**MEETING MINUTES**

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| Meeting: | SPAN MRI Meeting Led by Dr. Ayata |
| Date and Time: | 02 April 2021 10-11am PDT |
| Present: | Cenk Ayata, Ryan Cabeen, Dan Thedens, Adnan Bibic, Basav Sanganahalli, Jelena Mihailovic, Peter Van Zijl, Ali Arbab, Shuning Huang, Karisma Nagarkatti |

**Discussion:**

1. In Stage 2, we are now moving to a different animal model and not all sites will be doing the same model
2. Ryan Presented specifics of Stage 1 Pipeline
   1. Denoise, parameter estimation, skull stripping, there were some cases where anterior/posterior were flipped but Ryan manually fixed those issues.
   2. Analysis shows that neural network approach accurately reproduces previous approach with 96% accuracy and a few fixed cases
   3. 1309 scans uploaded, 779 early timepoint, 530 late. 13 failed due to incomplete data, 35 failed due to motion. There were some repeat T2 scans which can be manually cleaned up.
   4. Correction for Midline shift quantification: Dr. Ayata proposes that when Ryan plots the parabolic midline he should use the actual midline rather than its vertical projection on the horizontal midline. The projection is only used for midline shift calculation.
3. Site Feedback
   1. Dr. Hyder asks: Does Network have access to non-ischemic brain in the IDA database? For lesion definition what are the chances for the lesion definition being picked up randomly? For the midline it should work just as well for a brain without an infarct. Dr. Ayata responds that this is a good point, Dr. Thedens (U Iowa) has two animals already scanned without infarct.
   2. Dr. Ayata asks group: For the pilot do we need strokes/infarcts, or should we just use normal animals scanned once? He points out that Obese mice must be kept on the diet for a while and SHRs will need to be ordered in advance.
      1. JH: You must prove that you have a normal reference frame in pilot project because brain may look a bit different in obese mice compared to young mice. He would endorse sites scan a normal animal in addition to stroked animals.
      2. YL: There are strong budget Concerns. This pilot could lead to issues with budget. Dr. Hyder states that NINDS must reconsider budget adjustments.
   3. Ryan points out that in pilot scans it would be helpful to have the same animal rescanned with a normal and a 10% larger field of view keeping the grid the same (i.e. 10% larger voxel size) to see how the automated segmentation performs under both conditions.
   4. Dr. Van Zijl asks: Why is lesion size different among all the sites?
      1. Dr. Ayata responds: As we can see JH had smaller lesions. It is not due to technical problems; Ryan and I reviewed this and in most cases there is no lesion, no midline shift or other evidence of a lesion. Our conclusion is that every site has a normal lesion volume distribution that is normal to them. These differences are attributed to technique, environment the animals are kept in, etc. It introduces the much-needed heterogeneity in this preclinical trial and helps us to determine if the treatments are robust enough to overcome these site differences in site lesion volumes. Some sites are waking their animals up, some keep their animals anesthetized. There are so many differences it is difficult to find one specific reason.
      2. Dr. Bibic (JH) observed that initially the site was seeing very large lesions and high mortality. They contacted the CC and made an adjustment and now he sees that scans show little to no lesion.
4. U Iowa Obese Mice Scans
   1. These scans were from non-lesioned mice using the existing Stage 1 protocol. These scans were typical with what has been done historically at U Iowa. ~50-60 grams. Read out direction is top to bottom.
   2. Unique perhaps to U Iowa system: Fat water shifts, frequency direction is in the direction of the brain. The subcutaneous fat will map into the brain, this could make skull stripping challenging. In U Iowa they would have to perhaps consider shifting direction or some sort of fat suppression. SNRs are on the lower side compared to what some other sites are used to. On RARE image, you can see ripples. The ADC perhaps is at the lower end of quality spectrum, like what has been seen in the past. There is a bit of a shift on these scans. There is a relatively low bandwidth, and a large fat water shift will result. However, the ADC is primarily being used to exclude CSF and these scans are still functional for that
   3. The bigger challenge seems to be it’s a little harder to keep the animal in place in the console. We may expect to end up with a lot more motion artifact with the obese mice. To combat this, U Iowa takes multiple scans and takes the best scans (those with minimal amount of motion artifact).
   4. Scans show that fat affects T1 and T2 which could be why U Iowa gets hyperintensities. We need to make sure holder is fixed tightly.
   5. Dr. Hyder requests that Dr. Thedens run the same scans with higher frequency?
   6. U Iowa responds we can do that. How much will changing this frequency affect analyses on the lesion sizes?
      1. There is a little bit of cropping at the anterior and posterior ends. Ryan added a step that crops the brain segmentation. Increasing frequency for FOV may not impact analysis
      2. Fat suppression should not affect TR or protocol in any which way because it chemically selects fat signal and crushes it out.
      3. U Iowa states that they do have a clinical console. The only other thing is there is a premium for tuning, i.e. suppressing water but states that this should not be a problem.
      4. Takeaway: with fat suppression and larger FOV would be the only changes to the current protocol.
      5. U Iowa concern: occasionally in the past at U Iowa they reported that the fat signal was so large that SNR would suffer. If aliasing would be limited to left right with an anti-alias filter and appropriate frequency direction site might be able to do the same FOV. Between the actual positioning of the restraint and where it pushes that breathing motion could affect the ADC.
   7. Proposal: Increase FOV (would increase voxel size and decrease the resolution). by 10%. We could keep voxel size the same but this would add to the scan time. Question is whether the algorithm is good enough to identify lesions and midline shift?
      1. Ryan believes proposal will provide reasonable estimates but could lead to some uncertainty with the decreased resolution. Ryan suggests that this be tested through the algorithm.
   8. Is the RARE image involved in segmentation?
      1. Ryan reports that segmentation is done with T2 and ADC.
   9. Sites agree that a pilot phase is needed to determine if an increase in FOV will make a difference to analysis. Additionally, fat suppression will need to be improved. Dr. Ayata brough up concern that if Network is dealing with smaller lesions at some sites, losing voxel size would make images noisier.
   10. Differences in frequency coding:
       1. UTH notes that they do frequency coding left and right.
       2. Dr. Ayata proposes that this would be a good reason to have a few sites scan in images because each site scans differently.
   11. During pilot scans, would sites support doing scans on two different FOVs to determine how skull stripping and midline performs on Ryan’s pipeline? Dr. Hyder believes that this will be needed.
   12. U Iowa: Do we need RARE images?
       1. Dr. Hyder states that Dr. Lyden brought up that at some point the Network wants to analyze brain volume and RARE images are one of the best ways to do this analysis. Dr. Hyder further explains that currently the RARE scans are not being used but sometime in the future the RARE should be put through a similar type of pipeline.
5. Dr. Hyder proposes a question to sites: Each site has raised their own curiosity about whether they can add something else to scan protocol. Does any site want to add something if this type of scanning is done within 20 min. Can we add something?
   1. U Iowa: it takes us 40 min. Because the T2 mapping now takes 3 discrete maps.
   2. Yale: that is where we are as well. But if we go from single coil to volume coil we can reduce this to ~30-35min.
   3. UTH: 40 min. per mouse including set up time
   4. AG: 50-55 min. We must cancel scanning if there is any movement
   5. JH: ~ 30-35 min. It takes 10 min. to adjust the animal
   6. MGH: ~30 min.
   7. Sites are requested to email this group with the average scan times being used in Stage 1. This would be a strong argument for requesting an increase in funding from NINDS.
6. How long can we keep obese mice anesthetized without introducing a confound?
   1. Based on Eng Lo’s presentation to Network, Anesthesia is definitely confound but we cannot avoid it.
   2. Regarding aged mice, MGH has done some scans in the past. These scans have never gone longer than 40-45 min. but this dependent on how large the lesion is
7. Rare scan time
   1. UIowa: 6 min added time
   2. Yale: 4 min added time
8. Should group consider dropping RARE sequence to reduce scan time?
   1. Yale: Agree to drop, we can get same info from T2 MAP.
   2. AG: In favor of dropping RARE. If you use middle TE from T2 map you get the same info
   3. U Iowa: In favor
   4. JH: Agrees. Does not see a reason for RARE can get volume from T2 scan
   5. UTH: Agrees. If you do not currently use it for analysis then we should eliminate it
   6. All site MRI investigators agree to drop RARE from protocol for Stage 2. This will be particularly helpful if aged mice show higher sensitivity to anesthesia during MRI.
   7. Ryan will experiment using the brain volume calculation on RARE images to see how well it matches the T2-based approach.
9. SHR
   1. AG plans to perform rat strokes next week. Site is requested to scan 1-2 animals using the Stage 1 protocol. AG will share these images to discuss at the next meeting next week.
   2. U Iowa reports that they have done 1 scan on a normal Sprague Dawley not SHR.
   3. The next discussion on April 6th, 2021 11am PST will focus on SHR acquisition protocol

**Summary: Decisions and Action Items**

1. Challenges to Obese mice scanning: restraining mouse to reduce motion artifact and the impacts to skull stripping because of the subcutaneous fat in obese mice
2. For Pilot scans:
   1. Sites agree to take 2 FOVs in pilot
   2. Sites agree to scan a normal animals (1-2 aged, obese and/or SHR) in addition to a stroked/lesioned mouse
3. Sites agree that **fat suppression and 10% larger FOV for obese mice, and elimination of RARE images for all animal models (aged, obese, SHR) would be the only changes to the current MRI acquisition protocol for now.**
4. Many sites brought up the issue of budget restrictions. **Each site is requested to email this MRI group with the average scan times that have been used for Stage 1.** This would be a strong argument for requesting an increase in funding from NINDS.
5. Sites will meet next Tuesday 4/06 11am PST to discuss changes to protocol for SHR

Minutes submitted by: Karisma Nagarkatti

Reviewed by: Cenk Ayata