University of California, Irvine
General Clinical Research Center

Transcranial Magnetic Stimulation Laboratory
Key Policies and Forms

CONTENTS
TMS Lab Policy
TMS Screening Form
Seizures and TMS
Instructions for using Brainsight
UCI TMS MRI File Retrieval & Conversion
TMS Lab Policy

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1. General: TMS may only be performed upon completion of the GCRC Neuroimaging Core TMS Training and with the subsequent written approval of the Core Director, Dr. Steve Cramer. This training includes confirmation of completion of required UCI Human Subjects and HIPAA training modules, training in human subjects research, familiarity with GCRC policies, and familiarity with the safe operation of the TMS software and hardware. TMS may only be performed in the General Clinical Research Center Hewitt Hall site, with the onsite availability of a GCRC nurse familiar with operations of the TMS lab.

A GAC-approved, IRB-approved, TMS-trained investigator may perform single pulse TMS studies, or low frequency (1 Hz or less) repetitive TMS, of healthy subjects without supervision if done in accordance with these policies. For single pulse TMS studies of subjects with a condition associated with reduced seizure threshold (such as structural brain abnormality) and for any for studies using TMS in the repetitive-TMS mode at a frequency > 1 Hz, the investigator has the additional responsibility of identifying an MD who is familiar with recognition and response to a seizure and who has agreed to be in the building during performance of each TMS study.

2. Hardware: Prior to performing TMS studies, the investigator must demonstrate familiarity with, and safe operation of, all hardware involved. This includes the computers, trigger cables, the TMS front panel, amplifiers, TMS coils, and (if used) the frameless stereotaxic components. These components are very expensive and the investigator assumes cost of replacement if devices are damaged due to improper or irresponsible usage. Familiarity with replaceable components, such as EMG lead materials, is also important. Please notify Dr. Cramer if replaceable supplies need re-ordering.

3. Software: The investigator must demonstrate familiarity with all software to be employed including Scope for motor evoked potential recordings, programs needed to transfer MRI data as needed, and (if used) Brainsight for frameless stereotaxic methods. No software is to be installed by users on TMS lab computers—software is to be installed only by the Neuroimaging Core personnel, otherwise software conflicts will be inevitable. The investigator must contact the Neuroimaging Core personnel for a TMS room computer account/login/password.

4. Compliance with rules: The investigator must comply with all UCI IRB and all GCRC rules, general and those specifically outlined herein. Approval must be obtained from UCI IRB and from the GCRC review board (GCRC Advisory Committee or “GAC”) for all studies performed. Paramount among these rules for the current context is that TMS may only be performed in the GCRC Hewitt Hall site (room 1311) at a time when a GCRC nurse is present in Hewitt Hall, which is achieved when one schedules with GCRC as per below. A TMS Screening Form must be completed as below.

5. Earplugs: All subjects in the TMS room during any TMS studies must wear protective earplugs.

6. TMS Screening Form: For all subjects, a TMS Screening Form, akin to an MRI Screening Form, must be completed for all subjects, signed prior to any TMS performance, and placed in the ‘signed form bin’ that sits on the TMS Room desk. Any Yes response on this form requires that the subject be explicitly approved by Dr. Cramer before any TMS is performed. Note that on this Form, items 1-7 are absolute contraindications, and a Yes to any of these precludes performance of any variety of TMS unless explicit exception is explicitly granted by Dr. Cramer. Items 8-13 are not absolute contraindications but in some cases could affect seizure threshold, and therefore any Yes response to an item 8-13 question means that the subject can only undergo TMS if Dr. Cramer has explicitly approved the subject for TMS. When a subject is studied a second time, either a new form must be completed or the prior form must be initialed/dated to indicate no change in responses.
7. Scheduling with GCRC: Subjects may only be studied with TMS after scheduling the subject via formal GCRC methods. Currently this involves phoning (714 456-2307) or emailing (<angelam@uci.edu>) Angela Mendoza. Support for the GCRC hinges on formal documentation of each subject’s visits. The contact to Angela achieves this. Also, confirmation of an appointment through Angela insures that a GCRC nurse will be on site when the subject is scheduled.

8. Reserving the TMS room: The TMS room is shared by many investigators. Angela Mendoza is not involved reservation of the TMS room. A second scheduling effort must be extended to insure the room and equipment are available. The investigator must login to http://www.gcrc.uci.edu/neuroimaging/tmscalendar/index.cfm ; if not on GCRC’s HS system, userID is "GCRCNeuro" and the password can be obtained from Dr. Cramer.

9. Familiarity with response to a seizure: While a seizure has never been reported with single pulse TMS using healthy subjects, the investigator must nevertheless be familiar with the Lab Policy for a seizure, which is: (a) Call the nurse for help. (b) Call 911 for emergency assistance in most cases. (c) Do not place objects or fingers near the subject’s mouth, and do not lift the subject unless it is critically necessary. (d) It is OK to loosen clothing around the neck, to place a pillow next to the head, or to increase subject safety. (e) Place an oxygen mask. The TMS room rules require that the door be left slightly ajar during TMS studies. One reason for this is to permit the GCRC nurse to enter the room without having the examiner leave the subject.

10. Pregnancy screen: Any woman of childbearing potential needs to have a negative pregnancy test prior to her first time TMS session. The GCRC can provide materials for instant urine test on site.

11. Two-way radio communication: The nurse on duty at the Hewitt Hall GCRC has in his/her possession a pair of two-way radios ("walky-talky's"). Prior to each TMS session, the TMS investigator must seek out the nurse on duty, to remind the nurse that a TMS session is beginning, and that the nurse's walky-talky needs to be in the nurse's possession. The second walky talky can be with the investigator in the TMS room, or can remain in the neighboring nursing station, in easy access to the investigator. This arrangement guarantees that if the person performing TMS suddenly needs nursing support, the nurse will be readily available, even if the nurse is in a different room in Hewitt Hall, without the need to physically search for the nurse.
Name of TMS Subject _______________________________________________

Your head will be exposed to a strong magnetic pulse. To maximize safety, please answer the questions below. Please do not hesitate to ask any questions you may have regarding below.

Do you have, or have you ever had, any of the following? If Yes, please explain on back

Y   N  1. Metallic hardware on the scalp
Y   N  2. Cardiac pacemaker
Y   N  3. Implanted medication pumps, intracardiac line, or central venous catheter
Y   N  4. History of cortical stroke or other cortical lesion such as brain tumor
Y   N  5. Prior diagnosis of seizure or epilepsy
Y   N  6. Previous brain neurosurgery
Y   N  7. Any chance you are pregnant? Date of last menstrual period: __________
Y   N  8. Any electrical, mechanical, or magnetic implants?
Y   N  9. Migraine headaches – if yes, are they controlled?
Y   N  10. List current medications on back of form (we are interested in medicines that affect seizure threshold such as tricyclic antidepressants and neuroleptics)
Y   N  11. Unstable medical conditions
Y   N  12. Any body or clothing metal above your shoulders? If so, please remove.
Y   N  13. Any metal on your body (i.e. watch or jewelry, hair holders or pins, eye glasses, body piercings, wallet, keys)? If so, please remove.

I have read and understand all questions in this document. My signature below indicates that I have accurately and completely answered all questions in this document.

Signature of TMS Subject: ________________________________  Date:  ___________________

Signature of investigator: _________________________________  Date:  ___________________
Seizures and TMS
UCI GCRC TMS Lab
version May 26, 2006

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Seizure types and their recognition
A seizure is an electric storm in the brain. A person can have a seizure for many different reasons. TMS has been reported to cause a seizure but this is very, very uncommon. A seizure can start very suddenly and unpredictably.

There are several types of seizure.
1. In some, there can be various types of repeated or jerking movements but no change in consciousness.
2. In other seizure types, a person is confused, with some alteration in consciousness, often accompanied by suddenly odd behavior.
3. The most severe type of seizure is characterized by severe jerking, writhing, and arching movements of the entire body, with complete loss of consciousness; in the few TMS-induced seizures reported in the literature, this third type is the most common.

Recognizing seizures types 1 and 2 is difficult, and a non-neurologist should likely label any suspicions for these as “possible.” Recognizing the third type of seizure above can be made with greater certainty by a non-neurologist.

Responding to a seizure
• If alone, call for help—this is why the door to TMS room is left ajar
• If two people are present, the first stays with the subject and the second should go to get a nurse, who will call 911
• Remove harmful objects from the person’s surrounding area
• If the person is in a chair, gently pull chair back away from metal instruments
• Loosen tight clothing from around the neck
• Cushion the head as possible
• Do NOT place anything or any fingers anywhere near the mouth
• Do not attempt to hold the person down
• Remain calm, seizures almost always stop after a few minutes
• Observe what is happening, how long, etc—this can help the person later
• If a person is having trouble breathing, turn them on their side
• After a seizure, stay with the person until paramedics arrive
• If there is concern for injury, do not move the person
Instructions for using Brainsight 1.5
Version May 26, 2006

Note: The program Brainsight is used for frameless stereotaxic TMS. Further details on Brainsight can be obtained from the website at http://www.rogue-research.com/

Make sure camera is on (flip switch on black box behind monitor). Do this early, so it has time to warm up – 2nd light on the black box should turn off when camera is ready.

SUBJECT

If this is the first appointment for the subject, open Brainsight 1.5 from the bar at the bottom of the screen and click “I agree”. If the subject already has a project saved, open the project and it will open the program.

1. To load images:
   • Click on File (on the top bar of the monitor screen) – Import Images – choose data format (typically Analyze – will depend on MRI software)
   • Select the subject’s .hdr file (or non-normalized anat or register & resample/reslice epi to anat.)
     Note: We need the full nose to tip and nose to upper lip, top of skull, and ears – ear canal for landmark capability.
   • Select transformation (typically MRI brain 3 with Analyze format).
     Note: If resulting picture is bad (can’t see it, or black and white), try entire process again (being sure to delete the .hdr file from the list- located in the small box that first opens with the program), with different transformation (MR Brain2 or MR Brain).

2. 3D reconstruction (or “Tell the program where “brain” is.”)
   • Use the curvilinear tool (bottom right icon of the group of 6 icons at top left of Volume View window) – click on it and select “new” from the buttons below the open box
   • In the small window that opens: make sure the coronal (middle picture) view is selected (it is highlighted by default, but hard to notice) – click Add Series: type 0 (start), 18 (end), 3 (step) and click Ok.
     Note: Select a sagittal or transverse view, if you are going to be activating an area of the brain that isn’t best seen from the coronal view.
   • In the Volume View, use apple key + mouse to center the crosshairs in the brain in the sagittal view.
   • Draw an outline of the brain only in the coronal display by clicking on the outline of the brain without using the apple key. Stay on the perimeter of the brain - no need to draw into sulci – stay around the outside layer of the brain.

Rules for drawing on the brain:
   • You must follow the direction of the red circle in the top left of the coronal view (or whatever view you plan to draw in). Start at the right inferior aspect of the midline, and follow a counter-clockwise direction around the brain, ending at the left inferior aspect of the midline. No need to connect the hemispheres at the bottom. You can also do just one half of the brain, if desired (to
more easily see down the midline.) Include temporal lobes, exclude cerebellum and eyes (or whatever you choose based on your study.)

- The program will automatically draw lines between your click points. Points (represented by the “x”) can be deleted by selecting and hitting delete on the keyboard, and/or moved by clicking on the x and dragging it.
- Start by drawing on the middle slice, then draw on one as far anterior and as posterior as you want representation for. The program will automatically draw on the areas in-between by interpolating between slices.
- On the sagittal view, use apple key + mouse to click between your manually drawn slices (represented by the red dashes on the left side of the sagittal picture area) to check that the program accurately drew around the brain.
- If you aren’t satisfied by where the automatic lines have been drawn (e.g. they aren’t correctly representing gray matter vs. CSF, or a true outline of the brain), redraw them manually by simply clicking in the window where you want to begin drawing – the automatic lines disappear and your clicks are recorded as before.
- When you are completely satisfied that the brain has been accurately outlined, turn off the ability to draw the outlines by unchecking the display box on the left (this is just to keep you from accidentally clicking around and messing up your work).

3. View 3D picture of the brain
   - Select one view box for 3D view and click on the blue sphere at the top of that box (second icon in from the top line of icons in each of the picture windows showing brain).
   - Go to the list icon (in the same line of icons at the top of the individual viewing box) and check the surface peeler box from the very bottom of the list. Click OK to close the list. A strangely shaded form of the brain in 3D should appear shortly.
   - Click on the peeler box in the upper right hand side of full screen column that’s on the left of the entire Volume View window. Slide the bar up and down to select to level of peel you desire (6 is typical). Slide the 2D bar (in upper left column of options under the curvilinear tool menu) to the right all the way to smooth the peel.
   - In the 3D view, you need to select from the list any item you wish to see. This includes any landmarks you placed on the brain for reference, any trajectories you saved, and pointer sticks or lines to show the position of the coil once you’re clicking.
   - Adjust the view of the brain by using the icons on the top bar of the 3D viewing window. You can zoom (be careful – it moves QUICKLY!!! If picture disappears, click on the “eye” icon and select a face. The program should bring the brain back into view in the orientation you selected), shift, and rotate the brain.

Note: The peeler box is only available in the curvilinear view. If you can’t find it, select the “tunnel”-like icon at the bottom right of the group of 6 icons in the column to the left of the brain pictures.

4. Mark landmarks
   - Click on the A+ icon in the group of 6 icons on the top left of the Volume View window.
   - Hold down the apple key while you click around to find the exact location you want to mark. Be sure to utilize each view (transverse, sagittal, coronal) to be assured that you’re in the correct spot. Mark a spot that is slightly into the skin, since you will likely push gently onto the subject’s face while registering.

Note: You may desire the pictures to be larger. You can change the 6-up to 4-up – so only 4 brain views are shown – by clicking on the 4-up button at the top middle of the Volume View window.
• Points to mark are: tip of nose, nasion (bridge of nose between brows), right and left (remember, radiological conventions: Left = Right) ear canal (just above tragus, one click in to find flesh). Optional: Motor area, generic starting spot on 3D view. Select the pointed finger in the 3D window, click on the spot to mark, and click on the A+ icon as before. View this spot in the 3D view once marked by clicking on the list again, and checking the point’s box.
• SAVE your project. (Click on “File” at the top of the monitor, then Save Project. Name it and navigate to the correct folder.)

5. Register subject to computer
• Make sure that camera is on (flip switch on black box behind monitor).
• Ask subject to rest their chin on the chin rest, and place either the tracker band or the glasses securely on their head.

Note: if starting at this point, click on File – open project – select subject’s data file, to open the previously saved brain image with landmarks.
• Click on pointer finger (top left of Volume View screen, in the group of 6 icons), then click on the drop down box “New” (left side of window, half-way down the column) – registration – assisted registration – go to next step - click auto registration and “go to next step” (be patient)

in the small Polaris window
• Click on the small arrow next to the small text “More” (located at the bottom left of the window)
• Click on the drop down box at the top of the panel that opens up, and select passive polaris C
• In the box immediately below that one, select Tool Cal (pick the most recent calibration file)
• Click Tracking ON
• Move the window out of the way, but do NOT close it

in the registration window
• Bring pointer into camera’s field of view, small red box should turn green.
• The landmarks you named will be selected one by one in the Volume View. Place the pointer at the correct spot on the subject’s head, and click “submit point” when ready.
• Select the points in order. When done with all points (except those on the brain), click “go to next step,” then close the window. Test the accuracy of your registration by pointing to various parts of the skull and making sure the registration is accurate.

Note: if having trouble with the pointer “being seen” by the camera, try clicking on pointer and active (in “mouse” mode) on the main window

5. Prepare to apply TMS pulses
• Go to volume view in pointer mode, select coil (drop down box on left side of main screen, towards the top.)
• Pick inline & inline 90 views (drop down box in individual window that shows i.e. “transverse” or “coronal”) for two of the 4 or 6 picture windows to use while placing the coil.
• Line up the coil with the motor area dot (or any other dot placed on the brain and selected to show on the 3D version), and bring the line of the coil through the point as it is visible on the inline and inline 90 views.
• Click on trajectory icon to save a “good” spot. Make sure you select this trajectory on the list in the 3D view if you want to see it in the 3D view.

Turn camera OFF
Quit the program (from the top of the monitor)

COIL CALIBRATION – only performed when tracker has been moved, or every few months

- Identify sweet spot on the bottom side of the coil
- Put calibration block (on table, behind monitor) in chin rest spot by removing chin rest. Locate Tool ROM file appropriate for the coil being calibrated: TMS lab Mac HD1-Applications-Brainsight-Tools-CT202.rom (for single pulse)
- Click on Tasks – Coil Calibration – follow steps and close window when “calibration complete” is displayed (save as single_pulse_Calyyymmdd)

Helpful Hints

- Quit between projects, otherwise file is appended.
- Don’t touch spheres (small balls on the tracker, pointer, calibration tool & coil) – they’ll get dirty & camera can’t find them easily.
- Must start program from bar, quit it from top.
- PURSUE THESE STEPS IN STRICT ORDER!!!!!! If you go backwards, or do something out of order, you may have to play around to figure out what is off track. Always check to be sure that the calibration file is still selected, or that the correct item is being tracked (coil, pointer, mouse, etc.) and whether or not the “Active” box is checked.
1 Retrieve data from RIC MRI computer
   I. Use FlashFXP (it can resume disrupted transfers)
      A. Suggest retrieving data from RIC within 1 day of the MRI scan
      B. Enter working local directory on left side. Press ‘connect’ (lightning bolt)/quick connect
      C. Fill the fields: server: ricdata.ric.uci.edu, user: cramer, pw: fmri2cramer. Press ‘Connect’
      D. Usually can determine correct folder by its name (for example, “BETAS” or “subject ID”)
      E. DO NOT DELETE FILES – THEY CANNOT BE RECOVERED!
      F. Select folder to transfer to, RH click, TRANSFER

G. Transfer is still going if: files appear in cue (lower left), or progress meter (in yellow at bottom) still appears. Can resume transfer by hitting ‘GO’ button. Transfer complete when # files matches in each column

H. Save data
   1. Create RAWDATA folder, copy .PAR and .REC files into the folder
   2. Burn backup data CD (use template for jewel case)
      a. In Nero – CD-ROM(ISO)/New/
      b. Drag files into the left side. Rename CD to subject ID
2 Process Files and prepare for analysis

I. SPM5
   A. Open SPM5, make sure MATLAB7/work contains uci3t_parec5.m
   B. Navigate to the folder containing the .PAR and .REC files. Make sure the entire path doesn’t contain any spaces.
   C. Type uci3t_parec5, hit enter
   D. A new window opens. Copy/paste the appropriate directory into the ‘Dir’ window; .PAR and .REC files should appear in right hand window
   E. Select all .PAR and .REC files. They should now appear in the window at the bottom. Click ‘Done’.
   F. The program should now create new folders for each run. However, within each folder, the .img and .hdr files will be assigned the same name, so they must be renamed based on session.

II. Rename each session (optional).
   A. Open the program Rename.exe
   B. Navigate to appropriate folder on the left. When the folder is opened, all .img and .hdr files will be shown on the right.
   C. Check the box next to ‘Insert/Append’. Type the desired prefix (ie. Session1) and hit ‘Start’. The program will automatically insert this prefix in front of the file name and save.
   D. Repeat for all sessions.