FUS Foundation Brain workshop
July 23-24, 2012

Overview

Jeff Elias, MD began the meeting with a summary of Parkinson's Disease and tremor. He covered the history of treatment, including early surgical removal of sections of brain tissue (Stereoencephalotome in about 1947). He discussed Thalamic targeting, showing how a line between the anterior and posterior commissure is used to target different regions in the thalamus, including the ventralis intermedius (Vim) nucleus of the thalamus for tremor suppression. Several different regions around the Vim nucleus are sensitive with other known functions. Tremor apparently has a single target, while the Globus paladin is also a target for Parkinson's disease. Deep brain stimulation was used on up to 3000 new patients in 2008 (up from 500 in 98). RF thalamotomy is also performed a lot.

Dr. Elias presented results from the UVA study of MRI guided FUS treatment of tremor. To date, 15 subjects have been treated with MRgFUS for unilateral thalamotomy. There was a significant reduction in tremor in the treated hand and also in the measure of disability. The reduction in tremor in the untreated hand was not significant. The procedure methods were reviewed. After patient setup and localization, FUS exposures were applied in 20 second bursts, beginning at low power and then increasing in power and the effects are monitored to ensure that the desired location has been attained. Location is adjusted until the tremor location has been found. Most lesions have averaged 3mm in diameter. The 2nd patient had 3 re-alignments and the lesion is over larger extent.

Dr. Elias presented a "wish list" of needs for the MRgFUS project.

1) There is a need for better target visualization:
    Higher Field MRI (up to 7T) to better image:
    Globus paladin, STN, Substantia Nigra (need to visualize targets better)
2) Need for connectivity-based thalamic segmentation (Pouratian, Zheng, Bari, …)
3) Need ability to overlay an atlas that is patient specific
4) From a question, there is need for temperature measurements in multiple planes to ensure that the focal spot is correctly located.
    Beat Werner: Need for 3D thermometry
    Jeff Elias: Currently spend an hour to measure temperature in 3 different planes to confirm focus.
5) Need for reduced noise in temperature images.
    Work is being done on improved RF coils.
    Zurich: Uses better receiver coils.

Jeff reviewed the steps and time requirements of procedure:
    Patient prep,
    interface setup,
    transducer alignment,
    planning images,

registration,
treatment planning,
targeting verification,
therapeutic sonications,
patient releases from system.

Question on adjusting focal spot size:

Jeff: better to have a tight focal spot when aligning things.

Treating tremor is ideal – FUS can knock out a small specific spot of the brain.

Beat: How does lesion size relate to volume of ablated tissue?

Jeff: Large part of apparent lesion is edematous.

Most of the T1w abnormality is ablated tissue (visible the next day). That cavity collapses – not necessarily a penumbra that recovers. A lot of the ablated tissue becomes necrotic.

DLP: Is there a temperature at which patient detects effect but damage does not occur? Jeff: spectrum of temperatures – damage is likely dose related.

Kim: Role of ARFI? Jeff thinks ARFI might be better than heating for spot localization? Need better anatomy, DTI, other advanced techniques. Immediate challenge is imaging –volumetric thermometry.

DTI could take the patient out of the procedure loop. Connectivity maps showing where the DBS electrode landed – connectivity map made at UCLA – identify the target area reasonably well.

After Breakfast:

Review of technical challenges

Eyal Zadicario presented an overview of the technical aspects of the InSightec system. He then presented a detailed set of images and artifacts from the 15 MRgFUS treatments performed at UVA and possibly others from other sites. Much of the issues addressed arise from the nature of the system:

Transducer is a large hemisphere with conductive materials – cables, connectors, and water (circulating and vibrating): 7 or 8 liters – only pause circulation while imaging.

Observations - Role of imaging and technical issues:

Stereotactic planning – accurate placement required

Technical issue: Displacement on images (frequency encoding, etc.)

Need to validate registration vs. scanner movement, image shifting, etc.

UVA patient 15, sonication 17: Swap phase freq direction gave shift of 1mm.

CT-MR mis-registration:

The table doesn't go back to the same place each time.

Nathan's experience: When sending the table to the scan position the location reached is different depending on whether the starting point of the table is in the MRI scanner or in or outside of the scanner.

DLP observation:

InSightec is using bilinear interpolation after reconstruction

They don't use zero-filled interpolation –

and the images show a vertical and horizontal pixelation.

Need better Image quality and accuracy for stereotactic navigation.

Need to solve registration

Thermal feedback:

Used for localizing focal spot

Temperture STD around 1 degree.

An artifact was observed that demonstrated signal in regions of the holder that should have been dark, and banding artifact similar to ssfp images. Several alternative causes were presented.

Movement detection:

Ensure that nothing has changed during the several hours required.

Focusing:

CT Fusion: prediction based phasing – correct phase based on CT

MR ARFI.

ARFI sensitivity

1.5T, Brain tissue elasticity mimicking phantom.

6" surface coil

EPI-ARFI invert sequence

Displacement std = 0.2um

Phantom-displacement: 2um/50watts (linear?)

Elena Kaye – comment that displacement and phase change may not be linear because of the time constant of the arfi displacement.

FSE Image quality:

Many FSE images showed very low SNR in the head/brain.

Discussion on development of RF coils

Matt Eames presented work on the UVA receive-ony loops.

Kim Butts-Pauly – Ron Watkins birdcage transmit-receive coil.

Craig Meyer summarized a set of experiments to be performed on Tuesday:

Bandwidth test – multiecho vs. single echo to reduce misregistration.

Test concomitant gradient potential (see if you get oblique shift)

Test B0 eddy current hypothesis – change sign of spoiler gradients.

Test FLAIR for water suppression

Test Sat bands and other methods for aliasing artifact elimination.

Find cause of loss of signal for the FSE sequence. – probably the transmit gain.

Summary of Tuesday Experiments:

1) Tested the frequency shifts – A/P vs. L/R and no shift was observed, though it was observed later.

2) Tested single echo vs. Two-echo acquisition:

Single Echo: BW = 5.7kHZ, TE= 13ms, STD = 0.14 °C

Dual echo: BW = 31kHz each echo – sequence would not allow lower BW.

TE = 13, 17.3 ms, STD = .19 °C

It was suggested that multi-echo be implemented with fly-back. Wilson Miller points out that doing multiple echoes without flyback would help nail down the frequency shifts in #1 above.

3) In heating tests, we observed 1 °C heating of the phantom background. We initially thought this was due to a B0 eddy current (a shift in the Bz due to a B0 eddy current), but we were able to verify that it is likely just an actual nearly uniform increase in temperature throughout the phantom due to the fact that the full phantom is being insonified. Viola did a separate experiment where a short heating pulse after many images had been acquired and there was no B0 shift.

4) We tried to reproduce the banding artifact seen on the DQA phantom. Kim adjusted the receiver gain and finally we adjusted the slice thickness and were able to get the data to exceed the A/D converter range and a nearly identical artifact was observed. Two factors contribute to the cause of the artifact: 1) The base of the phantom holder has metal screws that cause a distortion in the field near the base and banding in the real and imaginary images. 2) The phantom and water nearly filled the entire field of view resulting in a very large term in k-space at the very center of k-space. When overranging occurs, it will eliminate the DC offset for one or both channels. The magnitude image will then have a constant value in black regions and the banding structure will appear. It was shown that this potential problem can be averted by proper receiver gain adjustment on manual prescan.

5) We attempted data acquisition using the GE zip512 option. The resulting images were more artifactual with zero padding – there were different motion artifacts and an increase in Gibbs artifact. It as noted that the images were also filtered differently. Will Grissom repeated the experiment during heating, collected the Pfiles, and performed the reconstructions off line with and without zerofilling (and applying the same filter to both sets of data). The images were presented later and were an excellent illustration of the added value of zero filling. There was no change in the maximum temperature reached and the zero-filled images were smoother without artifactual high frequencies that are inserted in the unzerofilled images.

6) We tested the folding artifact in the SI direction. A phantom was placed close to the transducer and reproduced the wraparound artifact observed when the phase encoding direction is S/I. Kim was able to solve this artifact by applying the no phase wrap. Because this option is not available, she modified the image field of

view and was able to achieve the desired effect with a small increase in scan time. We also tested using saturation band. Again the sequence doesn't allow saturation in the multiphase option, but the images obtained did not eliminate the wraparound and there were additional artifacts from incomplete spoiling of the saturated signal.

7) We tried FLAIR to eliminate water signal with many adjustments in transmit gain, but this was not able to eliminate the water signal. We don't know what the actual flip angle was. If we had revisited this topic after #9 below, we might have had a better chance of improving the images.

8) In conjunction with the ZFI experiments, we succeeded to demonstrate the shifts of the hot spot between AP/ LR and the shift was not exactly the same relative to the desired focus. We applied a 40 Hz reduction in the readout frequency and the shift disappeared in both directions. In our discussion, it would appear that the shift includes another component as well. In other words, the change in each direction seen when you change the freq direction (the diagonal spatial shift) is due to off resonance, while other shifts are from other causes.

9) We studied the transmit gain for the FSE sequence and found that the TG of 99 obtained from the automatic prescan gave strong water signal and reasonable image of the head phantom. We set the TG to 140 and the phantom in the image essential disappeared (poor image quality). We then did manual prescan and found that a TG = 50 gave a much better signal from the center of the image which included the head phantom. We ran the FSE and the image was much better than TG=99. **Conclusion:** It is very important to set the TG manually at least once per subject and then monitor if the TG changes. This is done by maximizing the signal (on MPS/TG) in the center of the signal where the brain is, ignoring the outer signal where the bulk of the water is). This needs to be verified in vivo in both FSE images and temperature images as it could potentially improve the accuracy of temperature measurements if TG is set correctly.

10) Back in the Darden, we had a discussion of acquiring multiple baselines before doing the acquisition. DLP suggested averaging the baselines if the data made sense, but Viola presented data showing that the effects of physiological motion causes image variations that make the average image less effective that choosing the image that matches the phase. Averaging images by phase, might be useful, but would take longer than the actual heating run.

Eyal: There were some final questions about whether eddy currents could be important, but it was felt that there are several similar magnitude potential causes of position shifts, and there is no guarantee that eddy currents are important for up to ½ pixel.

Final discussion – we addressed the question of whether we need 3D temperature measurements. Because there is not a 3D segmented EPI pulse sequence on the GE MRI scanner, we discussed creating an interleaved multiple-slice option. Craig,

Dennis, and Kim presented the argument that multiple slices could be obtained using the existing GE 2D interleaved segmented EPI sequence. This is similar to the method used by others including the Utah group. We returned to the MRI scanner, and Kim set up the pulse sequence with variations in echo train length, bandwidth, etc. The GE sequence includes a reference scan, that takes some time, but then the images are excellent and only show distortion that results from the effective bandwidth in the phase encoding direction. Flyback is not enabled. Tested ETL=4, 8, 16, 32 (32 was too many), 8 seemed ok. Set ETL = 8, RBW = 128. 5 slices acquired in 3 seconds – with excellent image quality. The SNR should be slightly better than the SNR obtained using the original InSightec protocol for a single slice and this obtains 5 slices in the same time.

In summary, on the whole the meeting was considered interesting to the attendees and successful in solving many of the issues of immediate concern to InSightec. Several artifacts were demystified and solutions found. It was found that it is critically important to check transmit and receiver gains on manual prescan, for improvements in FSE image quality, to improve thermometry signal to noise, as well as to avoid overranging artifcts. A potential protocol for 5-slice thermometry with multishot EPI was found. Future discussion points that weren't fully discussed at this meeting include eddy currents and ARFI.