EIBALL/QIBA ASL Profile Call

January 13, 2022

Attendees

Xavier Golay
Aaron Oliver-Taylor
Erin Kelly
Gudrun Zahlmann
Karl-Olof Lovblad
Marion Smits
Nancy Obuchowski
Particia Clement
Valentin Prevost
Hangzhang Lu
Thijs van Osch
Peter Gordebeke

Summary

Xavier opens the call and thanks everyone for their attendance and continued effort. He intends to complete the ASL Profile as soon as possible, so it can move to clinical trial following a validated set of measures defined in the Profile.

PROFILE (Xavier Golay): The Profile was initially based on the original white paper. There are a series of updates to this white paper, but Xavier does not believe this changes the recommendations in the ASL Profile. There are some papers coming about ASL in clinical settings, and any protocols and recommendations from these papers need to of course be considered.

The Profile aims to be as simple as possible, while allowing to validate its claims. It is not intended for brain disorders in which the reduction in blood flow is a primary event. In particular, neurovascular diseases are not included. The upcoming paper on clinical use also describes multi-timepoint measurements for neurovascular disorders, which in comparison to the ASL Profile is much more complicated.

CLAIMS (Patricia Clement): Work on the systematic review is continuing, and an abstract about it has been submitted and accepted for the upcoming perfusion workshop. The search strategy has been improved to increase sensitivity. The main message is that a lot of work has been done already, but it is nevertheless hard to summarize it and gather any conclusions, since sequences and protocols differed. A lot of the work has been done prior to publication of the white paper.

CLINICAL APPLICATIONS: Xavier asks who is using ASL daily in clinical practice e.g. for the assessment of dementia and what their approach is, if there are any threshold values, or how it can work visually or what the minimum detectable difference is. Marion shares that she does not use cut-off values in a clinical setting. The cingulate should be higher than the normal cortex, if it's equal to or lower than the cingulate is hypoperfused. Similarly, for hyperperfusion in tumors, she uses the cortex as a reference.

The way the claims are laid out is mostly in statistical terms. The problem is that for any claim laid out in such a way, linearity between the measured biomarker and a ground truth has to be shown. Nancy

indicates that Marion's approach describes a cross-sectional claim, rather than a longitudinal claim. It's not clear if linearity needs to be proven for cross-sectional claims.

Karl-Olof agrees with Marion. In clinical settings the measurements are not quantified (often), and it is more important that you have a good signal in your reference area. In some cases, it is difficult, for instance in Alzheimer's disease, where even the reference area would be affected in terms of perfusion. It is difficult to make something subjective like this objective. A large reference cohort would be needed to quantify accurately. Marion agrees, an absolute quantification would be nice, but the question if how feasible or simple it is to achieve.

There are other Profiles that rely on relative values. Nancy indicates that if there's not too much between-subject variability, maybe a reference value could work as a claim. However, if the reference value doesn't apply to different patients very well, then it would be difficult. Xavier indicates that the reference value in this case would be specific to that individual and not a value for the general population. Nancy indicates that this would work.

Marion believes the big question is how this is linked with the disease. For hyperperfusion in tumours this is most likely easier to establish, but for hypoperfusion in for instance dementia it's unclear how strong the biological link is and whether it's possible to accurately claim that a certain measured difference reflects an actual change in perfusion. Xavier adds that the Profile is more about the technical aspects and not about the biological links.

Xavier states that for a lot of disorders the reproducibility and repeatability are known, and the systematic review may lead to exact numbers for quantification. Still, it would be easier to base the claim on a certain amount of change within an individual that reflects an actual change with 95% confidence. Nancy believes this would be a valid claim, but it's not clear whether it addresses Marion's concerns about the changing values (and differences) within an individual as disorders progress. Marion agrees that this is indeed problematic for dementia patients.

Marion asks Xavier if the reference value would be from a healthy population in this case. Xavier replies that it would need to be reference values directly measured within each individual, as the within subject variance is too large for it to be used. Marion confirms that this could then be problematic for dementia.

DECCISION TO FOCUS on BRAIN TUMOURS: Gudrun asks if the Profile wants to position ASL as disease-agnostic. It was her understanding that the Profile focused on brain tumours, but it appears as if the community would gain a lot if dementia is also included. Xavier replies that it's possible to have different claims for tumours and dementia, and suggests to first focus on tumours, as neurodegenerative diseases prove to be more difficult. Currently, it's indeed set up to be disease-agnostic, but maybe it's better for the initial completion of the Profile to focus on one disease. Karl-Olof and Marion state that for brain tumours it might not be as straight-forward either with the differences between white and grey matter, and the different vascularization levels of tumors.

Xavier states that the most important goal now is to define the exact claim. A lot of the technical parts are done, but still the claim is the main part of any Profile. Then as a last step the Profile can be simplified as much as possible. Hangzhang asks if claims from other Profiles are pathology specific. Xavier replies that they're almost always pathology specific. Hangzhang asks what pathology has most data to establish ASL as a biomarker. Xavier replies that it's important to establish what the biomarker is for and whether it only needs to detect or actually measure the status/severity of the pathology. Marion adds that for this, only providing technical details would probably not be sufficient, information on the biological link is also important.

Marion thinks considering the previously discussed, patient recruitment for clinical trial based on tumour treatment effect in brain tumours is most likely the best aspect to focus on, with most available data. Karl-Olof agrees. Xavier reiterates that the Profile would only provide a way on how to assess the blood flow. The biological question whether this is treatment effect or recurrence is not something the Profile is looking to answer. Marion replies that assessing what exactly an elevated/increased blood flow is, is the difficult question.

If we move forward this way, Nancy believes linearity does not need to be established, since it's cross-sectional. Xavier states that this would make things much easier.

Marion asks if partial volume correction needs to be discussed. Thijs answers that for brain tumours it's probably not the most important aspect. For dementia it's more relevant, and probably should be applied. Marion replies that if the grey matter is used for reference, then there is some influence of the white matter, but this could be argued as the same for everyone.

NEW CO-CHAIR (CLINICAL): Xavier asks if anyone would like to join as co-chair. Karl-Olof agrees to co-chair as clinician.

Xavier suggests advancing the ASL Profile draft so it is nearly complete in early March, as this would coincide with the relevant meetings in Los Angeles. He thanks the participants for their attendance and effort, and closes the meeting.