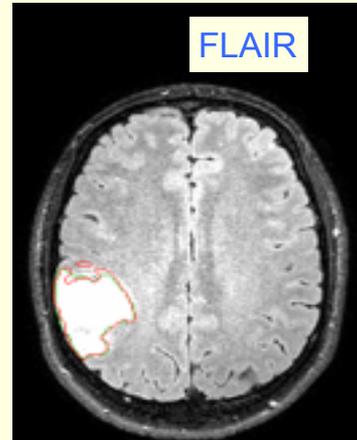
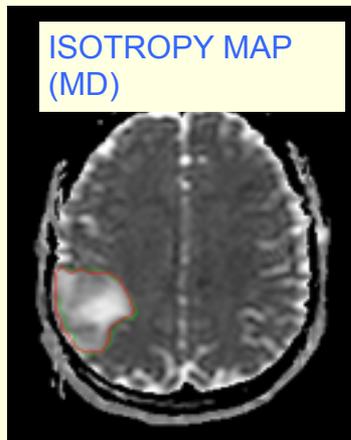


From TESLA to nextMR

Giorgio De Nunzio &Co

TESLA *(Technological Equipment and Software for Life-Science Applications)*

- Contesto generale:
 - Realizzazione di sistemi software e hardware per applicazioni mediche, in Risonanza Magnetica
- Sedi
 - Pisa, L'Aquila, Lecce
- Compito della sezione di Lecce:
 - **individuazione di tipo istologico e grado dei gliomi cerebrali** tramite analisi tessiturale in immagini di Risonanza Magnetica convenzionale e in tensore di diffusione;
 - tipo istologico: astrocitomi / oligodendrogliomi / oligoastrocitomi / glioblastomi
 - gradazione di malignità: I e II (basso grado, LGG), III e IV (alto grado, HGG)



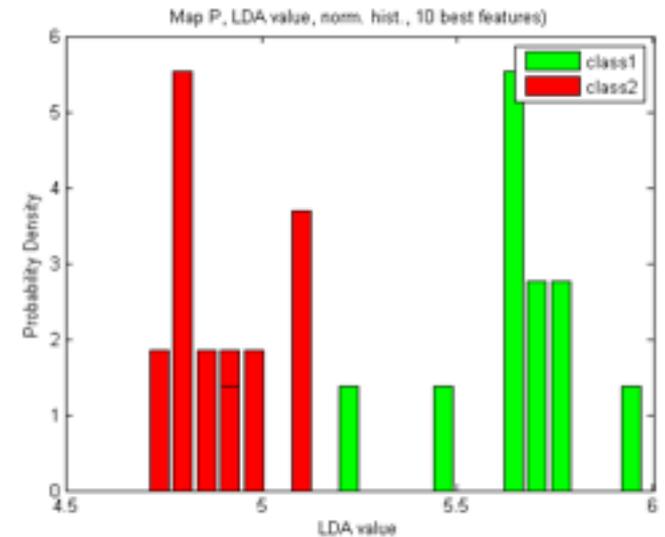
GLIOMA: tumore della glia (cellule con funzione nutritiva e di sostegno per i neuroni).

Il più comune tumore maligno del SNC, difficile da trattare a causa dell'elevata malignità e invasività.

Comportamento altamente invasivo → **fallimento delle terapie disponibili**; Trattamento chirurgico seguito da radioterapia e/o cicli chemioterapici

METODOLOGIA

1. fissata una tipologia di immagini (e.g. MD)...
2. fissato il tipo di classificazione da indagare (e.g. distinguere tra astrocitoma e oligodendroglioma, di basso grado)
3. separare i pazienti in due classi disgiunte in base alla classificazione istologica
4. calcolare le feature tessiturali di primo e secondo ordine nelle ROI tumorali dei pazienti
5. applicare un metodo di classificazione supervisionato (e.g. LDA, ANN, SVM, random forests...) e valutare il potere predittivo (LOPO)



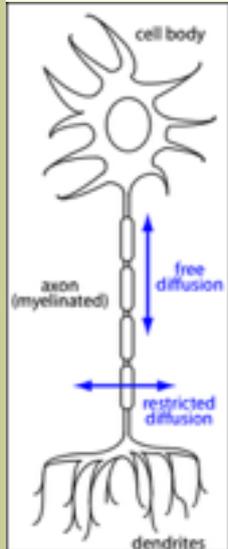
Classificazione di pazienti con oligodendroglioma basso grado (rosso) e con astrocitoma basso grado (verde)

Calcoli effettuati anche in porzioni delle ROI tumorali, per massimizzare l'accuratezza



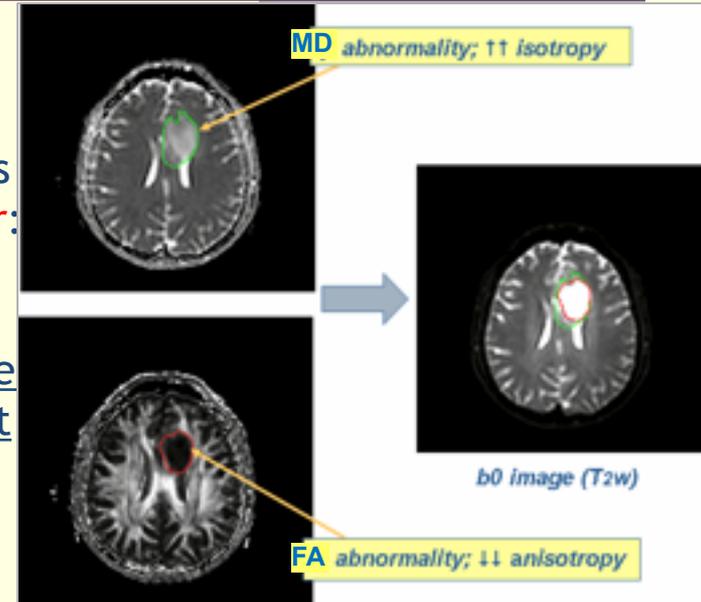
METODOLOGIA

Diffusion Tensor Imaging

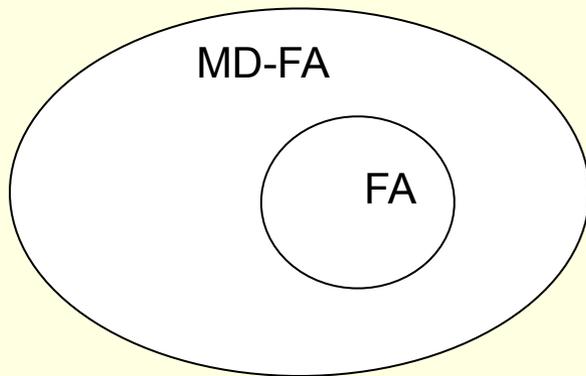


By splitting the diffusion tensor into its **isotropic and anisotropic components**, it is possible to **define two regions of a tumour**: the central part is characterized by reduced anisotropy which corresponds to the gross tumour core, and around this there is a region of increased isotropic but normal anisotropic diffusion which correlate with glioma infiltration

Price et al., Eur Rad. 2007



MD



Calcoli effettuati anche in porzioni delle ROI tumorali, per massimizzare la sensibilità

ROI(MD), ROI(FA), e il margine ROI(MD-FA)

DATABASE INDIVIDUATI:

U.O. Neuroradiologia, Ospedale San Raffaele e Università Vita-Salute;

U.O. Neurochirurgia, Ist. clinico Humanitas, Univ. di Milano

50 pazienti, di cui abbiamo mappe e roi manuali e automatiche (GlioCAD) (MD, FA, B0 (T2w), FLAIR, P e Q. Tipo/grado: 16 oligo II, 4 oligo III, 6 astro II, 8 astro III, 8 oligoastro II, 2 oligoastro III, 4 gbm sec

Unita' di neurochirurgia dell'ospedale San Salvatore dell'Aquila

Stiamo collezionando/valutando il dataset in questione

7 pazienti al momento ricevuti

Pazienti con risultato istologico, modalità T1, T2, FLAIR, DWI. Con e senza MDC.

Unita' di neuroradiologia dell'ospedale di Casarano "Francesco Ferrari"

Stiamo collezionando/valutando il dataset in questione

17 pazienti al momento ricevuti

Modalità T1, T2, FLAIR, DWI. Con e senza MDC.

Database pubblico BraTS

20 casi HGG e 10 casi LGG

Modalità T1mdc, T2, FLAIR.

Milestones for 2013 and 2014

WP3

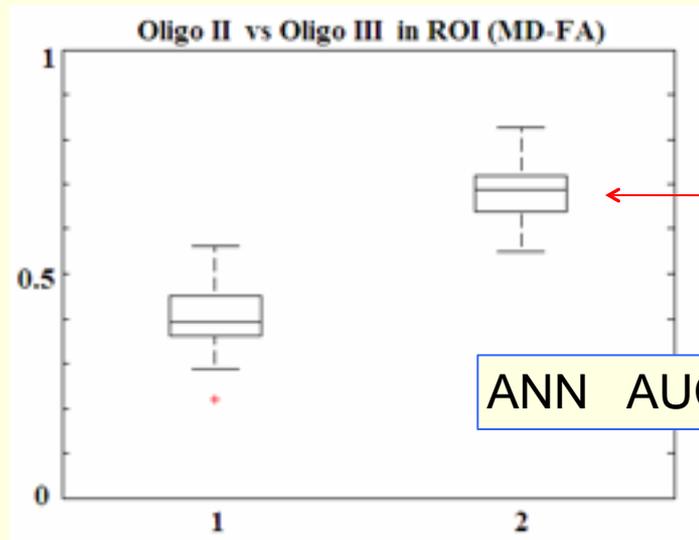
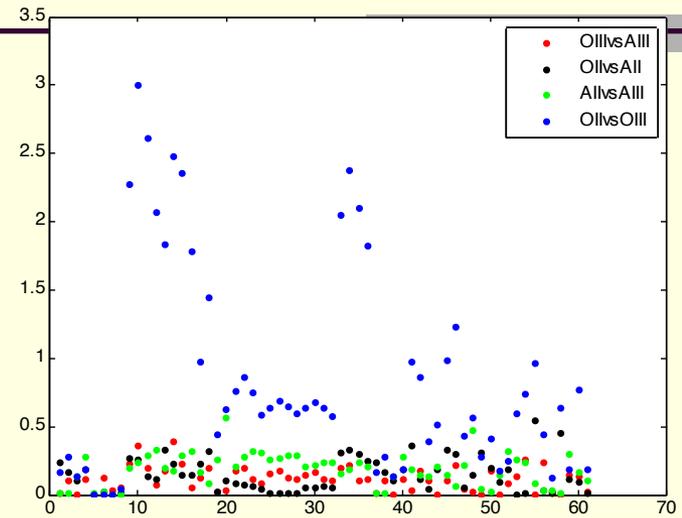
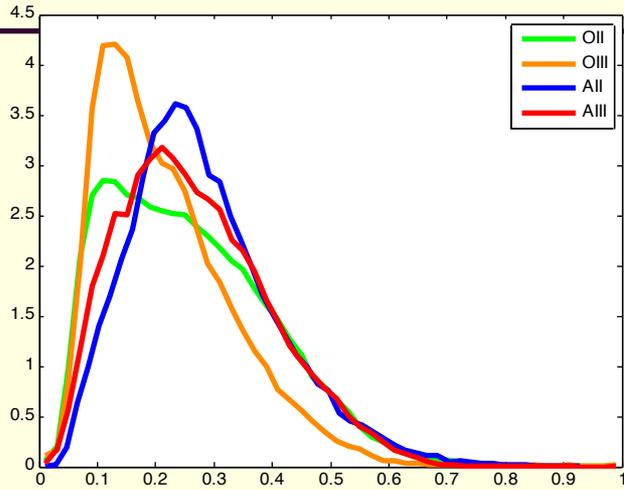
	PI	LE	AQ
2013	<p>4.3.1 Development of image filtering techniques to recover homogeneity in 7 T structural images of the brain</p>		
	<p>4.3.2 Acquisition of suitable diamagnetic pads and optimization of acquisition sequences from imaging the wrist at 7T with the available 32-ch coil for human head (Nova Medical Inc.). Wrist data acquisition of few volunteers (healthy and with osteoporosis at different degrees</p>		
	<p>4.3.3.1 Design and implementation of whole-brain classification techniques to analyze brain data of subjects with Autism Spectrum Disorder (ASD).</p>	<p>4.3.3.2 Multimodality glioma data collection. Histological glioma data collection. Data analysis for the estimation of the discriminant power of textural features (search for correlation between in-vivo and ex-vivo measures). Tuning the software system for MR image standardization.</p>	<p>4.3.3.2 Data analysis to help in the correlation between in-vivo and ex-vivo measures, using if appropriate fluorescent microscopy data.</p>
	<p>4.3.3.2 Retrospective choice of a suitable data sample for connectome study (HARDI acquisition protocol).</p>		
	<p>4.3.1 Evaluation standard registration and cortical segmentation tools on filtered 7 T structural images of the brain.</p>		
	<p>4.3.2 Evaluation of SNR and SCR for trabecular bone and cartilage. Segmentation of relevant structures. Evaluation of: total bone volume (TBV), bone volume fraction(BVF), surface curve ratio (SCR), erosion index (EI).</p>		

1-6 m

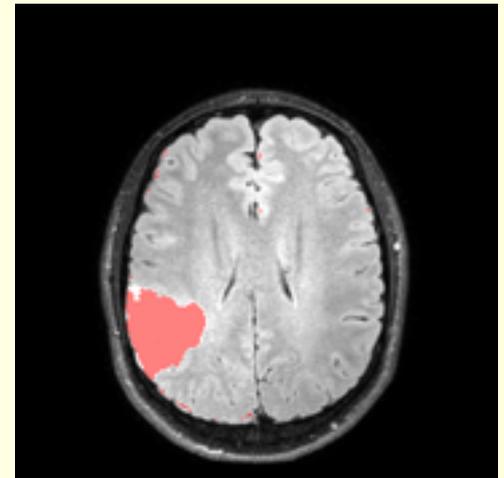
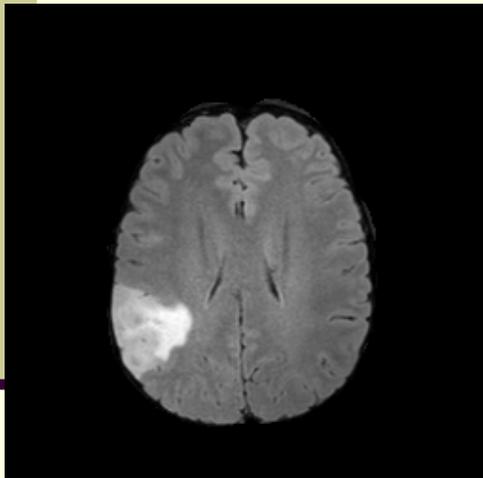
2013

		PI	LE	AQ
2014	7-12 m	4.3.2 Acquisition of suitable diamagnetic pads and optimization of acquisition sequences for imaging the ex-vivo vertebrae and knees at 7T with the available 32-ch coil for human head (Nova Medical Inc.).		
		4.3.3.1 Design and implementation of Region-of interest (ROI) based classification techniques to analyze brain data of ASD subjects.	4.3.3.2 Building the multivariate/ multimodality classification system with SVM and ANN.	
		4.3.3.2 Implementation of fiber tractography and cortical parcellation algorithms on each subject.		
	1-6 m	4.3.3.1 Implementation of a combination technique to integrate the whole-brain and ROI-based classification protocols to maximize the classification performance.	4.3.3.2 Optimization of the classification system; test on new clinical data.	4.3.3.2 Providing guidelines for design of the Graphical User Interface for the glioma classification software.
		4.3.3.2 Connectome map extraction. Implementation of decisional systems (SVM) for connectome interpretation.		
	7-12 m	4.3.2 Acquisition at 7 T of knees/vertebrae of human volunteer with osteoarthritis/osteoporosis with PA16 and NEC coil prototypes (WP1).		
4.3.2 Analysis of images of knees and vertebrae of human volunteers; Evaluation of SNR and SCR for trabecular bone and cartilage. Segmentation of relevant structures. Evaluation of: total bone volume (TBV), bone volume fraction(BVF), surface curve ratio (SCR), erosion index (EI).				
	4.3.3.1 Evaluation of all classification methods on the whole data sample of ASD subjects acquired.	4.3.3.2 Building of the Graphical User Interface for the glioma classification software.		
	4.3.3.2 Evaluation of the impact of multivariate classification techniques on connectome data.	4.3.3.2 Final evaluation of the system performance		

ALCUNI RISULTATI (PRELIMINARI!!)



SEGMENTAZIONE NON SUPERVISIONATA:

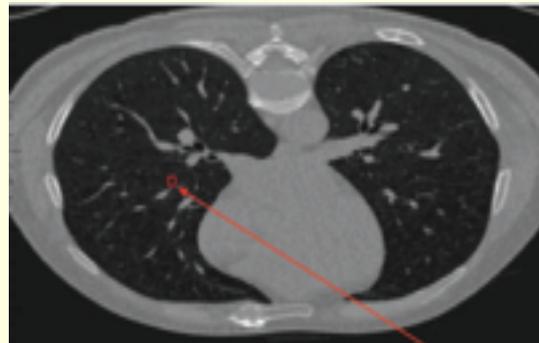


CAD per i NODULI POLMONARI:

Computer Assisted Detection per la diagnosi precoce dei noduli polmonari in TAC, il sistema CAD già sviluppato dalle collaborazioni MAGIC5 e poi M5I, è stato attualmente reso fruibile via Rete da parte dei medici radiologi interessati

E' stato pianificato il seguito della sperimentazione, con l'unità di radiologia dell'ASL Lecce (nella persona del Direttore Dott. Massimo Torsello).

E' anche in corso la definizione di un'interfaccia per l'utente in ambiente ImageJ.



PUBBLICAZIONI E CONFERENZE:

Conferenze

G. De Nunzio, R. Cataldo, A. Carlà, "Robust gray-level standardization in brain Magnetic-Resonance images." Dagli atomi al cervello - Le Scienze di Base per la comprensione delle funzioni del cervello. Milano 27/1/2014

G. De Nunzio, R. Cataldo, A. Carlà, "Robust gray-level standardization in brain Magnetic Resonance images", 8° Congresso Nazionale dell'Associazione Italiana di Fisica Medica (AIFM), Torino 16-19 novembre 2013.

S. Batzella, G. De Nunzio, M. Donativi, R. Buccolieri, R. Quarta, S. Di Sabatino, P. Ialongo, G. Culla, G. Galluccio, "Stenosi tracheale e Fluidodinamica Computazionale(CFD): una nuova tecnica per lo studio della limitazione al flusso aereo?" XIV Congresso Nazionale UIP-FIP / XLII Congresso Nazionale AIPO "Clinica, Ricerca, Organizzazione: la centralità della persona in Pneumologia", Verona 27-30 Novembre 2013

M. Rucco, A. Castellano, M. Donativi, G. De Nunzio, E. Merelli, D. Herman, T. Petrossian, G. Pastore, L. Bello, A. Falini, "Segmentazione di immagini FLAIR assiali basata su analisi topologica dei dati", 4° Congresso Annuale dell'Italian Chapter dell'ISMRM Risonanza Magnetica in Medicina 2013: dalla ricerca tecnologica avanzata alla pratica clinica, PERUGIA, 24 - 25 ottobre 2013

Pubblicazioni

G. De Nunzio, R. Cataldo, A. Carlà, Robust intensity standardization in brain Magnetic Resonance images, submitted to Journal of Digital Imaging

R. Cataldo, A. Agrusti, G. De Nunzio, A. Carlà, I. De Mitri, M. Favetta, M. Quarta, L. Monno, L. Rei, E. Fiorina, Generating a minimal set of templates for the hippocampal region in MR neuroimages. J Neuroimaging. 2013 Jul;23(3):473-83. doi: 10.1111/j.1552-6569.2012.00713.x. Epub 2012 Nov 15. Lavoro svolto nell'ambito della collaborazione MAGIC-5.

The core of this proposal is to advance in the understanding of MR-based imaging and their data analysis, to serve as better quantitative measurements in clinical practice thus increasing the prognostic value. This goal is pursued by addressing a selected number of current topics most relevant for clinical research and by developing novel knowledge in physics, mathematics and information technology as appropriate.

From the scientific activity point of view, nextMR is planned *in continuity* with past INFN-CSN5 experiences - namely MIND¹ and TESLA² - and the proponents' expertise.

The nextMR project is structured to be a long-term activity, that is, it configures to be a line of research. The proponents past experience on physics methods applied to bio-medical research

Sedi: Genova, Pisa, Trieste, L'Aquila, Catania, Lecce, Bari

Obiettivi

- O.1: MRI techniques: disease-specific image enhancement through dedicated acquisition modality and instrumentation [coils, sequences...]
- O.2: Advanced protocols and analyses: connectomics, brain network studies, lesion characterization [fMRI, DTI, DKI, pattern recognition, connectome, biomarkers, autism, gliomas, ...]
- O.3: Enhanced MRI-driven markers in the measure of the neurodegeneration process.

TESLA to nextMR: from experimental tests to clinical practice

WP.3.A

Reference pathologies are brain gliomas. Inspection of available data, **MR/DTI as the current best option.** Check of data completeness and homogeneity. Goal to be achieved: **non-invasive glioma grading and type assessment by the analysis of DTI-derived maps.** When **DKI datasets of glioma patients become available** within the Collaboration, the goal will be **glioma automatic segmentation, grading, and type assessment by DKI maps.** Eventually, the characterization techniques will be applied to **different types of brain lesions (e.g. metastases)** depending on the research lines agreed on with the clinical partners

WP.3.C

Definition, implementation, and test of algorithmic procedures (software) for preprocessing and pattern recognition, for the achievement of the goal(s) defined in WP.3.A. **Code optimization (parallel and/or CUDA programming when advisable).** Grading and type assessment of gliomas through the analysis of DTI-derived maps.

WP.3.E, WP.3.F

Validation of the strategies implemented in WP.3.C, by the assessment of procedure performance on **different/new datasets, and by blind trials with expert readers (clinicians).**

WP.3.I

Deployment and dissemination. **GUI (Graphical User Interface) implementation for software enjoyment by the clinical partners.** Application to conferences and journals.

CLINICAL PARTNERS! Necessità di attrarre fondi esterni!

LE	<u>G. De Nunzio</u>	Uni. LE	0.4
	R. Cataldo	Uni. LE	0.4
	M. Quarta	Uni. LE	0.4
	M. Donativi	Grant (Ministry of Health)	0.4

2015 (k€)

INFN site	Inventory	Travel	Consumables	Software
GE	1.5	5.0	1.0	1.0
PI	0.0	3.0	11.0	4.5
TS	0.0	1.0	1.0	0.0
AQ	0.0	3.0	10.0	2.5
CT	5.0	3.0	0.0	1.0
LE	0.0	3.0	3.0	1.0
BA	0.0	5.0	1.0	1.0



2016 (estimated total, k€)

INFN site	Inventory	Travel	Consumables	Software
All sites	3.0	20.0	25.0	11.0

2017 (estimated total, k€)

INFN site	Inventory	Travel	Consumables	Software
All sites	0.0	15.0	10.0	11.0