Optimization and harmonization of quantitative MRI protocols for clinical applications

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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

Il sottoscritto Claudia Gandini Wheeler-Kingshott in qualità di:

☐ responsabile scientifico ☐ moderatore ☐ docente X 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

X 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):~~

_____ _____
_____ _____
_____ _____
_____ _____

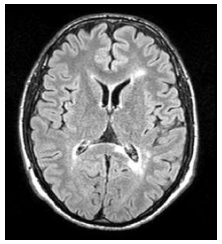
Aims:

- Promote the use of *quantitative* MRI in the clinic;
- Harmonise protocols to create a critical mass of quantitative data for large studies:
  - Use of phantoms for monitoring scanner performance;
  - Set up of detailed SOPs for data acquisition.
- Resolve clinical questions that are impossible to solve by single centres.

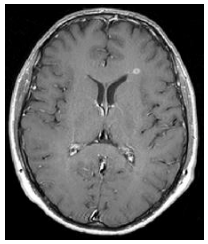
Advanced Neuroimaging

STRUCTURAL

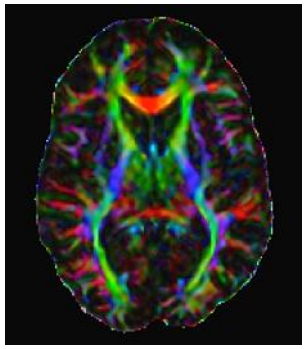
FLAIR

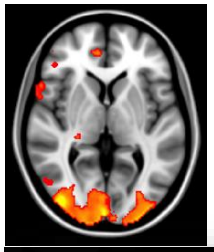


T1 gad

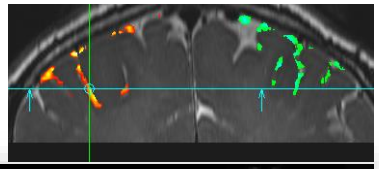


DIFFUSION & TRACTOGRAPHY

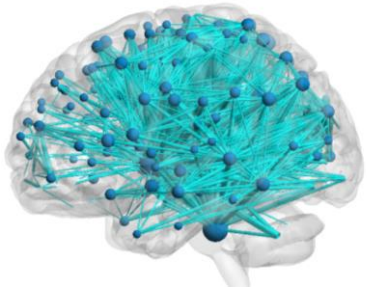




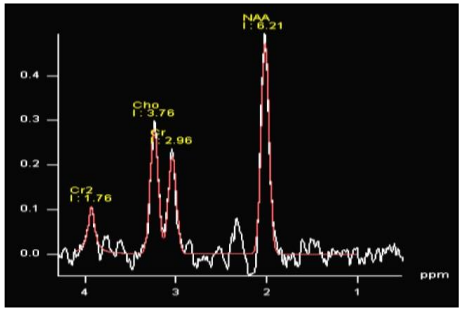
FUNCTIONAL



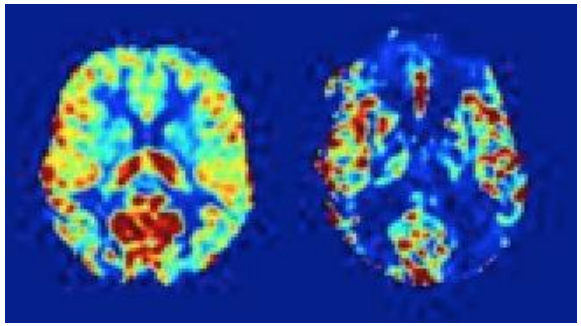
CONNECTOMIC



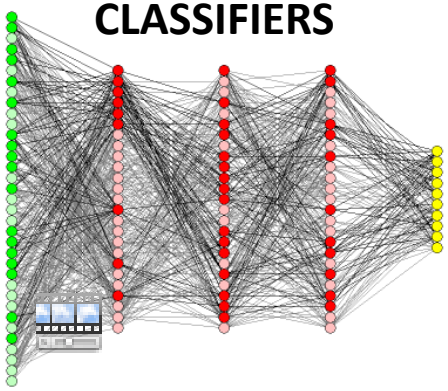
SPECTROSCOPY (MRS)



PERFUSION (ASL)

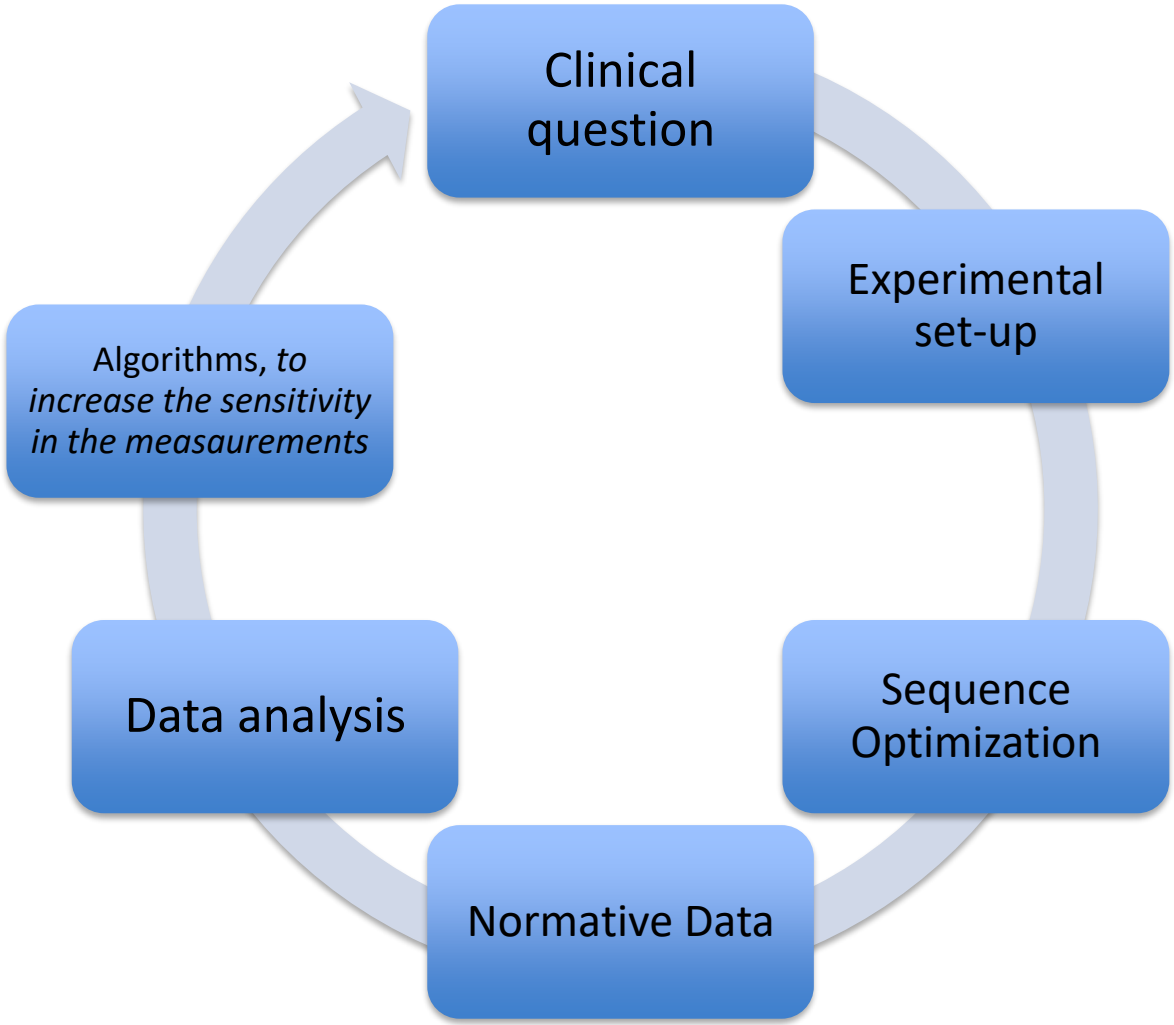


CLASSIFIERS



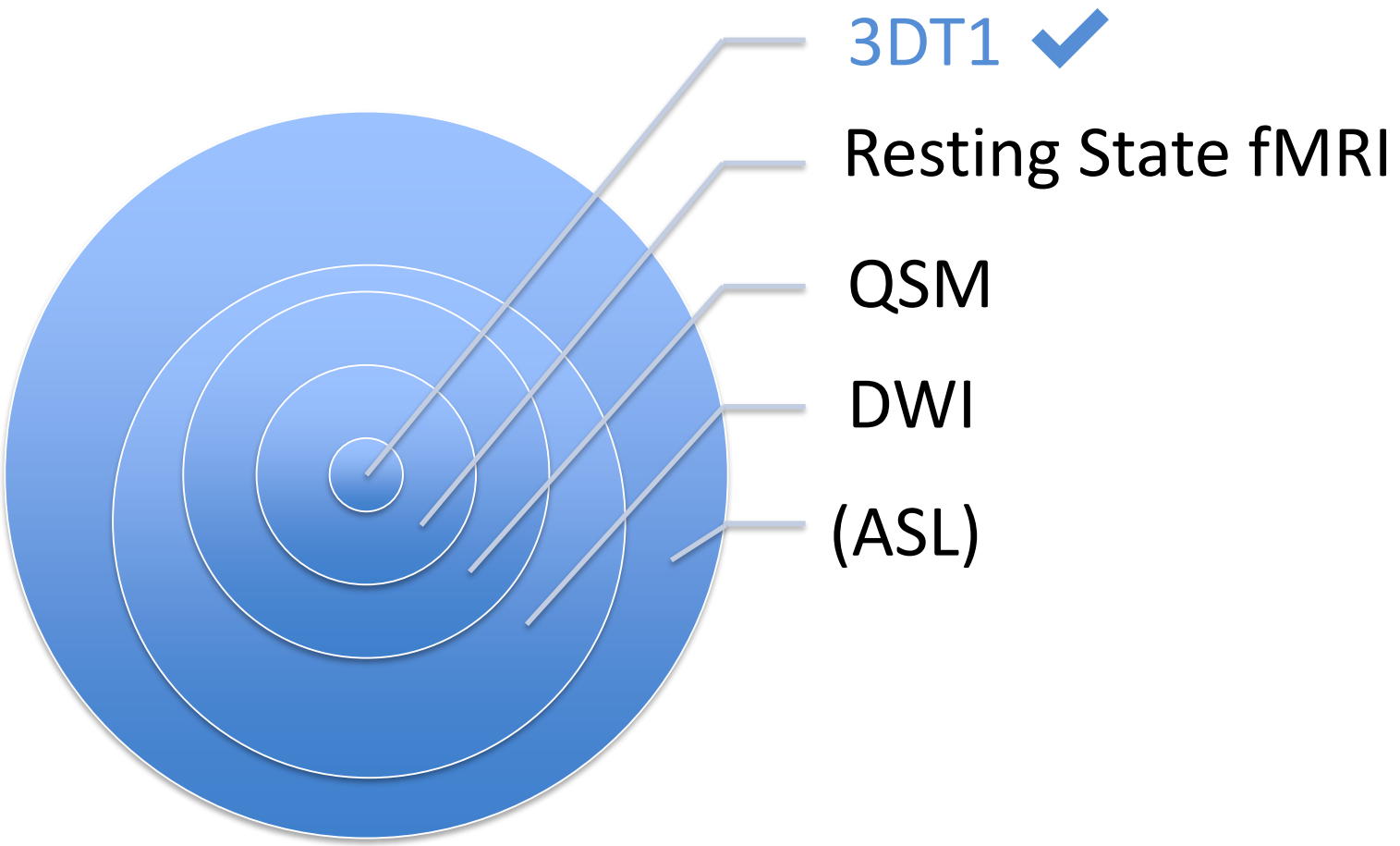
Italian IRCCS Network for Advanced Neuroimaging Research.

NETWORK of *Advanced MRI*
Looking for *quantitative* biomarkers



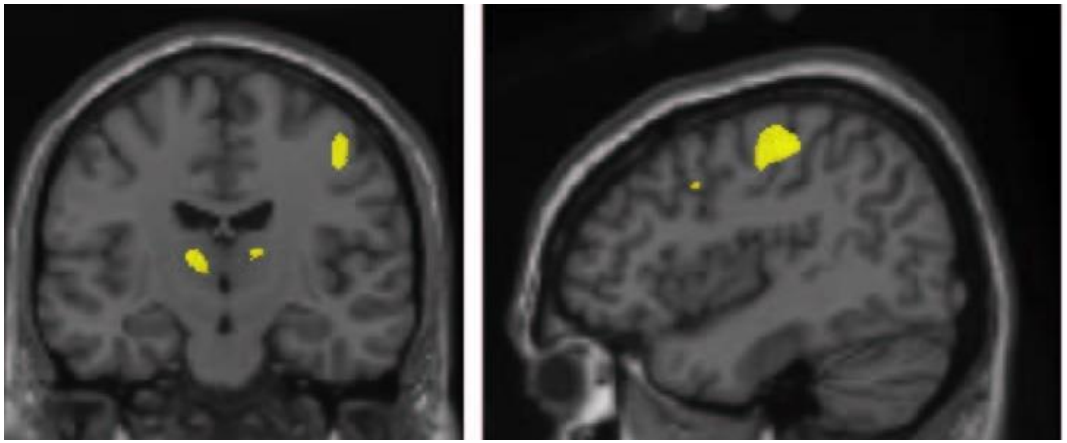
Italian IRCCS Network for Advanced Neuroimaging Research.

RETE's normative dataset
5-10 subjects per site

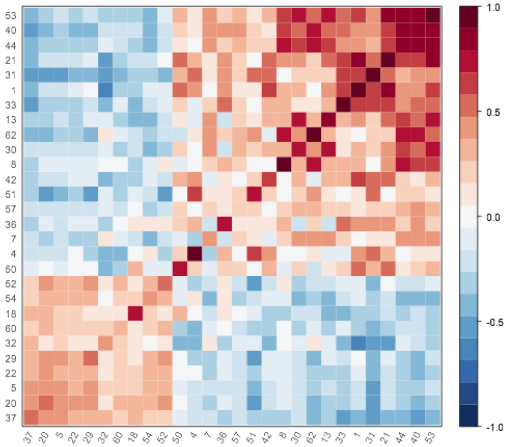


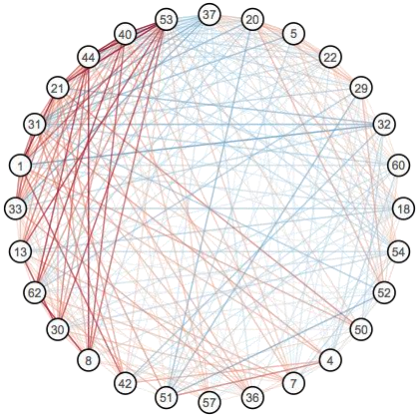
3DT1 - What can we measure?

Group level analysis



Tissue density loss or **localised atrophy (VBM)**, NOT visible with naked eye



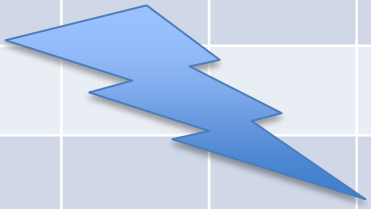


Brain «network» properties calculated with **graph theory**, based on cortical thickness measures

3DT1 - How can we exploit these measurements?

ID	TIV	GMV	WMV	Hip	Thal	CTh1	CTh2	CTh3	CTh4	VBM1	VBM2
S1											
S2											
S3											
AD1											
AD2											
AD3											
FTD1											
FTD2											
FTD3											

BIG DATA



WP4

Where shall we start from?

- Advanced **quantitative** protocols:
  - Our IRCCS network must aim to promote the clinical use of quantitative magnetic resonance imaging (qMRI) to exploit information that is **objective**, **reproducible** & **comparable**

Where shall we start from?

- Introducing the use of phantoms:
  - Phantoms can help assessing the scanner performance over time;
  - Phantoms help quantification of metrics;
  - Phantoms help metrics comparisons.
- Limitations:
  - Phantoms are not biological tissues!

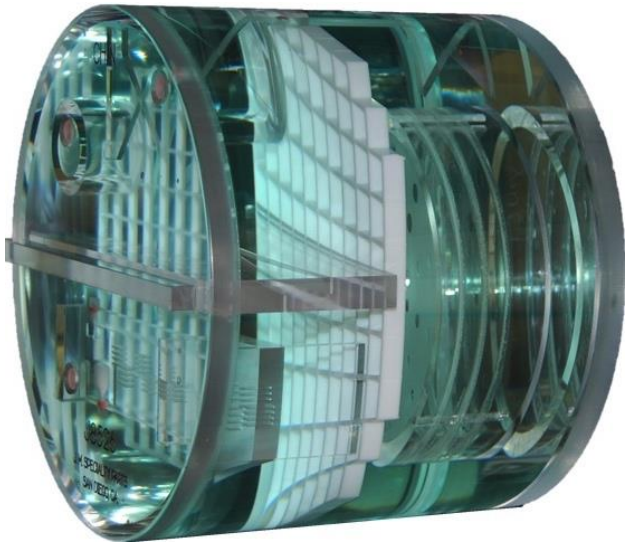
Where shall we start from?

- Standard Operating Procedures for in vivo acquisitions:
  - SOPs are essential for reproducible acquisitions;
  - Improve the intra-subject reproducibility;
  - Improve inter-subjects and inter-site reproducibility.
- Limitations:
  - We have a large variety of scanners !

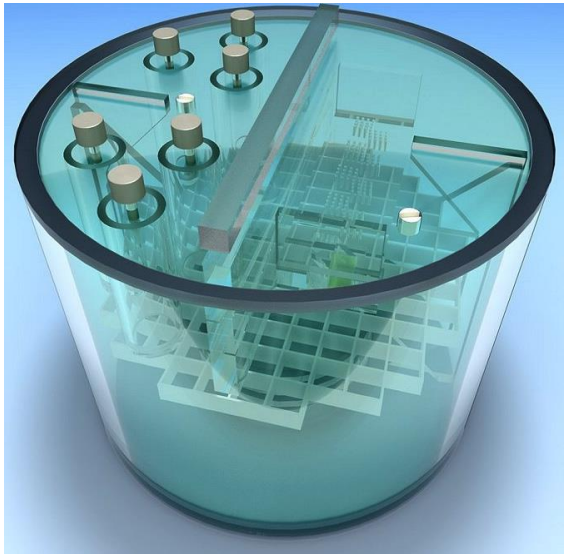
Phantom work

- For structural measures (e.g cortical thickness) The scanner has to be stable in terms of:
  - Resolution
  - Geometric distortions
  - Contrast
  - Signal to noise ratio
  - Contrast to noise ratio
- For quantitative measures such as diffusion and functional MRI that use Echo Planar Imaging (EPI), the scanner has to be stable over time.

ACR Large Phantom



- Cylinder 20.4 cm in diameter by 16.5 cm in length
- Internal dimensions are 19.0 cm diameter by 15.0 cm in length
- Acrylate plastic, glass, and silicone rubber
- Filled with 10 millimolar (mmol) nickel chloride solution containing sodium chloride (45 mmol) to simulate biological conductivity
- Reference points for nose and chin



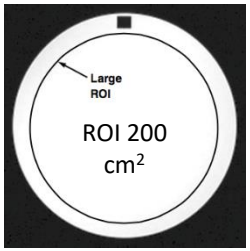
Software for analysis

codice MATLAB

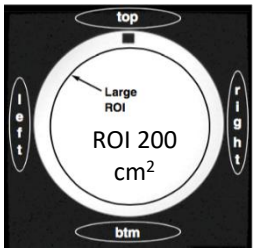
ACR_figures.m | run_ACR_large_test.m | fun_ACR_large_7_S8S9S10S11.m | fun_ACR_large_H

```
% This RUN script runs all the functions to test ACR phantom
%
% A log file summarises the QA result and a spreadsheet of result will be
% created and saved to the directory of the QA images. The path is
% displayed in cmd window.
%
% Author: Jidi Sun
% Email: jidi.sun@uon.edu.au
% Version: v.1 (17/05/13)
%          v.2 (13/10/13)(search for v2)
%          v.3 (30/04/14)
% History: v.1
%          v.2 changed the output Excel format to single row
%              changed PIU to % before saving, to be consistent to Michael
%              save the Excel sheet in localiser folder
%              add instruction to high contrast test message box
%          v.3 major change: -create a log file store results info
%                            -check if an output exists, so don't repeat
%                             the same measurement if 1st time went wrong
% Copyright: please see license.txt
% Acknowledgement: My study is funded by the Cancer Council NSW, Australia,
%                  project grant RG11-05. PhD under the University of
%                  Newcastle and the Calvary Mater Newcastle Hospital
%                  provides me the office and the MR scanner to work with.
```

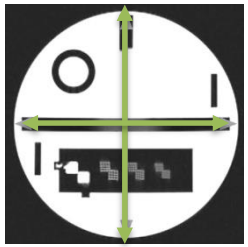
UNIFORMITY

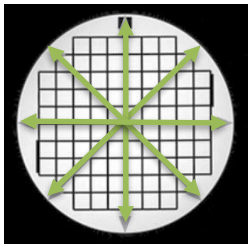


GHOST

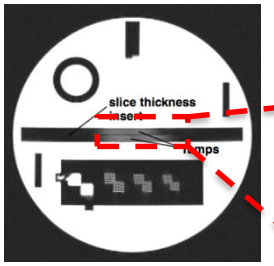


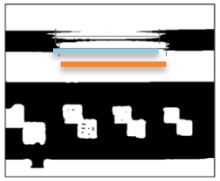
GEOMETRICAL ACCURACY



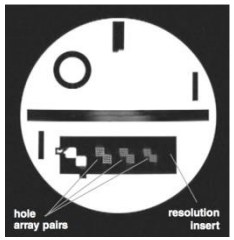


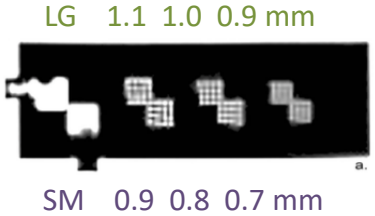
SLICE THICKNESS



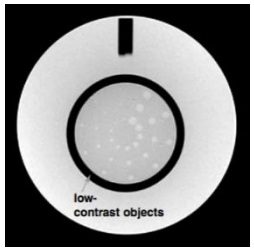


HIGH CONTRAST

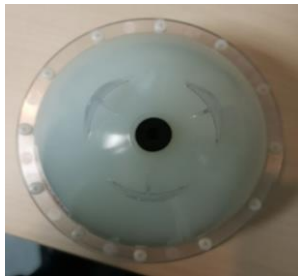




LOW CONTRAST



Phantom selected for Stability Assessment



FUNSTAR phantom

- sphere with diameter 17.5 cm
- filled with agar gel
- comparable T1 and T2 to that of gray matter
- produced by Gold Standard Phantoms ltd

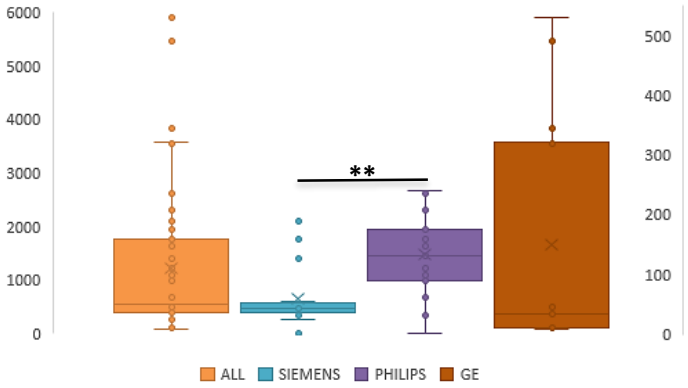
Acquisition protocol

Field of view	220 mm
Slices	32 , 4-mm-thick , 1-mm-interslice gap
TR	2000 ms
TE	30 ms
FA	90 degrees
Bandwidth	>100 kHz (~1590 Hz/pix)
Matrix	64 x 64
Fat suppression	NO
Parrallel Imaging	NO

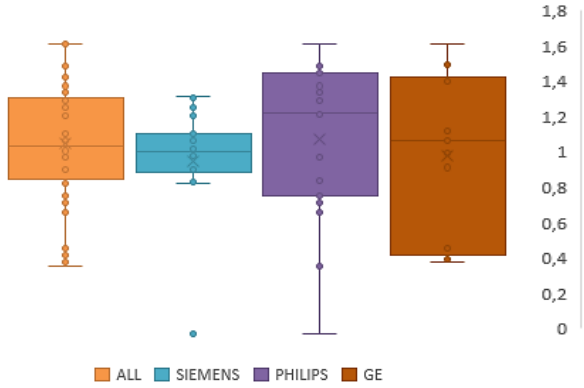
Friedman L., Glover GH. Report on a multicenter fMRI quality assurance protocol (2006). *Journal of Magnetic Resonance Imaging 23:827–839*

SNR, SFNR and Drift% - STATIC ANALYSIS within Central ROI

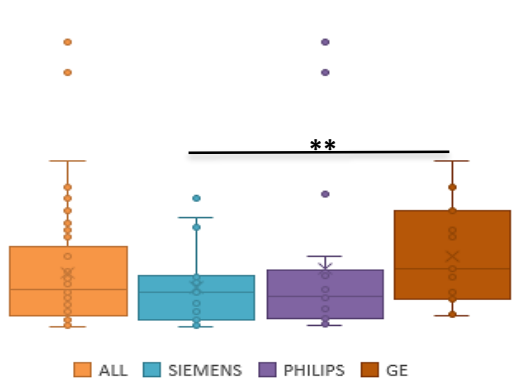
SNR Central ROI



SFNR Central ROI



Drift% Central ROI



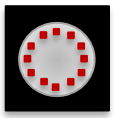
$$SNR = \frac{Central\ ROI\ spatial\ mean}{Background\ ROI\ spatial\ dev}$$

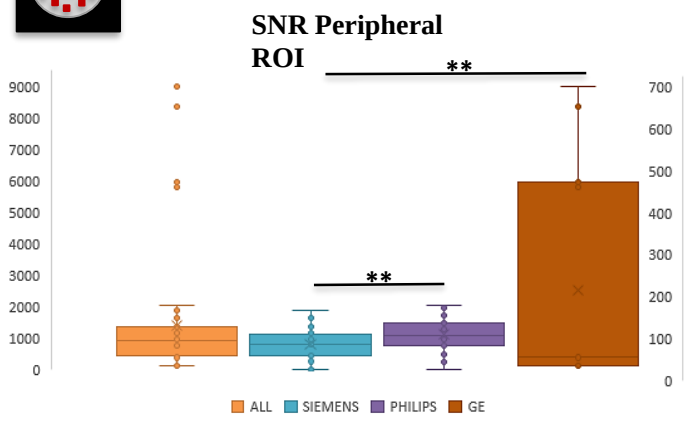
$$SFNR = \frac{Temporal\ mean}{Temporal\ standard\ deviation}$$

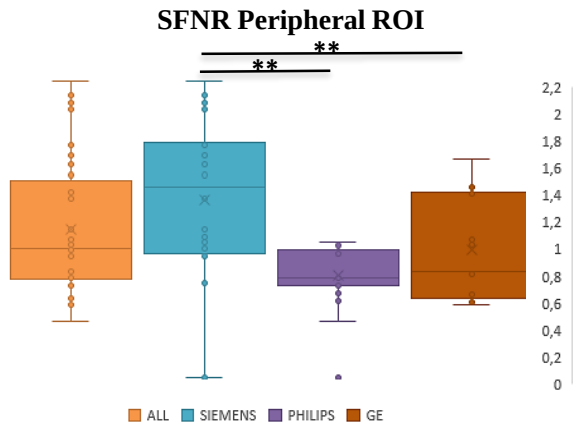
Vendor	SNR (mean ± stddev)	SFNR (mean ± stddev)	Drift% (mean ± stddev)
ALL	1221,21 ± 1272,63	319,47 ± 96,42	0,32 ± 0,33
Siemens	696,66 ± 509,17	314,27 ± 43,70	0,24 ± 0,21
Philips	1563,58 ± 701,94	344,51 ± 107,07	0,34 ± 0,47
GE	1649,65 ± 2152,92	297,73 ± 137	0,41 ± 0,28

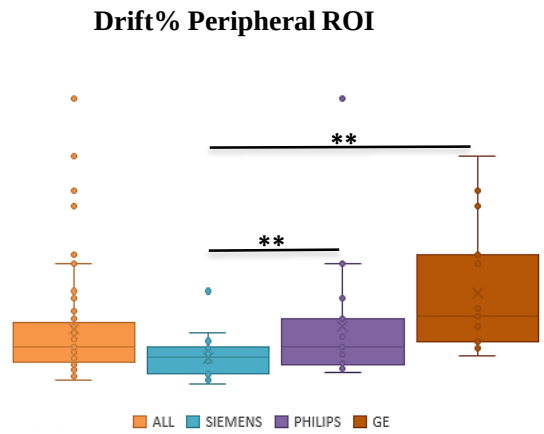
- **SNR:** $pval_{Siemens\text{-}Philips}$ = 5,8e-5
- **Drift%:** $pval_{Siemens\text{-}GE}$ = 0,0281

SNR, SFNR and Drift% - STATIC ANALYSIS within Peripheral ROI









$$SNR = \frac{Central\ ROI\ spatial\ mean}{Background\ ROI\ spatial\ dev}$$

$$SFNR = \frac{Temporal\ mean}{Temporal\ standard\ deviation}$$

Vendor	SNR (mean ± stddev)	SFNR (mean ± stddev)	Drift% (mean ± stddev)
ALL	1396,72 ± 1877,75	354,40 ± 150,32	0,40 ± 0,41
Siemens	854,39 ± 436,14	458,75 ± 151,23	0,21 ± 0,14
Philips	1184,96 ± 534,99	256,22 ± 54,97	0,44 ± 0,48
GE	2518,56 ± 3396,10	305,28 ± 124,50	0,67 ± 0,47

- **SNR:** $pval_{Siemens\text{-}Philips}$ = 0,0199 ; $pval_{Siemens\text{-}GE}$ = 0,0397
- **SFNR:** $pval_{Siemens\text{-}Philips}$ = 5,65e-7 ; $pval_{Siemens\text{-}GE}$ = 7e-4
- **Drift%:** $pval_{Siemens\text{-}Philips}$ = 0,0306; $pval_{Siemens\text{-}GE}$ = 0,001

HEALTHY SUBJECTS

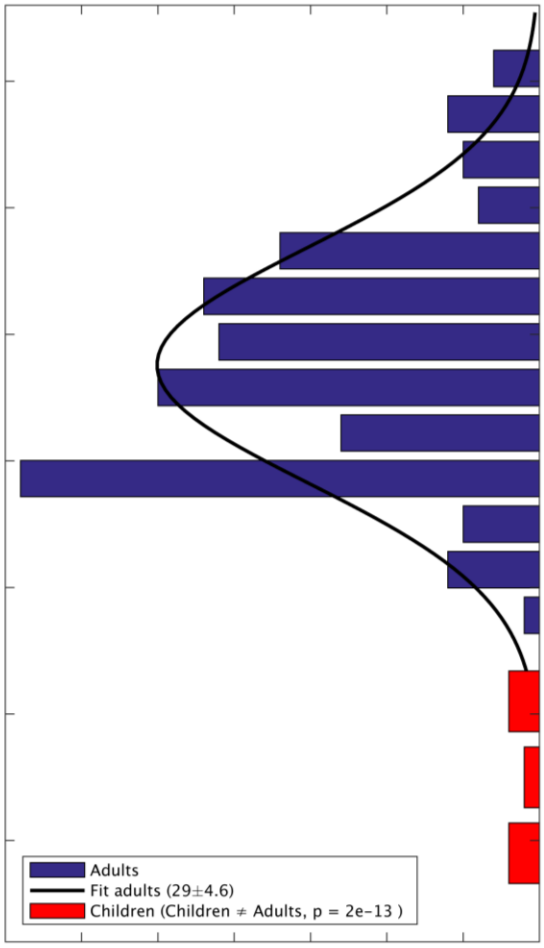
- 3DT1
- fMRI
  - Resting state
- DWI
  - Multi-shell
- QSM
  - 3D gradient echo

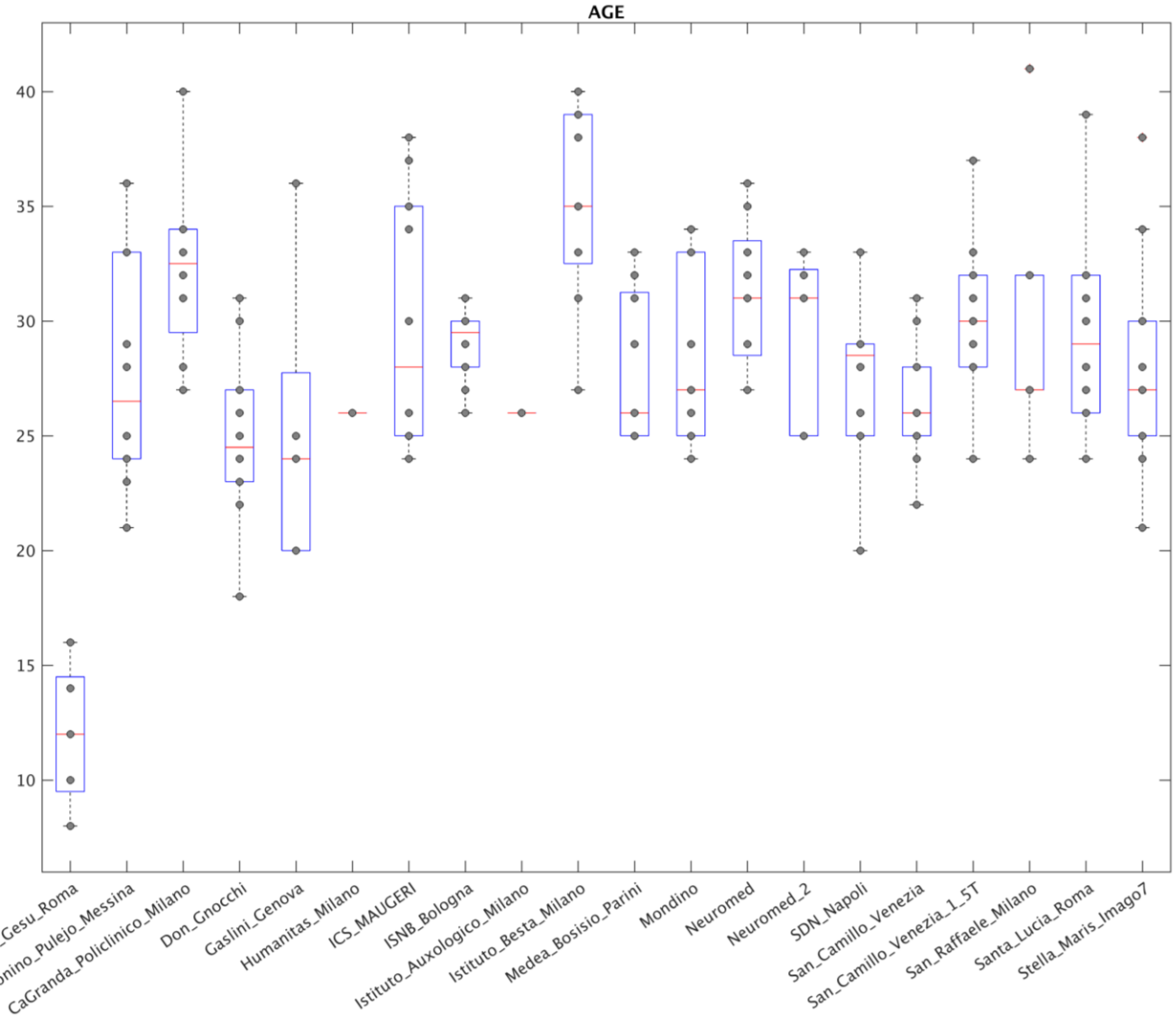
3DT1 Data overview (174 scans)

Site	Manufacturer	Model Name	Field Strength	#scan
Istituto Besta, Milano	Philips Medical Systems	Achieva	3 T	9
Bambin Gesu, Roma	SIEMENS	Skyra	3 T	5
Fondazione Santa Lucia, Roma	Philips Medical Systems	Achieva	3 T	10
Centro neurolesi Bonino Pulejo, Messina	Philips Medical Systems	Achieva	3 T	10
IRCCS Stella Maris, Pisa	GE MEDICAL SYSTEMS	Signa HDxt	1,5 T	11
ICS Maugeri, Pavia	GE MEDICAL SYSTEMS	DISCOVERY MR750	3 T	10
Istituto Clinico Humanitas, Milano	SIEMENS	Verio	3 T	1
SDN, Napoli	SIEMENS	Biograph_mMR	3 T	10
Ospedale San Raffaele, Milano	Philips Medical Systems	Ingenia CX	3 T	10
IRCCS Medea, Bosisio Parini	Philips Medical Systems	Achieva dStream	3 T	9
Neuromed, Pozzilli	GE MEDICAL SYSTEMS	Signa HDxt	3 T	16
IRCCS Ca 'Granda Policlinico, Milano	Philips Medical Systems	Achieva	1,5 T e 3T	6+2
Ospedale Pediatrico Gaslini, Genova	Philips Medical Systems	Ingenia	3 T	5
Fondazione Mondino, Pavia	SIEMENS	Skyra	3 T	10
Fondazione Don Gnocchi, Milano	SIEMENS	Avanto	1,5 T	14
Istituto Auxologico San Luca, Milano	GE MEDICAL SYSTEMS	DISCOVERY MR750	3 T	6
San Camillo, Venezia	Philips Medical Systems	Ingenia CX	3 T	10
San Camillo, Venezia	Philips Medical Systems	Achieva	1,5 T	10
IBNB_Bologna	SIEMENS	Skyra	3T	10

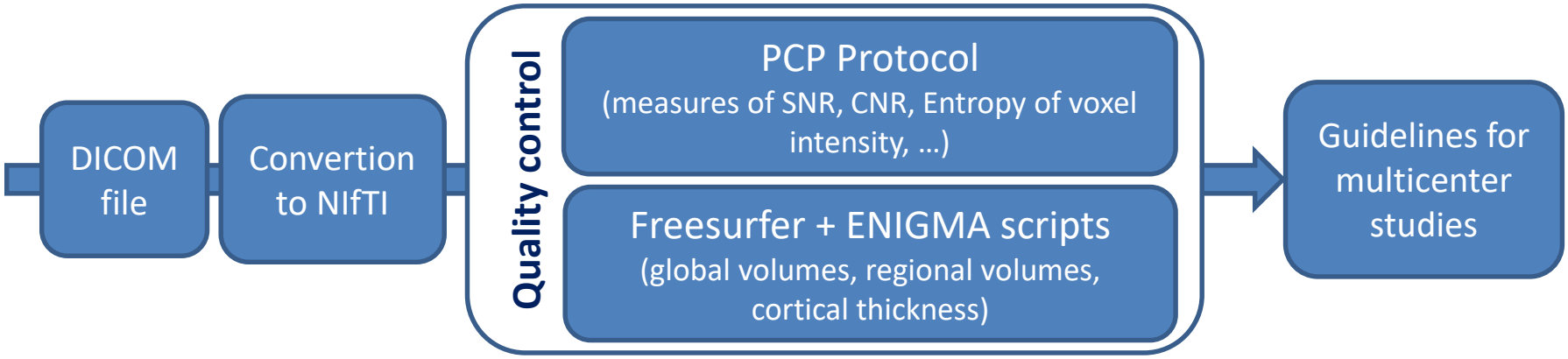
Italian IRCCS Network for Advanced Neuroimaging Research.

Age distribution





Quality Control Measurements

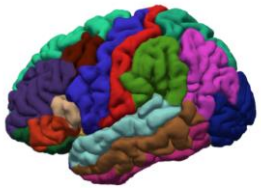


PCP Protocol

Proposed by R. Cameron Craddock and Pierre Bellec
(Center for the Developing Brain, Child Mind Institute, New York, USA)
http://preprocessed-connectomes-project.org/quality-assessment-protocol/

This quality control protocol was used on the multicenter ABIDE data sample:
http://preprocessed-connectomes-project.org/abide/quality_assessment.html

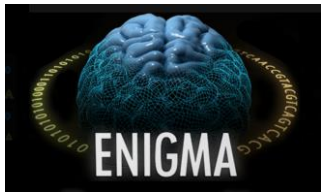
Freesurfer v6.0



Fischl B, et al.,
Neuron 2002;33:341–55
https://surfer.nmr.mgh.harvard.edu

+

ENIGMA Quality Control scripts

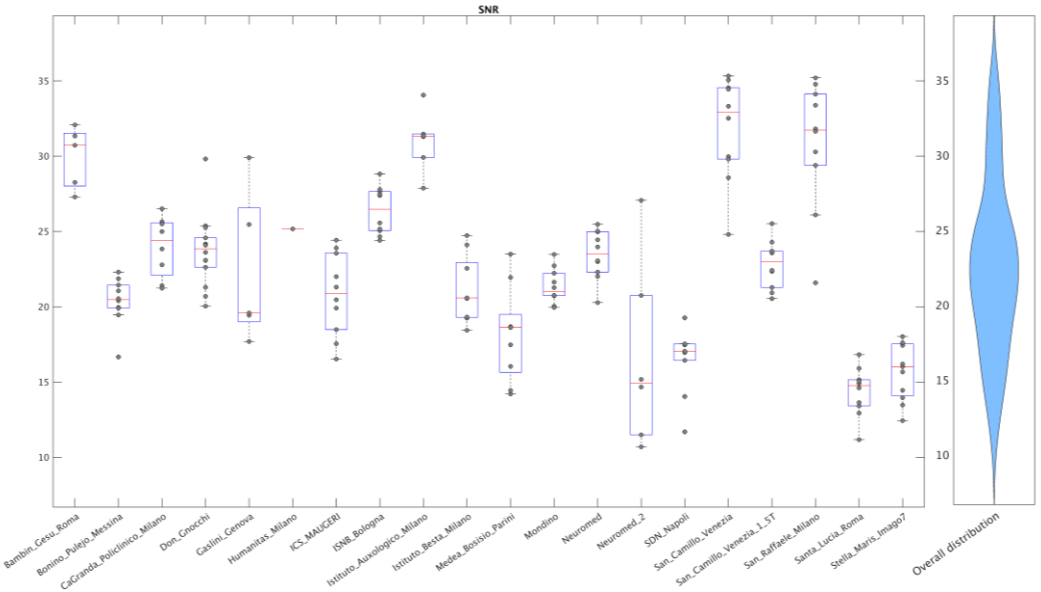


http://enigma.ini.usc.edu/protocols/imaging-protocols/

Quality Control Measurements

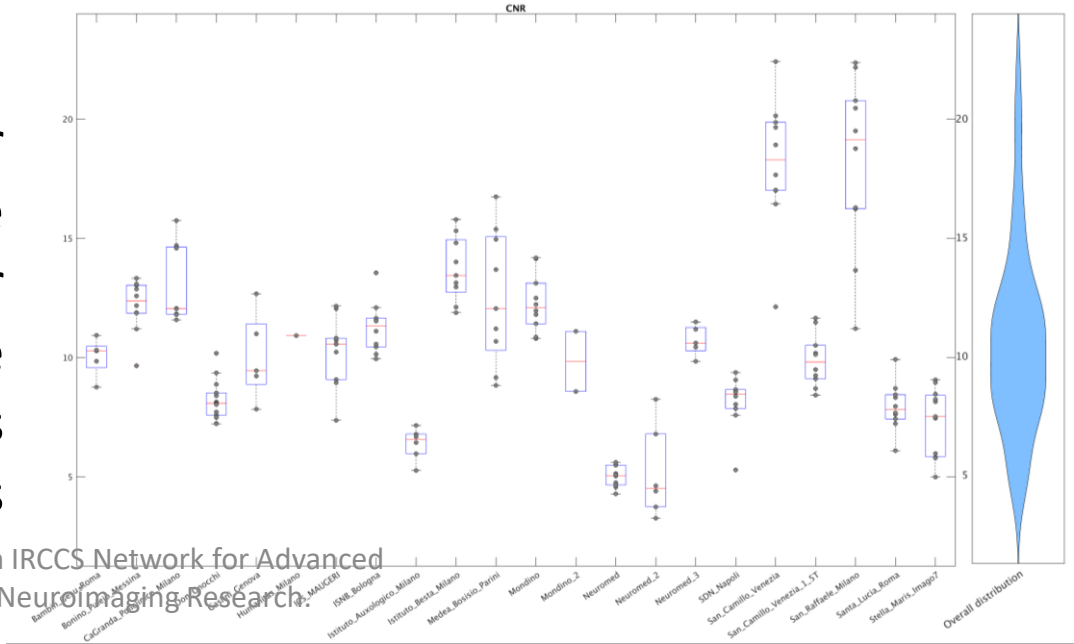
Signal-to-Noise Ratio (SNR):

The mean intensity within gray matter divided by the standard deviation of the values outside the brain. Higher values are better.



Contrast to Noise Ratio (CNR):

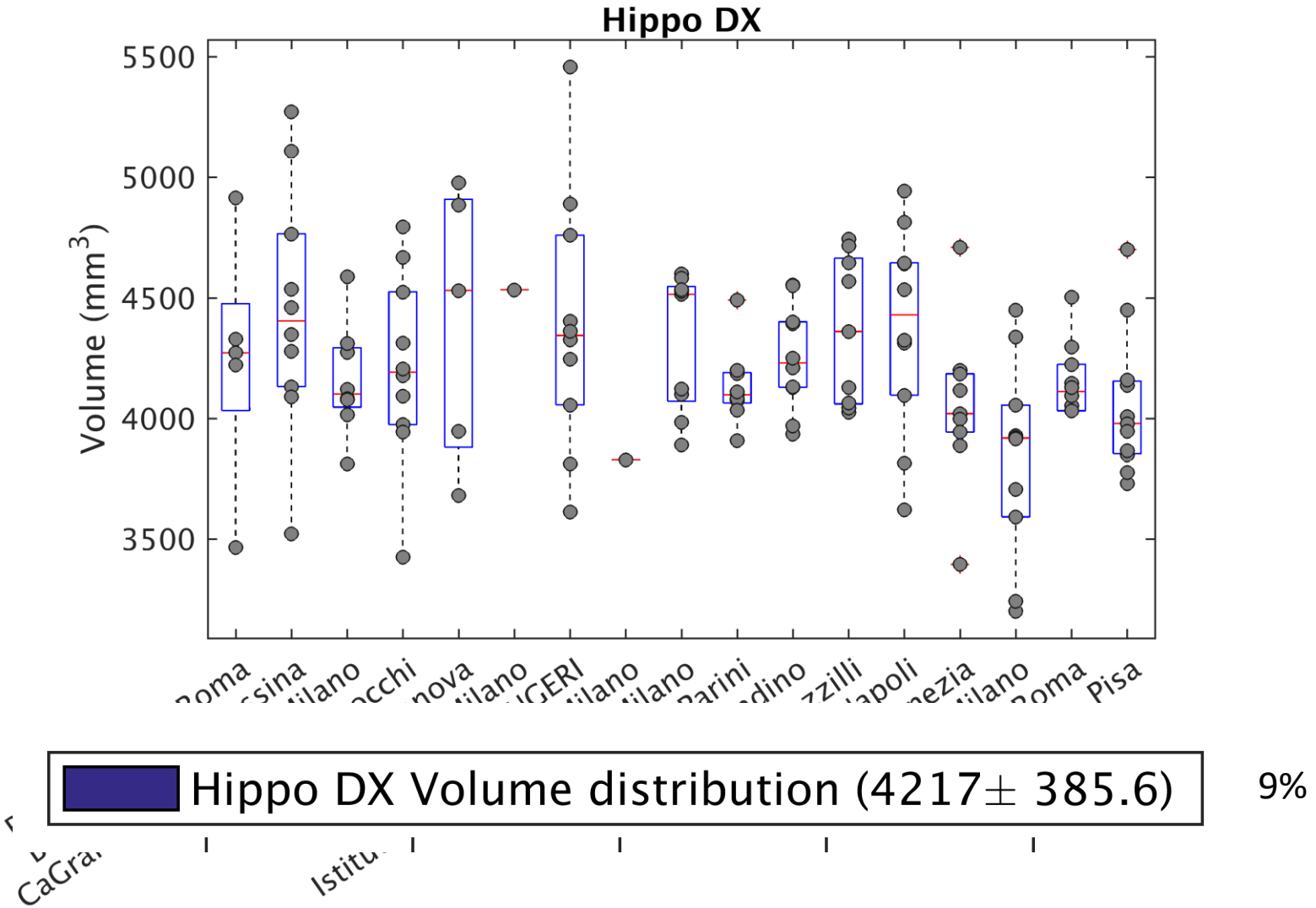
The mean of the gray matter intensity values minus the mean of the white matter intensity values divided by the standard deviation of the values outside the brain. Higher values are better



Sub-cortical structure volume

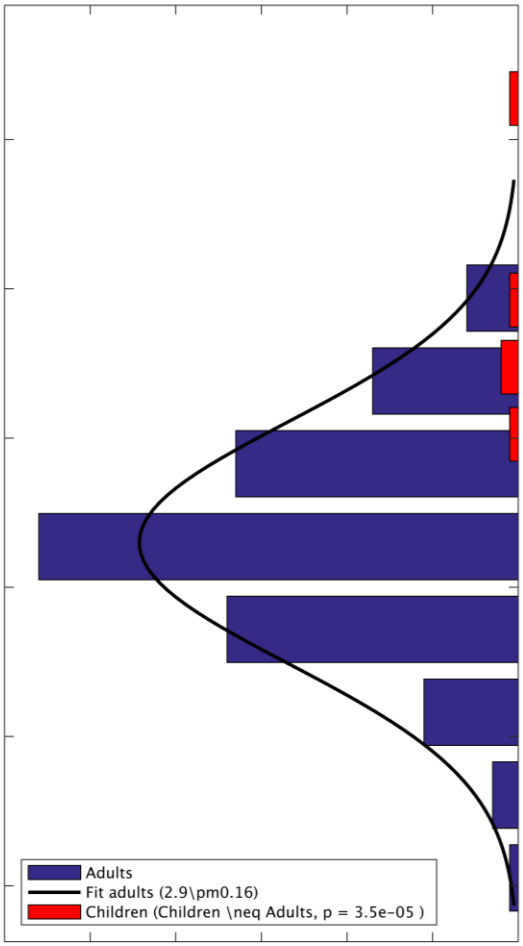
Freesurfer 6.0

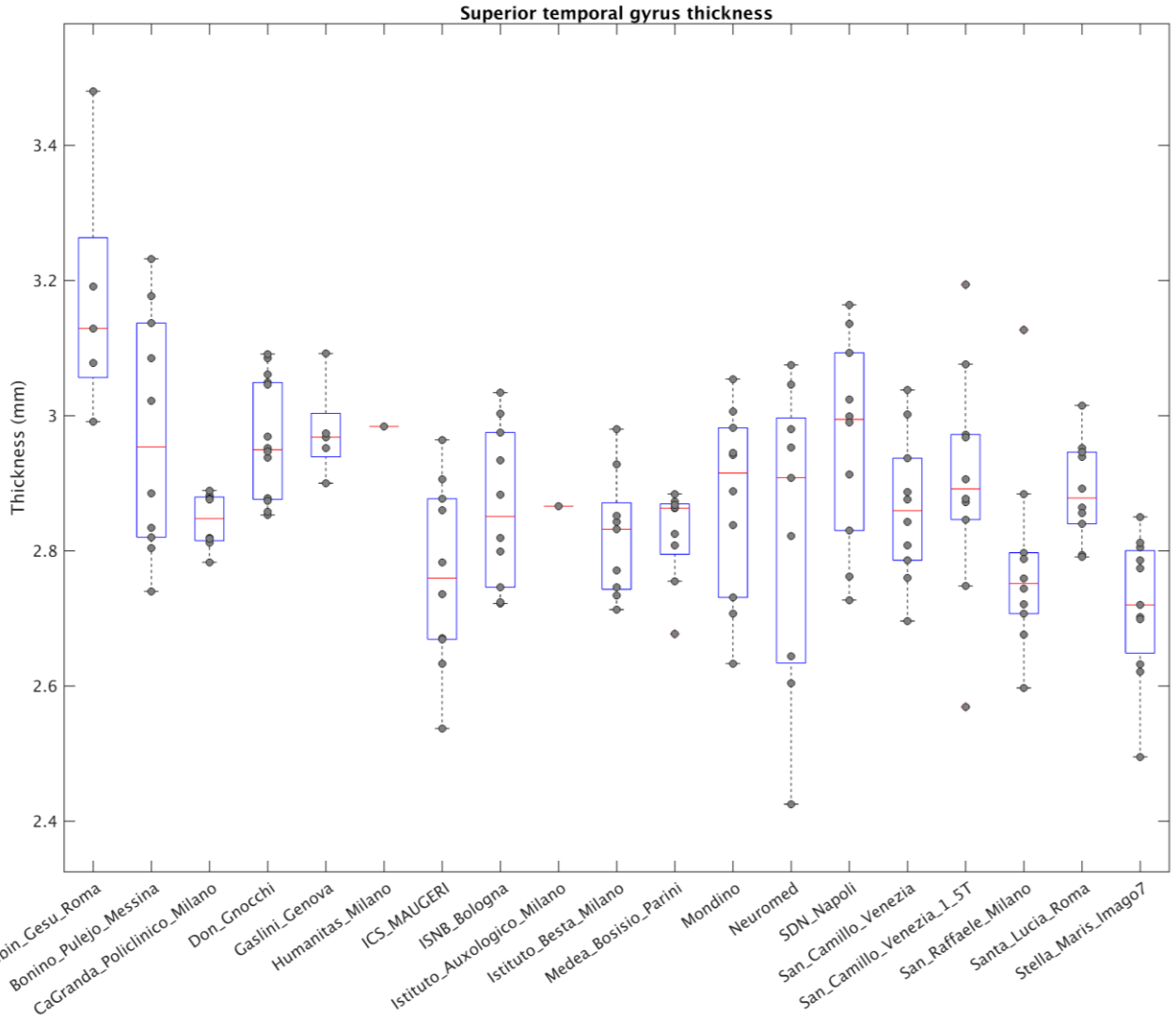
Hippocampus



cortical structure
Freesurfer 6.0 - ENIGMA

Superior Temporal Gyrus





Italian IRCCS Network for Advanced Neuroimaging Research.

Fit adults (2.9 ± 0.16) 5%

Shared standardised 3D T1 protocol

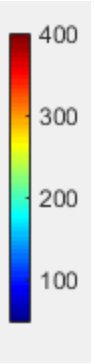
Parameters	sT1W_3D		
Vendors	Philips	Siemens	GE
Sequence type	3D FFE	MP-RAGE	3D BRAVO
Slice orientation	sagittal	sagittal	oblique
FOV [mm]	240 x 240	256 x 256	256 x 256
Resolution [mm^3]	1 × 1 × 1	1 × 1 × 1	1 × 1 × 1
Matrix (Base Resolution)	240x240	256x256	256x256
Slice thickness	1	1	1
Slice gap (mm)	-	-	-
n. slices	175 – 180 (**)	175 – 180 (**)	175 – 180 (**)
Phase Encoding direction	AP	AP	AP
Slice order	Interleaved	Interleaved	Interleaved
NSA/Averages/NEX	1	1	1
1TR [ms]	2300	2300	non modif
TE [ms]	2.96	2.96	3.2
TI [ms]	900	900	900
Flip angle	9°	9°	9°
Fat Suppression	No	No	No
k-space coverage (Halfscan/Partial Fourier)	No	No	No
Acceleration factor	SENSE≤ 2.3	GRAPPA=2	ARC=2
Filter	CLEAR on	Prescan Normalize on	PURE on
Bandwidth [Hz/Px]	191	240	244
Duration [min]	**≈ 5.30**	**≈ 5.30**	**≈ 5.30**

Shared standardised rs-fMRI protocol

Parameters	RS_fMRI_200vol_vox3_PA			RS_fMRI_GE_AP		
Vendors	Philips	Siemens	GE	Philips	Siemens	GE
Sequence type	GE EPI		GE EPI FMRI BOLD	GE EPI		GE EPI
Slice orientation	transversal	transversal	oblique	transversal	transversal	oblique
FOV [mm]	240 x 240	240 x 240	240 x 240	240 x 240	240 x 240	240 x 240
Resolution [mm^3]	3.0 × 3.0 × 3.0	3.0 × 3.0 × 3.0	3.0 × 3.0 × 3.0	3.0 × 3.0 × 3.0	3.0 × 3.0 × 3.0	3.0 × 3.0 × 3.0
Matrix (Base Resolution)	80x80	80x80	80x80 * (rhimsize=80)	80x80	80x80	80x80 * (rhimsize=80)
Slice thickness	3.0	3.0	3.0	3.0	3.0	3.0
Slice gap [mm]	0.5	0.5	0.5	0.5	0.5	0.5
n. slices	40	40	40	40	40	40
Phase Encoding direction	PA	PA	PA * (pepolar = 0)	AP	AP	AP * (pepolar = 1)
Slice order	interleaved descending	interleaved descending	interleaved (multi-phase) * (opslice _order=1)	interleaved descending	interleaved descending	interleaved (multi-phase) * (opslice _order=1)
TR [ms]	2300	2300	2300	2300	2300	2300
TE [ms]	28	28	28	28	28	28
Flip angle	80°	80°	80°	80°	80°	80°
Fat suppression	yes	yes	yes	yes	yes	yes
k-space coverage (Halfscan/Partial Fourier)	No	No	No	No	No	No
Acceleration factor	SENSE= 2	GRAPPA=2	ASSET=2	SENSE= 2	GRAPPA=2	ASSET=2
Filter	CLEAR on	Prescan Normalize on	PURE on	CLEAR on	Prescan Normalize on	PURE on
Dynamic scans (phases)	200	200	200	3	3	3
Dummies scans	3	-	-	0	0	0
Bandwidth [Hz/Px]	2560	2404	2500 * (rbw=100)	2560	2404	2500 * (rbw=100)
Echo spacing [ms]		0.5			0.5	
EPI factor		80			80	

Triantafyllou 2005

rs-fMRI: analisi preliminari



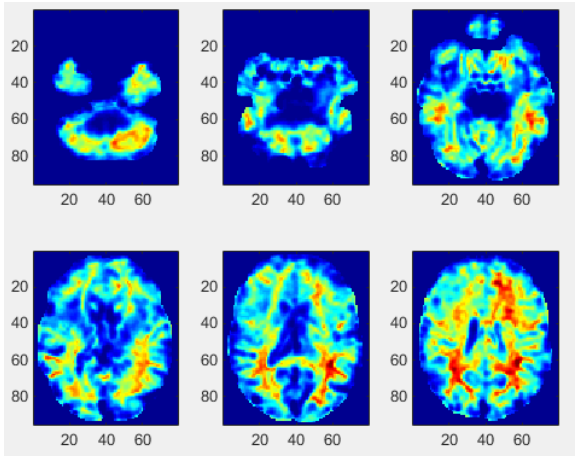
Philips 32 canali

Siemens 32 canali

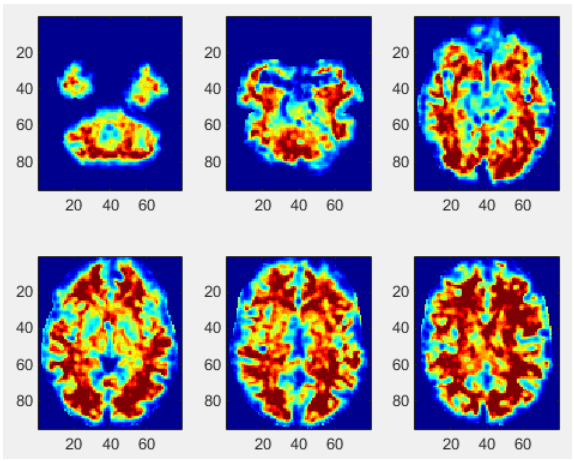
GE 8 canali

TEST01

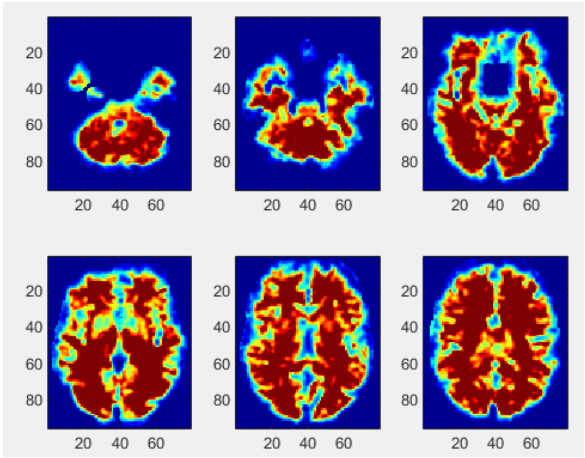
Voxel 3x3



Voxel 3x3

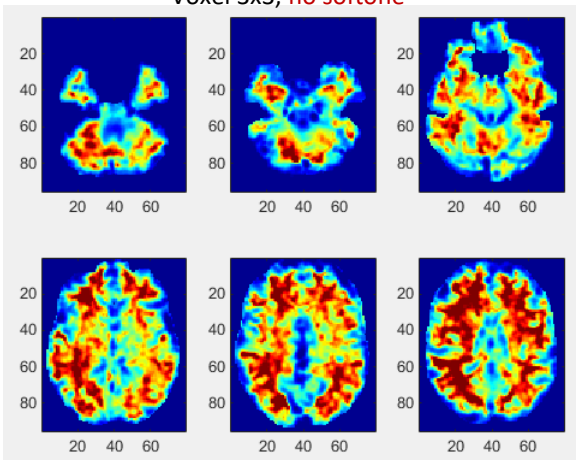


Voxel 3.25x3.25

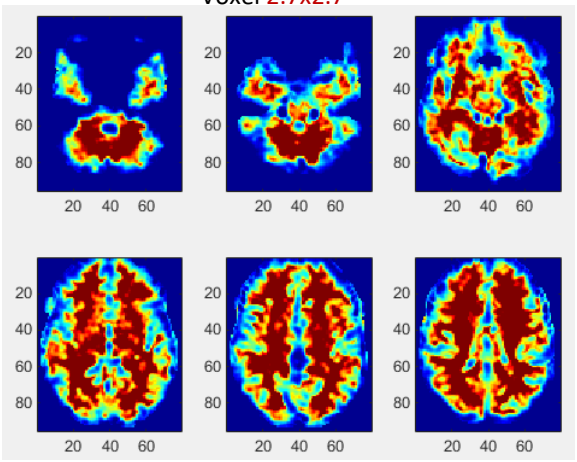


TEST02

Voxel 3x3, no softone



Voxel 2.7x2.7



tSNR

Shared standardised DWI protocol

Parameters	sT1W_3D		
Vendors	Philips	Siemens	GE
Sequence type	3D FFE	MP-RAGE	3D BRAVO
Slice orientation	sagittal	sagittal	oblique
FOV [mm]	240 x 240	256 x 256	256 x 256
Resolution [mm^3]	1 × 1 × 1	1 × 1 × 1	1 × 1 × 1
Matrix (Base Resolution)	240x240	256x256	256x256
Slice thickness	1	1	1
Slice gap (mm)	-	-	-
n. slices	175 – 180 (**)	175 – 180 (**)	175 – 180 (**)
Phase Encoding direction	AP	AP	AP
Slice order	Interleaved	Interleaved	Interleaved
NSA/Averages/NEX	1	1	1
1TR [ms]	2300	2300	non modif
TE [ms]	2.96	2.96	3.2
TI [ms]	900	900	900
Flip angle	9°	9°	9°
Fat Suppression	No	No	No
k-space coverage (Halfscan/Partial Fourier)	No	No	No
Acceleration factor	SENSE≤ 2.3	GRAPPA=2	ARC=2
Filter	CLEAR on	Prescan Normalize on	PURE on
Bandwidth [Hz/Px]	191	240	244
Duration [min]	**≈ 5.30**	**≈ 5.30**	**≈ 5.30**

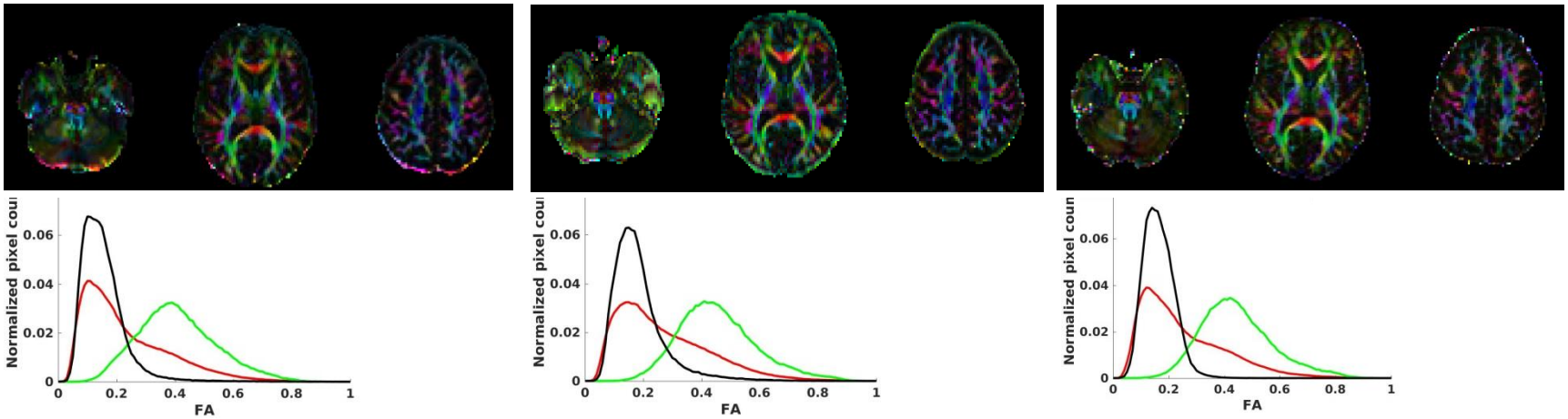
DTI: analisi preliminari

NABT
NAWM
GM

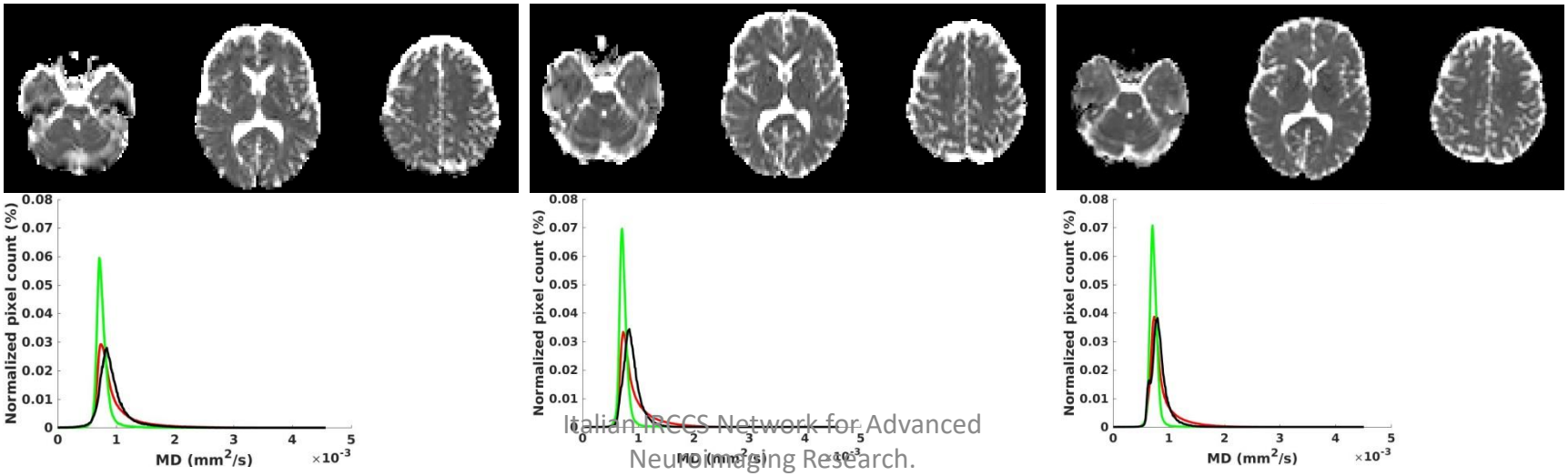
- Istogrammi FA e MD (DWI-32 direzioni)

Philips 32 canali ***Siemens 32 canali*** ***GE 8 canali***

FA



MD



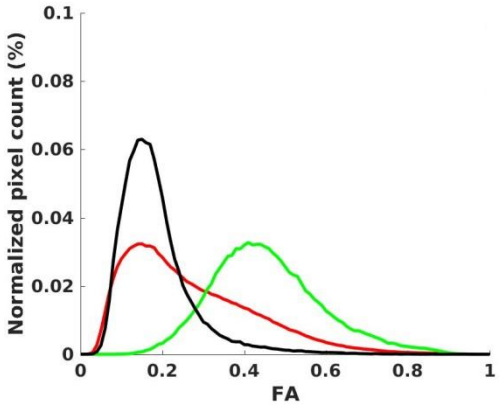
DTI: analisi preliminari

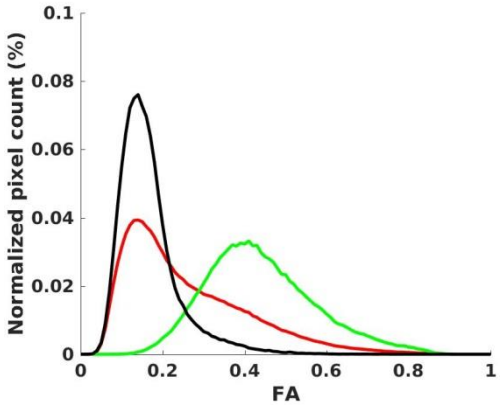
NABT
NAWM
GM

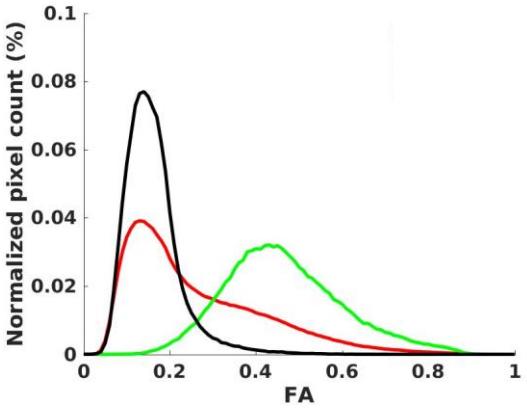
- Istogrammi FA e MD (Siemens)

32 direzioni ***64 direzioni*** ***2 shells: 32 – 64***

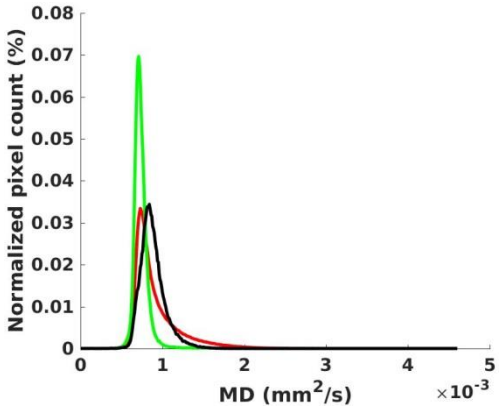
FA

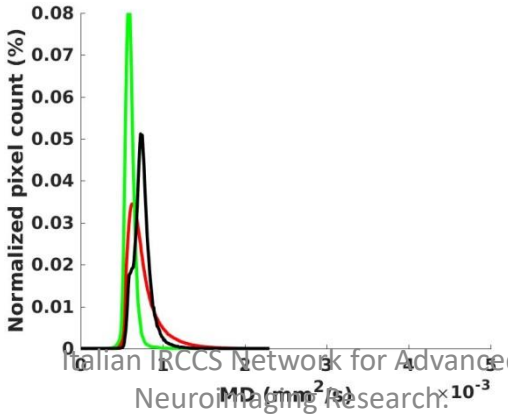


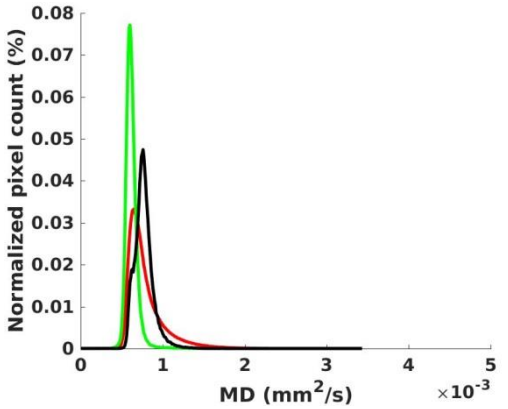




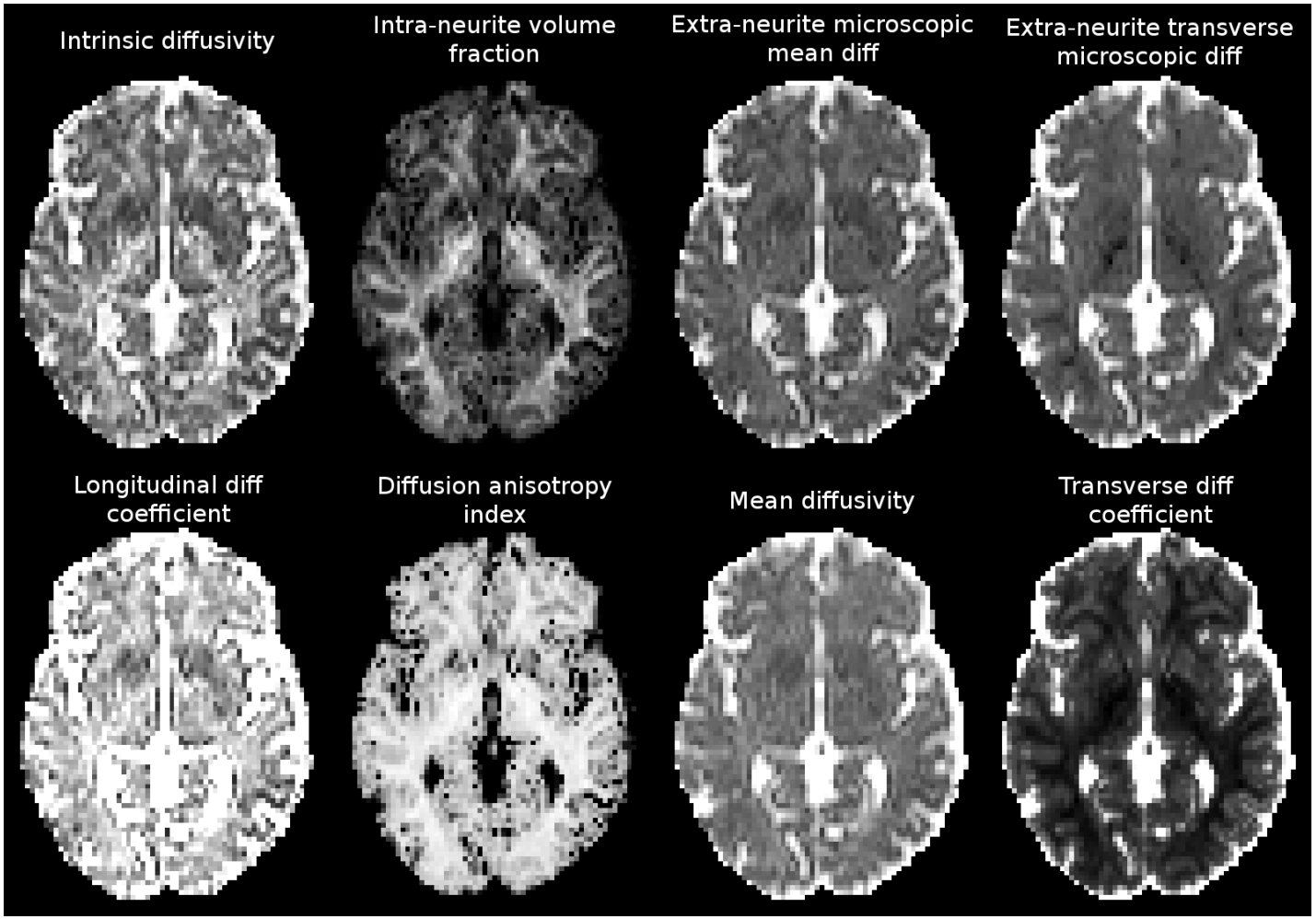
MD







Multi-shell DWI



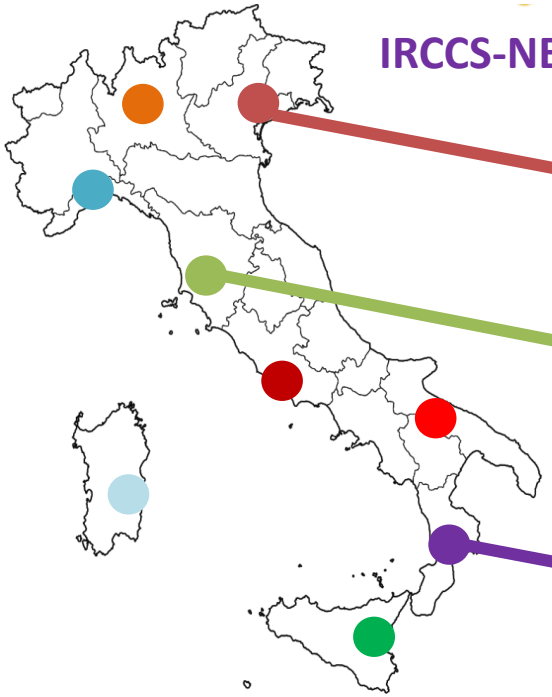
Quantitative MR Techniques

3DT1	RS-fMRI	QSM	DWI	ASL	…….
• ISO VOXEL • 1×1×1mm^3	• GRE • AC-PC • EPI • ISO VOXEL • TR- 2-3 s • TE 20 - 30 ms • FA 70 -90 deg • 180-200 frames • 5 – 12min	• GRE • AC-PC • multiecho o SWAN • Voxels 1 mm • TE_1 5-15 ms • ΔTE 3-6 ms • TE_n 60-80 ms • N-echo 1-16 • TR=50-70 ms	• EPI • ISO voxel 2x2x2 mm^3 • 2 shells • 32-64 Dirs • b-value = 1000; 2000	• PCASL • Single shot EPI • Matrix size 64×64 • Field of view 224×224mm • Thk 6mm • TR Inter-pulse time 1.24 ms • TE 21- 28 ms • TR 4500 - 4800 ms • PLD ? • Labeling duration ? • Labeling position ?	

Conclusions

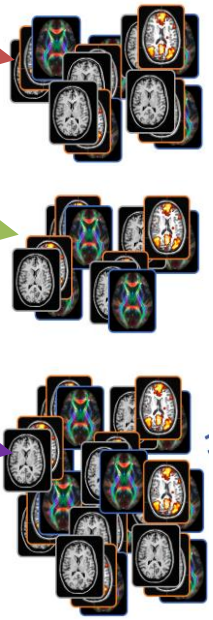
- Phantom acquisitions ongoing for:
  - Geometrical distortions
  - Stability over time
- In vivo optimised acquisitions:
  - 3DT1
  - rs-fMRI
  - 2-shells DWI
  - qSM
- Next steps:
  - Comparison of healthy subjects between IRCCS
  - Traveling brain
  - Application to pathologies (dementia and development)
- Data analysis:
  - Quantitative features extraction
- Data collection:
  - Centralised features stored for advanced precision medicine

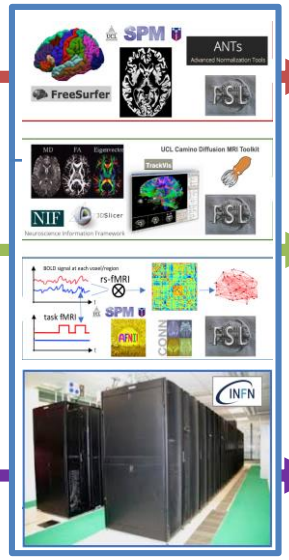
Thank you for your attention!



IRCCS-NET

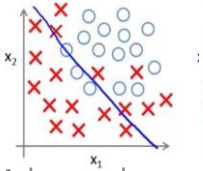
ARIANNA project x IRCCS-NET

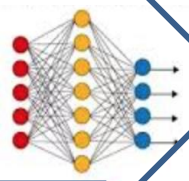




MIP platform

Data driven predictive models





Precision medicine