Per quanto concerne i moderatori, relatori, formatori, tutor, docenti è richiesta dall'Accordo Stato-Regioni vigente apposita dichiarazione esplicita dell'interessato, di trasparenza delle fonti di finanziamento e dei rapporti con soggetti portatori di interessi commerciali relativi agli ultimi due anni dalla data dell'evento.
La documentazione deve essere disponibile presso il Provider e conservata per almeno 5 anni.

Dichiarazione sul Conflitto di Interessi

Nicoletta Anzalone
Il sottoscritto_____ in qualità di:

☐ responsabile scientifico ☐ moderatore ☐ docente ☒ relatore ☐ tutor

dell'evento "X CONGRESSO AIRMM - RISONANZA MAGNETICA IN MEDICINA 2019:
DALLA RICERCA TECNOLOGICA AVANZATA ALLA PRATICA CLINICA"
Milano, 28-29 marzo 2019

da tenersi per conto di **Biomedia srl Provider n. 148,**

ai sensi dell'Accordo Stato-Regione in materia di formazione continua nel settore "Salute" (Formazione ECM) vigente,

Dichiara

che negli ultimi due anni NON ha avuto rapporti anche di finanziamento con soggetti portatori di interessi commerciali in campo sanitario

☐ che negli ultimi due anni ha avuto rapporti anche di finanziamento con soggetti portatori di interessi commerciali in campo sanitario (indicare quali):

Relatore Bayer Healthcare
Advisory board Bracco Diagnostics

_____ _____
_____ _____
_____ _____
_____ _____

Innovation in perfusion MRI, is Gadolinium still necessary?

Auditorium Testori
di Palazzo Lombardia

MILANO
28-29 marzo 2019

Nicoletta Anzalone, Claudia Godi

Neuroradiologia,
Universita' Vita e Salute,
IRCCS Ospedale S Raffaele , Milano

OSPEDALE
SAN RAFFAELE

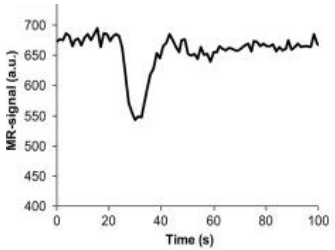
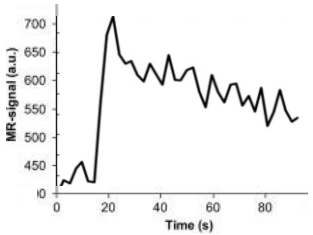
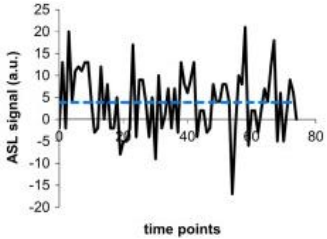
UNIVERSITÀ VITA-SALUTE SAN RAFFAELE
UniSR
QUID EST HOMO?

Brain MR Perfusion Techniques

- *Dynamic Susceptibility Contrast MRI (DSC-MRI)**
- *Dynamic Contrast Enhanced MRI (DCE-MRI)**
- *Arterial Spin Labelling (ASL)*

* Gadolinium

Brain MR Perfusion Techniques

	DSC	DCE	ASL
Signal Contribution	Changes in T2/T2* relaxation	Changes in T1 relaxation	Magnetic Blood labeling
Contrast	Gadolinium-based	Gadolinium-based	Labeled blood water
Acquisition Time	Short (1-2 min)	Long (5-10 min)	Intermediate (4-6 min)
BBB	Intact	Intact/Disrupted	Intact/Disrupted
Signal Time Course			

ADVANTAGES AND DISADVANTAGES OF PERFUSION SIGNALS

	DSC	DCE	ASL
Basis	T_2/T_2^*	T_1	Spin tag
Contrast agent	Gd-based	Gd-based	Blood label
SNR	Very good	Good	Fair
CBF	Fair	Poor	Very good
CBV	Good	Very good	Poor
Transit	Very good (MTT)	Very good (K^{trans})	Fair
Coverage	Very good	Good	Good
Scan time	Very good	Fair	Good
Repeatable	Good	Fair	Very good
Child application	Good	Fair	Very good
Image artifact	Fair	Very good	Good

Jahng et al, 2014

TWO MOST IMPORTANT REQUIREMENTS FOR PERFUSION

DSC: temp res 1-2 sec , spatial res 2-3 x 3-5mm
White paper AJNR 2015

DCE: temp res < 5sec, spatial res 1-2 x 4-5mm
Qiba 2012

ASL: temp res < 1-2 sec, spatial res 3x3x5 mm
White paper Magn Res Med 2015

DIFFERENT PERFUSION SEQUENCES DIFFERENT MARKERS

DSC: *CBF, CBV, MTT, TMAX, TTP*

DCE: *VP, Ktrans, Ve, Kep (extended Toft model)*

ASL: *CBF, BAT, aBV but also different sequences (PASL vs pCASL, Multiple TI), 3T*

Perfusion applications in neuroradiology

Brain tumor
Stroke , stroke mimics
Chronic vascular insufficiency
Degenerative disease
Neonates
Infections

Choice of techniques depends on: Clinical question, Target parameters (MTT,CBF,CBV, Vp,Ktrans...) Temporal /Spatial resolution

BRAIN TUMOR

Neuro-Oncology

Neuro-Oncology 17(9), 1188–1198, 2015
doi:10.1093/neuonc/nov095
Advance Access date 6 August 2015

Consensus recommendations for a standardized Brain Tumor Imaging Protocol in clinical trials

Benjamin M. Ellingson, Martin Bendszus, Jerrold Boxerman, Daniel Barboriak, Bradley J. Erickson, Marion Smits, Sarah J. Nelson, Elizabeth Gerstner, Brian Alexander, Gregory Goldmacher, Wolfgang Wick, Michael Vogelbaum, Michael Weller, Evanthia Galanis, Jayashree Kalpathy-Cramer, Lalitha Shankar, Paula Jacobs, Whitney B. Pope, Dewen Yang, Caroline Chung, Michael V. Knopp, Soonme Cha, Martin J. van den Bent, Susan Chang, W.K. Al Yung, Timothy F. Cloughesy, Patrick Y. Wen, Mark R. Gilbert, and the Jumpstarting Brain Tumor Drug Development Coalition Imaging Standardization Steering Committee

Table 1. Minimum standard 1.5 T & 3 T MRI protocol

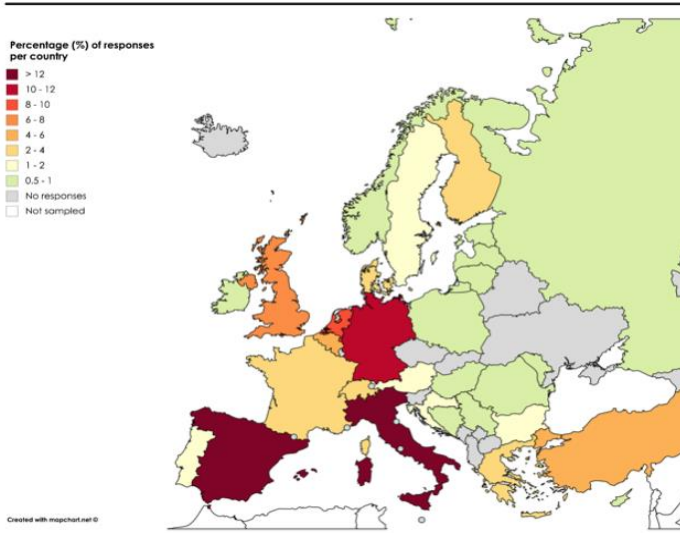
	3D T1w Pre[b]	Ax 2D FLAIR[j]	Ax 2D DWI	Ax 2D T2w[h,j]	3D T1w Post[b]
Sequence	IR-GRE[e,f]	TSE[c]	SS-EPI[g]	TSE[c]	IR-GRE[e,f]
Plane	Sagittal/axial	Axial	Axial	Axial	Sagittal/axial
Mode	3D	2D	2D	2D	3D
TR [ms]	2100[m]	>6000	>5000	>2500	2100[m]
TE [ms]	Min	100–140	Min	80–120	Min
TI [ms]	1100[n]	2000–2500[k]			1100[n]
Flip angle	10°–15°	90°/≥160°	90°/180°	90°/≥160°	10°–15°
Frequency	≥172	≥256	≥128	≥256	≥172
Phase	≥172	≥256	≥128	≥256	≥172
NEX	≥1	≥1	≥1	≥1	≥1
FOV	256 mm	240 mm	240 mm	240 mm	256 mm
Slice thickness	≤1.5 mm	≤4 mm[i]	≤4 mm[i]	≤4 mm[i]	≤1.5 mm
Gap/spacing	0	0	0	0	0
Diffusion options[p]			$b = 0, 500, 1000$ s/mm^2 ≥3 directions		
Parallel imaging	Up to 2x	Up to 2x	Up to 2x	Up to 2x	Up to 2x
Scan time (approx) [benchmarked on 3 T Skyra]	5–10 min [5:49 for 1 mm isotropic]	4–8 min [3:22 for 2D FLAIR]	2–4 min [1:22 for 3 direction DWI and 3 b-values]	4–8 min [5:10 for dual echo]	5–10 min [5:49 for 1 mm isotropic]

Contrast Injection[a]

Glioma imaging in Europe: A survey of 220 centres and recommendations for best clinical practice

S. C. Thust,[1,2,3] S. Heiland,[4] A. Falini,[5] H. R. Jäger,[1,2,3] A. D. Waldman,[6] P. C. Sundgren,[7,8] C. Godi,[5] V. K. Katsaros,[9,10,11] A. Ramos,[12] N. Bargallo,[13,14] M. W. Vernooij,[15,16] T. Yousry,[1] M. Bendszus,[4] and M. Smits[15]

European Radiology 2018



Perfusion MRI (pMRI)

When do you acquire pMRI?			
Always in glioma	Primary diagnosis only	Follow up only	Upon indication only
49.1 *(108)*	10.9 *(24)*	3.6 *(8)*	21.4 *(47)*

Reasons for using pMRI				pMRI protocol duration		
For clinical diagnosis	Biopsy guidance	To guide therapy	Mainly research	≤5 mins	≤2 mins	Don't know
79.7 *(149)*	46 *(86)*	61.5 *(115)*	13.4 *(25)*	83.5 *(71)*	45 *(38)*	5 *(4)*

Reasons for always acquiring pMRI	
I want it to be available when I need it	43.6 *(61)*
I (almost) always find it useful	55.7 *(78)*
It impacts patient care and management	56.4 *(79)*
Clinicians always want it	7.9 *(11)*
I acquire it for logistical reasons (e.g. standardised protocols)	30 *(42)*
For research purposes	24.3 *(34)*
To maintain radiographers' level of experience	15.7 *(22)*

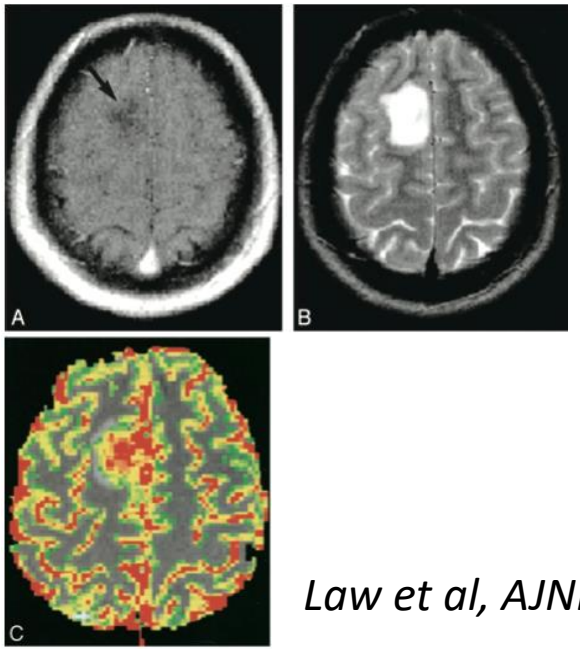
pMRI method				Preload		
DSC	DCE	ASL	≥ 2 methods	Yes	No	Don't know
81.8 *(153)*	29.4 *(55)*	12.3 *(23)*	21.4 *(40)*	46.5 *(87)*	46 *(86)*	7.5 *(14)*

DSC - State of the art

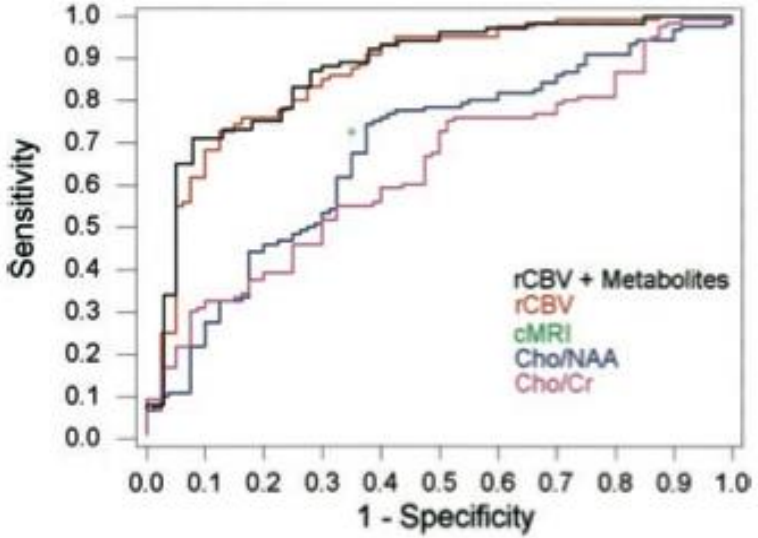
DSC Glioma grading: added value

Diagnostic accuracy

Comparison with conventional studies



Law et al, AJNR 2003

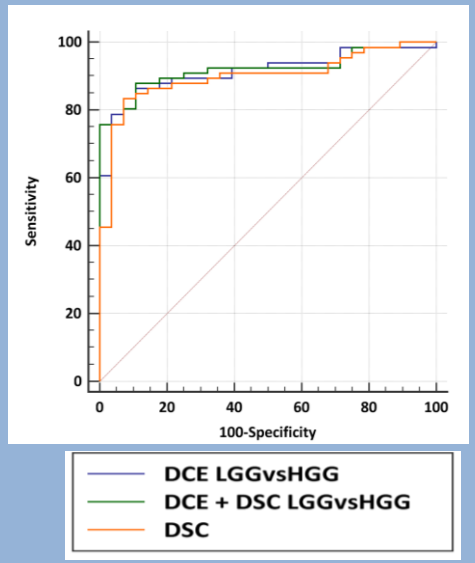


DSC - State of the art

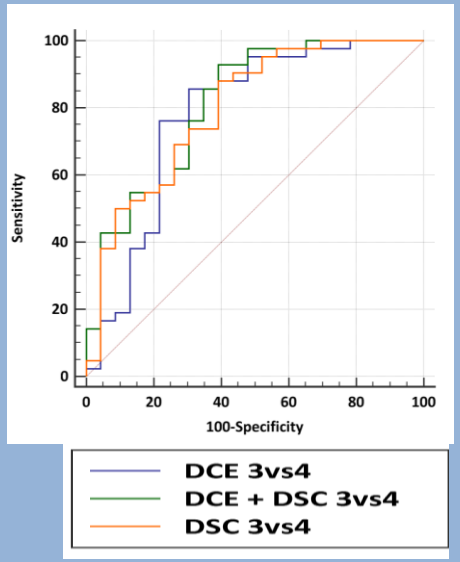
DSC /DCE – Glioma grading

A Multi-center, Standardized Assessment of Dynamic Contrast-Enhanced and Dynamic Susceptibility Contrast MRI in Grading Gliomas

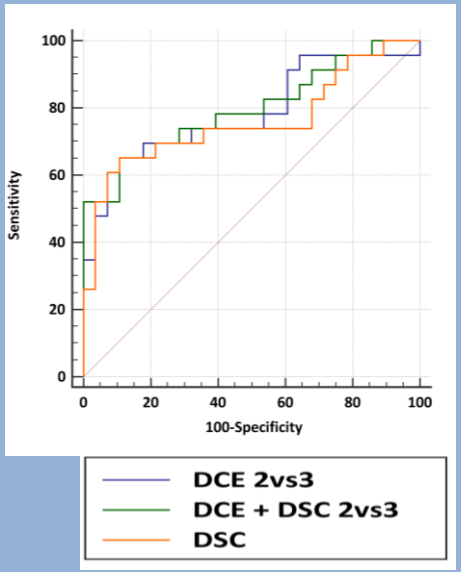
Anzalone N, Castellano A, Cadioli M, et al ***Radiology, 2018***



Low vs High Grade



Grade III vs Grade IV



Grade II vs Grade III

DSC - State of the art

DSC/DCE – Radiogenomic

SCIENTIFIC REPORTS

OPEN

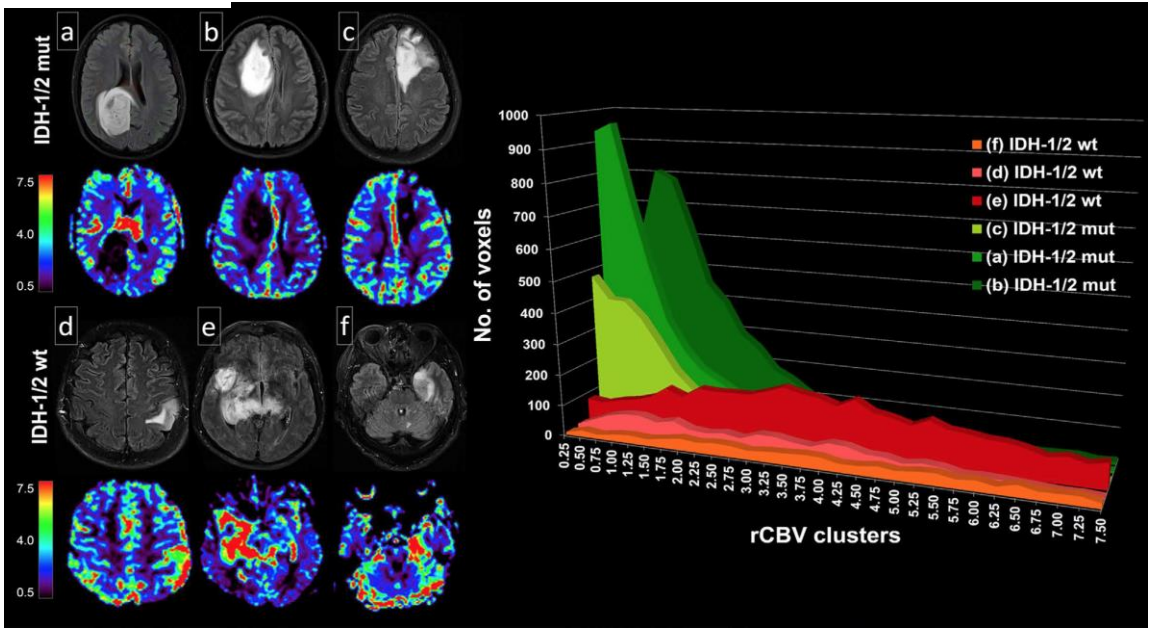
Received: 06 July 2015
Accepted: 14 October 2015
Published: 05 November 2015

IDH mutation status is associated with a distinct hypoxia/ angiogenesis transcriptome signature which is non-invasively predictable with rCBV imaging in human glioma

Philipp Kickingereder[1], Felix Sahm[2,3], Alexander Radbruch[1,4], Wolfgang Wick[2,3], Sabine Heiland[1], Andreas von Deimling[2,3], Martin Bendszus[1] & Benedikt Wiestler[1,4,4,1]

a-c: IDH mut -> lower CBV values

d-f: IDH wt -> higher CBV values

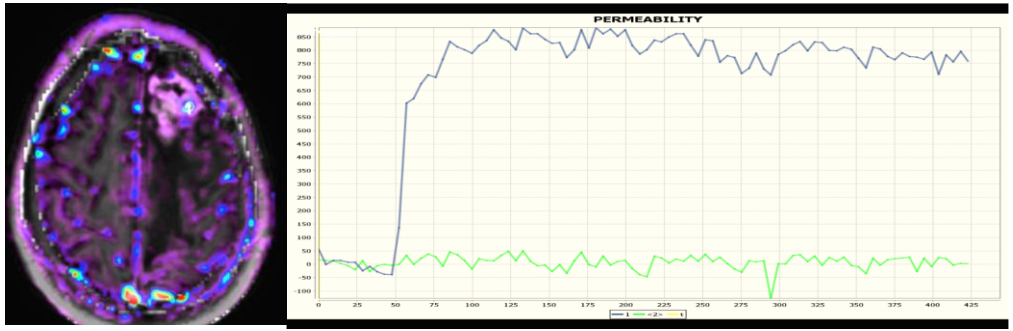


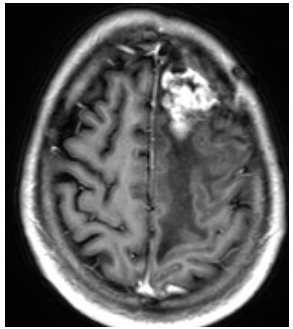
DSC - State of the art

DCE/DSC – Treatment response

Vp: 15.4-Ktrans 0,3

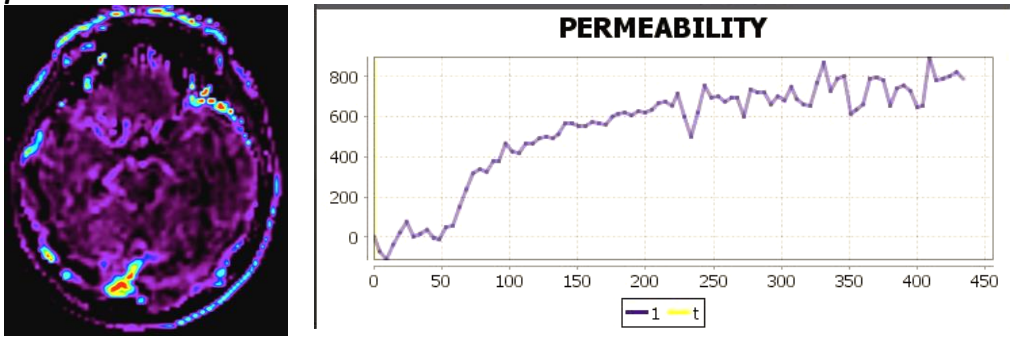
Anaplastic oligodendroglioma relapse

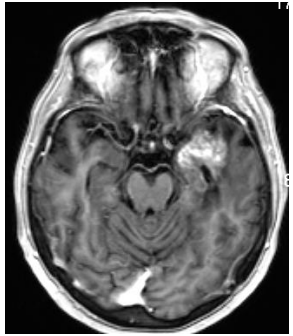




Vp: 3.9-Ktrans 0.08

Radionecrosis





ASL – Glioma grading Added value

Diagnostic accuracy

Comparison with conventional studies (ADC)

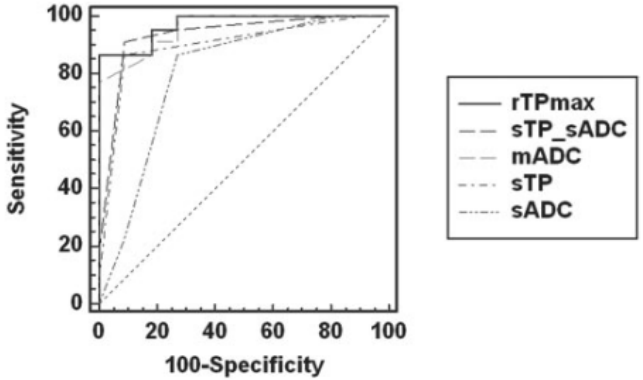


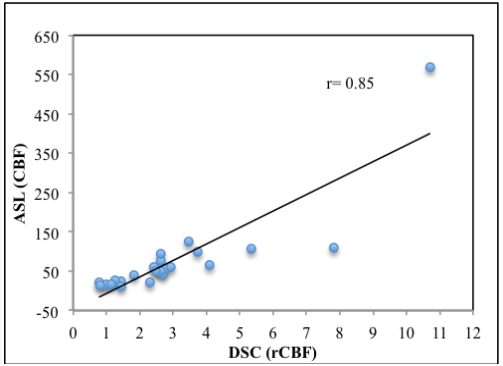
Table 2: Sensitivity, specificity, PPV, and NPV for conventional imaging and the five qualitative and quantitative methods of PASL and ADC for distinguishing high-grade from low-grade gliomas

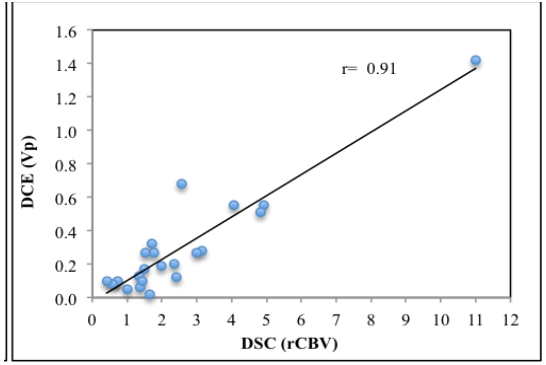
	CI	rTPmax	mADC	sTP	sADC	sTP and sADC
Sensitivity (%)	77.3	95.5	90.9	86.4	86.4	90.9
Specificity (%)	72.7	81.8	81.8	90.9	72.7	90.9
PPV (%)	85.0	91.3	90.9	95.0	86.4	95.2
NPV (%)	66.7	90.1	81.8	76.9	72.7	83.3

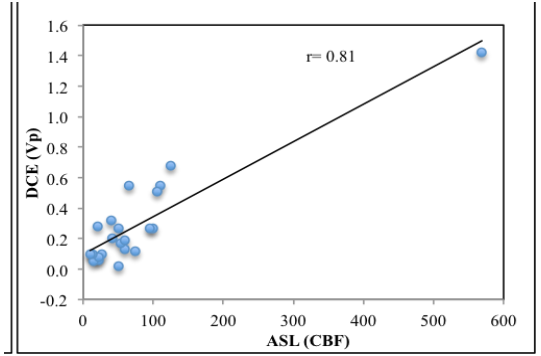
Kim et al, AJNR 2007

ASL versus DSC/DCE

- *23 patients*
- *gliomas WHO II (n=12), glioma WHO III (n=8),*
- *radiation necrosis (n=1), metastasis (n=1), haemangioblastoma (n=1).*

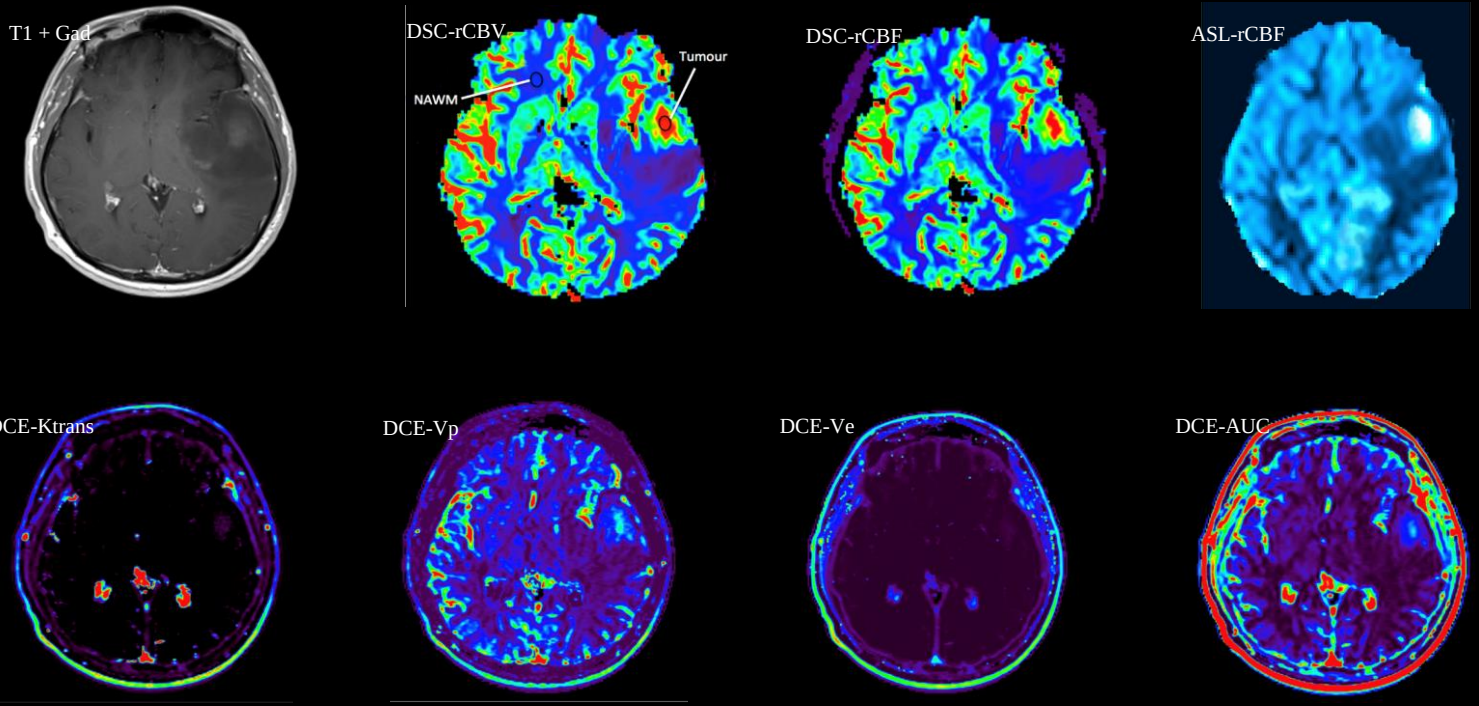






Courtesy of Sameeha Fallatah

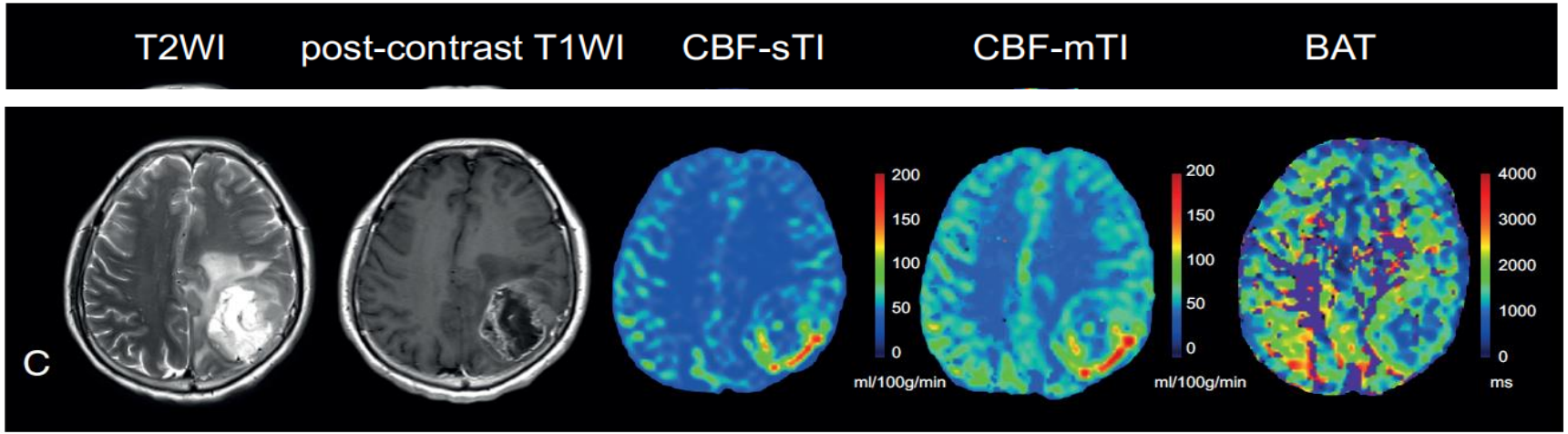
ASL versus DSC/DCE



ASL : no use of leakage correction algorithms
possible false positive in oligodendrogliomas

Courtesy of Sameeha Fallatah

ASL in Glioma Grading: Single TI vs Multi-TI *

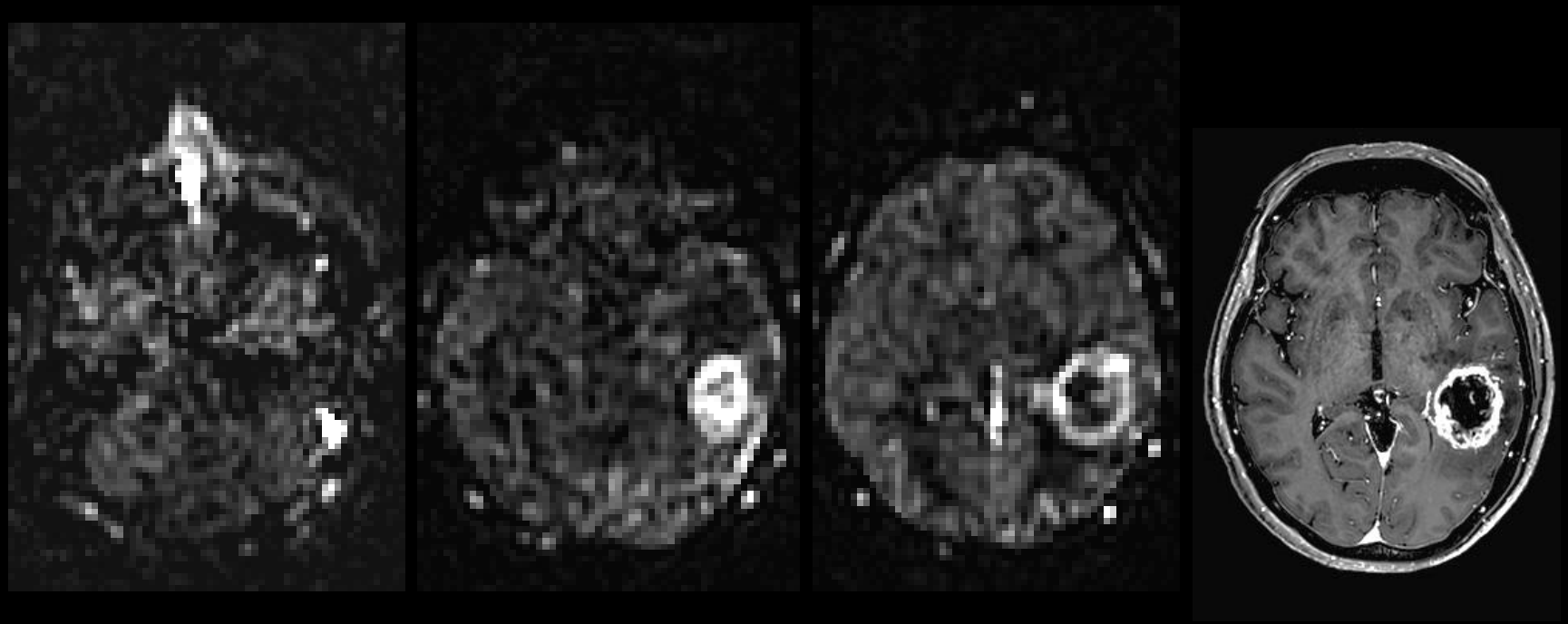


WHO Grade	Sum of Scores (Median) (Range)	nCBF-sTI (Median) (Range)	nCBF-mTI (Median) (Range)	nBAT (Median) (Range)
II (LGGs)	13 (8.5–19)	1.28 (0.36–8.7)	1.62 (0.68–8.56)	1.21 (0.68–4.52)
III	15 (12–19)	3.33 (0.72–10.78)	4.93 (1.78–14.85)	0.77 (0.53–1.70)
IV	16.5 (11.5–19.5)	4.07 (1.07–15.23)	13.40 (5.18–22.36)	0.90 (0.53–1.55)
III and IV (HGGs)	16.5 (11.5–19.5)	3.7 (0.72–14.51)	6.7 (1.78–22.36)	0.86 (0.53–1.70)

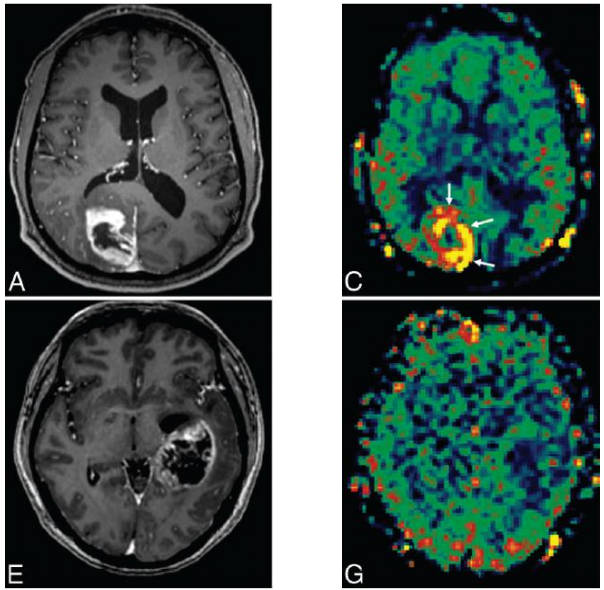
[a] Values are presented as median and range.

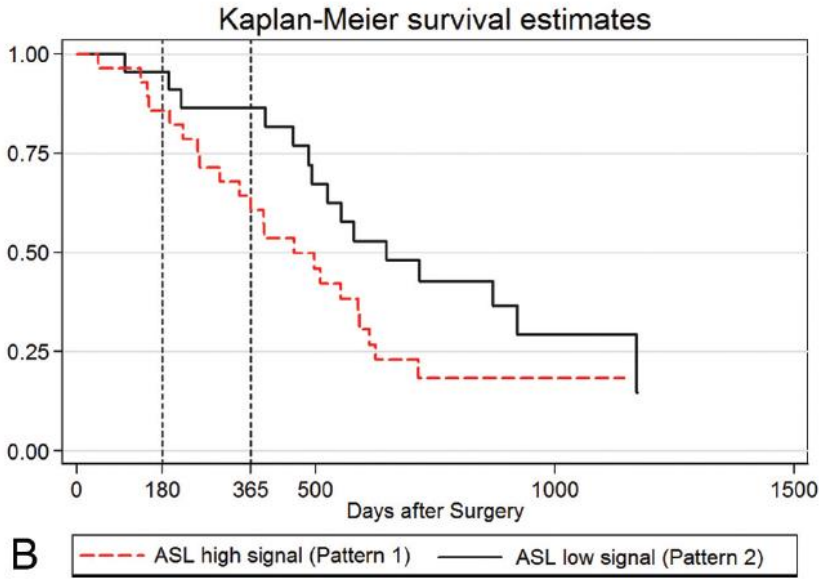
Yang et al AJNR 2016

* ASL in Higher Grade Gliomas: A-V Shunt



ASL and Stratification of Survival in Glioblastoma

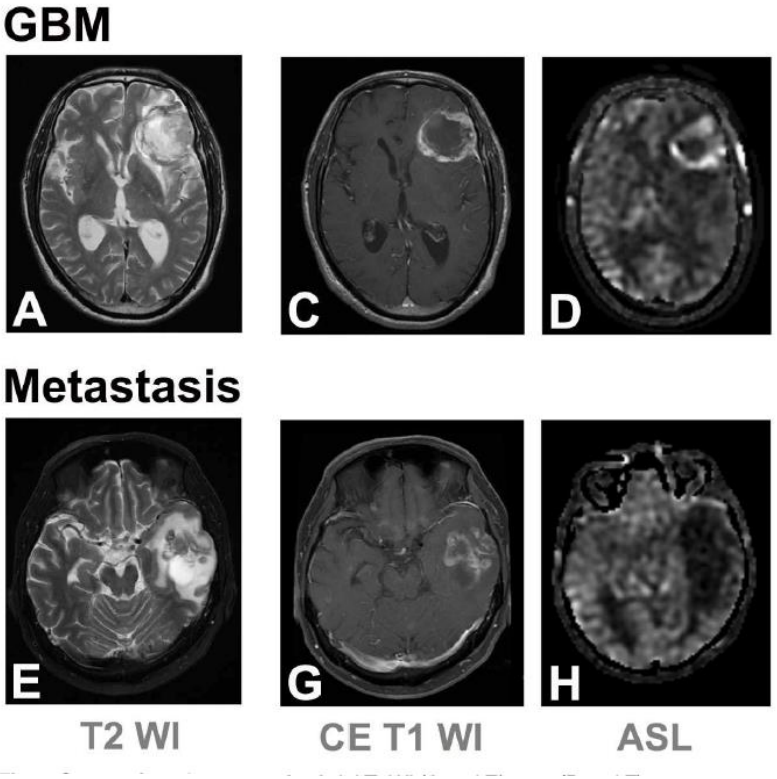




- *Pattern 1 associated with shorter progression free survival*
- *Pattern 1 associated epidermal growth factor receptor variant III expression*

Qiao et al AJNR 2015

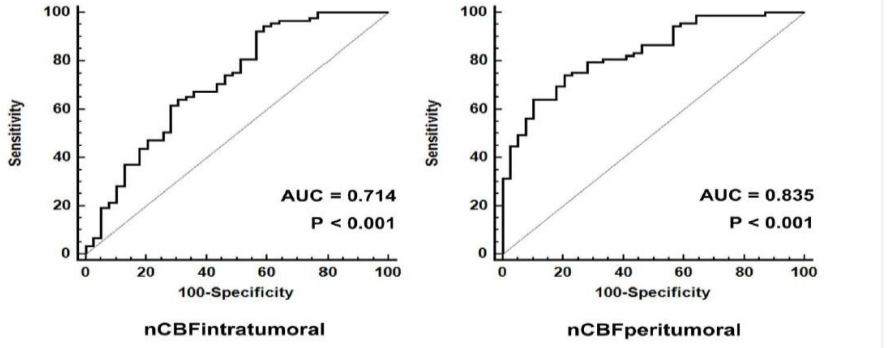
ASL and Differentiation of GBM from Metastases/Small lesions



RESEARCH ARTICLE

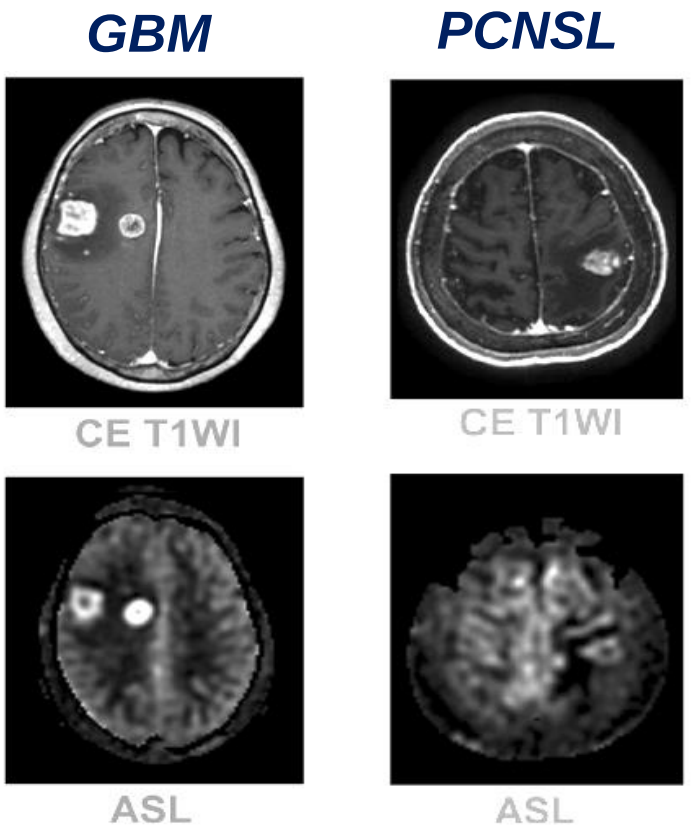
Differentiation of Glioblastoma from Brain Metastasis: Qualitative and Quantitative Analysis Using Arterial Spin Labeling MR Imaging

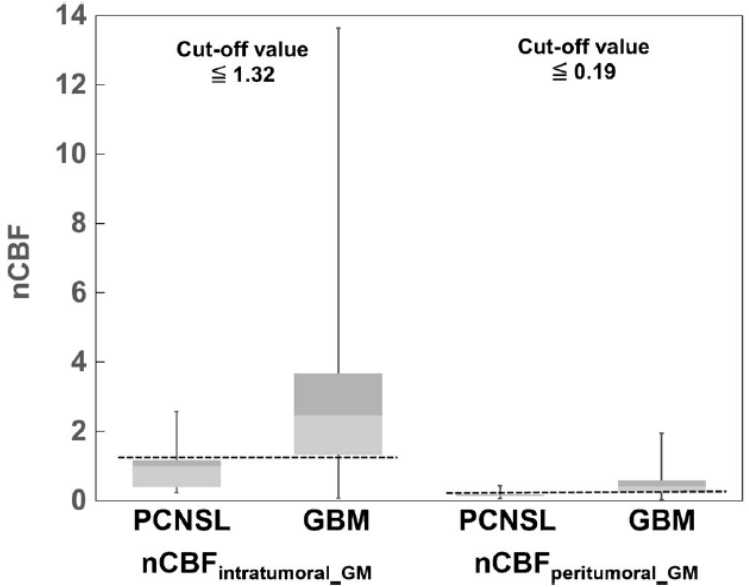
Leonard Sunwoo[1,2], Tae Jin Yun[1,3]*, Sung-Hye You[3], Roh-Eul Yoo[1,3], Koung Mi Kang[1,3], Seung Hong Choi[1,3], Ji-hoon Kim[1,3], Chul-Ho Sohn[1,3], Sun-Won Park[1,4], Cheolkyu Jung[1,2], Chul-Kee Park[5]



Sunwoo et al PLoS ONE 2016

ASL and Differentiation of GBM from PCNSL

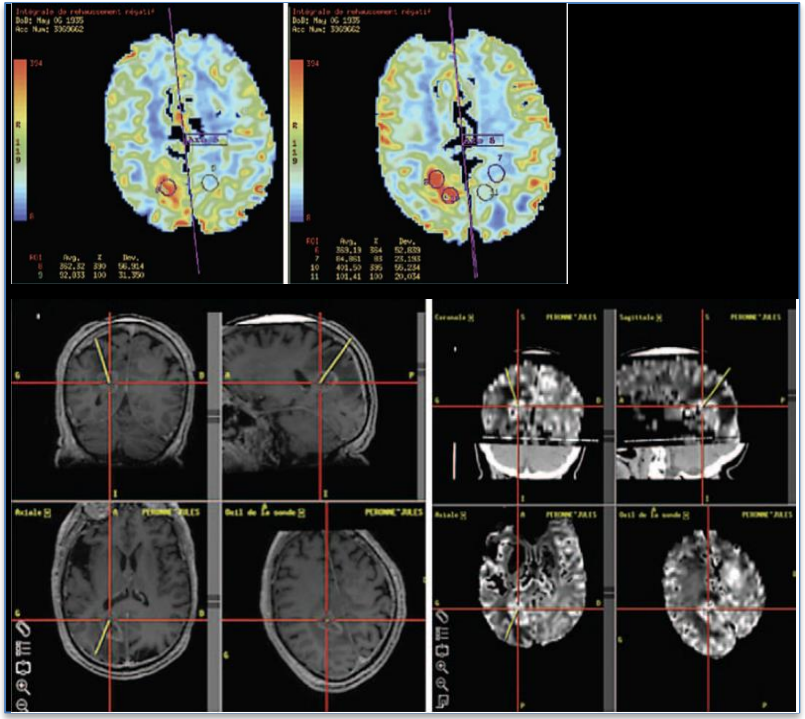




You S et al Eur Rad 2018

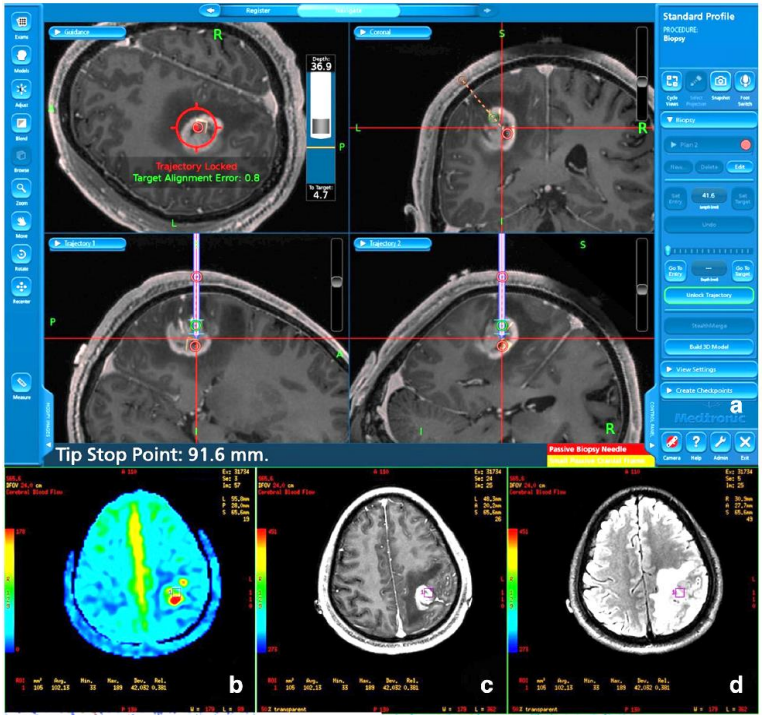
ASL-Targeting Surgical Biopsy

DSC- CBV



Lefrance et al. Stereotact Funct Neurosurg 2012

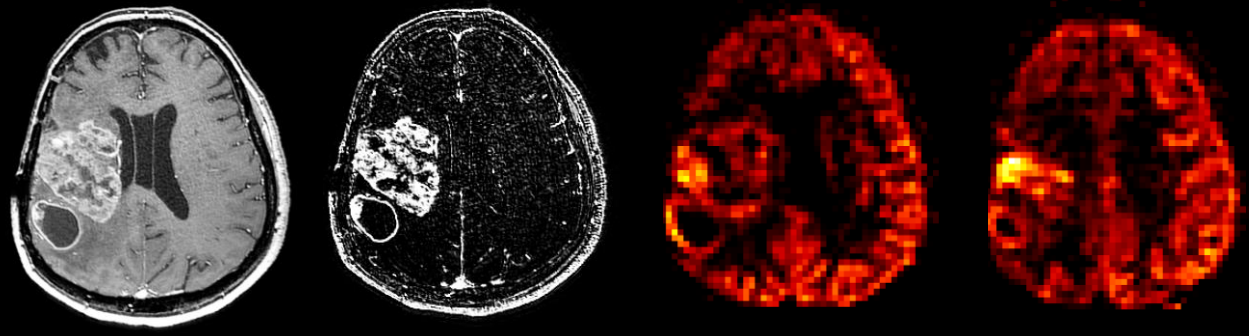
ASL-CBF



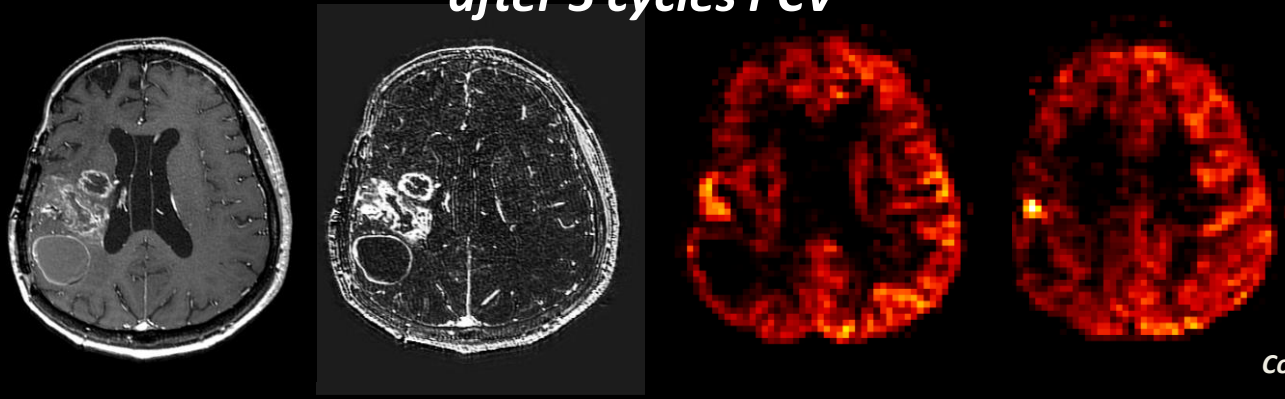
Di Ningning et al. Neruroradiology 2017

ASL and Treatment Response

Oligo WHO III IDH 1 mutant 1p19q codeletion



after 3 cycles PCV

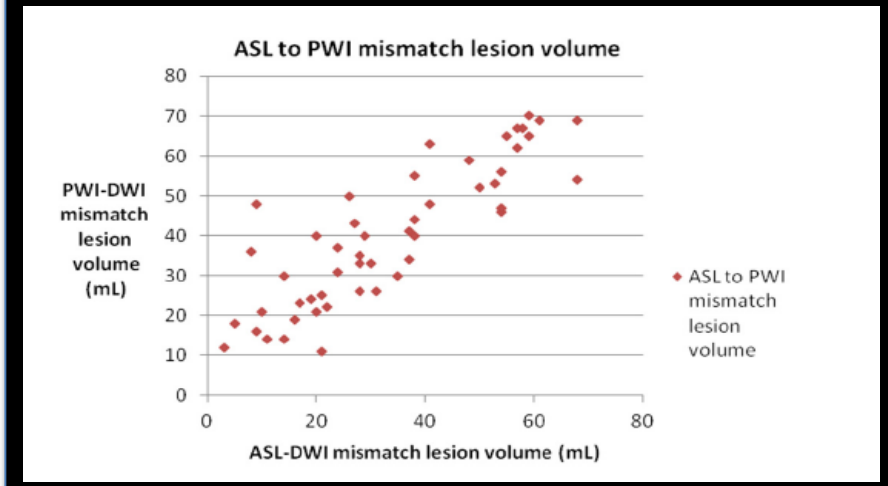


Courtesy of Rolph Jager

ASL – Acute Stroke

Mismatch PWI - DWI

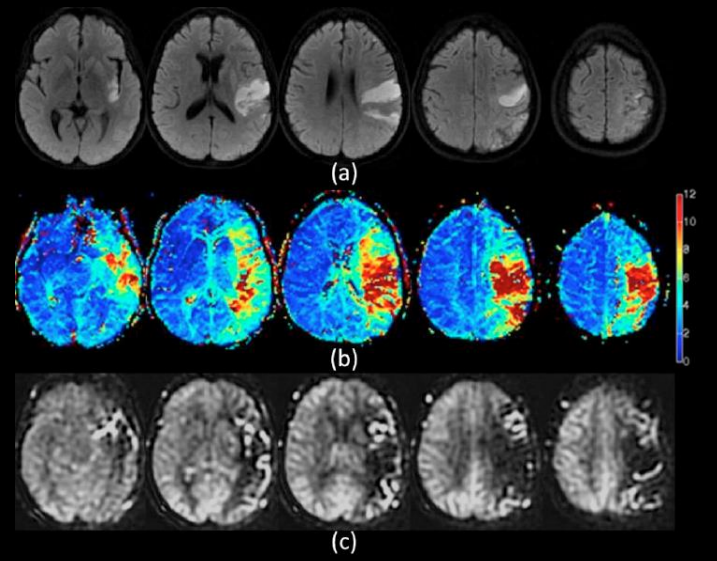
3T



PWI (Tmax,CBF)-DWI Mismatch is well correlated

Bivard et al, Stroke 2014

1.5T



Mismatch overestimation with ASL

Zaharchuk et al, Stroke 2012

ASL – Acute Stroke *

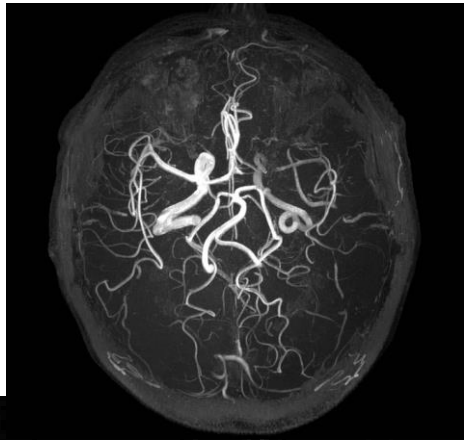
Collaterals

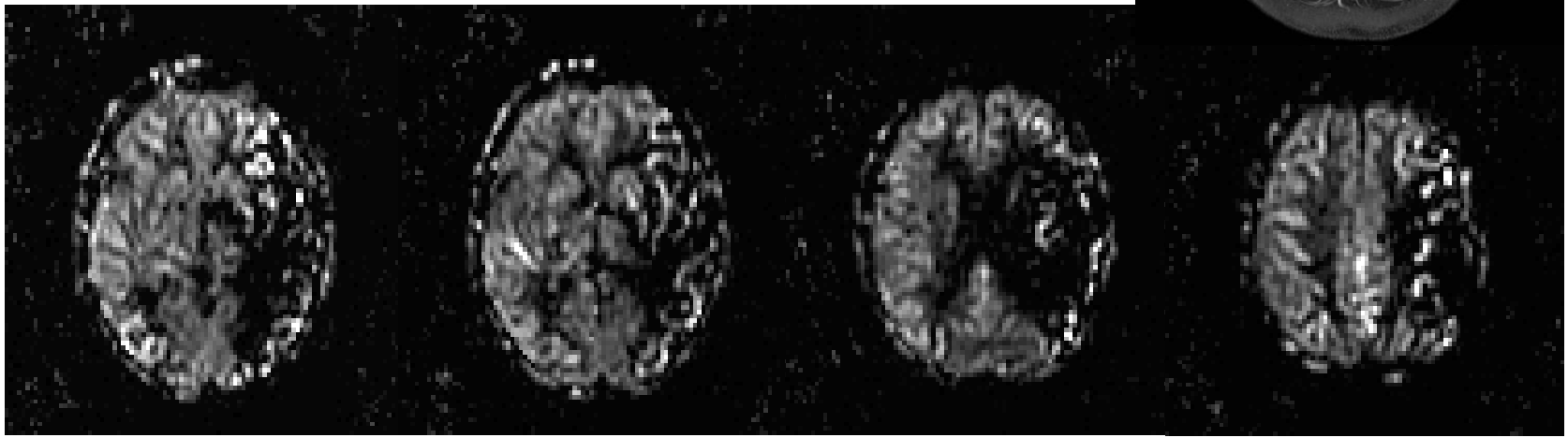
JAMA Neurology | Original Investigation

Association of Collateral Blood Vessels Detected by Arterial Spin Labeling Magnetic Resonance Imaging With Neurological Outcome After Ischemic Stroke

Adam de Havenon, MD; David R. Haynor, MD, PhD; David L. Tirschwell, MD, MSc; Jennifer J. Majersik, MD, MS; Gordon Smith, MD; Wendy Cohen, MD; Jalal B. Andre, MD

JAMA Neurol 2017

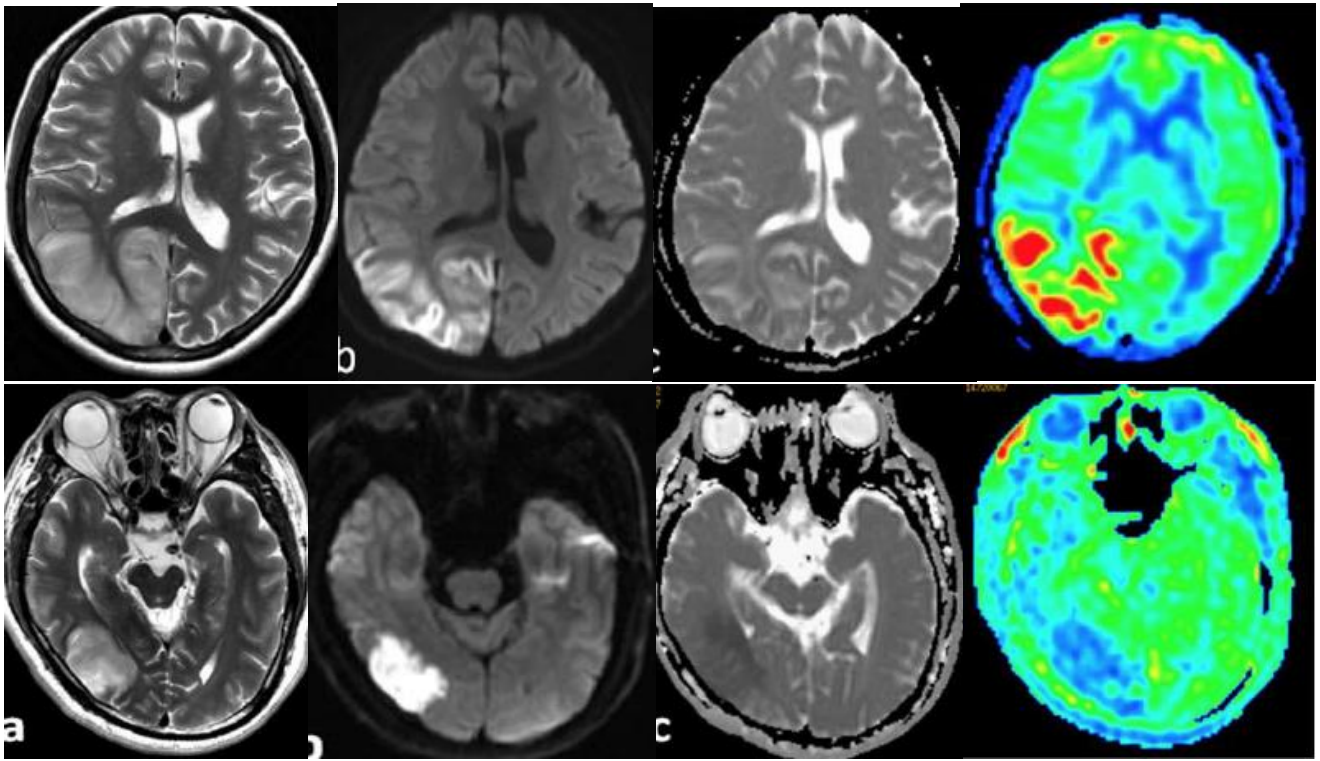




ASL – Acute Stroke

Stroke mimics

MELAS



ISCHEMIC STROKE

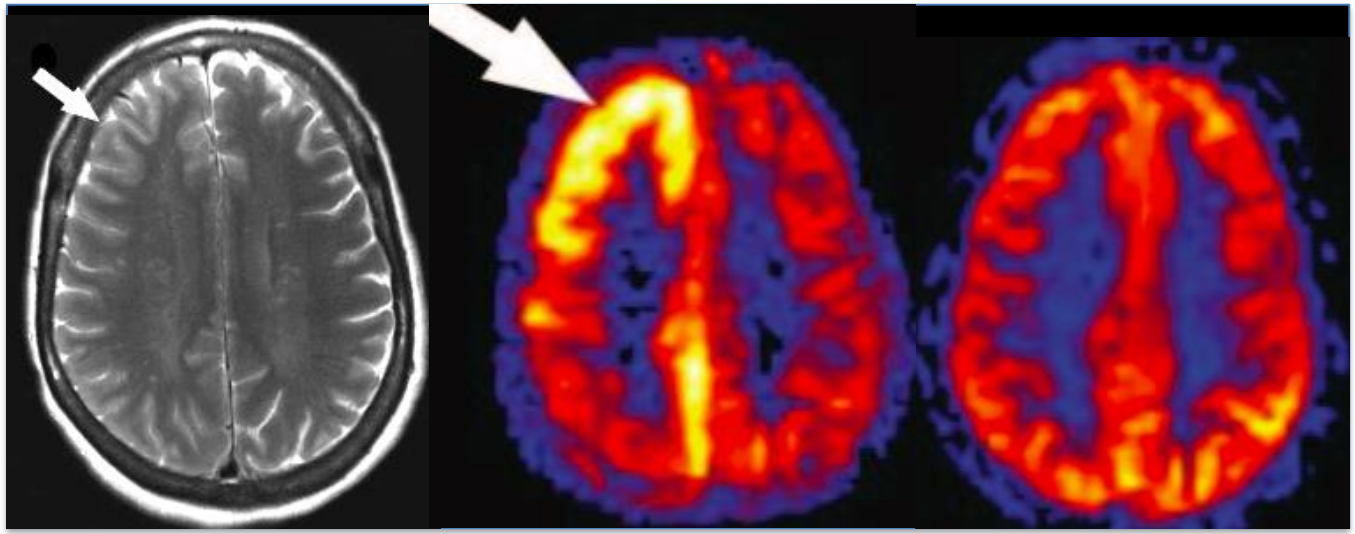
Li et al, J magn Reson Imaging 2017

ASL – Acute Stroke

Stroke mimics

MIGRAINE

55 ys male, right frontal headache, left arms numbness, weakness dysartria 6hs before



6 HS ***6 DAYS FU***

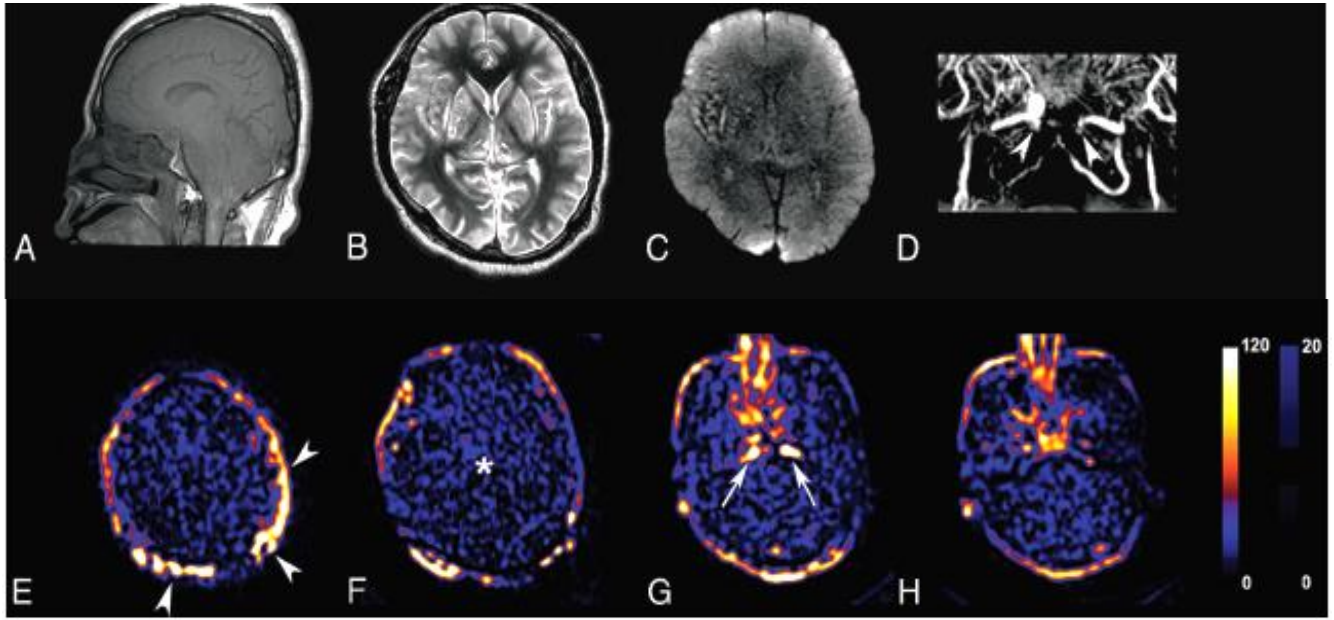
But...Boulouis et al, Develop med and child neurol 2016

ASL – Anoxic Brain Injury

CLINICAL REPORT
BRAIN

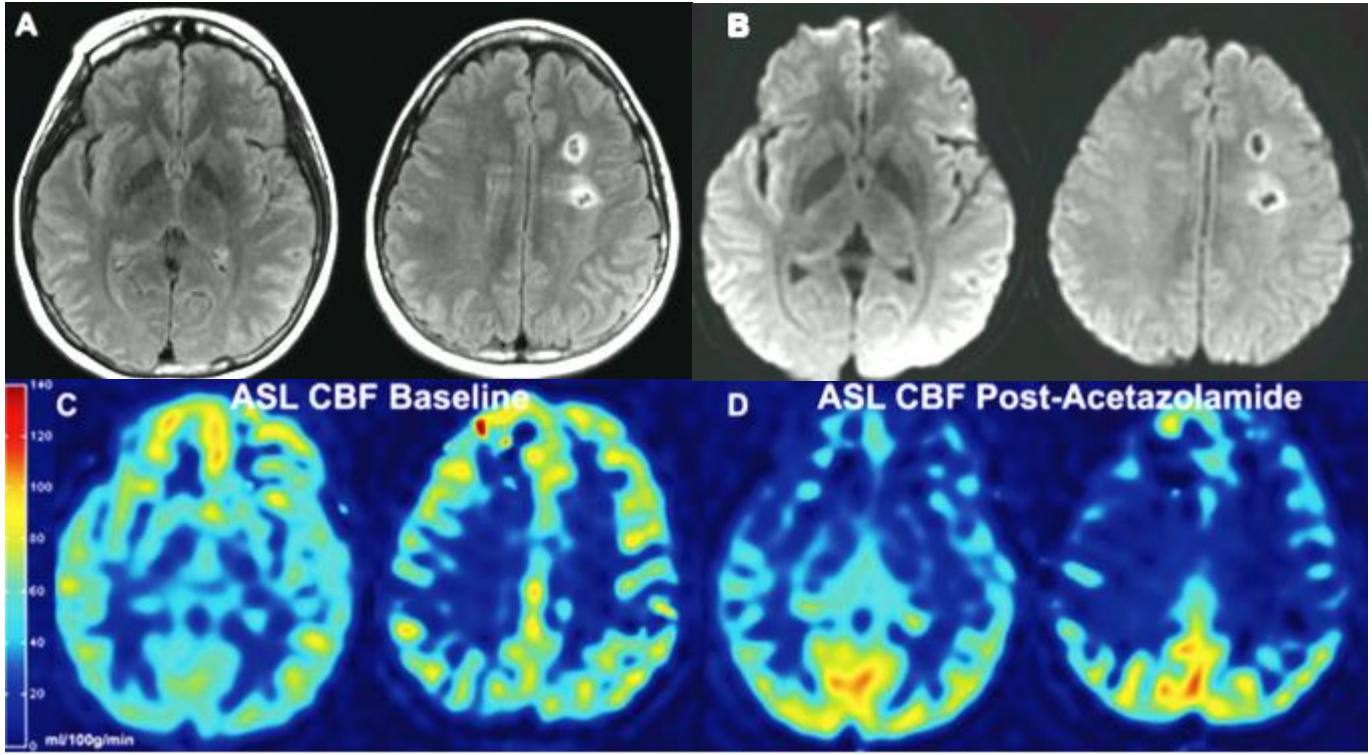
Clinical Utility of Arterial Spin-Labeling as a Confirmatory Test for Suspected Brain Death

K.M. Kang, T.J. Yun, B.-W. Yoon, B.S. Jeon, S.H. Choi, J.-h. Kim, J.E. Kim, C.-H. Sohn, and M.H. Han



ASL – Cerebrovascular reserve evaluation

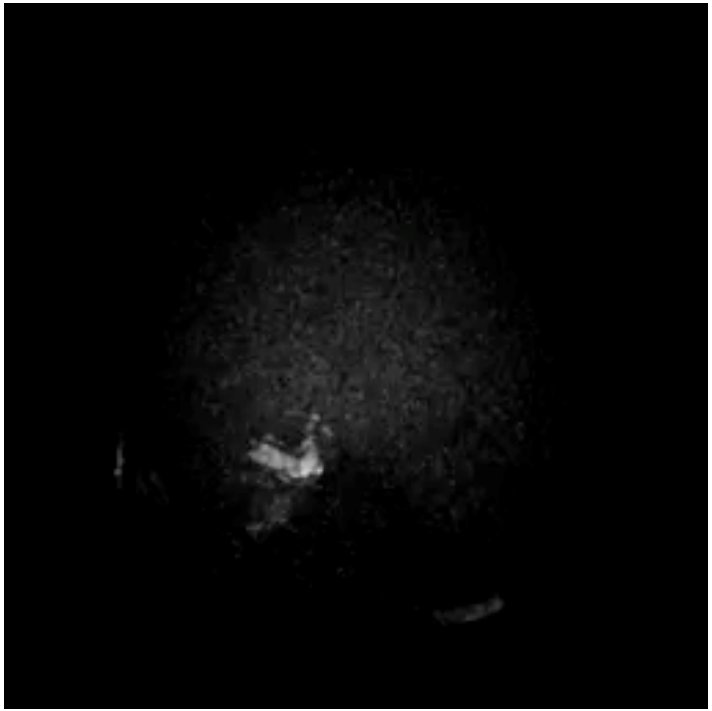
MOYA-MOYA



Haller et al, Radiology 2016

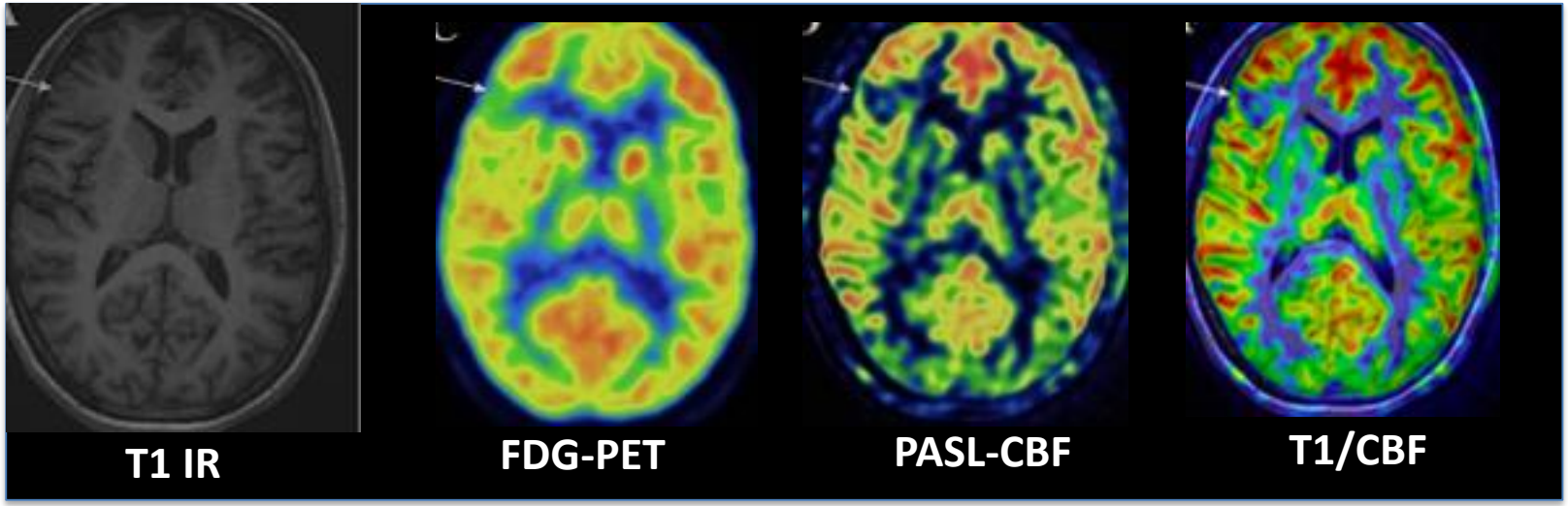
ASL – Chronic vascular disease

4D angio ASL to study brain blood supply



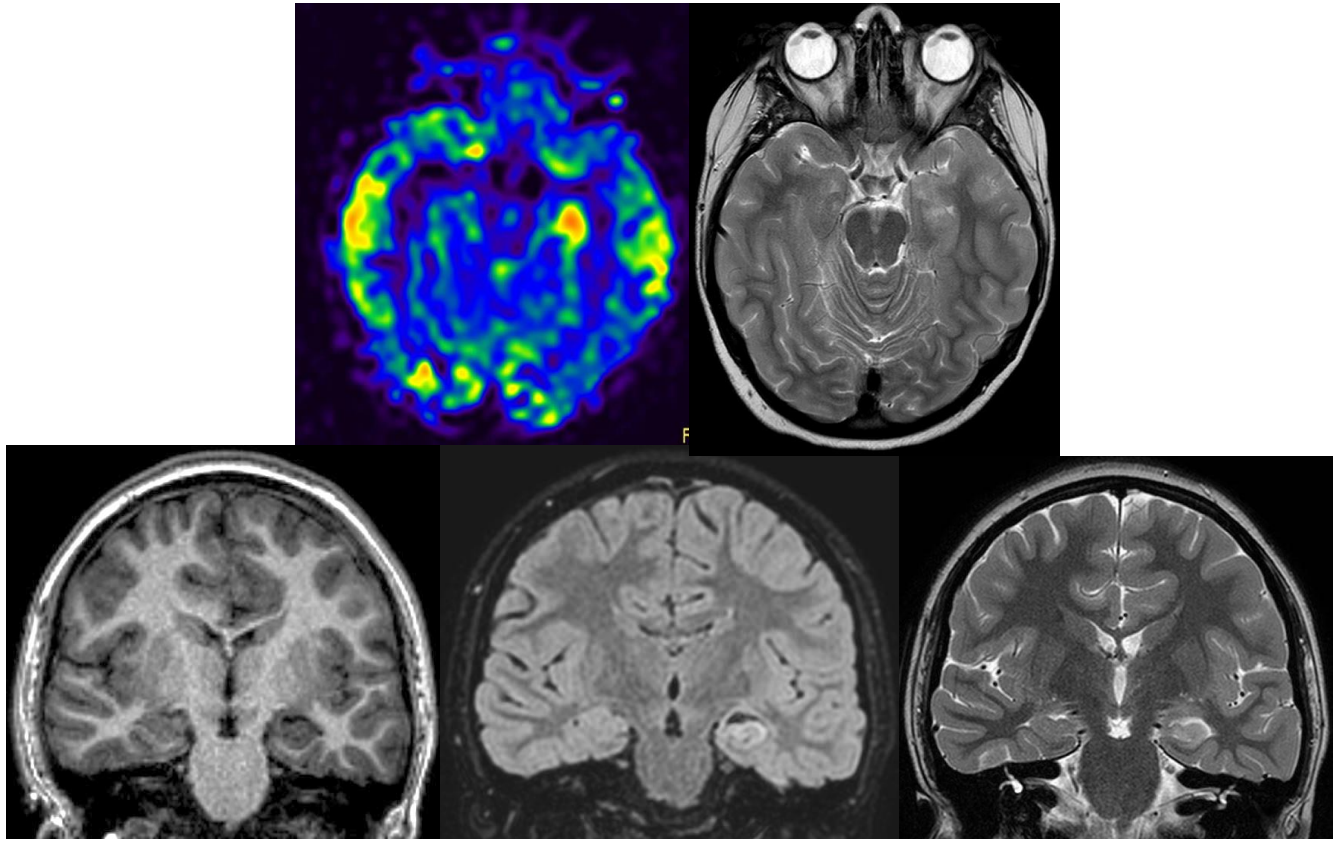
ASL – Focus epilepticus

Cortical malformation



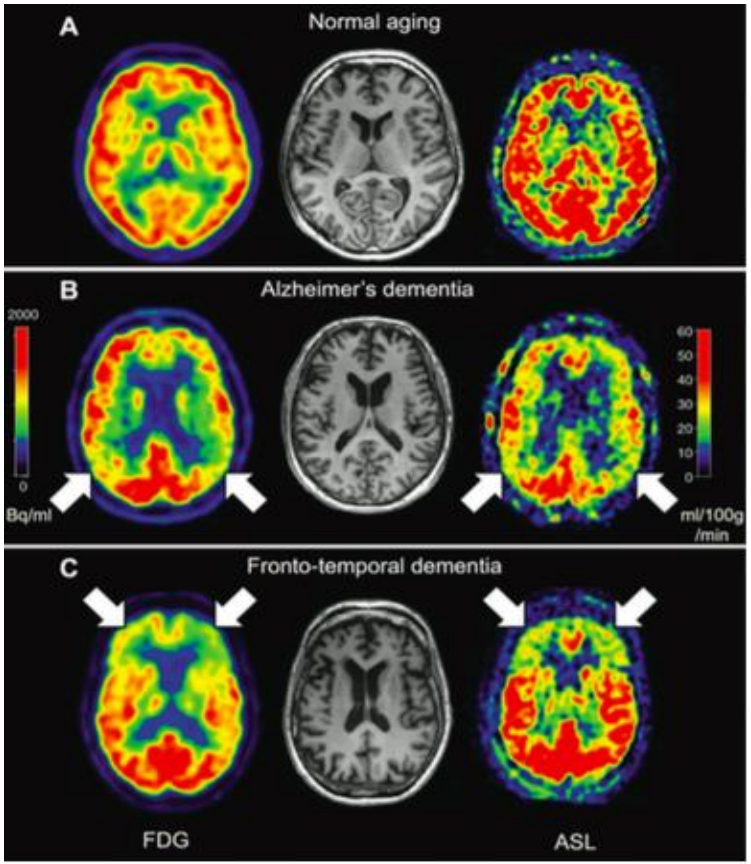
Blawblomme et al, Epilepsy research 2014

ASL – Focus epilepticus



Courtesy of Claudia Cinnante

ASL – Degenerative diseases



FDG-PET
ASL-CBF

Haller et al, Radiology 2016

Conclusions

DSC and, to a lesser extent, DCE are well established techniques that improve our diagnostic accuracy especially in tumors

ASL despite its "age" it is not yet part of our clinical daily practice Nevertheless it has many advantages and promises especially in vascular field that need to be again and continuously explored