EIBALL: QIBA ASL profile meeting

14:00 BST / 15:00 CEST, July 14th 2017 – online meeting

Attendees

- Xavier Golay
- Peter Gordebeke
- Grudrun Zahlmann
- Edward Jackson
- Patrick Hales
- George Harston
- Arastoo Vossough
- Rik Achten
- Ona Wu
- Henk Mutsaerts
- Patricia Cole

Summary

Xavier Golay opens the meeting, thanks all attendees for joining call, and summarizes the recent activities. The previous call (July 12) discussed statistics and the need to perform a literature meta-analysis on repeatability and reproducibility, as well as possibly performing re-analysis of existing data to back up claims about ASL as a biomarker. The meta-analyses, and possible re-analyses, will form the basis for the technical part of the claim.

This call is focused on the clinical context and significance, which are important parts of the QIBA profile. An extensive discussion on the meaning of signal increase/decrease needs to be included. A signal decrease can represent a decrease in perfusion, or a delayed arrival time.

From the previous discussion, it seems that from a clinical context perspective, the focus will be on a few selected diseases in the brain, e.g. tumours, epilepsy, stroke and dementia. Xavier Golay asks if attendees agree with this selection.

Rik Achten suggests to add psychiatric problems as well, as FDG-PET is often used in these situations. Xavier Golay adds that these diseases need to be assessed in terms of the use of ASL. Meta-analyses need to be performed for any disease that will be described in the profile.

Arastoo Vossough asks if stroke includes chronic cerebrovascular disease without an acute stroke. Xavier Golay confirms this is the case.

Xavier Golay indicates that one of the best uses of ASL has been for the detection of arteriovenous malformation (AVM). The ASL signal in AVM is actually an artefact, but nonetheless very useful. Xavier Golay asks how claims on this could be included. Ed Jackson answers that in this case two different claims would have to be included in the profile. There are ways how the profile can be structured to include both use-cases.

Gudrun Zahlmann asks if the claim will be different per clinical use-case, as some claims may not cover everything. Xavier Golay answers that in many use-cases perfusion is a surrogate marker of metabolism. Claims could be separated based on diseases of the cerebrovascular system and diseases in which the measurement is really a reflection of the underlying metabolism. Furthermore, claims for signal increase and decrease may have to be different.

Patricia Cole suggests it might be more efficient to have separate profiles for the different claims. Xavier Golay replies that this may be a good idea. The profile should then be separated based on diseases where the measurement is a surrogate marker for metabolism, such as epilepsy, tumour, Alzheimer's, and neurovascular disease. Ed Jackson recommends not to rush decisions on claims and keep everything centralised until it becomes evident that 1 profile is not sufficient. If section 3 and 4 of the Profile are similar, or the same, it would be better and simpler to include two claims in the same document. This is also easier for sites and vendors to show compliance. Xavier Golay agrees.

Xavier Golay asks for Rik Achten's opinion on continuous/longitudinal assessment of patients with ASL as a number of factors can affect perfusion. Rik Achten answers that his paper provides possible steps that can be taken to ensure measurements are standardised and corrected for certain factors. Henk-Jan Mutsaerts adds that these factors will have different effects on different individuals. Should measurements be of global perfusion, or are relative values satisfactory? Many physiological variations have an effect on the whole brain. Rik Achten confirms that several factors have general effects, but others have psychotropic effects and that patterns are changing. It is very difficult to put absolute values to perfusion. If certain factors are changing patterns, these should be taken into account.

Xavier Golay indicates longitudinal assessment is important, in particular in ongoing diseases like epilepsy or brain tumours to assess treatment efficacy. This needs to be carefully considered for the Profile. Xavier Golay believes a thorough review of ASL in several diseases should be performed to see what clinical interpretations can be included in the Profile. This should be backed up by data.

Xavier Golay asks if anyone would be happy to do a systematic review/meta-analysis on their preferred disease in terms of perfusion changes. Xavier Golay will work on brain tumours. George Harston has done a lot of work reviewing ASL in stroke and is happy to include this. XG asks if anyone worked on Alzheimer's disease. Henk-Jan Mutsaerts replies that a literature review is difficult as many studies report absolute perfusion changes, which are difficult to compare. Xavier Golay mentions a study by Sven Haller, which may be a good resource. Rik Achten indicates there is a review available for for psychiatric disease. Xavier Golay adds the information should be condensed even more if possible.

Xavier Golay summarises that for volunteers are needed for meta-analyses of ASL in Alzheimer and epilepsy, and asks with Rik Achten would volunteer for the analysis of ASL in psychiatry disease. Rick Achten answers that he would be interested, but believes Antonio would be better fit.

Ona Wu add that she has relevant references available (11 references for ASL/dementia, 74 ASL/tumours, 15 ASL/epilepsy 15 items).

Rik Achten asks about the timeline for the Profile. Xavier Golay indicates efforts will be made to have a good draft of the Profile by the end of the year.

Xavier Golay states that per disease only a couple of paragraphs based on literature should be included to keep the Profile streamlined. E.g., in Alzheimer's disease an average signal reduction in the posterior cingulate is a predictor of mild cognitive impairment. This needs to be put in context, and then have claims based on this: If we have reduction in perfusion of X within the context of a known non-vascular disease, this reduction can be considered to be true with 95% confidence.

Particia Cole adds that more longitudinal data from ADNI will be available soon. Information on test/retest is also needed to describe what kind of changes are meaningful. Xavier Golay states that test/retest has been discussed at length in the in previous call. Henk-Jan Mutsaerts shares that he wrote software to harmonize image processing and statistics for large perfusion studies. Within-sequence test/retest can be used to calculate the group levels and a within-study validation. Xavier Golay adds that numbers are available in many cases, and that the coefficient of variation is of interest. George Harston comments that the technical and clinical aspects have been demonstrated and established well, and wouldn't worry too much about factors influencing measurements. If it's shown to work/have clinical utility, that's the important part to include. Xavier Golay agrees.

Henk-Jan Mutsaerts asks whether it is important for clinicians to compare scans between hospitals. Rik Achten answers that it is important to at least be able to compare relevant patterns. Xavier Golay shares that Nancy Smith indicated repeatability is most important. Patricia Cole and Henk-Jan Mutsaerts agree.

Ona Wu asks if the Profile will focus on a particular ASL sequence. Patricia Cole answers that typically longitudinal repeatability is most important in clinical trials and suggests to have a standardised sequence. Henk-Jan Mutsaerts comments that repeatability can become reproducibility, e.g. through updates on the scanner. Ona Wu suggests to power trials by reproducibility. Ed Jackson agrees.

Ed Jackson indicates that the Profile should be aimed at commercially available packages and also engage vendors. Vendor specific settings can be included in the Profile under Appendix D. Don't tell vendors they must use specific sequence, but indicate they need to show certain aspects to meet a particular claim. Regarding the use of the same scanner, Ed Jackson states that the taskforce writing the Profile needs to address if they feel the data indicates that the same scanner needs to be used.

Henk-Jan Mutsaerts asks the clinicians for input on their need of relative values or absolute quantifications. Relative values are much easier to measure. Xavier Golay comments that this will be dependent on claims as well and that it could be disease specific.

Xavier Golay thanks everyone for their attendance and closes the meeting. Xavier Golay will distribute a to-do list via email with next steps for writing.