EIBALL-QIBA Collaboration: ASL as a Biomarker

Xavier Golay
On behalf of the European Biomarkers Alliance

European Society of Radiology Statutory Committees

- Communications and external affairs
- Education
- Quality, Safety and Standards
- Patient Advisory Group
- Finance and Internal Affairs
- ECR Programme planning
- National Societies
- Subspecialities and Allied Sciences
- Publications

RESEARCH

EIBALL
EIBALL Mission Statement

To facilitate imaging biomarker development and standardization;

To promote imaging biomarker use in clinical trials and in clinical practice by collaboration with specialist societies, international standards agencies and trials organizations within a network of excellence.

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Activity on Pillar 2 - Validating Biomarkers

Validation pipeline A Alberich-Bayarri

<table>
<thead>
<tr>
<th>Performance Indicator</th>
<th>Assays</th>
<th>Statistics</th>
<th>Acceptable*</th>
<th>Minimum</th>
</tr>
</thead>
<tbody>
<tr>
<td>CoV (%)</td>
<td>Coefficient of Variation</td>
<td>&lt; 15% (20% LLOQ)</td>
<td>2/2</td>
<td></td>
</tr>
<tr>
<td>ε (%)</td>
<td>Relative Error</td>
<td>&lt; 15% (20% LLOQ)</td>
<td>0/2</td>
<td></td>
</tr>
<tr>
<td>Correlation</td>
<td>Pearson, Spearman</td>
<td>p&lt;0.05</td>
<td>1/2</td>
<td></td>
</tr>
</tbody>
</table>

Validated Imaging Biomarker 3/6

*European Medicines Agency. Guideline on bioanalytical method validation. 21 July 2011
1st Step: Precision (harmonization / methodologies)

Recommended Implementation of Arterial Spin-Labeled Perfusion MRI for Clinical Applications: A Consensus of the ISMRM Perfusion Study Group and the European Consortium for ASL in Dementia

David C. Alsop,1 John A. Detre,2 Xavier Golay,3 Matthias Günther,4,5,6 Jeroen Hendrikse,7 Luis Hernandez-Garcia,8 Hanzhang Lu,9 Bradley J. MacIntosh,10,11 Laura M. Parkes,12 Marion Smits,13 Matthias J. P. van Osch,14 Danny J. J. Wang,15 Eric C. Wong16, and Greg Zaharchuk17

This review provides a summary statement of recommended implementations of arterial spin labeling (ASL) for clinical applications. It is a consensus of the ISMRM Perfusion Study Group and the European ASL in Dementia consortium, both of whom met to reach this consensus in October 2012 in Amsterdam. Although ASL continues to undergo rapid technical development, we believe that current ASL methods are robust and ready to provide useful clinical information, and that a consensus statement on recommended implementations will help the clinical community to adopt a standardized approach. In this review, we describe the major considerations and trade-offs in implementing an ASL protocol and provide specific recommendations for a standard approach. Our conclusion is that as an optimal default implementation, we recommend pseudo-continuous labeling, background suppression, a segmented three-dimensional readout without vascular crushing gradients, and calculation and presentation of both label/control difference images and cerebral blood flow in absolute units using a simplified model. Magn Reson Med 73:102-116, 2015. © 2014 Wiley Periodicals, Inc.

1st Step: Precision (QIBA Profile Development)

- First draft of Profile completed on 16/02/2018 by EIBALL task force:
  - Rik Achten
  - Matthias Guenther
  - Henk-Jan Mutsaerts
  - Xavier Golay
- Working towards consensus:
  - Claims
  - Clinical implications
Meta-analysis of ASL as QIB for LGG vs. HGG

- 18 studies
- All comparing HGG vs LGG
- QADAS-2 for bias assessment:

A. Alsaedi, S. Bisdas, et al.

LGG <-> HGG: Relative vs. absolute TBF

A. Alsaedi, S. Bisdas, et al.
Diagnostic Performance

<table>
<thead>
<tr>
<th>Comparison</th>
<th>Number studies</th>
<th>Sensitivity (95% CI)</th>
<th>Specificity (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>II vs. III</td>
<td>4</td>
<td>94% (75%, 99%)</td>
<td>61% (48%, 73%)</td>
</tr>
<tr>
<td>II vs. IV</td>
<td>3</td>
<td>(*)</td>
<td>(*)</td>
</tr>
<tr>
<td>III vs IV</td>
<td>9</td>
<td>86% (75%, 93%)</td>
<td>69% (57%, 79%)</td>
</tr>
</tbody>
</table>

(*) Unable to calculate pooled results due to a lack of studies

2\textsuperscript{nd} step: Accuracy & Gold Standard
ASL Perfusion Phantom

Perfusion Exchange Unit

Existence of a true Gold Standard

Geometric model
Velocity Map
Particle simulation


Bluetooth Connectivity

Average Flow Rate = 349.9 ± 1.6 ml/min
Maximum deviation 2.7% of desired 350ml/min

Results: Single PLD pCASL
Ongoing developments

• Beta-test study (reproducibility across 10 sites, supported by an SBRI grant):
  – UK: Oxford, UCL
  – EU: Bremen (DE), Leiden (NL), Erasmus MC (NL)
  – US: MGH (MA), U Michigan (MI), U Wisc (WI)

• Automatic QC analysis using ExploreASL (H. Mutsaerts)

Next steps

• Finalizing QIBA Profile to get it to Public stage (ETA Summer 2018)
  – Performing the Beta-test study for ASL Phantoms
  – Estimating ICC, CoV, etc... from clinical studies (ExploreASL)

• 3rd step: Short term and long term diagnostic value
  – Diagnostic & therapeutic value of ASL as QIB
  – Prognostic value