

Re: SPAN: MRI Fat Suppression and Scan time in Stage 1

From: **Karisma A Nagarkatti** | nagarkat@usc.edu

Friday,
Apr 9,
9:28
AM

To: **Basavaraju Ganganna** | basavaraju.ganganna@yale.edu, **Fahmeed Hyder** | fahmeed.hyder@yale.edu, **Joe Mandeville** | jbm@nmr.mgh.harvard.edu, **Arbab, Ali** | AARBAB@augusta.edu, **Bibic, Adnan** | Bibic@kennedykrieger.org, **Huang, Shuning** | Shuning.Huang@uth.tmc.edu, **Thedens, Daniel R** | dan-thedens@uiowa.edu, **Mihailovic, Jelena** | jelena.mihailovic@yale.edu

Cc: **Ryan Cabeen** | Ryan.Cabeen@loni.usc.edu, **Ayata, Cenk, M.D.** | CAYATA@mgh.harvard.edu

Dear SPAN MRI Investigators,

Thank you for your attendance at the MRI call on Monday 4/06. I am emailing to follow up on a few work items discussed at the meeting.

Please **reply to this group with your responses** to the below questions:

1. Did your site use fat suppression for Stage 1 imaging, and if so, which sequences did you use it in?
2. What was the average scan time per animal for Stage 1?

Thank you for your time,
Karisma

From: **Thedens, Daniel R** | dan-thedens@uiowa.edu

Friday,
Apr 9,
9:31
AM

To: **Karisma A Nagarkatti** | nagarkat@usc.edu, **Basavaraju Ganganna** | basavaraju.ganganna@yale.edu, **Fahmeed Hyder** | fahmeed.hyder@yale.edu, **Joe Mandeville** | jbm@nmr.mgh.harvard.edu, **Arbab, Ali** | AARBAB@augusta.edu, **Bibic, Adnan** | Bibic@kennedykrieger.org, **Huang, Shuning** | Shuning.Huang@uth.tmc.edu, **Mihailovic, Jelena** | jelena.mihailovic@yale.edu

Cc: **Ryan Cabeen** | Ryan.Cabeen@loni.usc.edu, **Ayata, Cenk, M.D.** | CAYATA@mgh.harvard.edu

Iowa:

- 1) No fat suppression used on any sequences
- 2) Average scan time 45 minutes, range 40-50 minutes depending whether any DWI repeats were needed to correct motion

--

Dan Thedens

dan-thedens@uiowa.edu

From: **Karisma A Nagarkatti** | nagarkat@usc.edu

To: **BasavarajuGanganna**

Friday, Apr 9, 11:27 AM

Dear SPAN MRI Investigators,

Thank you for your attendance at the MRI call on Monday 4/06. I am emailing to follow up on a few work items discussed at the meeting.

Please reply to this group with your responses to the below questions:

1. Did your site use fat suppression for Stage 1 imaging, and if so, which sequences did you use it in?
2. What was the average scan time per animal for Stage 1?

Thank you for your time,

Karisma

Notice: This UI Health Care e-mail (including attachments) is covered by the Electronic Communications Privacy Act, 18 U.S.C. 2510-2521 and is intended only for the use of the individual or entity to which it is addressed, and may contain information that is privileged, confidential, and exempt from disclosure under applicable law. If you are not the intended recipient, any dissemination, distribution or copying of this communication is strictly prohibited. If you have received this communication in error, please notify the sender immediately and delete or destroy all copies of the original message and attachments thereto. Email sent to or from UI Health Care may be retained as required by law or regulation. Thank you.

From: **Huang, Shuning** | Shuning.Huang@uth.tmc.edu

Friday, Apr 9, 9:39 AM

To: **Karisma A Nagarkatti** | nagarkat@usc.edu

Cc: **Basavaraju Ganganna** | basavaraju.ganganna@yale.edu, **Fahmeed Hyder** | fahmeed.hyder@yale.edu, **Joe Mandeville** | jbm@nmr.mgh.harvard.edu, **Arbab, Ali** | AARBAB@augusta.edu, **Bibic, Adnan** | Bibic@kennedykrieger.org, **Thedens, Daniel R** | dan-thedens@uiowa.edu, **Mihailovic, Jelena** | jelena.mihailovic@yale.edu, **Ryan Cabeen** | Ryan.Cabeen@loni.usc.edu, **Ayata, Cenk, M.D.** | CAYATA@mgh.harvard.edu

At UTH, we have fat suppression on for all sequences. The average scan time is about 35 to 40 minutes.

Shuning

From: **Karisma A Nagarkatti** | nagarkat@usc.edu

Friday, Apr 9, 11:27 AM

**** EXTERNAL EMAIL ****

Dear SPAN MRI Investigators,

Thank you for your attendance at the MRI call on Monday 4/06. I am emailing to follow up on a few work items discussed at the meeting.

Please **reply to this group with your responses** to the below questions:

1. Did your site use fat suppression for Stage 1 imaging, and if so, which sequences did you use it in?
2. What was the average scan time per animal for Stage 1?

Thank you for your time,
Karisma

<06Apr21_SPAN_MRI_MeetingMinutes.docx>

From: **Ganganna, Basavaraju Sangannahalli** | basavaraju.ganganna@yale.edu

Friday,
Apr 9,
9:46
AM

To: **Karisma A Nagarkatti** | nagarkat@usc.edu, **Hyder, Fahmeed** | fahmeed.hyder@yale.edu, **Joe Mandeville** | jbm@nmr.mgh.harvard.edu, **Arbab, Ali** | AARBAB@augusta.edu, **Bibic, Adnan** | Bibic@kennedykrieger.org, **Huang, Shuning** | Shuning.Huang@uth.tmc.edu, **Thedens, Daniel R** | dan-thedens@uiowa.edu, **Mihailovic, Jelena** | jelena.mihailovic@yale.edu

Cc: **Ryan Cabeen** | Ryan.Cabeen@loni.usc.edu, **Ayata, Cenk, M.D.** | CAYATA@mgh.harvard.edu

Yale 9.4T:

1. We did not apply fat suppression on any of the sequences in stage 1
2. Average scan time / mouse was 40- 45 minutes

Basav

From: **Karisma A Nagarkatti** | nagarkat@usc.edu

To: **Ganganna**

Friday, Apr 9, 12:27 PM

Dear SPAN MRI Investigators,

Thank you for your attendance at the MRI call on Monday 4/06. I am emailing to follow up on a few work items discussed at the meeting.

Please **reply to this group with your responses** to the below questions:

1. Did your site use fat suppression for Stage 1 imaging, and if so, which sequences did you use it in?
2. What was the average scan time per animal for Stage 1?

Thank you for your time,
Karisma

From: **Ayata, Cenk, M.D.** | CAYATA@mgh.harvard.edu

Friday,
Apr 9,
9:57
AM

To: **Basavaraju Ganganna** | basavaraju.ganganna@yale.edu, **Fahmeed Hyder** | fahmeed.hyder@yale.edu, **Joe Mandeville** | jbm@nmr.mgh.harvard.edu, **Arbab, Ali** | AARBAB@augusta.edu, **Bibic, Adnan** | Bibic@kennedykrieger.org, **Huang, Shuning** | Shuning.Huang@uth.tmc.edu, **The dens, Daniel R** | dan-thedens@uiowa.edu, **Mihailovic, Jelena** | jelena.mihailovic@yale.edu, **Ryan Cabeen** | Ryan.Cabeen@loni.usc.edu
Cc: **Karisma Nagarkatti (USC)** | nagarkat@usc.edu, **Patrick Lyden (USC)** | plyden@usc.edu

Dear All,

Here is the bottomline that emerged from the two discussion on MRI for the animal models for stage 2.

MRI acquisition protocol for Stage 2 Pilot:

- Scan n=3 normal brains and n=3 stroked animals for each animal model for each site. You may scan the same animal before and 48 hours after stroke.
- Obtain RARE + T2 map + ADC map
- Field of view:
- Aged and obese mice: (a) original 19.2 mm in-plane x 15 mm in slice direction, and (b) 10% larger (21.12 mm).
- Spontaneously hypertensive rats: 25.6 mm in-plane, 0.8 mm slice thickness.

- Matrix density 128 x 128 x 30 slices in all scans.
- Use fat suppression for all scans.

This is specifically for the pilot scans. Based on the observations in the pilot, we will finalize the FoV and RARE decisions on stage 2 MRI protocols. We will decide whether we need a larger FoV, and we may drop RARE from both time points or perform RARE-only 30d scans. One way or another, scan times will be reduced.

In pilot, we will scan RARE because Fahmeed raised the possibility of eliminating T2/ADC from 30d scan and performing RARE only. This is based on the fact that 30d scan readout is only the brain volume to quantify tissue loss, and RARE can potentially achieve this. If it works, it would be a tremendous time save. There are potential problems, however, which is the reason why we will keep RARE/T2/ADC in the pilot and compare the RARE-only approach to T2/ADC approach in the pilot. In the meantime, Ryan is working to see if a RARE-only neural net might be developed using stage 1 MRI. But we do not know whether aged/obese mouse or hypertensive rat images will perform as well in the neural net, hence the ask for n=3 animals.

It is imperative that all sites sac the mice after 48h scan and perform TTC staining based on a standardized protocol that will be distributed by the CC as part of the Stage 2 Pilot SOP. The latter is important because validation requires comparing MRI to TTC, and TTCs from different sites must be comparable.

Please REPLY ALL if you agree, or send suggestions to revise further if I made an error. Once final, this will be inserted in the Stage 2 Pilot SOP.

Thanks!
Cenk

PS: Karisma, would you please kindly plan to use this summary, and responses to it, to revise the working draft for the Stage 2 Pilot SOP?

From: **Thedens, Daniel R** | dan-thedens@uiowa.edu

Friday,
Apr 9,
10:08
AM

To: **Ayata, Cenk, M.D.** | CAYATA@mgh.harvard.edu, **Basavaraju Ganganna** | basavaraju.ganganna@yale.edu, **Fahmeed Hyder** | fahmeed.hyder@yale.edu, **Joe Mandeville** | jbm@nmr.mgh.harvard.edu, **Arbab, Ali** | AARBAB@augusta.edu, **Bibic, Adnan** | Bibic@kennedykrieger.org, **Huang, Shuning** | Shuning.Huang@uth.tmc.edu, **Mihailovic, Jelena** | jelena.mihailovic@yale.edu, **Ryan Cabeen** | Ryan.Cabeen@loni.usc.edu

Cc: **Karisma Nagarkatti (USC)** | nagarkat@usc.edu, **Patrick Lyden (USC)** | plyden@usc.edu

Question/clarification:

From:

- * Obtain RARE + T2 map + ADC map
- * Field of view:
- * Aged and obese mice: (a) original 19.2 mm in-plane x 15 mm in slice direction, and (b) 10% larger (21.12 mm).

Is it intended these will be in a single session for both pre-stroke and 48 hour scans? With RARE still included in these, at our site this results in a roughly 90 minute total scan time. Based on the pilot scans we did on non-surgical obese mice, I think those will be OK, but I don't know post-stroke how fragile they will be for a lengthy scan.

--

Dan Thedens

dan-thedens@uiowa.edu

From: **Ayata** | CAYATA@mgh.harvard.edu

To: **BasavarajuGanganna**

Friday, Apr 9, 11:57 AM

Dear All,

Here is the bottomline that emerged from the two discussion on MRI for the animal models for stage 2.

MRI acquisition protocol for Stage 2 Pilot:

- * Scan n=3 normal brains and n=3 stroked animals for each animal model for each site. You may scan the same animal before and 48 hours after stroke.
- * Obtain RARE + T2 map + ADC map
- * Field of view:
- * Aged and obese mice: (a) original 19.2 mm in-plane x 15 mm in slice direction, and (b) 10% larger (21.12 mm).
- * Spontaneously hypertensive rats: 25.6 mm in-plane, 0.8 mm slice thickness.
- * Matrix density 128 x 128 x 30 slices in all scans.
- * Use fat suppression for all scans.

This is specifically for the pilot scans. Based on the observations in the pilot, we will finalize the FoV and RARE decisions on stage 2 MRI protocols. We will decide whether we need a larger FoV, and we may drop RARE from both time points or perform RARE-only 30d scans. One way or another, scan times will be reduced.

In pilot, we will scan RARE because Fahmeed raised the possibility of eliminating T2/ADC from 30d scan and performing RARE only. This is based on the fact that 30d scan readout is only the brain volume to quantify tissue loss, and RARE can potentially achieve this. If it works, it would be a tremendous time save. There are potential problems, however, which is the reason why we will keep RARE/T2/ADC in the pilot and compare the RARE-only approach to T2/ADC approach in the pilot. In the meantime, Ryan is working to see if a RARE-only neural net might be developed using stage 1 MRI. But we do not know whether aged/obese mouse or hypertensive rat images will perform as well in the neural net, hence the ask for n=3 animals.

It is imperative that all sites sac the mice after 48h scan and perform TTC staining based on a standardized protocol that will be distributed by the CC as part of the Stage 2 Pilot SOP. The latter is important because validation requires comparing MRI to TTC, and TTCs from different sites must be comparable.

Please REPLY ALL if you agree, or send suggestions to revise further if I made an error. Once final, this will be inserted in the Stage 2 Pilot SOP.

Thanks!
Cenk

PS: Karisma, would you please kindly plan to use this summary, and responses to it, to revise the working draft for the Stage 2 Pilot SOP?

Notice: This UI Health Care e-mail (including attachments) is covered by the Electronic Communications Privacy Act, 18 U.S.C. 2510-2521 and is intended only for the use of the individual or entity to which it is addressed, and may contain information that is privileged, confidential, and exempt from disclosure under applicable law. If you are not the intended recipient, any dissemination, distribution or copying of this communication is strictly prohibited. If you have received this communication in error, please notify the sender immediately and delete or destroy all copies of the original message and attachments thereto. Email sent to or from UI Health Care may be retained as required by law or regulation. Thank you.

From: **Ayata, Cenk, M.D.** | CAYATA@mgh.harvard.edu

Friday, Apr 9, 10:16 AM

To: **The dens, Daniel R** | dan-the dens@uiowa.edu

Cc: **Basavaraju Ganganna** | basavaraju.ganganna@yale.edu, **Fahmeed Hyder** | fahmeed.hyder@yale.edu, **Joe Mandeville** | jbm@nmr.mgh.harvard.edu, **Arbab, Ali** | AARBAB@augusta.edu, **Bibic, Adnan** | Bibic@kennedykrieger.org, **Huang, Shuning** | Shuning.Huang@uth.tmc.edu, **Mihailovic, Jelena** | jelena.mihailovic@yale.edu, **Ryan Cabeen** | Ryan.Cabeen@loni.usc.edu, **Karisma Nagarkatti (USC)** | nagarkat@usc.edu, **Patrick Lyden (USC)** | plyden@usc.edu

Good point. Yes, the intent to compare two FoVs essentially duplicates the scan time.

As a group we must decide whether 10% larger FoV is really essential. Correct me if I am wrong but this was out of concern for the increased fat content in obese mice. If fat suppression can eliminate this concern, or the problem can be overcome by tweaking other scan parameters, then we can drop it from the pilot, which simplifies things a lot.

On the other hand, mice will be sac'ed at the end of the scan in pilot, so post-MRI health or mortality is not a concern. But if larger FoV is not felt to be essential, then I would rather keep thing simple and efficient.

What do others think?

From: **Daniel R** | dan-thedens@uiowa.edu

Friday, Apr 9, 1:08 PM

External Email - Use Caution

Question/clarification:

From:

- * Obtain RARE + T2 map + ADC map
- * Field of view:
- * Aged and obese mice: (a) original 19.2 mm in-plane x 15 mm in slice direction, and (b) 10% larger (21.12 mm).

Is it intended these will be in a single session for both pre-stroke and 48 hour scans? With RARE still included in these, at our site this results in a roughly 90 minute total scan time. Based on the pilot scans we did on non-surgical obese mice, I think those will be OK, but I don't know post-stroke how fragile they will be for a lengthy scan.

--

Dan Thedens

dan-thedens@uiowa.edu

From: **Ayata** | CAYATA@mgh.harvard.edu

To: **BasavarajuGanganna**

Friday, Apr 9, 11:57 AM

Dear All,

Here is the bottomline that emerged from the two discussion on MRI for the animal models for stage 2.

MRI acquisition protocol for Stage 2 Pilot:

- * Scan n=3 normal brains and n=3 stroked animals for each animal model for each site. You may scan the same animal before and 48 hours after stroke.
- * Obtain RARE + T2 map + ADC map
- * Field of view:
- * Aged and obese mice: (a) original 19.2 mm in-plane x 15 mm in slice direction, and (b) 10% larger (21.12 mm).
- * Spontaneously hypertensive rats: 25.6 mm in-plane, 0.8 mm slice thickness.
- * Matrix density 128 x 128 x 30 slices in all scans.
- * Use fat suppression for all scans.

This is specifically for the pilot scans. Based on the observations in the pilot, we will finalize the FoV and RARE decisions on stage 2 MRI protocols. We will decide whether we need a larger FoV, and we may drop RARE from both time points or perform RARE-only 30d scans. One way or another, scan times will be reduced.

In pilot, we will scan RARE because Fahmeed raised the possibility of eliminating T2/ADC from 30d scan and performing RARE only. This is based on the fact that 30d scan readout is only the brain volume to quantify tissue loss, and RARE can potentially achieve this. If it works, it would be a tremendous time save. There are potential problems, however, which is the reason why we will keep RARE/T2/ADC in the pilot and compare the RARE-only approach to T2/ADC approach in the pilot. In the meantime, Ryan is working to see if a RARE-only neural net might be developed using stage 1 MRI. But we do not know whether aged/obese mouse or hypertensive rat images will perform as well in the neural net, hence the ask for n=3 animals.

It is imperative that all sites sac the mice after 48h scan and perform TTC staining based on a standardized protocol that will be distributed by the CC as part of the Stage 2 Pilot SOP. The latter is important because validation requires comparing MRI to TTC, and TTCs from different sites must be comparable.

Please REPLY ALL if you agree, or send suggestions to revise further if I made an error. Once final, this will be inserted in the Stage 2 Pilot SOP.

Thanks!
Cenk

PS: Karisma, would you please kindly plan to use this summary, and responses to it, to revise the working draft for the Stage 2 Pilot SOP?

Notice: This UI Health Care e-mail (including attachments) is covered by the Electronic Communications Privacy Act, 18 U.S.C. 2510-2521 and is intended only for the use of the individual or entity to which it is addressed, and may contain information that is privileged, confidential, and exempt from disclosure under applicable law. If you are not the intended recipient, any dissemination, distribution or copying of this communication is strictly prohibited. If you have received this communication in error, please notify the sender immediately and delete or destroy all copies of the original message and attachments thereto. Email sent to or from UI Health Care may be retained as required by law or regulation. Thank you.

From: **Fahmeed Hyder** | fahmeed.hyder@yale.edu

Friday, Apr 9, 10:56 AM

To: **Ayata, Cenk, M.D.** | CAYATA@mgh.harvard.edu, **The dens, Daniel R** | dan-the dens@uiowa.edu

Cc: **Basavaraju Ganganna** | basavaraju.ganganna@yale.edu, **Joe Mandeville** | jbm@nmr.mgh.harvard.edu, **Arbab, Ali** | aarbab@augusta.edu, **Bibic, Adnan** | Bibic@kennedykrieger.org, **Huang, Shuning** | Shuning.Huang@uth.tmc.edu, **Mihailovic, Jelena** | jelena.mihailovic@yale.edu, **Ryan Cabeen** | Ryan.Cabeen@loni.usc.edu, **Karisma Nagarkatti (USC)** | nagarkat@usc.edu, **Patrick Lyden (USC)** | plyden@usc.edu

Larger FOVs are primarily for avoiding fold over artifacts in rats, but also larger mice.

From: **Ayata**

Friday, Apr 9, 1:16 PM

Good point. Yes, the intent to compare two FoVs essentially duplicates the scan time.

As a group we must decide whether 10% larger FoV is really essential. Correct me if I am wrong but this was out of concern for the increased fat content in obese mice. If fat suppression can eliminate this concern, or the problem can be overcome by tweaking other scan parameters, then we can drop it from the pilot, which simplifies things a lot.

On the other hand, mice will be sac'ed at the end of the scan in pilot, so post-MRI health or mortality is not a concern. But if larger FoV is not felt to be essential, then I would rather keep thing simple and efficient.

What do others think?

Cenk

From: **Daniel R** | dan-thedens@uiowa.edu

Friday, Apr 9, 1:08 PM

External Email - Use Caution

Question/clarification:

From:

- * Obtain RARE + T2 map + ADC map
- * Field of view:
- * Aged and obese mice: (a) original 19.2 mm in-plane x 15 mm in slice direction, and (b) 10% larger (21.12 mm).

Is it intended these will be in a single session for both pre-stroke and 48 hour scans? With RARE still included in these, at our site this results in a roughly 90 minute total scan time. Based on the pilot scans we did on non-surgical obese mice, I think those will be OK, but I don't know post-stroke how fragile they will be for a lengthy scan.

--

Dan Thedens

dan-thedens@uiowa.edu

From: **Ayata** | CAYATA@mgh.harvard.edu

To: **BasavarajuGanganna**

Friday, Apr 9, 11:57 AM

Dear All,

Here is the bottomline that emerged from the two discussion on MRI for the animal models for stage 2.

MRI acquisition protocol for Stage 2 Pilot:

- * Scan n=3 normal brains and n=3 stroked animals for each animal model for each site. You may scan the

same animal before and 48 hours after stroke.

- * Obtain RARE + T2 map + ADC map

- * Field of view:

- * Aged and obese mice: (a) original 19.2 mm in-plane x 15 mm in slice direction, and (b) 10% larger (21.12 mm).

- * Spontaneously hypertensive rats: 25.6 mm in-plane, 0.8 mm slice thickness.

- * Matrix density 128 x 128 x 30 slices in all scans.

- * Use fat suppression for all scans.

This is specifically for the pilot scans. Based on the observations in the pilot, we will finalize the FoV and RARE decisions on stage 2 MRI protocols. We will decide whether we need a larger FoV, and we may drop RARE from both time points or perform RARE-only 30d scans. One way or another, scan times will be reduced.

In pilot, we will scan RARE because Fahmeed raised the possibility of eliminating T2/ADC from 30d scan and performing RARE only. This is based on the fact that 30d scan readout is only the brain volume to quantify tissue loss, and RARE can potentially achieve this. If it works, it would be a tremendous time save. There are potential problems, however, which is the reason why we will keep RARE/T2/ADC in the pilot and compare the RARE-only approach to T2/ADC approach in the pilot. In the meantime, Ryan is working to see if a RARE-only neural net might be developed using stage 1 MRI. But we do not know whether aged/obese mouse or hypertensive rat images will perform as well in the neural net, hence the ask for n=3 animals.

It is imperative that all sites sac the mice after 48h scan and perform TTC staining based on a standardized protocol that will be distributed by the CC as part of the Stage 2 Pilot SOP. The latter is important because validation requires comparing MRI to TTC, and TTCs from different sites must be comparable.

Please REPLY ALL if you agree, or send suggestions to revise further if I made an error. Once final, this will be inserted in the Stage 2 Pilot SOP.

Thanks!

Cenk

PS: Karisma, would you please kindly plan to use this summary, and responses to it, to revise the working draft for the Stage 2 Pilot SOP?

Notice: This UI Health Care e-mail (including attachments) is covered by the Electronic Communications Privacy Act, 18 U.S.C. 2510-2521 and is intended only for the use of the individual or entity to which it is addressed, and may contain information that is privileged, confidential, and exempt from disclosure under applicable law. If you are not the intended recipient, any dissemination, distribution or copying of this communication is strictly prohibited. If you have received this communication in error, please notify the

sender immediately and delete or destroy all copies of the original message and attachments thereto. Email sent to or from UI Health Care may be retained as required by law or regulation. Thank you.

From: **Thedens, Daniel R** | dan-thedens@uiowa.edu

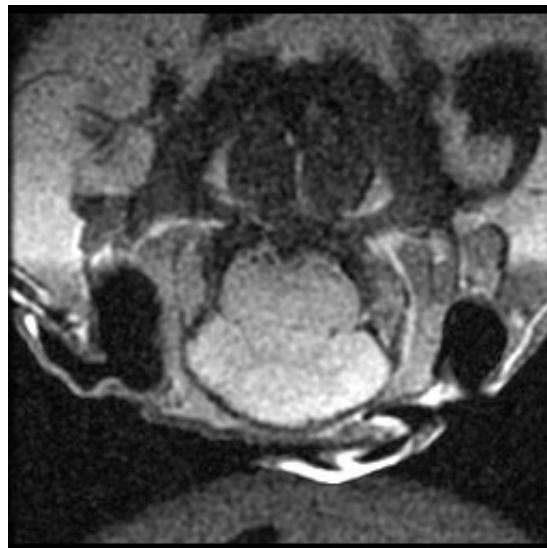
Friday, Apr 9, 12:33 PM

To: **Fahmeed Hyder** | fahmeed.hyder@yale.edu, **Ayata, Cenk, M.D.** | CAYATA@mgh.harvard.edu

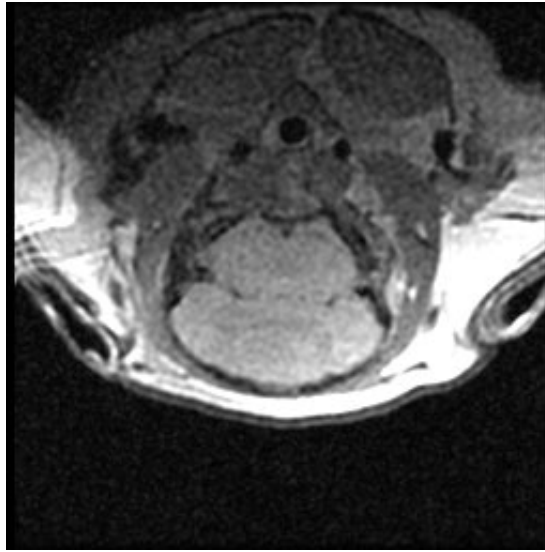
Cc: **Basavaraju Ganganna** | basavaraju.ganganna@yale.edu, **Joe Mandeville** | jbm@nmr.mgh.harvard.edu, **Arbab, Ali** | AARBAB@augusta.edu, **Bibic, Adnan** | Bibic@kennedykrieger.org, **Huang, Shuning** | Shuning.Huang@uth.tmc.edu, **Mihailovic, Jelena** | jelena.mihailovic@yale.edu, **Ryan Cabeen** | Ryan.Cabeen@loni.usc.edu, **Karisma Nagarkatti (USC)** | nagarkat@usc.edu, **Patrick Lyden (USC)** | plyden@usc.edu

This is a slice from an obese mouse that we did this week (weight 42g). This is slice #4 at the cerebellar end of the brain. This is from the TE=15ms set with the regular field of view (19.2mm), readout L/R, and fat saturation on. As you can see in our case the fat saturation is not very good away from the center of the bore (it's OK nearer the center, but I'm not sure if this is RF inhomogeneity or the fact that we are shimming on the brain; I may investigate if we have another method for this, e.g. adiabatic).

In any case, in this slice we are cutting it close in terms of wrap/foldover. This is probably the worst-case area in the volume since we're closer into the body, and it's not an area we'd expect lesion, but I think there is a possibility of wrap into the brain over the range of animals at 19.2mm FOV.



In the previous obese mice we scanned, we did frequency top/bottom (as we had in stage 1) and also saw wrap in these slices (L/R of course), but it was anatomically far enough from the brain that it did not wrap into the brain and in fact was less of a 'close call'. This scan did not have fat saturation.



--

Dan Thedens

dan-thedens@uiowa.edu

From: **Fahmeed Hyder** | fahmeed.hyder@yale.edu

To: **Ayata**

Friday, Apr 9, 12:56 PM

Larger FOVs are primarily for avoiding fold over artifacts in rats, but also larger mice.

Notice: This UI Health Care e-mail (including attachments) is covered by the Electronic Communications Privacy Act, 18 U.S.C. 2510-2521 and is intended only for the use of the individual or entity to which it is addressed, and may contain information that is privileged, confidential, and exempt from disclosure under applicable law. If you are not the intended recipient, any dissemination, distribution or copying of this communication is strictly prohibited. If you have received this communication in error, please notify the sender immediately and delete or destroy all copies of the original message and attachments thereto. Email sent to or from UI Health Care may be retained as required by law or regulation. Thank you.

From: **Ayata**

Friday, Apr 9, 1:16 PM

Good point. Yes, the intent to compare two FoVs essentially duplicates the scan time.

As a group we must decide whether 10% larger FoV is really essential. Correct me if I am wrong but this was out of concern for the increased fat content in obese mice. If fat suppression can eliminate this concern, or the problem can be overcome by tweaking other scan parameters, then we can drop it from the pilot, which simplifies things a lot.

On the other hand, mice will be sac'ed at the end of the scan in pilot, so post-MRI health or mortality is not a concern. But if larger FoV is not felt to be essential, then I would rather keep thing simple and efficient.

What do others think?

Cenk

From: **Daniel R** | dan-thedens@uiowa.edu

Friday, Apr 9, 1:08 PM

External Email - Use Caution

Question/clarification:

From:

- * Obtain RARE + T2 map + ADC map
- * Field of view:
- * Aged and obese mice: (a) original 19.2 mm in-plane x 15 mm in slice direction, and (b) 10% larger (21.12 mm).

Is it intended these will be in a single session for both pre-stroke and 48 hour scans? With RARE still included in these, at our site this results in a roughly 90 minute total scan time. Based on the pilot scans we did on non-surgical obese mice, I think those will be OK, but I don't know post-stroke how fragile they will be for a lengthy scan.

--

Dan Thedens

dan-thedens@uiowa.edu

From: **Ayata** | CAYATA@mgh.harvard.edu

To: **BasavarajuGanganna**

Friday, Apr 9, 11:57 AM

Dear All,

Here is the bottomline that emerged from the two discussion on MRI for the animal models for stage 2.

MRI acquisition protocol for Stage 2 Pilot:

- * Scan n=3 normal brains and n=3 stroked animals for each animal model for each site. You may scan the same animal before and 48 hours after stroke.
- * Obtain RARE + T2 map + ADC map
- * Field of view:
- * Aged and obese mice: (a) original 19.2 mm in-plane x 15 mm in slice direction, and (b) 10% larger (21.12 mm).
- * Spontaneously hypertensive rats: 25.6 mm in-plane, 0.8 mm slice thickness.

- * Matrix density 128 x 128 x 30 slices in all scans.
- * Use fat suppression for all scans.

This is specifically for the pilot scans. Based on the observations in the pilot, we will finalize the FoV and RARE decisions on stage 2 MRI protocols. We will decide whether we need a larger FoV, and we may drop RARE from both time points or perform RARE-only 30d scans. One way or another, scan times will be reduced.

In pilot, we will scan RARE because Fahmeed raised the possibility of eliminating T2/ADC from 30d scan and performing RARE only. This is based on the fact that 30d scan readout is only the brain volume to quantify tissue loss, and RARE can potentially achieve this. If it works, it would be a tremendous time save. There are potential problems, however, which is the reason why we will keep RARE/T2/ADC in the pilot and compare the RARE-only approach to T2/ADC approach in the pilot. In the meantime, Ryan is working to see if a RARE-only neural net might be developed using stage 1 MRI. But we do not know whether aged/obese mouse or hypertensive rat images will perform as well in the neural net, hence the ask for n=3 animals.

It is imperative that all sites sac the mice after 48h scan and perform TTC staining based on a standardized protocol that will be distributed by the CC as part of the Stage 2 Pilot SOP. The latter is important because validation requires comparing MRI to TTC, and TTCs from different sites must be comparable.

Please REPLY ALL if you agree, or send suggestions to revise further if I made an error. Once final, this will be inserted in the Stage 2 Pilot SOP.

Thanks!
Cenk

PS: Karisma, would you please kindly plan to use this summary, and responses to it, to revise the working draft for the Stage 2 Pilot SOP?

Notice: This UI Health Care e-mail (including attachments) is covered by the Electronic Communications Privacy Act, 18 U.S.C. 2510-2521 and is intended only for the use of the individual or entity to which it is addressed, and may contain information that is privileged, confidential, and exempt from disclosure under applicable law. If you are not the intended recipient, any dissemination, distribution or copying of this communication is strictly

prohibited. If you have received this communication in error, please notify the sender immediately and delete or destroy all copies of the original message and attachments thereto. Email sent to or from UI Health Care may be retained as required by law or regulation. Thank you.

From: **jbm** | jbm@nmr.mgh.harvard.edu

Friday, Apr 9, 2:44 PM

To: **Thedens, Daniel R** | dan-thedens@uiowa.edu

Cc: **Fahmeed Hyder** | fahmeed.hyder@yale.edu, **Ayata, Cenk, M.D.** | CAYATA@mgh.harvard.edu, **Basavaraju Ganganna** | basavaraju.ganganna@yale.edu, **Arbab, Ali** | AARBAB@augusta.edu, **Bibic, Adnan** | Bibic@kennedykrieger.org, **Huang, Shuning** | Shuning.Huang@uth.tmc.edu, **Mihailovic, Jelena** | jelena.mihailovic@yale.edu, **Ryan Cabeen** | Ryan.Cabeen@loni.usc.edu, **Karisma Nagarkatti (USC)** | nagarkat@usc.edu, **Patrick Lyden (USC)** | plyden@usc.edu

Hi Dan,

Could you use part-k and increase the FOV & matrix proportionally to maintain roughly the same resolution with the same scan time?

It does look dicey keeping the lower FOV. Those guys must be really fat.

Best,

Joe

From: **Daniel R** | dan-thedens@uiowa.edu

Friday, Apr 9, 3:33 PM

External Email - Use Caution

This is a slice from an obese mouse that we did this week (weight 42g). This is slice #4 at the cerebellar end of the brain. This is from the TE=15ms set with the regular field of view (19.2mm), readout L/R, and fat saturation on. As you can see in our case the fat saturation is not very good away from the center of the bore (it's OK nearer the center, but I'm not sure if this is RF inhomogeneity or the fact that we are shimming on the brain; I may investigate if we have another method for this, e.g. adiabatic).

In any case, in this slice we are cutting it close in terms of wrap/foldover. This is probably the worst-case area in the volume since we're closer into the body, and it's not an area we'd expect lesion, but I think there is a possibility of wrap into the brain over the range of animals at 19.2mm FOV.

<4-T2_map_TE___15.jpg>

In the previous obese mice we scanned, we did frequency top/bottom (as we had in stage 1) and also saw wrap in these slices (L/R of course), but it was anatomically far enough from the brain that it did not wrap into the brain and in fact was less of a 'close call'. This scan did not have fat

saturation.

<5-T2_map_TE____15.jpg>

--

Dan Thedens

dan-thedens@uiowa.edu

From: **Fahmeed Hyder** | fahmeed.hyder@yale.edu

To: **Ayata**

Friday, Apr 9, 12:56 PM

Larger FOVs are primarily for avoiding fold over artifacts in rats, but also larger mice.

Notice: This UI Health Care e-mail (including attachments) is covered by the Electronic Communications Privacy Act, 18 U.S.C. 2510-2521 and is intended only for the use of the individual or entity to which it is addressed, and may contain information that is privileged, confidential, and exempt from disclosure under applicable law. If you are not the intended recipient, any dissemination, distribution or copying of this communication is strictly prohibited. If you have received this communication in error, please notify the sender immediately and delete or destroy all copies of the original message and attachments thereto. Email sent to or from UI Health Care may be retained as required by law or regulation. Thank you.

From: **Ayata**

Friday, Apr 9, 1:16 PM

Good point. Yes, the intent to compare two FoVs essentially duplicates the scan time.

As a group we must decide whether 10% larger FoV is really essential. Correct me if I am wrong but this was out of concern for the increased fat content in obese mice. If fat suppression can eliminate this concern, or the problem can be overcome by tweaking other scan parameters, then we can drop it from the pilot, which simplifies things a lot.

On the other hand, mice will be sac'ed at the end of the scan in pilot, so post-MRI health or mortality is not a concern. But if larger FoV is not felt to be essential, then I would rather keep thing simple and efficient.

What do others think?

Cenk

From: **Daniel R** | dan-thedens@uiowa.edu

Friday, Apr 9, 1:08 PM

External Email - Use Caution

Question/clarification:

.

From:

- * Obtain RARE + T2 map + ADC map
- * Field of view:
- * Aged and obese mice: (a) original 19.2 mm in-plane x 15 mm in slice direction, and (b) 10% larger (21.12 mm).

Is it intended these will be in a single session for both pre-stroke and 48 hour scans? With RARE still included in these, at our site this results in a roughly 90 minute total scan time. Based on the pilot scans we did on non-surgical obese mice, I think those will be OK, but I don't know post-stroke how fragile they will be for a lengthy scan.

--

Dan Thedens

dan-thedens@uiowa.edu

From: **Ayata** | CAYATA@mgh.harvard.edu

To: **BasavarajuGanganna**

Friday, Apr 9, 11:57 AM

Dear All,

Here is the bottomline that emerged from the two discussion on MRI for the animal models for stage 2.

MRI acquisition protocol for Stage 2 Pilot:

- * Scan n=3 normal brains and n=3 stroked animals for each animal model for each site. You may scan the same animal before and 48 hours after stroke.
- * Obtain RARE + T2 map + ADC map
- * Field of view:
- * Aged and obese mice: (a) original 19.2 mm in-plane x 15 mm in slice direction, and (b) 10% larger (21.12 mm).
- * Spontaneously hypertensive rats: 25.6 mm in-plane, 0.8 mm slice thickness.
- * Matrix density 128 x 128 x 30 slices in all scans.
- * Use fat suppression for all scans.

This is specifically for the pilot scans. Based on the observations in the pilot, we will finalize the FoV and RARE decisions on stage 2 MRI protocols. We will decide whether we need a larger FoV, and we may drop RARE from both time points or perform RARE-only 30d scans. One way or another, scan times will be reduced.

In pilot, we will scan RARE because Fahmeed raised the possibility of eliminating T2/ADC from 30d scan and performing RARE only. This is based on the fact that 30d scan readout is only the brain volume to quantify tissue loss, and RARE can potentially achieve this. If it works, it would be a tremendous time save. There are potential problems, however, which is the reason why we will keep RARE/T2/ADC in the pilot and compare the RARE-only approach to T2/ADC approach in the pilot. In the meantime, Ryan is working to see if a RARE-only neural net might be developed using stage 1 MRI. But we do not know whether aged/obese mouse or hypertensive rat images will perform as well in the neural net, hence the ask for n=3 animals.

It is imperative that all sites sac the mice after 48h scan and perform TTC staining based on a standardized protocol that will be distributed by the CC as part of the Stage 2 Pilot SOP. The latter is important because validation requires comparing MRI to TTC, and TTCs from different sites must be comparable.

Please REPLY ALL if you agree, or send suggestions to revise further if I made an error. Once final, this will be inserted in the Stage 2 Pilot SOP.

Thanks!

Cenk

PS: Karisma, would you please kindly plan to use this summary, and responses to it, to revise the working draft for the Stage 2 Pilot SOP?

Notice: This UI Health Care e-mail (including attachments) is covered by the Electronic Communications Privacy Act, 18 U.S.C. 2510-2521 and is intended only for the use of the individual or entity to which it is addressed, and may contain information that is privileged, confidential, and exempt from disclosure under applicable law. If you are not the intended recipient, any dissemination, distribution or copying of this communication is strictly prohibited. If you have received this communication in error, please notify the sender immediately and delete or destroy all copies of the original message and attachments thereto. Email sent to or from UI Health Care may be retained as required by law or regulation. Thank you.
