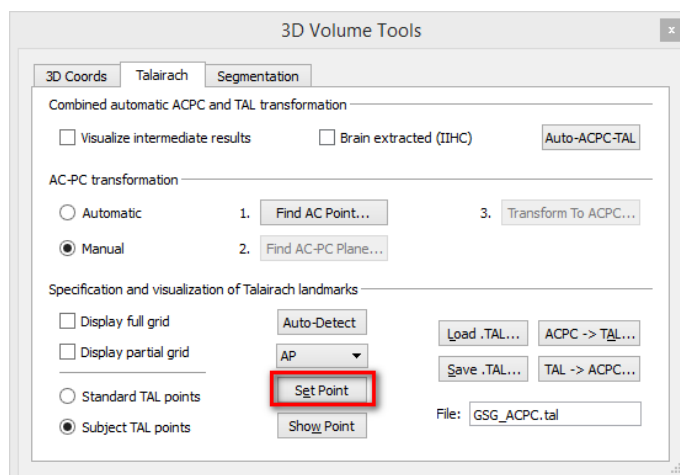
i As a result a green box is overlaid on the data set, representing the identified cerebrum border (see image on the right).



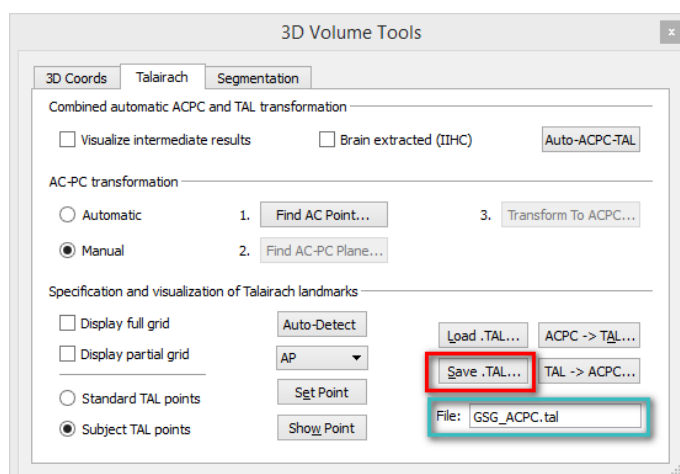
12. As a next step, you need to check whether the landmarks were correctly identified by the program. In order to do that hide the partial Talairach grid first (1). Then select each Talairach landmark in the list (2) and confirm the correct location in the image (3). Make sure that the cerebrum border points represent the most outer points of the grey matter. If a point was not correctly identified, correct the point by left clicking on the correct position in the data set.



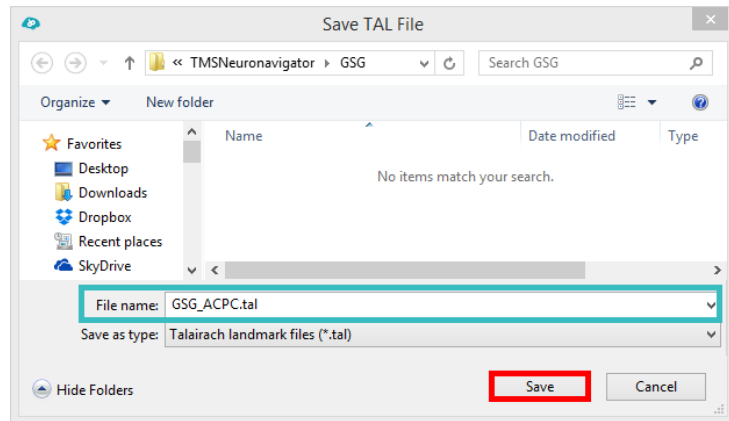
13. Confirm the corrected landmark position by clicking on "Set Point".



14. After all landmarks have been checked and corrected if necessary, you can save the corrected Talairach landmarks to disk, by clicking on "Save TAL..."



15. Keep the suggested filename and save the GSG_ACPC.tal.



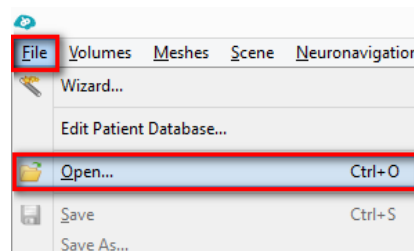
You can now continue with the creation of the head mesh.

Step 3: Manual Initiation of the Surface Reconstruction of the Head

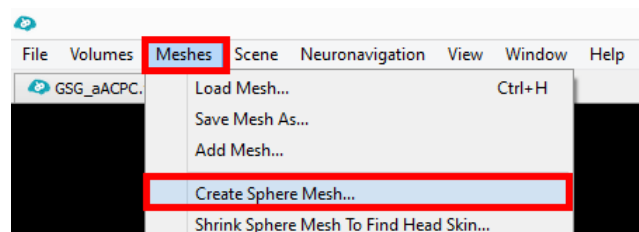
1. Open the TMS Neuronavigator and close the TMS Neuronavigator Wizard.



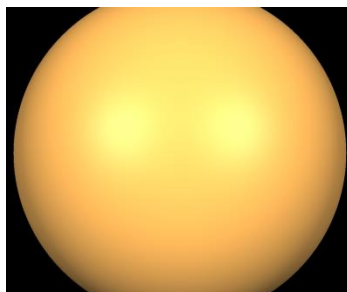
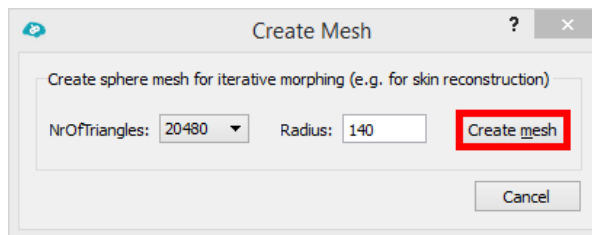
2. Go to "File -> Open" and select the GSG_aACPC.vmr.



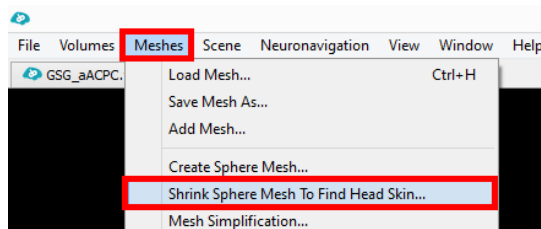
3. Go to Meshes -> "Create Sphere Mesh..."



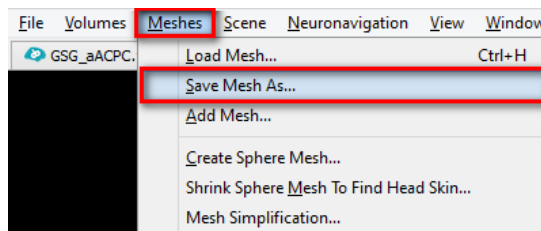
4. In a new surface window tab the Create Mesh dialog will open. Click on “Create Mesh” to create a sphere mesh.



5. Go to “Meshes -> Shrink Sphere Mesh To Find Head Skin” to start the iterative morphing procedure.



6. Save the resulting mesh to disk via Meshes -> “Save Mesh As...”. Use the file name: “GSG_aACPC_Head.srf”

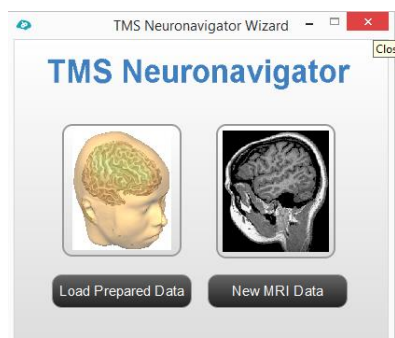


You can now continue with the creation of the cortex mesh.

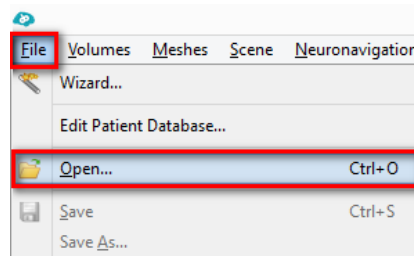
Step 4: Manual Initiation of the Automatic Cortex Segmentation

- ① The cortex segmentation can be started manually in case one of the earlier steps had to be performed manually or if the brain peeling step (removal of non-brain tissue) needs to be improved.

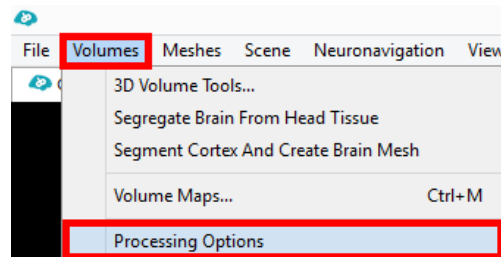
1. Open the TMS Neuronavigator and close the TMS Neuronavigator Wizard.



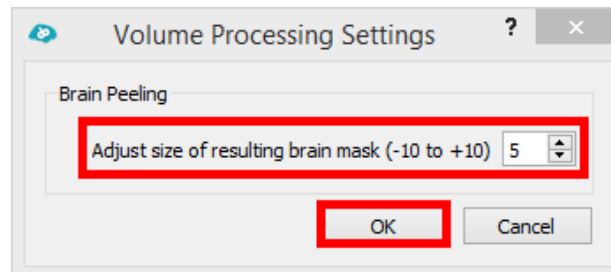
2. Go to “File -> Open” and select the GSG_aACPC.vmr.



3. In case not enough non-brain tissue is removed during the brain peeling, go to “Volumes -> Processing Options”.

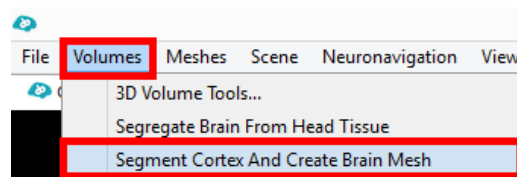


4. You can adjust how conservative the brain peeling is applied, by adapting the “Adjust size of resulting brain mask (-10 to +10)” field.



By default the brain peeling procedure is rather conservative to avoid an unintentional removal of brain tissue. By reducing the number in the spin box, the brain peeling becomes more liberal. Leave the dialog by clicking “OK”.

5. Start the automatic cortex segmentation (including the brain peeling) via “Volumes -> Segment Cortex And Create Brain Mesh”.



Overview of File Formats

All files required for neuronavigation are BOLD.

| Step | Input | Output |
|-------------------------------|--|--|
| Part II, Step 1 | miclue_140514_GSG -0002-0001-00001.dcm | GSG.vmr |
| | – | GSG.v16 |
| | miclue_140514_GSG -0002-0001-00192.dcm | GSG_VMR.pos |
| Part II, Step 2 | GSG.vmr, GSG.v16 | GSG_ToMSP.trf |
| | | GSG_aACPC.trf |
| | | GSG_aACPC.vmr |
| | | GSG_aACPC.tal |
| Part II, Step 3 | GSG_aACPC.vmr | GSG_aACPC_Head.srf |
| | | GSG_aACPC_Head.vwp |
| Part II, Step 4 | GSG_aACPC.vmr | GSG_aACPC_Brain.vmr |
| | | GSG_aACPC_Brain_BrainTalMask_ACPC.vmr |
| | | GSG_aACPC_Brain_RH_WM.vmr |
| | | GSG_aACPC_Brain_LH_WM.vmr |
| | | GSG_aACPC_Brain_LH_RECO.vwp |
| | | GSG_aACPC_Brain_LH_RECO.srf |
| | | GSG_aACPC_Brain_RH_RECO.vwp |
| | | GSG_aACPC_Brain_RH_RECO.srf |
| | | GSG_aACPC_Brain_LH_RECOSM.vwp |
| | | GSG_aACPC_Brain_LH_RECOSM.srf |
| | | GSG_aACPC_Brain_RH_RECOSM.vwp |
| | | GSG_aACPC_Brain_RH_RECOSM.srf |
| | | GSG_aACPC_Brain.vwp |
| | | GSG_aACPC_Brain.srf |
| | | GSG_aACPC_Brain_LH_GM.vmr |
| | | GSG_aACPC_Brain_RH_GM.vmr |
| | | GSG_aACPC_Brain_LH_GM.vwp |
| GSG_aACPC_Brain_LH_GM.srf | | |
| GSG_aACPC_Brain_RH_GM.vwp | | |
| GSG_aACPC_Brain_RH_GM.srf | | |
| GSG_aACPC_Brain_GM.vwp | | |
| GSG_aACPC_Brain_GM.srf | | |
| Part II, Step 8 | GSG_aACPC.vmr | GSG_aACPC_Head.fdp |
| | GSG_aACPC_Head.srf | |
| Part II, | GSG_aACPC.vmr | Step 10: GSG_Brain_GM_AL_M1.tgp |

Appendix

| | | |
|---------|------------------------|---|
| Step 10 | GSG_aACPC_Brain_GM.srf | Step 11: GSG_Brain_GM_TAL_M1.tgp |
| Step 11 | Step12: | Step 12: GSG_FingerTapping_Brain_GM.smp |
| Step 12 | GSG_FingerTapping.vmp | Step 12: GSG_Brain_GM_FL_M1.tgp |

Literature

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