Declaration of Financial Interests or Relationships

Speaker Name: Aaron Oliver-Taylor

I have the following financial interest or relationship to disclose with regard to the subject matter of this presentation:

Company Name: Gold Standard Phantoms Limited
Type of Relationship: Employee, Shareholder

A multi-site round-robin assessment of ASL using a perfusion phantom

A. Oliver-Taylor[1], T. Hampshire[1], H.J. Mutsaerts[2,3,4], P. Clement[5], E. Warnert[6], A. Harteveld[4], J.P.A. Kuijer[2], K. Baas[3], J. Petr[7,8], J.C.W. Siero[4,9], J.P. Marques[10], F. Vanhevel[15], S. Sunaert[11], R.J.H. Borra[12], M.J.P. van Osch[13], X. Golay[1,14], E. Achten[5]

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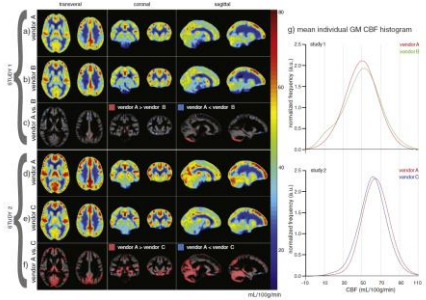
Introduction

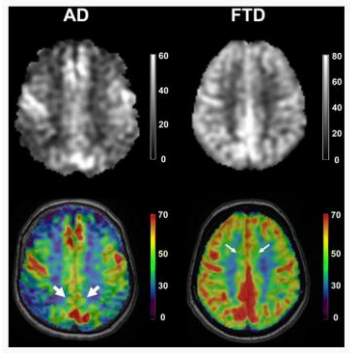
Recommended Implementation of Arterial Spin-Labeled Perfusion MRI for Clinical Applications: A Consensus of the ISMRM Perfusion Study Group and the European Consortium for ASL in Dementia

Since the publication of the ASL White Paper[1] in 2015, there is renewed interest in ASL .



Mutsaerts et al. Neuroimage (2015)

Numerous reproducibility studies[4] have determined the CoV of CBF, leading to its use as biomarker in cross-sectional studies[5].

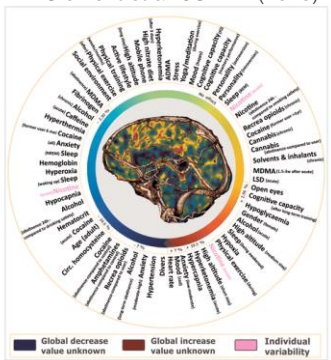


Steketee et al. Eur. Radiol. (2015)

ASL has been shown to be a valid biomarker of neurological disease onset[2] and response to therapy[3].

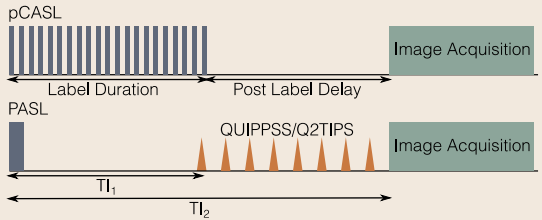
Sources of potential physiological confounds have been established[6].

Clement et al. JCBFM (2018)



However…

Different MRI system hardware



Different labelling strategies

So far, it has not been possible to compare across ASL implementations, accounting only for differences in hardware. In this study we set out to assess the effective reproducibility of CBF estimates using a perfusion phantom[7].

1. Alsop et al. MRM 2015; 73: 102-116. 2. Steketee, et al. Eur. Radiol. 26, 244–253, 2016. 3. Wang, et al. J. Pharmacol. Exp. Ther. 337, 359–366, 2011. 4. Mutsaerts, et al. Neuroimage 113, 2015. 5. Sullivan, et al. Radiology. 2015 Dec;277(3):813-25. 6. Clement, et al. JCBFM, 2018 Sep;38(9):1418-1437. 7. Oliver-Taylor et al. Proc. ISMRM, 2017, Abstract #0681.

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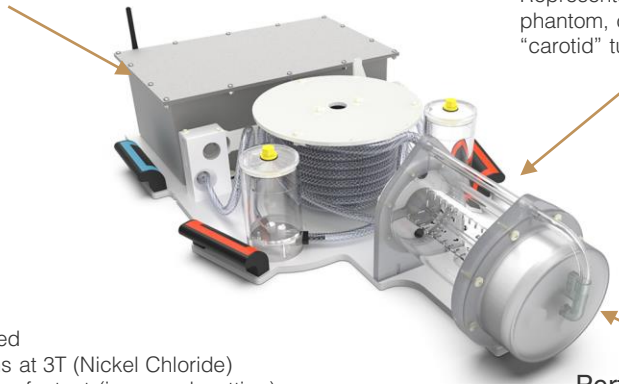
Perfusion Phantom

MRI Compatible Piezoelectric pump

Delivers perfusate at a controlled known flow rate round the system. Automatic flow control using a ARM microcontroller and calibrated flow meter. Wireless communications for control and real-time telemetry of measured flow rate and temperature



Label Chamber

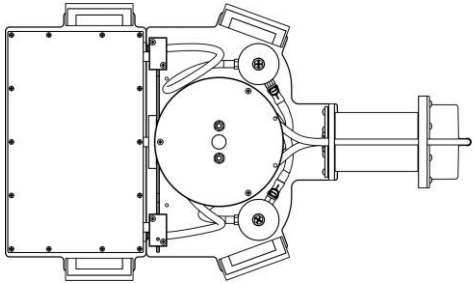
Represents the 'neck' of the phantom, containing the inflow "carotid" tube.

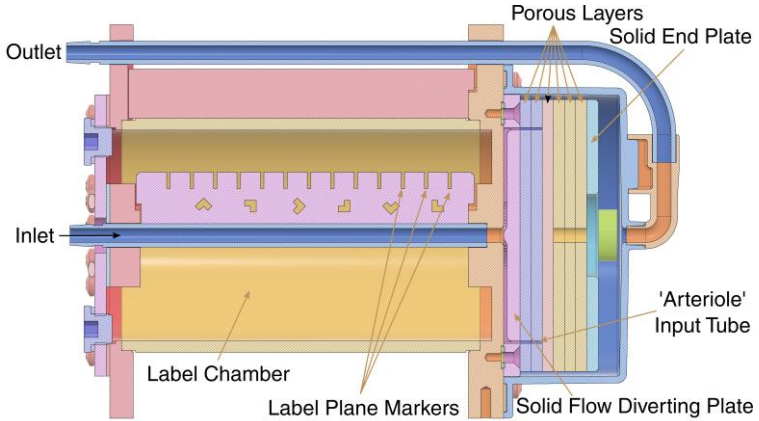
Perfusate

- Water based
- T_1 ~1800ms at 3T (Nickel Chloride)
- Non-ionic surfactant (improved wetting)
- viscosity ~1.65mPA.s @ 20°C (water soluble polymer)
- Non-toxic preservative (methylisothiazolinone based).

Perfusion Chamber

Simulates the capillary bed by using six 4.75x116mm discs of sintered UHMW Polyethylene (mean pore size 7um, porosity 32%)





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Study Design

Phantom transported by car to 11 sites in a 2 week period

No.	Site	MRI Vendor	Model	SW	Coil	ASL Sequence	Label Type	Acquisition	Label Duration / TI1 (ms)	PLD/TI (ms)
1	1	Siemens	Prisma Fit	VE11	64ch	C2P (Bremen)	pCASL	3D-GRASE	1800	1800
2	2	GE	Sigma PET/MR	DV26	8ch	Product	pCASL	Spiral FSE	1450	2025
3	2	Philips	Achieva	R5.4.0		Product	pCASL	3D-GRASE	1800	1800
4	3	Siemens	Prisma Fit	VE11	32ch	C2P (Bremen)	pCASL	3D-GRASE	1800	1800
5	4	Siemens	Prisma	VE11C	32/64ch	Product	PASL (FAIR)	3D-GRASE	700	1800
6	4	Siemens	Skyra	VE11C	64ch	Product	PASL (FAIR)	3D-GRASE	700	1800
7	5	Siemens	Prisma	VE11C	32ch	Product	PASL (FAIR)	3D-GRASE	700	1800
8	5	Siemens	Skyra	VE11C	32ch	Product	PASL (FAIR)	3D-GRASE	700	1800
9	6	Philips	Ingenia	R5.3.1	32ch	Product	pCASL	2D-EPI	1800	1800
10	6	Philips	Achieva	R5.3.1	8ch	Product	pCASL	2D-EPI	1800	1800
11	7	Philips	Ingenia	R5.4.0	32ch	Product	pCASL	3D-GRASE	1800	1800
12	8	Philips	PET/MR	R3.2.2	8ch	Product	pCASL	2D-EPI	1800	1800
13	8	GE	Discovery MR750	DV25	8ch	Product	pCASL	Spiral FSE	1450	1525/2025
14	9	Philips	Ingenia	R5.3.1	32ch	Product	pCASL	2D-EPI	1800	1800
15	9	Philips	Ingenia	R5.3.0	32ch	Product	pCASL	2D-EPI	1800	1800
16	10	GE	Discovery MR750	DV25	8ch/32ch	Product	pCASL	Spiral FSE	1450	1525/2025
17	11	Philips	Achieva	R5.3.1	32ch	Product	pCASL	2D-EPI	1800	1800

Acquire ASL measurements at 2 bulk flow rates: 200ml/min and 350ml/min

Laser marker was set to the same reference point on the phantom, the phantom aligned in the head-foot direction, and levelled using foam pads.

Analysis Groups

pCASL

- 2D-EPI: Philips
- 3D-GRASE: Siemens C2P Bremen
- 3D-Spiral: GE

PASL

- 3D-GRASE: Siemens

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Analysis

Convert DICOM to NIFTI[8]

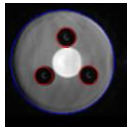
Calculate CBF using single subtraction equation[1]

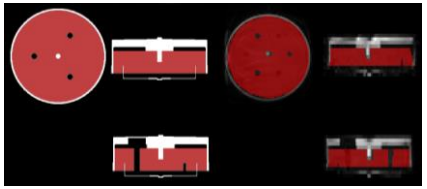
$$CBF_{pCASL} = \frac{6000\lambda \cdot (SI_{control} - SI_{label}) \cdot e^{\frac{PLD}{T_{1b}}}}{2 \cdot \alpha \cdot T_{1b} \cdot SI_{PD} \cdot \left(1 - e^{-\frac{\tau}{T_{1b}}}\right)}$$

$$CBF_{PASL} = \frac{6000\lambda \cdot (SI_{control} - SI_{label}) \cdot e^{\frac{PLD}{T_{1b}}}}{2 \cdot \alpha \cdot T_{1b} \cdot SI_{PD}}$$

$$\alpha = 0.85, \lambda = 0.32, T_{1,b} = 1800ms$$

a. Hough transform provides candidates for known circular features on M0 image

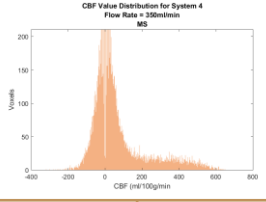




c. The porous mask in the atlas image is transformed to the image space using the registration results, resulting in an ROI mask of the porous material in the perfusion chamber.

b. Detected features used as initialisation to a multi-resolution, multi-transformation (including B-spline) registration to the phantom 'atlas' image, produced from the phantom CAD model.

Extract CBF value distribution within this ROI.
Calculate mean and standard devation



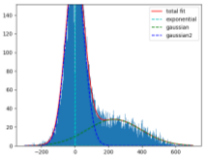
Fit to a signal distribution model

$$F(x) = A \cdot e^{\frac{-(x-\mu)^2}{2\sigma_1^2}} + Be^{\frac{-x^2}{2\sigma_2^2}} + C\lambda e^{-\lambda x}$$

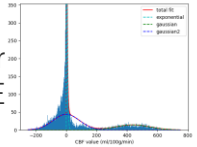
Perfusion signal distribution, $\mu > 0$

Noise distribution

Signal dispersion distribution, $\lambda > 0$



Example fit for 2D-EPI



Example fit for 3D-GRASE

1. Alsop et al. MRM 2015; 73: 102-116. 8. dicm2nii: https://github.com/xiangruili/dicm2nii

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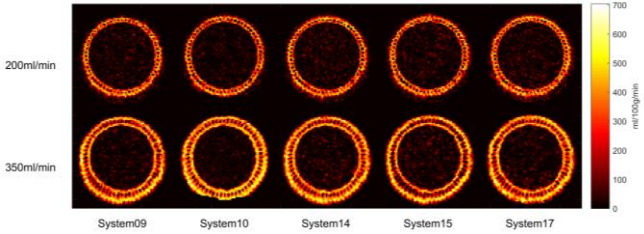
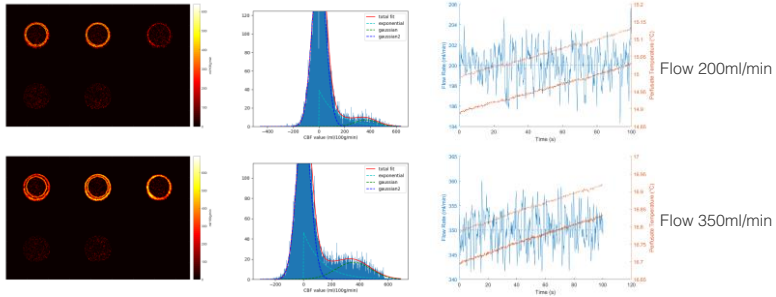
Results Philips 2D-EPI pCASL



CBF in the middle slice across all systems. Image quality, including artefacts and distortions are comparable.

Example data from System 17



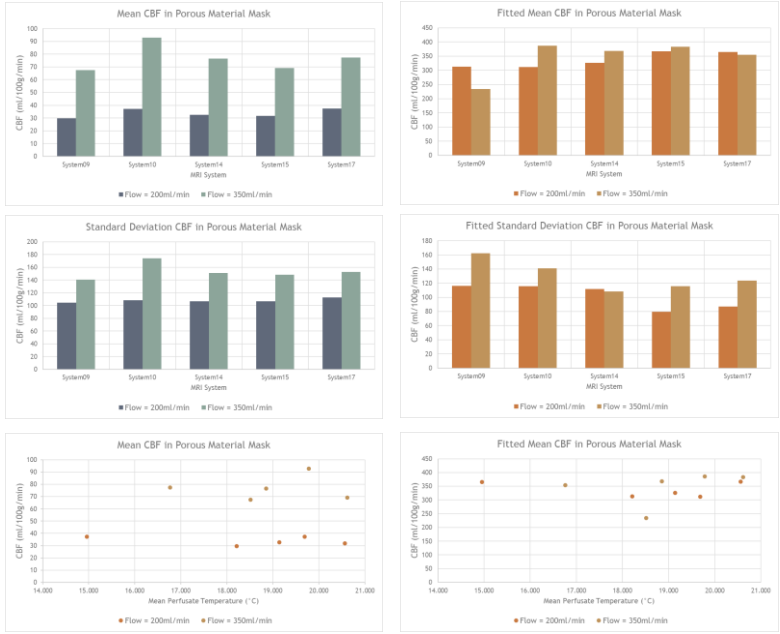
CBF Map | CBF Value Distribution | Recorded flow rate and perfusate temperatures during scan

No.	Site	MRI Vendor	Model	SW	Coil
9	6	Philips	Ingenia	R5.3.1	32ch
10	6	Philips	Achieva	R5.3.1	8ch
14	9	Philips	Ingenia	R5.3.1	32ch
15	9	Philips	Ingenia	R5.3.0	32ch
17	11	Philips	Achieva	R5.3.1	32ch

Label Duration	1800ms	Background suppression	4 pulse default
Post Label Delay	1800ms	TR	5000ms
Label Plane Location	60mm from centre of FOV	TE	Min TE (10.16-11.27ms)
No. dynamics	1 M0 + 3 control label pairs	Acq matrix	128x96
No. shots	4	No. Slices	12
SENSE Factor	2.3	Slice thickness/gap	4mm/1mm
FOV	256x192x59mm	PE Direction	AP

Mean CBF values are reasonably consistent for both flow rates

Fitted Mean CBF values are less so – especially at 200ml/min. This is possibly an artefact of the fitting algorithm



No observable temperature dependence on phantom CBF values

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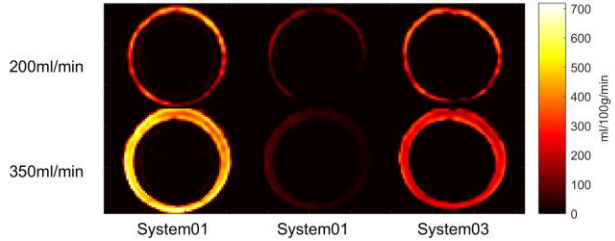
Results Siemens C2P (Bremen) 3D-GRASE pCASL

Label Duration	1800ms	Background suppression	Yes
Post Label Delay	1800ms	TR	5000ms
Label Plane Location	60mm from centre of FOV	TE	17.86ms
No. dynamics	1 M0 + 4 control label pairs	Acq matrix	64x48
No. shots	2	No. Slices	12
EPI Factor	24	Slice thickness	5mm
FOV	256x192x59mm	PE Direction	AP

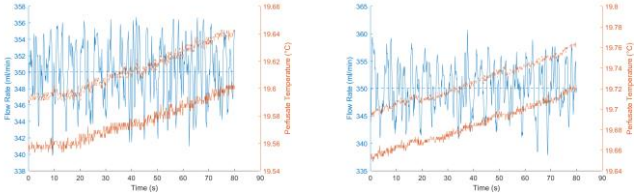
No.	Site	MRI Vendor	Model	SW	Coil
1	1	Siemens	Prisma Fit	VE11	64ch
4	3	Siemens	Prisma Fit	VE11	32ch



First Round Robin Scan
Last Round Robin Scan
Phantom operated similarly for each scan.
Why so different?

- Label efficiency?
- Distortions?

Slightly different version of the sequence (older), is this the cause of the difference or is it also label efficiency/distortions.



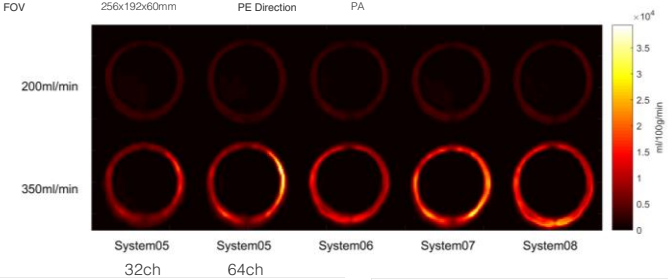
First Scan

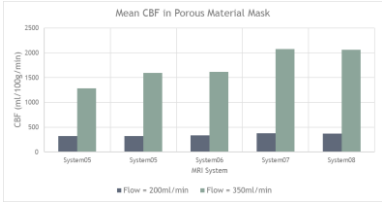
Last Scan

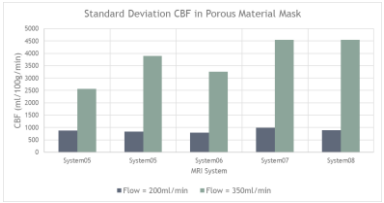
Results Siemens 3D-GRASE FAIR

Bolus Duration	700ms	Background suppression	Yes
Inversion Time	1800ms	TR	5000ms
M0	Pseudo M0 (Bolus Duration=100ms, Inversion Time=7000ms)	TE	16.94ms
No. dynamics	1 M0 + 4 control label pairs	Acq matrix	64x48
No. shots	2	No. Slices	12
EPI Factor	23	Slice thickness	5mm
FOV	256x192x60mm	PE Direction	PA

No.	Site	MRI Vendor	Model	SW	Coil
5	4	Siemens	Prisma	VE11C	32/64ch
6	4	Siemens	Skyra	VE11C	64ch
7	5	Siemens	Prisma	VE11C	32ch
8	5	Siemens	Skyra	VE11C	32ch







CBF values much higher than with pCASL because TI (1800ms) is half of the label duration + PLD (3600ms).
Fitting was not successful for this data. Global mean values are similar, however there's a significant difference between Systems 5&6 and 7&8.

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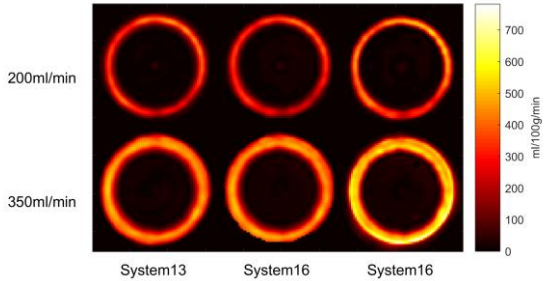
Results GE 3D Spiral FSE pCASL

No.	Site	MRI Vendor	Model	SW	Coil
13	8	GE	Discovery MR750	DV25	8ch
16	10	GE	Discovery MR750	DV25	8ch/32ch

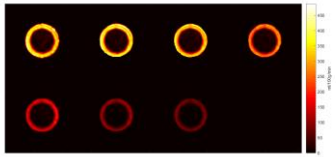
Label Duration	1450ms	Background suppression	Yes
Post Label Delay	1525/2025ms	TR	4590/4802ms
Label Plane Location	76.8mm from centre of FOV	TE	10.536ms
No. dynamics	3	Recon matrix	128x128
No. arms	8	No. Slices	32
Points per arm	512	Slice thickness	4mm
FOV	256x192x59mm		

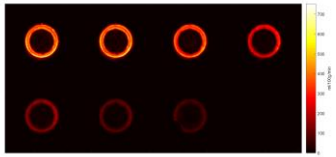
PLD=1525ms



System 16, PLD=2025ms

8 channel

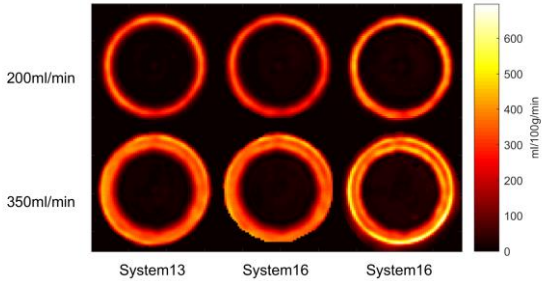


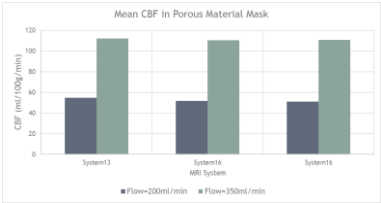


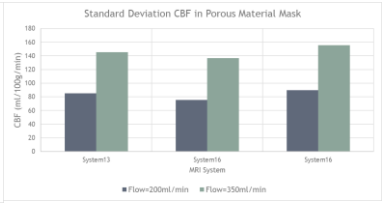
32 channel

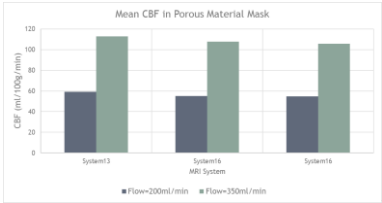
Similar mean CBF values for 8 and 32ch, however visibly different perfusion signal.

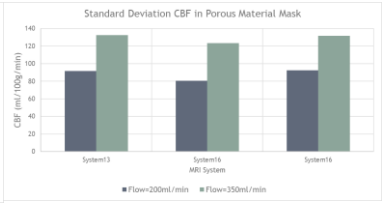
PLD=2025ms











A multi-site round-robin assessment of ASL using a perfusion phantom

A. Oliver-Taylor[1], T. Hampshire[1], H.J. Mutsaerts[2,3,4], P. Clement[5], E. Warnert[6], A. Harteveld[4], J.P.A. Kuijer[2], K. Baas[3], J. Petr[7,8], J.C.W. Siero[4,9], J.P. Marques[10], F. Vanhevel[15], S. Sunaert[11], R.J.H. Borra[12], M.J.P. van Osch[13], X. Golay[1,14], E. Achten[5]

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Discussion and Conclusions

Coefficient of Variation for each sub-group

Philips 2D-EPI pCASL

Flow Rate (ml/min)	CoV CBF Mean (%)
200	9.1
350	11.8

Siemens 3D-GRASE FAIR

Flow Rate (ml/min)	CoV CBF Mean (%)
200	7.3
350	17.6

GE 3D-Spiral pCASL

PLD (ms)	Flow Rate (ml/min)	CoV CBF Mean (%)
1525	200	3.1
1525	350	0.7
2025	200	3.5
2025	350	2.8

- Significant variation in the quantitative values obtained within the sub-groups.
- Not possible to make comparisons between implementations.
- No measure of variability on a single system has been made – difficult to know if differences are systematic or random.
- Fitting to signal distributions needs some more work as they don't work so well for some implementations.
- Phantom reproducibility seems good, but this is not known quantitatively to give a lower bound of measurable variability.

Future work

- Establish phantom reproducibility (including effects of placement, alignment etc)
- Perform test-retest on each system.
- Standardise by using similar ASL flavours and common label/acquisition parameters.
- Better statistics to determine statistically significant differences between systems.

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GOLD STANDARD PHANTOMS