EIBALL: QIBA ASL profile meeting

13:00 BST / 14:00 CEST, July 12th 2017 – online meeting

Attendees

- Ishtiaq Bercha
- Nic Blockley
- Fernando Calamante
- Tom Chenevert
- John Detre
- Xavier Golay
- Peter Gordebeke
- George Harston
- Luis Hernandez-Garcia
- Roger Hughes
- Henk-Jan Mutsaerts
- Nancy Obuchowski
- Nadia Smith
- Ona Wu

Summary

Xavier Golay opens the meeting and thanks all attendees for joining call.

Xavier Golay shares that work on the profile has just begun and the claim need to be discussed. For this, it is important to review the literature to determine the achievable precision of measurements done by ASL.

Most papers look at the within-subject standard deviation either in the whole grey matter, or in a region of interest (ROI). Xavier Golay prefers methods based on ROI, and asks attendees what statistics are necessary to establish such claims.

Claims should be outside of clinical context. The claims are based on differences that can be measured and the confidence intervals for such measurements. Nancy Obuchowksi elaborates on the three kinds of claims:

1) Technical performance claims stating the precision, e.g. the within-subject coefficient of variation should be less than or equal to [value], or the bias is expected to be less than or equal to [value].

2) Cross-sectional claims, which give a confidence interval for the true value of the measurement at a single time-point, e.g. a measurement of X, then there is a 95% confidence that the true value will be in [range]. In order to get a cross-sectional claim, the within-subject variability (precision) and the bias need to be known.
3) Longitudinal claims, where changes over two time-points are compared. For such claims, the within-subject variability is the focus, and it is assumed that the bias is constant and therefore cancelled out in comparing measurements.

Xavier Golay proposes to review existing literature to find within-subject and between-subject variances.

Xavier Golay presents results from a previous multicenter study looking at whole grey matter, and asks if the results can be used as a starting point. Scans were performed on 10 volunteers in 30 sites, using an outdated method. Between-subject standard deviation, standard deviation between sites, within-subject standard deviation are available with confidence intervals and corresponding repeatability. Nancy Obuchowski believes this data can be used, and asks if the study assumes the standard deviation is constant. In multiple QIBA imaging biomarker analyses the variability increases as the biomarker value increases, and the coefficient of variation is used instead of standard deviation. Xavier Golay indicates that the inter-session within-subject coefficient of variation was also calculated. Xavier Golay asks if taking an average across different regions is acceptable. Nancy Obuchowksi answers that this is up to experts. If the coefficient of variation is the same over these regions then it does make sense to take an average.

Fernando Calamante asks if the measurement values depend on the protocol used. Xavier Golay answers that papers shown have similar coefficients of variation. Measured values are generally in the same range even though studies use different methods with years between them.

John Detre asks what the advantage is of making increasingly difficult claims, and suggests making basic, technical claims. Xavier Golay answers that the rationale behind it is to promote ASL as a biomarker. John Detre thinks that a very basic claim that stands up to different methods and quantification models opens doors for other uses. Ona Wu agrees, and shares that QIBA prefers such precise, conservative definitions. Nancy Obuchowksi agrees as well.

Xavier Golay proposes the following claim: A measure of X% difference in measured perfusion signal in certain area can be considered as effectively different from the average with 95% confidence.

Fernando Calamante believes such a claim can't be made without relating back to the signal-to-noise ratio (SNR) of the underlying data. Xavier Golay explains that claims are based on a certain number of procedures that are going to be included in the profile. The profile has to specify image acquisition among others.

Henk-Jan Mutsaerts thinks it is difficult to determine whether a change should be additive or multiplicative. In some cases, a change could be a 20% change, in others just 5% because the maximum dilation capacity is already reached. Xavier Golay agrees. The profile should indicate what the minimum difference in flow is we can measure with certainty. Ona Wu suggests to explicitly state these claims are for specific SNR of raw data. For instance, a measured change of more than 11% signal difference indicates true change occurred with 95%. Henk-Jan Mutsaerts agrees. Changes greater than 5% to 10% within- or between-session variability reach the ceiling of instrumental variability and hit the physiological variability, greater changes can be detected with high confidence.

Xavier Golay asks if a claim about general signal amplitude difference between sessions should also be included, related to not only regional but also global cerebral blood flow variability. John Detre asks if this describes longitudinal variability. Xavier Golay confirms that it is longitudinal variability over global cerebral blood flow rather than local, because the change locally is easier to define longitudinally than globally. John Detre replies there is a lot of physiological variability, i.e. coffee consumptions can have an impact. Assuming identical conditions, claims like this can be made but with caveat that there are extenuating circumstances as well as technical factors like labelling efficiency. John Detre asks what the advantage is of pushing the claims much past the minimum needed to make ASL an official measurement of perfusion. Xavier Golay indicates it is not clear where to set the minimum. The precision and the bias need to be defined for this. Henk-Jan Mutsaerts asks if there is no concern for physiological variability because the main point is the measurement itself. Xavier Golay confirms. The physiological variability will be part of the profile document. It is about the measurement, not about the clinical interpretation or the clinical interpretation within context of natural physiological variation. It is about the kind of measurement that can be made, and what the repeatability and bias are. Based on that rest will follow.

John Detre asks if the profile will be limited to the brain. Xavier Golay replies that it is easier to start with brain, based on available publications. Henk-Jan Mutsaerts agrees.

Henk-Jan Mutsaerts asks if a meta-analysis of existing literature or new analyses on existing data should be done for the profile. Xavier Golay believes a meta-analysis would be the best way to start, and asks if Nancy Obuchowski is willing to help. Nancy Obuchowksi confirms. Nadia Smith also could help.

Xavier Golay asks if the following claim is possible: A 15% measured difference in an ROI can be considered a true measurement of difference. John Detre thinks a general claim about how the pattern of blood flow in image reflects pattern of perfusion in brain is pretty reasonable. This needs to be carefully formulated, since it does depend on many factors. Fundamental claims are label – control difference reflects perfusion, that you can calculate cerebral blood flow based on this using different models, and there's plenty data to show this for global or ROI measurements. Longitudinal stability doesn't depend on precision of measurement, and depends too much on underlying physiology. John Detre indicates he would be hesitant to say 15% hemispheric difference in any ROI is significant, because it depends on many factors, including where the ROI is, how big ROI is, and how good data is. Fernando Calamante adds that a perfusion phantom might come in handy to restrict variability of the measurement itself. Henk-Jan Mutsaerts agrees. Xavier Golay adds that it is clear that for longitudinal claims, a perfusion phantom is needed. Otherwise, it's not possible to separate physiology from technique. The perfusion phantoms are being produced now by Gold Standard Phantoms and are ready for testing. The phantom data will be very beneficial for profile.

Xavier Golay asks who would like to contribute to the meta-analysis and who would like to work on the claims. Xavier Golay indicates he would like to work on the claims, and believes John Detre should also work on them. Nancy Obuchowksi prefers to work on the claims as well, and can also do a review of the meta-analysis. John Detre suggests a fellow or trainee could publish the meta-analysis. Henk-Jan Mutsaerts agrees and offers to help with the meta-analysis.

Ona Wu will share her collection of papers, which can be used as a starting point for the meta-analysis. Luis Hernandez-Garcia suggests using the literature database from the ASL Network. The collection from Ona Wu and the ASL Network should be enough for the meta-analysis, and there is no need for new literature searches.

John Detre asks if the literature database contains papers comparing ASL and other methods, e.g. “gold standards”. Xavier Golay thinks this is a good point, and asks if this could establish a potential bias. Nancy Obuchowski also thinks this is an important point.

Fernando Calamante asks if reproducibility papers are consistent enough regarding technique used. Xavier Golay answers these are not consistent at all, but models will average those differences out. Henk-Jan Mutsaerts adds that within-session reproducibility is also important and often overlooked. It may be essential to reassess datasets to look at within-session reproducibility. George Harston agrees, and indicates he previously looked at healthy volunteers and stroke patients and saw within-session reproducibility differences. Xavier Golay agrees as well. Henk-Jan Mutsaerts suggests looking at a small number of clinical cases (approx. 100) and their within-session repeatability. Nancy Obuchowksi thinks this is a good idea that will result in lot of valuable data.

Xavier Golay thanks everyone for participating and closes the meeting.