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**COD. C01**

**Comparison of multiple multi-compartment diffusion models in temporal lobe epilepsy**

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Introduction

Neuroimaging and neuropathological studies have reported that the structural network affected in Temporal Lobe Epilepsy (TLE) extend to both temporal and extra-temporal brain structures. Diffusion MRI has made it possible to detect pathology-derived alterations in specific white matter (WM) regions (1). The aim of this pilot study was to evaluate WM microstructural abnormalities in TLE by means of diffusion tensor imaging (DTI) and different advanced diffusion models (2), in order to identify temporal and extratemporal abnormalities.

Methods

Thirty-two TLE patients (18 left: 32.8±10.1yrs, 10males, 14 right: 39.5±10.7yrs, 6males) and 30 controls (CTR) (32.5±8.5yrs, 15males) were recruited within the 3TLE* project. After temporal lobectomy, histopathology revealed hippocampal sclerosis (HS) in seven (4 left and 3 right) and heterogeneous lesions in the remaining patients.

Diffusion images were acquired with a two-shell twice-refocused SE-EPI (TR/TE=8400/93ms, 70 slices, 2.2mm isotropic voxel, 48 non-collinear diffusion directions with b=1000/2000s/mm$^2$) using a 3T scanner (Skyra, Siemens Healthcare GmbH, Germany).

Diffusion images were corrected for Gibbs artifacts, noise, eddy and geometrical distortions, and motion. Fractional anisotropy, mean, axial and radial diffusivity maps were calculated from DTI model, while diffusion kurtosis imaging (DKI) provided maps of mean, axial and radial kurtosis. Multi-compartment WM DKI (WMDK) and spherical mean technique (SMT) models were fit to obtain microstructural metrics of axonal density, intra and extra-axonal diffusivity and entropy. Neurite orientation dispersion and density imaging (NODDI) provided similar metrics in left TLE. For each metric, mean values were calculated in temporal, limbic and other main axonal tracts. A one-way ANOVA ($p<0.05$, Bonferroni corrected) was performed between TLE and CTR and repeated between HS patients and CTR.

Results

DTI detected some temporal microstructural abnormalities: right stria terminalis, inferior fronto-occipital (IFOF), inferior longitudinal (ILF) and uncinate tracts in right TLE, left parahippocampus and IFOF in left TLE. Multi-compartment models showed the same temporal alterations as well as right parahippocampus in right TLE and left uncinate in left TLE.

All models detected extra-temporal alterations: right fornix, anterior thalamic radiations and forceps minor in right TLE, left cingulum, anterior thalamic radiations and corticospinal tract in left TLE.

In a subgroup of patients with HS, DTI revealed alterations in the limbic circuit (stria terminalis, fornix and left cingulum), while the advanced models revealed both limbic (stria terminalis, fornix and cinguli) and extra-limbic temporal abnormalities (bilateral IFOF and ILF).

Discussion

Our findings showed that some parameters (e.g. fractional anisotropy, axonal density, entropy) obtained with different diffusion models identified alterations in the same regions but other parameters (e.g. axial diffusivity/kurtosis) were not informative of pathology. In the relatively homogeneous subgroup of patients with HS, advanced models detected not only limbic but also extra-limbic deep temporal WM alteration. These preliminary results suggest that DKI and multi-compartment diffusion models may be more sensitive than conventional DTI to detect temporal and extratemporal WM alterations in TLE.

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**COD. C02**

**Estimate of vacuoles size and density in sporadic Creutzfeldt-Jakob disease by diffusion MRI and biophysical modelling**

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Introduction

Sporadic Creutzfeldt-Jakob disease (sCJD) is the most common human form of prion disease, a rare, rapidly progressive, and fatal neurological disorder. The five sCJD subtypes are characterized by different diameter and distribution of intracellular vacuoles (spongiform degeneration) in brain tissues. Fine spongiosis is typical of the most common sCJD subtypes (MM1 and MV1), having a survival time of few months, while others (MM2 and MV2C) have large confluent vacuoles and longer survival time. Unfortunately, no reliable non-invasive method for subtype identification is currently available. Diffusion MRI (dMRI) identifies sCJD lesions in the cortex, striatum, and thalami with high diagnostic accuracy (>95%). The neuropathological basis of dMRI is unknown, but a few studies suggested that the spongiform degeneration may be the main determinant. We aim at estimating vacuoles size and density from dMRI. Estimate of vacuoles size may improve pre-mortem non-invasive sCJD subtype diagnosis.

Methods

Multi-shell dMRI images from 9 probable sCJD patients and 10 age-matched healthy controls were acquired at 3T (Philips Achieva) using a Pulsed-Gradients-Stimulated-Echo (STEAM) sequence. Constant diffusion time (67ms) and different b values (1000-8000s/mm$^2$) were used in the shells. After standard data pre-processing, a tissue-inspired three-compartment model

$$S(b)/S(b=0)=f_{sticks}S_{sticks}(b,D_a)+f_{sphere}S_{sphere}(b,D_0=3\mu m^2/ms,d_{sphere})+(1-f_{sticks}-f_{sphere})S(b,D_{iso})$$

was fitted to the direction-averaged signal S(b) to estimate $f_{sticks}$ (neurites MR signal fraction), axial diffusivity $D_a$, $f_{sphere}$ (vacuoles MR signal fraction), $d_{sphere}$ (vacuoles diameter) and extra-cellular isotropic diffusivity $D_{iso}$. Bilateral regions of interest (ROIs) were manually drawn in eleven regions: precuneus, parietal, frontal, temporal, occipital and anterior cingulate cortex, insula, hippocampus, caudate, putamen, dorso-medial thalamus. The distribution of vacuole diameters, weighted by the fraction of the spherical compartment, was evaluated in the hyperintense part of each ROI.

Results

Hyperintensities on diffusion-weighted images (DWI) were found in the cortex and basal nuclei in all patients with probable sCJD. Maps of the volumetric MR signal fraction of the spherical restricted compartment showed focal areas of high density largely corresponding to DWI hyperintensities. MR-measured diameter of the spheres (vacuoles) was between 4-18µm, in agreement with histological values reported in the literature. Vacuolar size distribution varied among patients: larger diameters (13-15µm) were found in five cases; small diameters (6-8µm) were estimated in the striatum of one patient; a broader diameter distribution was found in the other three. Vacuolar size was in the noise range (0-2µm) in 10 healthy subjects.

Conclusion

Quantitative maps of MR-measured vacuolar size and density in the brain of sCJD patients are feasible. The estimated vacuolar sizes range is compatible with histopathology results. We found different distributions in 9 sCJD patients with presumably different subtypes: larger diameters were estimated in the cortex than in the striatum. In the near future, these preliminary results will have to be validated by neuropathology on the brains of these patients obtained at autopsy. If the results will be confirmed, this method will become extremely valuable for the non-invasive diagnosis of sCJD subtype, with an impact on more accurate prognosis and personalized therapy.

**COD. C03**

**Chasing True FLAIR: a three-component Magnetic Resonance Fingerprinting approach to synthetic MRI**

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Recently, there has been a development of multiparametric quantification techniques, such as QRAPMASTER[1] or Magnetic Resonance Fingerprinting (MRF)[2], providing maps of Proton Density (PD), T1 and T2 within a single acquisition. These maps can be exploited to obtain any desired contrast-weighted image by using the appropriate signal equation, potentially replacing a whole clinical exam. This approach is called Synthetic MRI. However, both the presence of multiple tissue per voxel and the effect of flowing blood are usually neglected in the signal model, leading to quantification error and artifacts in the synthetic images. This is particularly evident in synthetic FLuid Attenuated Inversion Recovery (FLAIR)[3] images, which are affected from Partial Volume Effect (PVE) due to Cerebrospinal Fluid (CSF) and signal hyperintensities due to flowing blood. It has been shown that CSF PVE can be corrected by using a multi-component signal model[4]. However, previous studies failed to correct for flowing blood: here, we incorporated this effect in the dictionary[5], correcting artifacts due to vessels, and we compared the resulting synthetic FLAIRs to true FLAIR[6] acquisitions.

Therefore, we wrote the dictionary as a weighted combination of tissue, CSF and vessel dictionaries. To compute the vessel dictionary, we used a previously introduced simplified model assuming a constant scalar velocity for the blood[5]. Velocity values from 0 to 100 cm/s were used for the blood simulation (T1=1500ms; T2=250ms).

This approach was used to reconstruct previously acquired data from 4 patients (age from 11 months to 6 years) without visible alterations and to compute corresponding synthetic FLAIR images (TI/TR/TE=1883/6000/117ms). Subject ages were chosen to test the technique for different stages of development of the brain. These synthetic images were compared to true FLAIR and to synthetic FLAIR using single-component mode and two-component model accounting only for CSF.

Our approach was able to suppress the signal from both CSF and vessels achieving a very similar contrast to the true FLAIR. This was true for each subject independently from the subject age (and therefore from the different stages of development of the brain). In contrast, naïve mono-compartment synthetic FLAIR suffered both from PVE artifacts near the ventricles and inconsistent hyperintensities within the vessels, while the two-compartment model neglecting blood flow was only able to correct PVE near the ventricles. Importantly, no modification of the acquisition pattern was required, thus previously acquired dataset can be retrospectively corrected. Moreover, the reconstruction time (420s) was still short enough to allow clinical use of the technique.

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**COD. C04**

**Changes in left ventricular volumes and mass during a 60-days head-down bed-rest assessed by cine MRI**

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Aims. Prolonged immobilization generates cardiac deconditioning, a risk factor for cardiovascular disease, also present in astronauts when returning to Earth after long-term exposure to microgravity. To measure this phenomenon, our aim was to assess the effects of 60 days strict head-down (-6 degrees) bed-rest (BR) on left ventricular volumes and mass by cine MRI.

Methods. Eleven healthy male volunteers (mean age 28±6 years, height 181±5 cm, weight 77±8 Kg) underwent 60 days BR, preceded and followed by 14 days of active hospitalization (i.e., lying in bed during the day was prohibited). The experiment was conducted at :envihab (Koln, DLR, Germany) as part of the European Space Agency BR studies, after ethical approval. A short-axis stack of cine MRI images (3T Biograph mMR, Siemens) with finger pulse gating was acquired, covering the whole left ventricle (LV) from base to apex (25 frames/cycle, slice thickness 8 mm, no overlap). Imaging was performed before (PRE), after 58 days (HDT58) of BR, and 5 days after its end (R+4).
The end-diastolic (ED) and end-systolic (ES) frames were manually selected, and semi-automatically analyzed using previously validated custom software based on 2D level-set methods to segment the LV endocardium (papillary muscles included in the cavity) and epicardium in each slice from base to apex, from which the ED and ES volumes were computed using the method of disks, and stroke volume (SV), ejection fraction (EF), and LV mass were derived, together with heart beat duration (RR) and cardiac output (CO). One-way ANOVA for repeated measures with multi-group Tukey test ($p<0.05$) was applied to test for effects of BR, and recovery.

Results. At HDT58, compared to baseline values at PRE, a significant shortening of the RR (14%) with a decrease in LV ED (19%) and ES (10%) volumes, SV (23%), EF (5%), CO (10%) and LV mass (9%) were observed. At R+4, during the recovery period, RR, ED and ES volumes, SV and EF returned to values not significantly different from PRE, while only CO resulted increased by 8% and LV mass was still decreased by 5%.

Conclusions. Cardiac adaptation to deconditioning due to immobilization induced by BR resulted in a reduction of cardiac volumes and function, together with a decrease in LV mass. Volumetric and functional variations were recovered in 5 days, while myocardial mass was only partially recovered. As BR also induces loss of plasma volume, the observed changes could be explained by a reduction in circulating blood volume, and loss of fluids in the extracellular matrix, thus reducing measured LV mass by dehydration effect. These effects are reversed once immobilization is interrupted. This information could be useful for better understanding of physiologic changes in patients undergoing long periods of immobilization and to test effectiveness of potential countermeasures to reduce cardiac deconditioning in space research.

**COD. C05**

**Machine learning classification of spinal lesions: compared accuracy of texture parameters extracted by different software**

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Purpose

To compare the accuracy of machine learning (ML) algorithms for classification of spinal lesions based on texture analysis (TA) parameters extracted by different software from unenhanced Magnetic Resonance images (MRI).

Methods and Materials

We retrospectively enrolled 146 patients with 146 spinal lesions (49 benign, 57 metastatic and 40 primary malignant lesions) imaged using MRI. Of them, 117 were subsequently histopathologically confirmed after surgery while 29 benign lesions were confirmed by follow-up. Patients were randomly divided in training (n=100) and test groups (n=46), respectively for classification model development and testing. Lesions were manually segmented on T1-weighted and T2-weighted images by drawing a bi-dimensional polygonal region of interest. These were used for first order and texture feature extraction on two software, 3D Slicer heterogeneityCAD module (hCAD) and Pyradiomics. For each of them, different data subsets, obtained by four feature selection methods were analyzed by 9 ML classification algorithms to evaluate their accuracy in identifying benign vs. malignant lesions and benign vs. primary malignant vs. metastatic lesions.

Results

In the test goup, a random forest (RF) algorithm correctly classified 89% of lesions as benign or malignant, based on hCAD TA, while a Support Vector Machine could achieve an accuracy of 87% from Pyradiomics TA. For the classification of benign, primary malignant and metastatic lesions, RF models accurately classified 70% of lesions for both TA software.

Conclusion

ML algorithms show good accuracy in spinal lesion classification based on non-contrast MRI exams. Furthermore, feature extraction performed using different software has shown consistent results at subsequent ML analysis.

**COD. C06**

## Feature Texture and Histogram Analyses of DTI and DSC to Predict Ki-67 Percentage in Brain Tumor Patients by SVM

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Introduction: Clinical MRI has an important role in diagnosis and treatment, but neoplasma has often heterogenous tissue, and tumour characterization is difficult. On the other hand, histopathology analysis has limitations, such as sampling error, variability in interpretation and aggressiveness. MRI protocols provide a rich source of information for treatment strategy. Our main purpose was to characterize DTI and PWI metrics to predict Ki-67 percentage as a cellular marker for proliferation. They may assist to planning treatment strategies and be a high accuracy predictor for prognosis. Methods: Seven with known Ki_67 index were used to represent in a machine learning analysis to predict Ki_67 percentage and prognosis. All patients underwent examination with a 3T Philips Achieve Scanner, and pre-operative brain tumour protocols consist of T1 with Gd and T2-w imaging, DTI with b-value of 800 and PWI.The ROIs were drawn on every T1-Gd and T2-w tumour section by a neuroradiologist. The registration was acquired to extract features from the ROIs on MD, FA, CBV and CBF maps.In this purpose, we extracted intensity-based features such as the mean values and standard deviation of maps and texture-based features such as contrast, correlation and homogeneity of FA and CBV maps in each slice.The predicted variables in this study was Ki_67 percentage. This index was considered to three groups, those with less than 10% , between 10% and 18%, more than 18%, respectively.We used support vector machine (SVM) for classification of Ki_67 among brain tumour patients. Results: A SVM trained model using all the features was able to classify patient Ki_67 index with accuracy 98.42% (permutation test, $P < 0.001$). The classification of Ki_67 index with using only DTImetrics achieved 96.85% accuracy (permutation test, $P < 0.001$)A SVM trained model using all the features was able to classify tumour grade with 97.38 % accuracy(permutation test, $P < 0.001$). The sensitivity and specificity for each SVM classifier were 98.41,100,95.65 and 100,97.24,100 respectively. The method might be used to investigate microstructural features of tumours. The Ki-67 protein is a cellular marker for proliferation. Since changes in diffusivity pattern of tumour are proportional with cell proliferation and cell density it might be used to predict Ki-67 index. Tumour cellularity increases with cell proliferation increase, and the ADC will be lowered due to environment restriction. Previous studies have shown that tumours with higher FA values have higher cell density, and they have high Ki-67 index which indicate greater malignancy.

**COD. C07**

**Cross-sectional approach for automatic detection of MS lesions using machine learning**

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Background

To date, no automated software for lesion outlining has been imposed in multiple sclerosis (MS). Recently, FSL has developed and validated in cerebrovascular patients, but not in MS, a supervised machine-learning algorithm (BIANCA) for the detection of white matter hyperintensities. BIANCA learns from manually segmented masks (training dataset) how to classify voxels as lesions, by using voxel intensity and spatial distribution of intensities as features. Once "trained", BIANCA can be used on a test dataset to obtain the lesion masks. BIANCA proved to be reliable and robust once the user sets a global threshold of lesion probability. Further, FSL recently developed an algorithm for determining the optimal local threshold of lesion probability (LOCATE).

Objective

To validate BIANCA on a MS patient dataset. We tested whether BIANCA performances are:

1) influenced by the training size

2) influenced by the selection of the training dataset, for a given training size

3) similar to those with BIANCA/LOCATE, making lesion segmentation fully automated

Methods

We used:

1) training dataset: 50 MS subjects

2) test dataset: 50 MS subjects

3) validation dataset: 100 MS subjects

T1, PD, FLAIR images and manually outlined masks were used. As pre-analysis, 108 different sets of lesion masks were obtained by running on the test dataset the fully trained BIANCA with 108 distinct feature combinations. Comparing these 108 sets of masks with those manually outlined, we retained the 2 settings with the highest DICE and the lowest number of false positive-negative clusters (nFPC, nFNC) for BIANCA (Setting 1) and BIANCA/LOCATE (Setting 2). For objectives 1 and 2, analyses were performed using BIANCA best setting. In detail:

1) Spearman correlation coefficient between DICE, nFPC and nFNC and training size was computed, with training size between 10 and 50

2) we created 10 distinct training datasets with size 20, generated by randomly selecting 20 subjects from the whole training dataset; for each of these datasets the masks were generated and the mean DICE obtained was used to measure the coefficient of variation (CV)

For objective 3, we ran the fully trained BIANCA and BIANCA/LOCATE for Setting1 and 2 on the validation dataset and compared with a Wilcoxon test the DICE, nFPC and nFNC obtained.

Results

1) The training size positively correlated with both DICE ($r=0.96$, $p<0.01$) and nFPC ($r=0.91$, $p<0.01$) while negatively correlated with nFNC ($r=-0.95$, $p<0.01$)

2) The mean CV was 5.02%

3) Setting 1: significant difference between BIANCA and BIANCA/LOCATE was found for nFPC (24±76, 34±133; $p<0.01$) but not for DICE and nFPN (0.59±0.18, 0.57±0.19; $p=0.59$; 5±9, 4±7; $p=0.11$). Setting 2: significant difference was found for nFPC and nFNC (16±28,37±81; $p<0.01$; 6.5±10,4±7; $p<0.01$) but not for DICE (0.57±0.17,0.59±0.19; $p=0.08$)

Discussion

BIANCA results improved as training size increased and were independent of the selection of subjects for the training dataset. BIANCA/LOCATE with optimized parameters can be equivalent to BIANCA.

**COD. C08**

**Predizione della disabilità clinica in pazienti affetti da Sclerosi Multipla tramite approccio di Machine Learning su parametri di Texture Analysis**

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IntroduzioneLa Sclerosi Multipla (SM) è una patologia demielinizzante e degenerativa cronica che rappresenta la prima causa di disabilità non traumatica in età giovanile-adulta. Nonostante il diffuso impiego di tecniche avanzate di risonanza magnetica (RM), ad oggi non è stato identificato alcun biomarcatore, che, in forma isolata, sia in grado di giustificare l'accumulo di disabilità clinica in tale patologia. Allo scopo di colmare il paradosso clinico-radiologico della SM si rivela molto promettente la Texture Analysis, che consente, attraverso l'analisi delle variazioni spaziali di intensità nei singoli voxel, l'identificazione di caratteristiche non risolvibili alla semplice analisi qualitativa delle immagini. Materiali e metodiPer questo studio sono stati arruolati 79 pazienti affetti da SM, con diagnosi secondo i criteri di McDonald. Per ognuno di questi soggetti, un neurologo ha valutato e documentato la scala Expanded Disability Status Scale (EDSS) come indice di gravità di malattia. Tutti i soggetti sono stati sottoposti ad esame RM su apparecchiatura a 3T con acquisizione di un volume 3D pesato in T1 insieme ad un volume 3D-FLAIR. Sulle immagini FLAIR le lesioni iperintense della sostanza bianca sono state segmentate tramite metodo semiautomatico (Jim 7; http://www.xinapse.com/home.php), mentre sul volume T1 sono stati segmentate sostanza grigia corticale e profonda, oltre che la sostanza bianca. La sequenza FLAIR è stata poi co-registrata al volume T1, per estrarre regioni di interesse da entrambe le sequenze.Per ogni regione di interesse sono state estratte 26818 feature utilizzando un software open source, Pyradiomics (v 2.1.2). Queste erano suddivise in provenienti dall'analisi dell'istogramma e dalle matrici di co-occorenza, run length, size zone, neighboring gray tone difference e dependence ottenute dalla distribuzione dei livelli di grigio dei voxel all'interno di ciascuna delle 11 ROI su ognuna delle 2 sequenze. Si è proceduto quindi alla selezione di sottogruppi di parametri da sottoporre ad analisi. I dataset così ottenuti sono stati quindi analizzati con un software di data mining (Weka, v3.8) per sviluppare un modello di regressione basato sul machine learning che fosse predittivo dell'EDSS. La validazione del modello è stata ottenuta su un gruppo di pazienti separato usato come test (25% della popolazione totale).RisultatiI 79 pazienti affetti da SM inclusi nell'analisi (M/F=44/35; età=41,5±11,0; 54 pazienti con forma Recidivante Remittente, 25 Progressivi) mostravano un valore mediano di EDSS di 3.5.L'approccio migliore per la selezione delle feature si è rivelato il subset evaluator che, tenendo conto del valore predittivo dei parametri contestualmente al loro grado di ridondanza, ha prodotto un dataset contenente 47 feature. In dettaglio, 22 provenienti dalla T1 e 25 dalla FLAIR con una prevalenza di parametri derivati dalla grigia profonda. La Support Vector Machine, con kernel Radial Basis Function, ha infine ottenuto un coefficiente di correlazione dall'analisi di regressione di 0.87, un errore assoluto medio di 0.53 ed un errore quadratico medio di 0.67.ConclusioniIl nostro approccio di machine learning, basato su parametri di texture analysis principalmente derivanti dalla sostanza grigia profonda, si è rivelato un metodo robusto ed efficace nella predizione della disabilità clinica globale in pazienti affetti da SM.

**COD. C09**

**MRI investigation of the therapeutic efficacy of liposomal doxorubicin modified with a bombesin peptide analogue in experimental model of prostate cancer.**

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Background: It is well known that anticancer drugs can increase their efficacy when incapsulated in nanoparticles thanks to enhanced blood half-life and selective delivery in cancer tissue where vasculature is caracterized by increased permeability. Moreover, nanoparticles can be functionalized in order to increase their uptake by cancer cells. In this study, liposomal doxorubicin, a clinically approved nanoparticle formulation of doxorubicin, has been modified with a synthetic bombesin peptide analogue able to target GRP (gastrin releasing peptide) receptors. The efficacy of this new nanotechnological fornmulation of doxorubicin has been investigated in vivo by MRI.

Methods: Xenografts of PC-3 cells were obtained by subcutaneously injecting 2-3*$10^6$ cells (50% in volume with Matrigel$^{TM}$) in nude mice. When tumors reached a volume of 100–150 $mm^3$, mice were randomly distributed into three groups (n = 12) and intravenously administered with a single dose of saline buffer (CTRL), pegylated liposomal Dox modified with the bombesin peptide (Doxil-BNAA1), and untargeted liposomal Dox at 10 mg/kg dosage (Doxil). MRI monitored tumor growth every 4 days for the following 36 days. 3D T2w and DW images were used. The synthesis of Doxil-BNAA1 has been described in Accardo et al., 2019.

Results: From 20 days after the treatment onward, both Doxil-BN-AA1 and Dox treated groups differ significantly from the CRTL group. Moreover, 32 and 36 days after the treatment, the Doxil-BNAA1 group showed significantly smaller average tumor volume than the Dox group. Results obtained by using DWI confirm the better therapeutic profile of Doxil-BN-AA1: the average apparent diffusion coefficient (ADC) in Doxil-BN-AA1 group is significantly higher than in pegylated liposomal Dox group ($p < 0.05$) and significantly higher than in CRTL group, at 12 days after treatment. The pegylated liposomal Dox group was not statistically different from CRTL. Interestingly enough, DWI was able to detect the effect of the drug after 12 days of treatment when no difference was detectable in the tumor volume.

Conclusions: MRI experiments performed in an animal model of PC-3 xenografts demonstrated that liposomal doxorubicin modified with a bombesin peptide analogue is more effective than clinically approved liposomal doxorubicin. In particular DWI was able to detect early the effect.

References: Accardo et al., Easy formulation of liposomal doxorubicin modified with a bombesin peptide analogue for selective targeting of GRP receptors overexpressed by cancer cells. Drug Deliv Transl Res. 2019 Feb;9(1):215-226.

**COD. C10**

**B3 breast lesions diagnosed at image-guided biopsy: can DWI spare surgical biopsy?**

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To evaluate diffusion weighted imaging (DWI) as an adjunct to contrast-enhanced MRI (CE-MRI) for lesion of uncertain malignant potential (B3) at percutaneous biopsy performed under mammography or ultrasound guidance.Eighty-two of 1,464 (5.6%) percutaneous core needle biopsies, were pathologically classified as B3. Thirty-one women aged 52 ± 10 years (mean ± standard deviation) having 32 B3 lesions and preoperative 1.5-T CE-MRI with DWI (b=0 and b= 750 s/mm$^2$) entered the analysis. Reference standard included final pathology of surgical specimens or negative imaging follow-up. DWI and apparent diffusion coefficient maps were qualitatively evaluated. Enhancing lesions with negative DWI were considered negative for combined assessment (CE-MRI+DWI).There were 10/32 (31%) atypical ductal hyperplasias, 20 (63%) papillary lesions with atypias, 1 (3%) phyllodes tumor, 1 (3%) fibroadenomatoid hyperplasia. All but one (31/32, 97%) were recommended for surgery. Upgrade rate was 8/32 (25%): 1 (13%) invasive ductal, 6 (19%) ductal in situ carcinomas (DCIS), and 1 (13%) malignant phyllodes tumor. Thirty of 32 (94%) lesions exhibited contrast-enhancement but only 8/30 (25%) were malignant. Of 22 false positive enhancing lesions, DWI correctly downgraded 4 (18%) while it missed 2/8 low-grade DCIS. Sensitivity and specificity were 8/8 (100%) and 2/24 (8%) for CE-MRI and 6/8 (75%) and 6/24 (25%) for CE-MRI+DWI. This preliminary series shows that DWI may be used for reducing the rate of false positive CE-MRI in the B3 setting, with only low-grade DCIS as false negative.

**COD. C11**

## Automated diagnosis of prostate cancer of the transition zone using multiparametric MRI and quantitative radiomic analysis

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Purpose: To implement a quantitative radiomic approach to develop a machine learning classifier based on multiparametrc MRI (mpMRI) images of the prostate, capable of diagnosing the presence of prostate cancer (PCa) of the transition zone.
Methods and Materials: Fifty-three patients with elevated PSA who underwent mpMRI were included in the study. Inclusion criteria were: PI-RADS score assessment of 3 or higher for lesions within the transition zone, a subsequent TRUS-MRI targeted fusion biopsy and no prostate biopsies or interventions in the previous 6 months. Lesions within the transition zone were manually segmented by a trained urogenital radiologist on the T2-weighted images and on the ADC maps using 3D Slicer, yielding a Volume of Interest (VOI) for each lesion. A radiomic approach was implemented in Python to extract features from the VOIs that correlated with the presence of histologically-proven PCa. Extracted features were then selected on univariate analysis and subsequently fed to a machine learning random forest classifier using the R statistical software package. Statistical analyses, including sensitivity, specificity, accuracy and ROC analysis, were performed on the trained classifier.
Results: Of the 53 patients 22 (42%) were positive for PCa at histopathology. Radiomic analysis calculated 368 quantitative features for each VOIs. A predictive model using the features selected on univariate analysis achieved a sensitivity of 0.74, specificity of 0.68 and overall accuracy of 0.71.
Conclusion: The machine learning classifier based on mpMRI radiomic analysis showed higher accuracy than radiologist assessment in detecting PCa of the transition zone.

**COD. C12**

**MRI predictive role in patients with adenoid cystic carcinoma treated with carbon ion radiotherapy**

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Purpose

To evaluate MRI parameters for prediction of carbon ion radiotherapy (CIRT) response in patients diagnosed with adenoid cystic carcinoma (ACC).

Methods and materials

We retrospectively enrolled 52 patients (56.5 ± 15.5 years old, male/female ratio = 25/27) diagnosed with ACC, who received CIRT at CNAO (National Center of Oncological Hadrontherapy) between 2013 and 2017. Morphological and DW-MRI with 3 b-values (0, 400, 800 or 1000 [s/mm$^2$]) were performed before (baseline-MRI) and after CIRT. Based on volume reduction, DWI and contrast enhancement features, patients were classified as complete response (CR), partial response (PR), stable disease (SD) or progression disease (PD) at the time of the best MRI response (Best-MRI) and the more recent MRI examination (Last-MRI). Volume, mean/median/skewness ADC values at baseline-MRI were compared with CR, PR, SD and PD subgroups of patients classified at best-MRI and last-MRI. ROC analysis was performed to calculate the optimal cutoff points for a global multiparametric model (volume, mean, median and skewness ADC values). Kruskal-Wallis test was used for statistical analysis.

Results

Best results were obtained when compared CR patients with the other subgroups (PR, SD, PD: ALL group). 15 patients were classified CR vs 37 classified ALL group at best-MRI, while 17 patients were classified CR vs 35 ALL group at last-MRI. Time difference between best-MRI and baseline-MRI was 7.4 ± 7.1 months; time difference between last-MRI and baseline-MRI was 25.7 ± 13.3 months. Baseline-MRI volume resulted significantly different between CR and ALL group at best-MRI ($p=0.004$). Baseline-MRI mean, median and skewness ADC values were significantly different between CR and ALL group at best-MRI ($p<0.04$). Baseline-MRI skewness ADC values were significantly different between CR and ALL group at last-MRI (p-value=0.008). Time difference between last-MRI and baseline-MRI was also significant between the two groups of patients ($p=0.03$).

0.053, 0.714 were the optimal cutoff points identified in CR vs ALL group at best-MRI (Sensitivity 71%, Specificity 95%, AUC 0.859)

Conclusion

In our study, volume and ADC values at baseline-MRI showed a good correlation in the assessment of treatment response, resulting effective in predicting therapy response.

**COD. C13**

**Quantitative susceptibility mapping of the precentral gyrus in motor neuron disease: a fully-automatic pipeline**

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Introduction

Motor Neuron Disease (MND) is a group of neurodegenerative disorders primarily affecting motor neurons. Regional variants restricted to the arms, legs or bulbar region as well as different patterns of clinical expression (distal or proximal, symmetric or asymmetric) are well-known [1]. Amyotrophic Lateral Sclerosis (ALS) is the most common MND and is characterized by degeneration of both upper and lower motor neurons. Precentral gyrus susceptibility changes have been investigated in ALS with T2*-weighed imaging, Susceptibility-weighted imaging (SWI) and Quantitative susceptibility mapping (QSM) based on hand-drawn ROIs and/or visual inspection [2,3,4]. Susceptibility increase is observed in both cortex and subcortical white matter probably due to iron overload and myelin content decrease respectively. However, measurements were strongly user-dependent and time consuming. We developed and applied a fully-automatic image processing pipeline to investigate the susceptibility properties of the precentral gyrus in MND.

Methods

51 MND (61.21 ±9.63 y) and 25 Healthy Controls (HC, 57.32 ±7.30 y) were enrolled and scanned in 3T General Electric (GE) SIGNA unit. A 3D sagittal FSPGR BRAVO T1w (TR=8.7ms, TE=3.2ms, TI=450ms; Pixel 0.5x0.5mm, thickness=1mm, spacing=1mm, FA=12°, matrix 256x256) and a spoiled gradient-echo multiecho (TR=39ms, 7 equally spaced echoes centered at 24ms, Pixel 0.47x0.47mm, thickness=1.4mm, spacing=0.7mm, FA=20°, matrix 416x320) whole-brain sequences were acquired. FSL Brain Extraction Tool provided the brain mask from magnitude image. QSM was perfomed by using the Matlab toolbox STI Suite [5]. Streaking artifacts reduction (STAR) QSM algorithm was adopted [6]. QSM was coregistered to T1w image with a mutual information-based rigid transformation in SPM12 and automatic segmentation of brain regions was performed in Freesurfer. Precentral gyrus cortex (PreGC) and subcortical white matter (PreGSubcWM) ROIs were extracted. Mean susceptibility and skewness of the susceptibility distribution were calculated in the PreGC and PreCSubcWM ROIs and statistically analyzed in SPSS.

Results

In PreGC, mean susceptibility was higher in MND but not statistically different from HC (p=0.139) while skewness was statistically significantly higher (p=0.002) in MND compared to HC. In PreGSubcWM, mean susceptibility (p=0.005) and skewness (p=0.039) were significantly higher in MND compared to HC. Mean susceptibility in PreGSubcWM showed a significant correlation with disease duration (Sig=0.033, r=0.26) and ALS Functional Rating Scale (ALSFRS, Sig=0.026, r=#0.42).

Discussion

The automatic ROI-based approach allows to obtain measurements that are irrespective of both pathology localization and lateralization. Automatic ROIs are not guided by the pathological changes occuring in precentral gyrus in MND patients that on the contrary may influence the ROI manual drawing. The hand drawn ROI-based approach is time consuming, user-dependent and difficult to perform due to the small size of the target structure leading to poor measure reproducibility. On the other hand, the metric of susceptibility mean calculated on this large automatic cortical ROI may lose significance: the values of the voxels with increased susceptibility are indeed averaged with all the other voxels compounding the bilateral PreGC. In addition, cortical voxels largely suffer from partial volume effects especially in standard resolution scans. On the contrary, skewness of susceptibility distribution in PreGC is sensitive to susceptibility changes in MND measured on the automatically-segmented bilateral PreGC. In PreGSubcWM, which is less affected by partial volume effects, automatically-measured mean susceptibility is able to highlight white matter anomalies likely linked to degeneration of myelinated fibers. The diagnosis of MND is a long process and there is no single definitive test, the process involves careful clinical and neurological examination during a long period of time [7]. An automatic non-invasive tool able to characterize the precentral gyrus with quantification of susceptibility properties of cortex and subcortical white matter would be beneficial in building a biomarker of pathology in MND.

Conclusion

A fully-automatic pipeline have been applied to quantitatively study the susceptibility properties of the precentral gyrus in MND. Our study suggests that the building of a MND biomarker might rely on susceptibility skewness in PreGC and susceptibility mean in PreGSubcWM automatically measured on clinical images. The pipeline may be easily adapted to widen the measurements pool and be applied on other neurodegenerative disorders.

**COD. C14**

**Quantitative Susceptibility Mapping in Parkinson's disease and atypical parkinsonisms**

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INTRODUCTION

Differential diagnosis among Parkinson's disease (PD), Progressive Supranuclear Palsy (PSP) and Multiple System Atrophy (MSA) can be challenging. In these diseases, abnormal iron deposition in the substantia nigra (SN) and in other brain structures has been documented but cannot be revealed using conventional MR techniques. Quantitative Susceptibility Mapping (QSM), which allows estimating tissue iron concentration, could improve the detection of early microstructural changes in the disease course. Therefore, we measured the magnetic susceptibility ($\chi$) of brain regions affected by pathology in order to explore QSM as a tool for an early differential diagnosis among PD, PSP and MSA.

METHODS

We enrolled 65 patients (36 PD, 14 MSA, 15 PSP) who underwent a clinical evaluation, including the assessment of disease severity with the Unified Parkinson's Disease Rating Scale II-III subscores, and a 3T-MRI exam of the brain.The MR protocol included two 3D multi-echo T2*-weighted sequences. One sequence targeted the midbrain, had spatial resolution of $0.4\times0.4\times2mm^3$ and was used for visual inspection of SN. The other one targeted basal ganglia and midbrain, had spatial resolution of $0.93\times0.93\times1mm^3$, and was used to generate QSM and measure relative $\chi$ ($\Delta\chi$) in 5 sub-regions of SN, in red nuclei (RN), subthalamic nuclei (STN), putamen, globus pallidus and caudate (reference ROI in the subcortical white matter of the right occipital lobe).

All statistical analyses were made using non-parametric tests.

RESULTS

The radiological anatomy of SN was abnormal in 88.6% of PD patients, 91.7% of MSA patients and in all PSP patients without difference among groups (P>0.68).

$\Delta\chi$ of each nigral ROI was higher in PSP then in MSA and PD patients, with significant differences in the medial (P=0.002) and ventral regions (P=0.044).

$\Delta\chi$ of RN was higher in PSP than in MSA and PD patients (P<0.001), and showed the highest accuracy in differentiating PSP from PD (AUC=0.93) and MSA patients (AUC=0.83).

$\Delta\chi$ of the putamen was higher in MSA than in PSP and PD patients (P=0.002), and showed the highest accuracy in differentiating MSA from PD patients (AUC=0.82).

In STN, the highest $\Delta\chi$ was recorded in PSP patients (P<0.001).

Disease severity showed a positive correlation (P<0.05) with $\Delta\chi$ of the medial, lateral and ventral region of SN, and with $\Delta\chi$ of STN, RN and putamen.

CONCLUSION

The visual inspection of SN using T2*-weighted images did not reveal differences among PD, MSA and PSP patients, whereas $\Delta\chi$ showed different patterns of iron accumulation within nigral and extranigral structures which reflect the pathology of each disease. Indeed, PSP patients showed the highest $\Delta\chi$, mainly in the medial part of SN and in the RN, whereas MSA patients showed the highest $\Delta\chi$ in the putamen. The correlation between disease severity and $\Delta\chi$ of many nigral and extranigral regions supports the hypothesis of a relationship between clinical worsening of patients and increasing iron deposition. Therefore, QSM could be explored as a tool to identify nigral end extranigral changes for an early discrimination among the main forms of degenerative parkinsonisms.

**COD. C15**

**A Machine Learning Approach to QSM: Susceptibility Map Reconstruction with Convolutional Autoencoders**

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Quantitative susceptibility mapping (QSM) is a recent MRI application, which provides maps of the magnetic susceptibility distribution in tissues from gradient echo phase data. Measurements of magnetic susceptibility allows us to investigate tissue composition and microstructure. QSM is a promising neuroimaging tool, which can be used to analyse traumatic brain injury, tumours, DBS electrode positioning, vascular and neurodegenerative diseases (A. Deistung et al., NMR Biomed,2017).

However, an ill-posed inversion problem has to be solved to obtain a magnetic susceptibility map. There are several methods to overcome this issue (S. Wharton et al.,Neuroimage,2010). One approach is based on multiple-orientation acquisitions (Calculation Of Susceptibility through Multiple Orientation Sampling - COSMOS). Others use single-orientation acquisition and they are based on numerical strategies, such as inverse filtering (Threshold-based K-space Division - TKD) and iterative methods.
The COSMOS technique aims to obtain high quality susceptibility distribution with reduced presence of artifacts, but requires a long acquisition time with the subjects having to move their head to different orientations with respect to the main magnetic field of the scanner. The TKD method is faster, but the results are more affected by artifacts and noise.
A compromise between accuracy and acquisition time has to be found in order to use the QSM method in clinical applications. Recently deep Neural Networks (NNs) have been applied to this problem (J. Yoon et al.,Neuroimage,2018).

Convolutional neural networks (CNNs) are a specific class of artificial NNs, which are nowadays being heavily used in many imaging tasks, including segmentation, recognition, denoising and reconstruction.
In this work, we have used NET, a fully convolutional autoencoder, to obtain the susceptibility map of a human brain, starting from single-orientation NMR phase measurements. The NET architecture includes long and short skip connections, as residual learning tools. Data from the $QSM_{2016}$ Challenge (C. Langkammer et al.,MR Med,2017) were used for this study. Supervised learning processes were performed, both with 2D (axial, sagittal and coronal slices) and 3D dimensional input data. Patches from multiple-orientation phase maps were used as input data, and the corresponding patches from the COSMOS map were used as label data. To create the training dataset, data augmentation techniques were computed.
NET susceptibility reconstructions were compared with those produced with the TKD method, using the COSMOS map as a reference for both. Similarity parameters (RMSE, pSNR, SSIM and HFEN) were studied, focusing on the caudate, putamen, red nucleus, globus pallidus and substantia nigra. The NET approach shows better performance with respect to all the criteria.
To enhance the results, contrast analysis inside the ROIs was also carried out, and the performance of the three techniques were compared. The NET and the COSMOS approaches shows similar results.

The proposed NET method is a single-orientation approach to QSM. It is as fast as other numerical approaches, but more accurate and less noisy than them. The NET method, applied to 2D- and 3D- data, produces results that are consistent with the gold-standard COSMOS method.

**COD. C16**

**Along-tract statistics of NODDI diffusion metrics enhances MR tractography quantitative analysis in healthy controls and in patients with glioma**

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INTRODUCTION: Novel techniques have been proposed to statistically quantify along white matter tracts 'classical' Diffusion Tensor Imaging (DTI)-derived metrics, such as mean, axial and radial diffusivities (MD, AD, RD) and fractional anisotropy (FA). Neurite orientation dispersion and density imaging (NODDI) enables an even more specific characterization of microstructure by estimating the relative contribution of different diffusion compartments to the total diffusion signal in each voxel, quantifying neurite density and orientation dispersion. Thus, we propose a novel along-tract quantitative analysis of NODDI-derived metrics within seven eloquent white matter tracts, combining the specificity of NODDI and the ability of along-tract approach to scrutinize microstructural tract variability in healthy volunteers and glioma patients.

METHODS: Fifteen controls and seven glioma patients underwent multi-compartmental diffusion MRI (dMRI) at 3T as part of the EU's Horizon EDEN2020 project, funded to our group. dMRI data were collected using simultaneous multislice EPI acquisition with two shells (b=711 and 3000s/mm$^2$, 35 and 60 directions). 60 slices with isotropic voxels of 2mm$^3$ and 12 b=0 images were obtained, one with reversed phase-encoding to correct susceptibility-induced distortions. Diffusion tensors were estimated and MD, AD, RD and FA maps were calculated at b=711 and b=3000s/mm$^2$. The NODDI model was fitted to data; maps were derived for orientation dispersion index (ODI) and for fraction of neurite density (FICV), extra-cellular volume (FECV) and free fluid (FISO). For every subject, 7 eloquent fiber bundles were reconstructed bilaterally by probabilistic HARDI Tractography based on a q-ball residual bootstrap algorithm. For each tract, raw streamlines were re-parameterized using cubic B-spline curves and resampled into 100 vertices spread evenly along their lengths. Correspondence between nearest points across the tract transverse sections was matched, obtaining a skeleton of each tract. Then, NODDI and DTI maps were resampled at the new streamline vertices and collapsed to gain average diffusion metrics at multiple locations along tracts. A group analysis was performed in healthy controls; average values and 95% CI were displayed in line graphs.

RESULTS: We constructed a robust reference database of along-tract microstructural values to describe the anatomical variability of NODDI metrics within tracts of healthy controls. Our analysis reliably segregates signals arising from the intraneurite, extraneurite and free CSF compartments for the entire fiber trajectories. Along healthy fascicles, free water is almost absent and the highest density of neurites is mirrored by the lowest extracellular volume fraction. Neurite density and orientation dispersion, the two key drivers for FA, were estimated individually along tracts. FA profiles show strong inverse correlation to ODI and weakly positive correlation with FICV. In glioma patients, we demonstrated the effectiveness of such along-tract approach in an example analysis of tracts running nearby tumor margins. When compared to reference control curves, patient-specific along-tract analysis localizes and quantifies microstructural differences of pathological tracts with respect to normal ones.

CONCLUSIONS: Estimating NODDI-derived microstructural diffusion along fibers enhances the specificity of quantitative tractography both at group and at subject-specific level. Initial observations in glioma patients possibly provide quantitative signatures of the microstructural changes of peritumoral tracts.

**COD. C17**

**How to improve the equivocal category PI-RADS score 3? Quantitative multiparametric MRI assessment of prostate cancerous and non-cancerous tissue using correlative histopathology.**

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Purpose: PI-RADSv2 is the most widespread scoring system for Multiparametric MRI of the prostate (mpMRI). However there is a consistent number of patients that fall in the equivocal group of PI-RADS 3. The aim of the study is to stratify patients with PI-RADS category 3, which might undergo TRUS-MRI targeted biopsy, by quantitatively analyzing mpMRI parameters (ADC, k-trans, K-ep and ve). Materials and Methods: Among the 1272 men who underwent mpMRI for PCa suspicion at our centre from January 2015 to March 2018, we retrospectively enrolled 98 patients who were subsequently treated with radical prostatectomy. We also selected 100 patients suspected of harboring PCa with at least one negative systematic prostate biopsy, at least two negative mpMRI exams, and a minimum follow-up of 60 months. All exams were performed at 3T and the protocol was PI-RADSv2-compliant. The mpMRI exams of the final patient population of 198 patients were randomly reviewed in consensus by two radiologists, blinded to both clinical data and histopathology reports. Quantitative analysis was performed on all lesion classified as PI-RADSv2 category 3, measuring pharmacokinetic parameters (k-trans, k-ep and ve) from perfusion study, and ADC values calculated from DWI sequences.

Results: The median patients age was 62, the median PSA was 6,32 ng/mL, the median PSA density was 0,12 ng/mL$^2$. A total of 95 PI-RADS 3 lesions were identified. Mean ADC value of 79,785 mm$^2$/s (95% CI = 75,427 to 84,143), mean k-trans of 0,273 min$^{-1}$ (95% CI= 0,229 to 0,316), mean k-ep of 0,532 min$^{-1}$ (95% CI = 0,462 to 0, 623) and mean ve of 0,71 (95% CI = 0,236 to 0, 317). Receiver operating characteristic analysis and area under curve were determined to identify a cut-off value to define which PI-RADS 3 lesion should be biopsied by TRUS-MRI targeted biopsy and which ones needed not to be biopsied. Patients were therefore stratified in two subgroups, according to their fate after mpMRI. Conclusion: Quantitative analysis of multiparametric MRI parameters might help to objectively stratify equivocal PI-RADS 3 lesions, to define the correct patients' diagnostic planning (biopsy or follow-up).

**COD. C18**

**Valutazione con RM della risposta a chemio-radioterapia nel tumore localmente avanzato del retto: ruolo delle volumetrie in T2 e in Diffusione e dell'analisi di istogramma dell'ADC volumetrica**

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Obiettivo del nostro studio è stato valutare il potenziale ruolo delle volumetrie nelle sequenze T2 e DWI pesate e dell'analisi di istogramma delle mappe di ADC nel predire la risposta istopatologica alla CRT neoadiuvante.Trentuno pazienti con adenocarcinoma localmente avanzato del retto sono stati sottoposti a RM a 1.5T prima, durante e dopo CRT. Ad ogni time-point sono stati calcolati i seguenti parametri: volume tumorale nelle sequenze pesate in T2 (VT2) e nelle sequenze ad alti valori di b(Vb1000), percentuale di variazione volumetrica nel tempo ($\Delta$VT2 e $\Delta$Vb1000) e parametri di texture di 1°ordine delle mappe volumetriche di ADC. Dopo chirurgia i pazienti sono stati classificati in relazione al Grado di Regressione Tumorale(TRG) in Responder Completi(RC-TRG4),Responder Parziali(RP-TRG3) e Non-Responder(NR-TRG 0-2). I predittori delle classi di risposta sono stati selezionati con l'analisi di regressione multipla e le curve ROC. In relazione al TRG,9 pazienti sono risultati RC,14 RP e 8 NR. Valori di 3D-ADC pre-trattamento più elevati (>1.198), maggiore $\Delta$VT2w durante(-58.5%) e dopo CRT(-82.5%) e minori valori di Vb,1000 post-trattamento(<2.52cc) sono risultati predire i RC con accuratezza rispettivamente del 84%,81%,84% e 87%. Vb1000 >36.35cc e 3D-ADC <1.085 prima della CRT sono risultati predire i NR con accuratezza di 87% e 81%, mentre $\Delta$VT2w -69% post-CRT prediva NR con accuratezza di 81%. Valori maggiori di skewness della 3D-ADC pre-CRT sono risultati associati a NR (p=0.05). La 3D-ADC potrebbe aiutare a predire la probabilità di risposta alla CRT pre-CRT , la $\Delta$VT2 è utile nel distinguere la risposta patologica durante trattamento, mentre Vb1000 sembra aiutare a identificare i RC post-CRT.La valutazione volumetrica della DWI potrebbe aiutare a predire il TRG preCRT e identificare i RC post-CRT mentre la $\Delta$VT2 sembra promettente nel distinguere la risposta patologica durante il trattamento.La 3D-ADC pre-CRT e il volume in b1000 potrebbero aiutare a predire la probabilità di risposta, mentre la $\Delta$VT2 sembra promettente nel distinguere la risposta patologica durante il trattamento.

**COD. C19**

**In vivo MRI detection of USPIO labeled exosomes in an experimental model of multiple sclerosis.**

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Background/Aims: Adipose stem cells (ASCs) are of great interest for potential therapeutic applications due to easy availability, to ability to migrate to damaged tissue and contribution in reparative processes [1-2] Literature findings indicate that ASCs exert their action through paracrine activity [3-4] mediated by the release of exosomes and several authors support the idea that exosomes can recapitulate the neuroprotective effect of stem cells and suggest their use for a noncell-based therapy of neurodegenerative diseases, including multiple sclerosis [5-6-7] Nevertheless, elucidation of the action mechanism of exosomes requires knowledge of their homing and the ability to track exosomes with a non-invasive and longitudinal imaging method, such as magnetic resonance imaging (MRI), becomes crucial. The aim of this work is to visualize and track labeled ASC-derived exosomes in vivo by MRI after intranasal administration in an experimental model of multiple sclerosis (EAE). The assessment of temporal and spatial homing of exosomes in EAE murine model, could provide further information on the site of action of exosomes giving insights in the cell target involved and in their therapeutic effect.

Methods: Exosomes were labeled as reported in Busato et al. [8] 2017 with USPIO (5 mg/ml Fe). A total of n = 10 animals was used: EAE (n =5 ) and healthy (n =5 ) mice. Mice were i.n injected with exosomes-USPIO at the onset of disease and MRI acquisition were performed after 3 and 24 hours from injection. T2* map images were acquired using a Multi Gradient Echo sequence with TR =2000 ms, TE =3.6 ms, FOV =2×1.5 cm2, MTX =160/120, slice thickness =0.5 mm. After the last MRI acquisition the brain was dissected out for histochemical analysis (Prussian Blue staining).

Results/Conclusion: The results show that with MRI we are able to detect exosomes-USPIO in the brain of the animals after 3 hours from the injection. In particular, in healthy mice the homing of exosomes seem to be randomly distributed, while in EAE mice we detected black spots (MRI decreased signal intensity) only in the cerebellum, near injured regions. The Prussian blue staining confirmed the presence of iron in the region detected by MRI in both healthy and EAE mice. After 24 hours, the iron nanoparticles were not detected in the brain, indicating that at this time point the exosomes have probably reached other target site, i.e the spinal cord. Further experiment will be conducted by Magnet Particle Imaging to confirm our results.

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**COD. C20**

**Cortico-striatal pathway integrity in Fabry Disease: a diffusion connectometry study**

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IntroductionRecent evidences have suggested the possible presence of an involvement of the extrapyramidal system in Fabry Disease (FD), a rare X-linked lysosomal storage disorders with a reduced functional connectivity between the motor cortex and the striatum. Although widespread alterations of the white matter (WM) microstructural integrity occur in FD, to date no information about integrity of cortico-striatal fibers are available.Aim of this study was to investigate the microstructural integrity of the cortico-striatal connections in FD patients to investigate the possible presence of structural connectivity changes in these connections, expanding the current knowledge about motor involvement in FD.MethodsIn this study, 47 FD patients (M/F=19/28, mean age 42.3±13.1 years), and 49 healthy controls (HC) (M/F=21/28, mean age 42.3±16.3 years) were enrolled. All subjects underwent MRI scan on the same 3T scanner (Trio, Siemens, Germany). Diffusion Tensor Images (DTI) were acquired with a voxel size of 2.2×2.2×2.2 $mm^3$, 64 directions with b-value=1000s/$mm^2$ and nine b=0s/$mm^2$, along with a 3D FLAIR sequence and a 3D T1-weighted volume, both with a voxel size of 1x1x1$mm^3$. WM lesions were segmented using a semi-automated method, and T1-weighted images were accordingly filled, with the intracranial volume (ICV, as the sum of GM, WM and cerebrospinal fluid) that was obtained for each participant. DTI images were then corrected for motion and eddy currents, and Fractional Anisotropy (FA), along with axial (AD), radial (RD) and mean diffusivity (MD) maps were computed for each subject using MRtrix. Anatomically-Constrained Tractography (ACT) with iFOD2 algorithm was performed to obtain 1 million streamlines. The connectomes were built using the standard Desikan-Killiany atlas, implemented in FreeSurfer. For each subject, DTI metrics and connectomes were combined to carry on diffusion MRI connectometry.Values corresponding to bundles connecting the precentral gyrus (PreCG) with the striatum (as caudate nucleus and putamen) were extracted, and a Generalized Linear Model was employed to compare the two groups, with age, gender and ICV added as covariates. Results were considered significant for $p<0.05$ (Bonferroni corrected for multiple comparisons).ResultsWe found a significant reduction of mean FA values of the left cortico-striatal fibers (0.43±0.02 vs 0.41±0.02 for HC and FD, respectively, p=0.001), coupled to an increase in MD ($0.67\cdot10^{-3}\pm0.02\cdot10^{-3}mm^2/s$ vs $0.68\cdot10^{-3}\pm0.03\cdot10^{-3}mm^2/s$, p=0.001) and RD ($0.50\cdot10^{-3}\pm0.02\cdot10^{-3}mm^2/s$ vs $0.52\cdot10^{-3}\pm0.03\cdot10^{-3}mm^2/s$, p<0.001) values, while no differences emerged when AD maps were evaluated ($1.00\cdot10^{-3}\pm0.03\cdot10^{-3}mm^2/s$ vs $1.01\cdot10^{-3}\pm0.03\cdot10^{-3}mm^2/s$, p=0.11). When evaluating cortico-striatal connection on the right side, a trend of reduced mean FA was found in FD patients compared to HC, not reaching the statistical significance (0.41±0.02 vs 0.40±0.03, p=0.07), while no differences emerged for the remaining variables (p=0.26, p=0.97 and p=0.14 for MD, AD and RD, respectively).ConclusionWe confirmed the presence of an alteration of the extrapyramidal system in FD patients, in line with the recent evidences suggesting the presence of brain changes as a possible reflection of the subtle motor symptoms present in this condition. In particular, our results show that along with functional changes, a microstructural damage of this pathway, predominantly affecting the left cortico-striatal connections, is present in FD patients.

**COD. C21**

**Cerebral blood flow hypoperfusion in TLE**

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Introduction: In drug refractory temporal lobe epilepsy (TLE) pathological examination after temporal lobectomy identifies hippocampal sclerosis (HS) or other focal lesions/malformations, which are often not detected at structural MRI (1). Arterial Spin Labeling (ASL) MRI measures cerebral blood flow (CBF) in a totally non-invasive way. Early studies in focal epilepsy have demonstrated ASL sensitivity to detect focal hypoperfusion within the epileptogenic area (2), which can be clinical relevant especially in MRI-negative patients.This pilot study attempted to characterize CBF alterations in TLE patients with or without HS at histological analysis after temporal lobectomy.

Methods: 18 TLE patients (9 left TLE, 6 males, and 9 right TLE, 2 males) and 26 controls (CTR) (13 males) were recruited within the 3TLE* project. After temporal lobectomy, histopatological analysis revealed HS (5 cases, 3 left and 2 rights), focal lesions (1 left cavernous hemangioma and 2 right ganglioglioma), focal cortical dysplasia (1 left and 1 right) and gliosis (4 left and 4 right). A multi-parameter mapping protocol, including 3D multi-echo PD, R1 and MT-weighted scans, and an ASL sequence (FAIR 3D GRASE multi-segment single-TI) were acquired using a Siemens Skyra 3T scanner (Siemens AG, Erlangen, Germany). ASL images were corrected for distortions and motion (FSL) and CBF maps were obtained following Buxton's model (3). CBF maps were deprived of negative (non-physiological) values and upper thresholded at 100 [ml/100 g/min] to remove vascular influence. High-resolution MT images were segmented, parcellated according to the MICCAI atlas and registered to CBF maps with ANT's. In this preliminary analysis, mean CBF and CBF asymmetry index, were obtained for each cerebral lobe and, within the temporal lobe, at gyral level.A one-way ANOVA analysis (significance at $p < 0.05$ corrected for multiple comparisons) was performed to identify significant differences in CBF and CBF asymmetry between CTR, right TLE and left TLE. The same comparison was performed between CTR and each histological subgroup.

Results: Hippocampal and parahippocampal asymmetry indexes were significant different between CTR, left and right TLE.Patients with HS showed decreased mean CBF values with respect to CTR and other histological groups not only in temporal lobe (specifically in left inferior temporal gyrus, right parahippocampal gyrus and right fusiform gyrus), but also in frontal, parietal, and occipital lobes.

Discussion: In this pilot study ASL perfusion differences between patients with HS and without HS were found. More consistent results in HS likely reflect their relative homogeneity. In fact, the patients without HS are heterogenous in term of epileptogenic area, which can be in any part of the temporal lobe, and presented both areas of hypoperfusion and hyperperfusion with respect to CTR.These findings are promising in order to characterize HS patients using non-invasive technique instead of other clinically accepted ones, such as PET. Nevertheless, further studies with larger cohorts are needed to confirm and improve our results.

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**COD. C22**

**GPU-accelerated analysis of DCE-MRI data from patients with glioblastoma.**

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BACKGROUND AND PURPOSE: Dynamic Contrast Enhanced (DCE) MRI ensures the assessment of the microvascular permeability. The method for the analysis of the DCE-MRI signal is well established and it is based on the theory of compartmental systems. The maps obtained with this technique can be used to locate tumors and to assess the treatment effect when comparing pre- and post-treatment scans.
There is a clinical relevance of having parameter maps for the whole volume acquired within an acceptable time. Due to the high volume of data, the voxel-wise CPU processing is very time consuming and, especially with complex models, it cannot be used in the clinical practice. The aim of the present work is, therefore, to develop a method to evaluate the perfusion parameters exploiting the acceleration produced by the parallelization of the algorithm through GPU computing.

MATERIALS AND METHODS: Four different pharmacokinetic models have been analyzed: the Tofts, the Patlak, the Extended Tofts and the Tissue Uptake model. The sample analyzed consisted of five patients with recurrent glioblastoma, randomly extracted from the RIDER Neuro Database.
A Levenberg-Marquardt minimization algorithm has been used to extract the perfusion parameters. Specifically, the four compartmental models were implemented running on Gpufit library, a publicly available and open source unconstrained GPU based optimization tool. Also, an extra step has been included to solve constrained optimization problems and to confine the solution between lower and upper boundaries. The analysis has been carried out with a single NVIDIA P5000 GPU card.
For comparison purposes, an algorithm that performs a similar analysis on the CPU has been performed.
The values of all the perfusion parameters have been obtained for the whole volume acquired.
A paired sample t-test has been carried out on the results obtained with the two different methods with a statistical significance level of 95 per cent.

RESULTS: The t-test has shown a significant difference in the value of the parameters averaged on the tumor region for two patients (model Extended Tofts and model Tofts) with $0.029 \leq$ p-value $\leq 0.045$.
The analogous t-test conducted on the value of the Root Mean Square Error has shown no significant difference between CPU and GPU processing.
The time performance of the proposed GPU-accelerated method is significantly better than a CPU-based method. On average, the GPU-based method performed approximately 168 times faster than the CPU-based method.

CONCLUSIONS: The findings of this study suggest that the proposed GPU-accelerated method can be an efficient alternative to previously reported DCE-MRI compartmental modelling analysis methods.
The method significantly reduces the computational time required to obtain important tumor physiological properties. Furthermore, although this work focuses on applying the GPU-accelerated method to brain tumor data and uses four different models for the analysis, the method can easily be extended to analyze various types of DCE-MRI data using other mathematical models.

**COD. C23**

**Low dose gadobutrol-enhanced breast MRI: a preliminary study.**

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Aims

To assess the performance of contrast-enhanced breast MRI using a reduced dose of gadobutrol through: 1) a correlation analysis between the tumor size on MRI the size obtained from the pathological report; 2) a qualitative evaluation of enhancement conspicuity.

Methods

We carried out a retrospective analysis of all breast MRI performed in our institution between September 2017 and December 2018. Patients with histologically confirmed benign conditions were excluded. All MRI scans were performed on a 1.5-T Siemens Symphony unit, using a three-dimensional axial fast low angle shot FLASH sequence with the following technical parameters: repetition time 11 ms; echo time 4.89 ms; flip angle 35°; echo train length 1; number of excitations 1; slice thickness 1.3mm mm; matrix 512x512mm; field of view 38x40 mm. Patients were administered with 0.080 mmol/kg of gadobutrol at a rate of 2 mL/min, followed by a 20 mL saline flush at the same injection rate. For size measurements, we used the longest diameter of each lesions on the first subtracted dataset. In the case of a multifocal or multicentric tumor we used the maximum diameter of the longest lesion. We evaluate the correlation between MRI and pathological measurements, also distinguishing between mass and non-mass lesions. In addition, a qualitative assessment of the contrast enhancement of the breasts was performed by two radiologists with 2 and 1 years of experience in breast MRI, using a Likert scale with four values on maximum intensity projection images (MIPs), taking into consideration vessels, normal gland and possible lesions, as follows: insufficient, sufficient, moderate, optimal. Spearman correlation and k-statistics were used.

Results

We retrieved from our database 61 patients with a breast cancer diagnosis confirmed by biopsy who underwent breast MRI between September 2017 and December 2018. For 23 patients, the pathological report was available. The medium size was 17.5 mm on MRI and 17 mm at pathology, with a highly significant correlation between the two measurements ($r = 0.729$; $p < 0.001$ ); the same data being 15 mm versus 16.5 mm for mass lesions (n=16) ($r = 0.787$; $p = 0.001$ ) and 30 versus 27.6 mm for non-mass lesions (n=9) ($r = 0.902$; $p = 0.001$). The qualitative assessment of the contrast enhancement was made in all 61 patients. The agreement between the two readers was moderate ($k= 0.561$). In particular, in 40 patients (66%) both readers judged the enhancement of breast good or optimal ($k=0.405$) and, of these, in 20 patients (33%) both readers judged the enhancement optimal.

Conclusion

Contrast-enhanced MRI with a low dose gadobutrol showed a high accuracy in determining the diameter of the lesions compared with the pathological measurements, both in the case of mass and non-mass lesions. The enhancement was judged as good or optimal in 66% of patients.

**COD. C24**

**DWI and perfusion MR in high grade serous ovarian cancer: preliminary results**

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Purpose:To evaluate if the perfusion and diffusion parameters from staging MR in Ovarian Cancer (OC) patients may predict the presence of residual tumor at surgery and the progression free survival in 12 months. Materials and Methods:At our Institution there is an ongoing prospective study for staging ovarian cancer patients by whole body MRI, including DWI and perfusion sequences. Among the patients included, a preliminary analysis was performed to evaluate the performance of perfusion and diffusion parameters. This preliminary study included 49 patients from 04/18/2016 to 07/24/2017 according to following inclusion criteria: pre-operative MR available with perfusion and diffusion-weighted imaging, cytoreductive surgery performed within a month from MRI, minimum follow-up of 12 months. Patients' characteristics including age, body mass index, surgical stage, presence of residual tumor at surgery (R0 or R1) and tumor markers were recorded.From MR perfusion parameters the following were included for analysis: bolus arrival time (BAT) area, contrast-enhancement ratio (CER) area, initial area under the gadolinium concentration time curve (IAUGC), rate transfer constant of gadolinium from the extravascular to the vascular space (Kep), volume transfer constant from vascular space to extravascular and extracellular space (Ktrans), maximum slope of increase area (MSL), volume of extracellular and extravascular space (Ve), intracellular space (INT). From diffusion-weighted parameters the following were included: ADC of the ovarian mass; normalized ovarian ADC as a ratio between the ovarian ADC and muscle ADC.Statistical analysis was performed and P-value was considered significant when < 0.05.Results:Mean ADC of ovarian mass and normalized ADC did not demonstrate significant association with patients characteristics. Association between MR perfusion parameters and progression free survival did not demonstrate significant difference between R0 and R1 patients. The evaluation of DWI parameters showed a slightly significant association between normalized ovarian ADC and the presence of residual disease at surgery (p=0.049).Conclusions: This preliminary study demonstrated a slightly significant association between normalized ovarian ADC and presence of residual tumor at surgery. The other perfusion and diffusion parameters were not significant for the endpoints of this study.

**COD. P01**

**DWI as a stand-alone method for breast cancer detection: a retrospective analysis in our institution**

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PURPOSE: To test diffusion-weighted imaging (DWI) for breast cancer (BC) detection.

METHODS: Single-center 1.5-T MR images of 790 breasts in 434 consecutive women (age 49±10, mean ± standard deviation) entered in the analysis. Two radiologists with 8- (R1) and 5-year (R2) experience, blindly assessed DWI images (b=0 and b=800 s/mm2), with a per-breast recall/no-recall reading. Apparent diffusion coefficient maps were qualitatively evaluated. Double reading (DR) was considered positive even with a single recall. Pathology and follow-up served as reference standard. McNemar and Cohen $\kappa$ were used.

RESULTS: Per-breast prevalence was 13% (101/790): 65 invasive ductal, 9 invasive lobular, 9 invasive ductal-lobular, 8 in situ ductal, 5 invasive not otherwise specified, 5 other type (median size 18 mm, interquartile range 11-25). Sensitivity was 88/101 (87%, 95% CI 79–93%) for R1, 84/101 (83%, 95% CI 74–90%) for R2, and 94/101 (93%, 95% CI 86–97%) for DR (DR versus R1, p=0.031); specificity 639/689 (93%, 95% CI 91–95%), 613/689 (89%, 95% CI 87–91%), and 603/689 (88%, 95% CI 85–90%), respectively (DR versus R1, p<0.001). For cancers ≤20 mm, ≤15 mm, or ≤10 mm, DR sensitivity resulted 60/65 (92%, 95% CI 83–98%), 39/44 (89%, 95% CI 75–96%), and 26/30 (87%, 95% CI 69–96%), respectively. Interobserver agreement was substantial ($\kappa$=0.739).

CONCLUSIONS: DWI showed a high sensitivity, favourably comparable with that of screening mammography, with an even acceptable specificity, in this enriched population. Prospective studies, in non-enriched populations, are needed for testing DWI as a new method of BC screening.

**COD. P02**

**Diffusional kurtosis imaging in head and neck cancer: On the use of trace-weighted images to estimate indices of non-Gaussian water diffusion**

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Purpose: While previous studies have demonstrated the feasibility and potential usefulness of quantitative non-Gaussian diffusional kurtosis imaging (DKI) of the brain, more recent research has focused on oncological application of DKI in various body regions such as prostate, breast, and head and neck (HN). Given the need to minimize scan time during most routine magnetic resonance imaging (MRI) acquisitions of body regions, diffusion-weighted imaging (DWI) with only three orthogonal diffusion weighting directions (x, y, z) is usually performed. Moreover, as water diffusion within malignant tumors is generically thought to be almost isotropic, DWI with only three diffusion weighting directions is considered sufficient for oncological application and it represents the de facto standard in body DKI. In this context, since the kurtosis tensor and diffusion tensor cannot be obtained, the averages of the three directional ($K_x$, $K_y$, $K_z$) and ($D_x$, $D_y$, $D_z$) — namely K and D, respectively — represent the best-possible surrogates of directionless DKI-derived indices of kurtosis and diffusivity, respectively. This would require fitting the DKI model to the diffusion-weighted images acquired along each direction (x, y, z) prior to averaging. However, there is a growing tendency to perform only a single fit of the DKI model to the geometric means of the images acquired with diffusion- sensitizing gradient along (x, y, z), referred to as trace-weighted (TW) images. To the best of our knowledge, no in vivo studies have evaluated how TW images affect estimates of DKI-derived indices of K and D. Thus, the aim of this study was to assess the potential bias and error introduced in estimated K and D by fitting the DKI model to the TW images in HN cancer patients.

Methods: Eighteen patients with histologically proven malignant tumors of the HN were enrolled in the study. They underwent pretreatment 3 T MRI, including DWI (b-values: 0, 500, 1000, 1500, 2000 s/mm$^2$). Some patients had multiple lesions, and thus a total of 34 lesions were analyzed. DKIderived indices were estimated, voxel-by-voxel, using single diffusion-weighted images along (x, y, z) as well as TW images. A comparison between the two estimation methods was performed by calculating the percentage error in D ($D_{err}$) and K ($K_{err}$). Also, diffusivity anisotropy ($D_{anis}$) and diffusional kurtosis anisotropy ($K_{anis}$) were estimated. Agreements between the two estimation methods were assessed by Bland–Altman plots. The Spearman rank correlation test was used to study the correlations between $K_{err}/D_{err}$ and $D_{anis}/K_{anis}$.

Results: The median (95% confidence interval) $K_{err}$ and $D_{err}$ were 5.1% (0.8%, 32.6%) and 1.7%(-2.5%, 5.3%), respectively. A significant relationship was observed between $K_{err}$ and $D_{anis}$ (correlation coefficient $R = 0.694$, $P < 0.0001$), as well as between $K_{err}$ and $K_{anis}$ ($R = 0.848$, $P < 0.0001$).

Conclusions: In HN cancer, the fit of the DKI model to TW images can introduce bias and error inthe estimation of K and D, which may be non-negligible for single lesions, and should hence be adopted with caution. These findings are likely to hold true for other body applications (e.g. prostate, breast); however, this deserves further specific investigation to be confirmed.

**COD. P03**

**Differences in lipid spectra among epicardial, pericardial and subcutaneous adipose tissue and the interventricular septum: an in vivo 1.5-T MRS study**

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Introduction

Proton magnetic resonance spectroscopy ($^1$H-MRS) can detect and quantify lipid accumulation in specific myocardial or peri-myocardial districts. Using $^1$H-MRS, peaks at 0.9 ppm (terminal methyl), 1.3 ppm (bulk methylene), 2.0 ppm (allylic methylene), and 5.3 ppm (olefinic methylene) could be detected. In this study we sought to evaluate differences in the lipid profile among epicardial (EAT), pericardial (PAT), and subcutaneous (SAT) adipose tissue in relation to body mass composition and blood cholesterol and triglycerides.

Methods

After Ethics Committee approval, we enrolled 33 patients (20 males, 60%; BMI 26±4 kg/m$^2$; age 64±10 years) with suspect of cardiovascular disease for a $^1$H-MRS using a water-suppressed chemical-shift imaging sequence to quantify the lipid profile of the interventricular septum (SEP), EAT, PAT, and SAT. All patients were examined with a 1.5-T MRI scanner (Magnetom Symphony, Siemens) using a dedicated 4-channel phased-array coil. Cine true-fisp sequences were acquired in short-axis and long-axis (2- and 4-chambers views). A water-suppressed chemical shift imaging (CSI) MRS sequence (TR=1200 ms, TE=30 ms, NEX=3) was acquired after automatic shimming in a matrix of VOI of 4×5×5 mm, positioned along the 4-chamber view. Pre-processing was performed using the proprietary software (Siemens Medical Solution, Germany). The integral of the lipid peaks at 0.9, 1.3, 2.0 and 5.3 ppm were measured in arbitrary units and each contribution was given in percent over the total amount of lipids. Patient weight, body mass index (BMI), visceral adipose tissue, EAT volume as well as blood glucose, cholesterol, triglyceride, and c-reactive protein were recorded. Pearson/Spearman correlation coefficients were calculated.

Results

The signal-to-noise ratio was very good in all patients. All peaks were measurable with very few exceptions, often distinguishing the doublet of the bulk methylene and the doublet of the allylic methylene. A subgroup of 15 subjects were identified as hyperglycemic (HG) (12 impaired-fasting-glucose and 3 diabetics: 121±26 mg/dL). Bulk methylene of SEP was higher in HG vs other patients (P=0.047). In HG patients, SEP was positively correlated to glucose, visceral fat, C-reactive protein (Spearman $\rho$>0.630, P<0.018); EAT had a positive correlation with visceral fat, age, body weight, and inversely to muscular-, fat free-, bone mass (Pearson r<|0.530|, P<0.039). In all subjects, the main lipid peaks correlated with metabolic parameters.

Discussion

A good quality $^1$H-MRS may be obtained in vivo at 1.5-T, and it allows measurement of lipid peaks in different adipose compartments. Lipid peaks may have cardiometabolic relevance: for instance hyperglycaemic patients showed higher levels of bulk methylene in the SEP compared to patients with normal glycaemia. Since modifications in the anatomo-physiology of the SEP are known to correlate with secondary heart events, SEP fat could be proposed as a biomarker, predicting future cardiovascular risk.

**COD. P04**

**Radiomics: a new approach to enable early diagnosis of breast foci in contrast-enhanced magnetic resonance mammography using machine learning**

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Background The aim of this study was to predict the malignancy of foci detected with contrast enhancement MR mammography (CE-MRm) through radiomic signature. Methods 45 female patients with enhancing mammary foci detected by CE-MRm were included in this study. Percutaneous, surgical biopsy or imaging imaging follow up served as reference standard. Among the 45 nodules, 33 were benign and 12 malignant. Unambiguous cases were added to the dataset to provide reference cases to the following analysis: 8 benign nodules (confirmed by follow-up > 5 years) and 15 radiologically unambiguous malignant tumours (confirmed histologically). MR Images were acquired with a 1.5T clinical scanner. One basal 3D T1w sequence and four dynamic T1w acquisitions after contrast injection were acquired. More than 200 radiomic features were extracted from lesions manually segmented by an expert radiologist from MR pre- and post-contrast images. Lastly, an evolutionary machine learning (ML) method was applied to find a diagnostic model for enhancing foci.. Results A k-Nearest Neighbour (KNN) classifier based on 35 features selected by a TWIST system was identified as the best performing machine learning ( ML) approach. Considering both the 45 enhancing foci and 23 unambiguous nodules, the classifier showed sensitivity and specificity of 100% and 90%, respectively. Moreover, 42 out of 45 enhancing foci were assigned to the right clinical outcome by the diagnostic model. Three misclassified cases were benign non-specific lesions classified as malignant. Conclusion This preliminary study shows the feasibility of a radiomic approach for the diagnosis of enhancing foci identified by CE-MRm.

**COD. P05**

**Investigating cerebral white matter structural changes associated with deafness through diffusion weighted MRI: a graph-based approach.**

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Deafness is usually accompanied by functional brain alterations that may be thought as an alteration to connectome scaffolding. The general goal of this study was to investigate brain structural network organization in early and profoundly deaf subjects (ED). The specific goal was to apply the structural white matter connectome formalism to evaluate network differences in primary, secondary sensory cortices, and higher cognitive system regions in ED relative to healthy controls and hearing signers.

A total of 44 subjects participated in this study: 14 ED, 15 age and gender-matched hearing controls (HC), and 15 age and gender-matched hearing signers (HS). Full-brain diffusion-weighted images (2.3 mm isotropic voxel, 60 DW volumes, 10 b=0 volumes, b=1500 s/mm$^2$, TE=99 ms) and T1 anatomical images (MPRAGE, 1 mm isotropic) were acquired with a 4T Bruker Medspec MRI scanner. Data were corrected for eddy currents and head motion followed by bias field correction and global intensity normalization. Probabilistic spherical deconvolution was adopted to estimate fibre orientation distributions (FODs), which were used for generating whole brain Anatomically-Constrained tractograms (ACT). A template of 638 similarly-sized regions, built from subdivision of regions from Anatomical Automated Labelling Atlas (AAL), was adopted for the anatomical parcellation in each subject. Three connectomes were derived for each subject based on the following white matter edge metrics between each pair of parcellation nodes: sum of weighted tracks, mean length and mean fractional anisotropy (FA) of interconnecting tracks. Connectomes were then analysed using Network-Based Statistics and Graph Analysis, to explore structural connectivity characteristics of deafness.

Network-based comparisons across groups showed significant reductions in ED relative to both HC and HS for mean FA ($p\text{-value}_{HC\text{-}ED}$ =0.003; $p\text{-value}_{HS\text{-}ED}$<0.001), mean length of interconnecting tracts ($p\text{-value}_{HC\text{-}ED}$ =0.002; $p\text{-value}_{HS\text{-}ED}$=0.003) and number of streamlines ($p\text{-value}_{HC\text{-}ED}$ =0.001; $p\text{-value}_{HS\text{-}ED}$=0.001). The global network efficiency, defined as the average of inverse shortest path length, did not differ across groups for the FA connectomes but was significantly reduced in ED compared to HC in both the mean tract length ($t\text{-value}_{ED\text{-}HC}$ =-2.45 $p\text{-value}_{ED\text{-}HC}$ = 0.02) and number of streamlines ($t\text{-value}_{ED\text{-}HC}$ = -2.11 $p\text{-value}_{ED\text{-}HC}$ = 0.04) connectomes. Node degree, defined as the number of edges connected to a node, was significantly reduced in ED regardless of group or connectome, especially in frontal, parietal and motor regions. Nodal strength, defined as the sum of the weights in edges to the node, showed significant reductions in ED with respect to HC (mainly in frontal, parietal, temporal and motor regions) as well as reductions in ED relative to HS (mainly in parieto-temporal regions). No statistically significant differences were detected, either at network level or in graph metrics, between HC and HS.

To the best of our knowledge, we identify for the first time white matter structural connectivity alterations in auditory sensory deprivation, using both network-level characteristics and graph indices. Further studies are needed to better understand if these network effects, mainly left lateralized, may be related to deafness-related plastic mechanisms or are due to sensory deprivation combined with a modified language experience.

**COD. P06**

**SIENAX2.0, an update of SIENAX tool for cross sectional brain volumes assessment**

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Introduction

SIENAX, the cross sectional version of SIENA, both from FSL, is one of the most widely used software for the analysis of brain volumes. However, it shows limitations in the brain extraction, especially when dura mater is isointense to gray matter (GM), in the deep GM segmentation and in the normalizing scaling factor, traditionally obtained with linear registration. In FSL, a new brain extraction tool was recently developed, adding to relatively new tools for deep GM segmentation and non-linear registration.

Objective

We tested whether an updated version of SIENAX, named as SIENAX2.0, which implements new brain extraction, segmentation of deep GM structures and new normalizing scaling factor, performed better than the previous version.

Methods

The new steps introduced in SIENAX2.0, applied to T1-W images, were the following:

1) the new brain mask was obtained by i) generating an initial brain mask trough the non-linear registration on the native brain of a standard brain mask; ii) adding to this mask all the contiguous voxels with a-posteriori probability to be parenchyma >50%.

2) the new GM-pve map, including the FIRST output, was obtained by replacing the pve of voxels falling in the deep GM masks, as generated by FIRST, with 1.

3) the new normalizing scaling factor was computed as the ratio between the volume of the non-linearly registered brain mask in standard space and the native brain volume.

We tested differences between SIENAX2.0 and SIENAX outputs by:

1) comparing, with a paired t-test and ICC analysis, the DICE and the percentage brain volume changes of the pairs of brain masks obtained with both the new brain extraction procedure and optimized-BET "-B -f 0.1" from 250 multi-center MRI datasets of healthy subjects (HS) scanned twice in a day;

2) comparing the masks of hippocampus and thalamus, manually outlined from 112 HS (GS-dGM) with, respectively, those obtained with FIRST (FIRST-dGM) and FAST by retaining GM-Pve voxels falling in the hippocampus and thalamus (FAST-dGM). The comparison, performed with a paired t-test and ICC analysis, included both DICE and volume changes of hippocampus and thalamus;

3) comparing, with a paired t-test, the new normalizing scaling factor with the "old" scaling factor provided by SIENAX.

Results

1) Brain masks obtained with the new brain extraction procedure had a significantly better spatial overlap and smaller absolute volumetric differences than those obtained with the optimized BET (DICE=0.989 ±0.002 vs 0.976±0.014, $p<0.001$; 0.3±35% vs 0.47±0.57%, $p<0.001$);

2) GS-dFM and FIRST-dGM showed modest but significantly higher concordance (ICC=0.54) than GS-dFM and FAST-dGM (ICC=0.02). The DICE between GS-dFM and First-dGM was high (DICE=0.88±01) and significantly higher ($p<0.01$) than the DICE between GS-dFM and FAST-dGM (DICE=0.57±0.02);

3) The new normalizing scaling factor had a significantly smaller variance than the old one (0.21±24 % vs 0.64±0.61 %, $p<0.001$).

Discussion

SIENAX2.0 shows to be more robust and reliable than the previous version for brain extraction, dGM segmentation and normalizing scaling factor.

**COD. P07**

**Brain volume asymmetries and 1H-MRS of Posterior Cingulate Cortex in the differential diagnosis of Primary Progressive Aphasia**

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INTRODUCTION

Primary progressive aphasia (PPA) is a neurodegenerative disorder with heterogeneous neuropathological patterns, characterised by an isolated and gradual dissolution of language function. Impairment of language abilities could also be an early manifestation of Alzheimer's disease (AD), therefore a differential diagnosis based on clinical grounds alone is sometimes difficult, especially in the early stages. The aim of this study was to investigate the ability of magnetic resonance spectroscopy (1H-MRS) of Posterior Cingulate Cortex (PCC) and brain volume asymmetries to differentiate PPA from AD.

METHODS

Nineteen PPA patients (age=69.88+6.91yrs), eighteen healthy controls (mean age=65.44+9.49) and twenty-three AD patients (mean age=71.13+9.48) were included in this study. All participants underwent a brain-MR protocol (1.5T GE scanner) including high-resolution T1-weighted volumetric sequence (isotropic 1mm3). Voxel-wise differences in brain volumetry (left and right side) were evaluated using FreeSurfer software and volumes were normalized by the total intracranial volume (TIV) of each participant. Asymmetry indexes (Right – Left)/(Right + Left) were also calculated for each brain area, and were compared among groups. Proton MR spectra of PCC were acquired using the point-resolved spectroscopy (PRESS) single voxel technique (TR=4000ms; TE=35ms; NEX=128; Volume =8ml) and were processed with the LCModel program.

The ANOVA and T-test, followed by post-hoc tests for multiple comparisons, were used. Receiver operating characteristics (ROC) curve analyses were also performed in order to determine the level of accuracy of the most significant parameters in discriminating between the two neurodegenerative groups.

RESULTS

The N-acetyl-aspartate (neuroaxonal marker) to myo-inositol (glial marker) ratio (NAA/mI ratio) in the PCC differentiates healthy controls from AD patients ($p < .001$) and it was also able to discriminate PPA from AD ($p = 0.004$) with an accuracy of 75.5%. Brain volume and cortical thickness analyses showed a left lateralized atrophy pattern in the PPA group compared to the AD group, however, these differences did not survive correction for multiple comparisons. Asymmetry indexes analyses were also performed between all groups and results showed significant differences in fronto-temporal areas when compared the PPA group with healthy controls; no asymmetry differences were found between the AD and the healthy control group. A comparison between the two neurodegenerative groups showed asymmetries in posterior cingulate volume ($p < .000$), inferior temporal volumes ($p = .001$), precuneus thickness ($p = .002$), inferior temporal ($p = .003$) and middle temporal thickness ($p = .003$), indicating a greater left-lateralized atrophy in the PPA group. ROC curve analyses of all asymmetry indexes were performed and the PCC showed the highest level of accuracy (83.3%) in discriminating between the two neurodegenerative groups.

DISCUSSION

The marked differences of N-acetyl-aspartate to myo-inositol in the PCC between the PPA and AD group suggests that proton MRS is accurate for differentiating between these two disorders. Furthermore, beside the well-known left-lateralized atrophy found in PPA patients, an asymmetrical volume reduction of PCC appears to be a highly sensitive indicator for distinguishing these two neurodegenerative pathologies. Additional studies with larger samples and follow-ups are needed to confirm these results and to monitor the progression of the disease.

**COD. P08**

**Clusterization of cortical areas based on tractography-derived intrahemispheric structural connectivity**

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INTRODUCTION

Brain atlasing studies aim to define brain regions that share common morphometric and connectivity properties (Eickhoff 2018). Cortical areas are interconnected by white matter (WM) tracts that can be visualised with diffusion MR tractography (Dell'Acqua and Catani 2019). Moreover, structural connectivity information can drive cortical parcellations (Fan et al. 2016), even if data quality and clustering criteria can influence results. In this work, we applied a data-driven approach previously proposed to parcellate the occipital and frontal lobe (Thiebaut de Schotten et al. 2014, 2017). Using Principal Component Analysis (PCA) we aimed to clusterize whole-brain cortical areas based on intrahemispheric connectivity profiles.

METHODS

Diffusion MR images of 50 right-handed males were obtained from the HCP S900 release (pre-processed b=2000s/mm$^2$). StarTrack (www.mr-startrack.com)software was used to extract diffusion tensor metrics and perform whole brain tractography (Euler tracking algorithm, 0.5mm step size, 30° and 0.2 FA threshold). Tractograms were non-linearly registered to the MNI space and concatenated into a group connectome using MegaTrack (Dell'Acqua et al. ISMRM 2015 proceedings). Subsequently, the group tractogram was filtered to exclude commissural and projection fibers evaluating only left intrahemispheric connections. A random fine parcellation of the MNI cortex was obtained running Freesurfer5 on the MNI-152 1mm and parcellating GM in 0.3cm$^3$ brain volumes. We obtained 1002 ROIs that were expanded into the underlying WM to increase tractogram overlapping (median ROI volume 0.5cm$^3$). Pairwise ROI connectivity was evaluated, a 1002x1002 adjacent matrix was extracted, weighted by the number of streamlines and normalized by ROI volume. The matrix was thresholded at the 10% of subjects and transformed in a z-score statistic (Matlab scripts). The connectivity matrix was entered in a PCA analysis using Orange3 software (https://orange.biolab.si). Eigenvalues associated to PCA components were fitted by a power law function to discriminate significant components.

RESULTS

PCA showed at least twenty significant components, although a clear cut-off was not identified. Positive weighted PCA components representing positive correlation across ROIs profiles, discriminated cortical areas connected by well-known large association pathways. Positive weights of PCA 1 defined frontal, temporal and parietal areas typically connected by the arcuate fasciculus. Medial limbic areas were identified by positive weights in PCA 2 and PCA 3. Cortical regions connected by intralobar parietal short fibres were defined by PCA 4 positive weights. PCA 5 identified the superior temporal and supramarginal gyrus connected by the posterior segment of the arcuate fasciculus (Catani et al. 2017, Dell'Acqua and Catani 2019).

CONCLUSION

In this study we demonstrated the feasibility of the PCA analysis of tractography-based structural connectomes for the parcellation of left hemisphere cortical areas. Further investigations are necessary to improve the validity of our results by reducing the number of artefactual reconstructions. The application of this novel approach to larger datasets could reveal interindividual variabilities among the general population in relation to differences between hemispheres, sexes and across the lifespan.

**COD. P09**

**Distribution of brain gray matter density and white matter microstructure abnormalities in MELAS patients**

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INTRODUCTION

MELAS syndrome is a rare genetic multi-organ disorder with broad manifestations including stroke-like episodes, dementia, epilepsy, lactic acidemia, myopathy. It is commonly associated with the m.3243A>G mutation in the MT-TL1 gene. The pathogenesis of MELAS is not fully understood. It comprises the co-occurrence of cellular mitochondrial dysfunction, microangiopathy with impaired microvasculature of several organs, as well as nitric oxide (NO) production deficiency.Conventional brain MRI findings in MELAS syndrome comprise the presence of stroke-like lesions, signal changes in pallidal nuclei related to calcifications, unspecific T2 hyperintense white matter lesions and both supratentorial and infratentorial brain atrophy. Advanced brain MRI techniques have been used so far in few studies, often with not homogeneous patient population, employing different image analysis methods to investigate possible brain MR atrophy in comparison to healthy subjects.The aim of this study was to test for brain grey and white matter alterations by VBM and TBSS analyses, in a cohort of adult MELAS patients.

METHODS

Sixteen patients with genetically confirmed MELAS diagnosis were enrolled (age 42.3±11.4 years, 9M/7F, 1 atypical mutation). Acquisitions were performed with a 1.5T GE Signa scanner. The standardized MR protocol included volumetric T1-w image (TR/TE/TI=12.5/5.1/600ms, 1mm3) and diffusion-weighted MRI (TR/TE=10.000/87.5ms, 25-directions, b-value=900 mm2s#1, voxel=1.25x1.25x4mm). Sex- and age-matched healthy controls were included. To evaluate grey matter (GM) density, voxel-based morphometry (VBM) analyses were performed on T1-w images using SPM 12.0, after white matter lesions refilling. To evaluate infratentorial structures, a specific and optimized software was used (Spatially Unbiased Infratentorial Toolbox, SUIT).Diffusion-weighted data underwent standard pre-processing and tensor fitting. Voxelwise analysis of tensor parameters was performed using TBSS (Tract-Based Spatial Statistics) for mean diffusivity (MD), fractional anisotropy (FA), longitudinal diffusivity (LONG) and radial diffusivity (RD) maps. Voxelwise comparisons were non-parametric (permutations). Statistical significance was set to $p<0.05$ (corrected for multiple comparisons).

RESULTS

Supratentorial VBM showed a widespread loss of GM density over the whole cortex, with a particular ($p<0.001$) involvement of occipital, insular and frontal cortices; cerebellum-specific VBM showed widespread loss of GM density.TBSS highlighted diffuse white matter alterations, with higher MD and lower FA (due to higher LONG and RAD) within all the main white-matter tracts, with a relative sparing of the posterior limb of the internal capsule.

DISCUSSION

Brain voxel-based morphometry in MELAS patients confirmed previous finding of gray matter volume reduction in the parieto-occipital cortex, confirming the susceptibility of posterior brain regions to the metabolic mitochondrial dysfunction. Moreover, it shows the presence of subtle brain atrophy also in bilateral frontal cortices even in absence of stroke-like lesions. We demonstrated for the first time a diffuse increase in the MD in multiple white matter tracts, driven by an increase of both the radial and axial components, which is in line with the presence of a diffuse microstructural alteration of the myelin compartment as well as with neuropathological studies reporting multiple necrotic foci, varying in size and stage, in the white matter of MELAS patients.

**COD. P10**

**Multivariate analysis of left hemisphere cortical thickness discriminates PPA, AD and healthy subjects**

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INTRODUCTION

Primary Progressive Aphasia (PPA), a neurodegenerative disorder affecting the language networks (Catani et al. 2013) has a pattern of cortical atrophy that is distinct from other neurodegenerative diseases, such as Alzheimer Disease (AD) (Seeley et al. 2009). Recently, it has been shown that Cortical Thickness (CT) measure is strictly related to white matter connectivity, and specifically language function in the left hemisphere (Qi et al. 2019). The purpose of this work is therefore to use multivariate analysis of cortical thickness as an index of network disruption to investigate anatomical differences across PPA, AD patients and Healthy Controls (HC).

MATERIAL AND METHODS

Three groups of equal size n.18: APP (69 ±7 years, 6M/12F), AD (68 ±8 years, 9M/9F,) and HC (65 ± 9 years, 10M/8F) underwent a standardised T1w brain protocol (1.5T FSPGR sequence, 1 $mm^3$ isotropic voxel). FreeSurfer (v6) software was used to extract CT measures according to the Desikan-Killiany atlas in the left hemisphere. The effect of sex and age on CT measures was evaluated in the HC and the estimated linear model (fitlm Matlab R2018a) was used to regressed out age and sex effects in all the groups. CT measures were normalized for each subject with respect to the hemispheric mean CT. Using SPSS (v.25) a MANOVA was performed and only the cortical regions that met the Levene's test of equality of error variances were selected as test variables. Subsequently, a discriminant analysis was performed using the leave-one-out classification as cross validation method.

RESULTS

MANOVA of the fourteen left cortical regions selected showed a significant group effect (Pillai's trace $p < 0.0001$). The discriminate analysis revealed two functions that significantly distinguished the three groups: the first function (f1) explained 76.6% of variance with canonical $R^2$=0.91, and the second function (f2) 23.4% with $R^2$=0.76. Middle temporal, supramarginal, superior frontal and pars opercularis cortical areas had the highest correlation with f1, while lateral occipital, isthmus cingulate and posterior cingulate mostly correlated with f2. The leave-one-out classification reported an accuracy of 96.3%: except 2 PPA subjects misclassified as AD all the remaining subjects were classified correctly.

DISCUSSION AND CONCLUSION

Multivariate analysis was successfully applied to structural MR images for the correct classification of patients with PPA and AD. The results showed that frontal, parietal and temporal areas involved in language and memory processing (Catani and Mesulam 2008, Ledig et al. 2018) had a prominent effect in the group differentiation. These results agree with previous findings that investigate CT in early-onset AD clinical variants (Ridgway et al. 2013) and suggest that it is possible to discriminate different neurodegenerative diseases based on the combination of CT measures of cortical brain regions.

**COD. P11**

**Silent fMRI with visual and auditory stimulation using 3D radial T2*-weighted ZTE-BURST sequence**

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Introduction

The detrimental effect of acoustic scanner noise (ASN) has been reported in several experimental conditions, such as fMRI experiments involving auditory stimulation, resting state scans and sleep. To overcome this limitation, we adapted a structural 3D radial sequence with T2*-contrast capability (ZTE-BURST) and minimal ASN (76 dBA) to fMRI. We then used auditory and visual stimulation to assess suitability of ZTE-BURST to enable silent BOLD-fMRI experiments.

Methods

Two healthy subjects (30 years-old male and 36 years-old female for the visual and auditory experiment respectively) underwent an MRI session on a 7T scanner including a T1-weigthed sequence and a train of 20 ZTE-BURST scans, each acquiring a volume with full-head coverage in 28s (voxel size=3x3x3mm$^3$, FA=3°, TE=16$\mu$s,11.1,22.2ms). fMRI analysis was performed on the third TE.Visual stimulation consisted of black and white checkerboard patterns on a grey background, positioned either along the horizontal or vertical meridian, which appeared alternately for 14s each, in a pseudo-random order so that the vertical meridian was presented during the first half of the k-space sampling in half of the volumes and in the second half in the others, and viceversa for the horizontal one. Auditory stimulation followed a similar paradigm, alternating 14s blocks of jittered pure tones (75ms each) sampled from either a low-frequency band (125-355Hz) or a high-frequency band (2000-5680Hz).Two halves of the raw data of two volumes acquired with different stimulus order were reconstructed separately, motion-corrected and recombined via a complex sum in a single fully-sampled image with consistent stimulation. Contrast maps (i.e., Vertical-Horizontal meridian and Low-High frequencies) were obtained by computing a voxelwise paired t-test between the two groups of images (10 volumes per stimulus condition) and transformed into the MNI152 space.The same stimulation paradigms were delivered also during a conventional EPI acquisition (TR=2s, TE=22.2ms, voxel size=2mm iso, 147 volumes). After standard preprocessing and GLM analysis in AFNI, statistical maps for the contrasts of interest were obtained and transformed into the MNI152 space.To compare the two acquisition schemes we masked the results using the anatomical definition of Heschl's gyrus and V1 for the auditory and visual experiment respectively. Similarity between sequences was quantified by correlating the corresponding patterns of activity.

Results

The ZTE-BURST activation maps closely resemble those obtained from the EPI acquisition. For both sequences, activations related to the vertical meridian are located in pericalcarine grey matter and the horizontal one is mapped at the fundus of the calcarine sulcus. Similarly, the activation map obtained for acoustic stimulation shows the expected pattern of response (rostrocaudal high-low-high organization) in the Heschl's gyrus. This high similarity is also testified by significant correlation ($p<0.001$) between response patterns both in visual ($r=0.73$) and auditory ($r=0.46$) experiments.

Conclusions

The ZTE-BURST acquisition scheme allowed the computation of activation maps compatible to those obtained via conventional EPI protocols, both with visual and acoustic stimulation, and can be used for silent fMRI. The current main limitation is related to temporal resolution, which will be improved by future work optimizing sequence parameters.

**COD. P12**

**Comparison between manual and automated quantification of sodium concentration in a 23Na MR clinical 3T stroke study**

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Aims: Sodium concentration ([Na]) promises to be a cellular biomarker in pathologic states, including ischemic stroke diagnostics. Our aim was to develop an algorithm to enhance the sodium image quality by a correction for relaxation effect and to quantify [Na] in tissue and stroke regions of interest (ROI), comparing results with manual analysis.

Materials and methods: Clinical $^{23}Na/^{1}H$ MR protocol was applied on 20 stroke patients (9 females, 75.2 ± 10.3 years old) using a MAGNETOM Trio (SIEMENS Healthineers, Erlangen, Germany) scanner with dual-tuned $^{1}H/^{23}Na$ birdcage head coil (Rapid Biomedical, Rimpar, Germany). Both proton and sodium images were acquired in the same session.
Two reference vials with [Na] of 100 mM and 50 mM respectively were placed in the field of view to allow the calculation of calibrated tissue sodium concentration (TSC) maps of the brain. The applied sequence for sodium images was a density-adapted 3D ultra-short echo time (isotropic resolution of 4 mm, echo time of 0.2 ms, repetition time of 100 ms). A phase-sensitive method was applied on quantitative images for the flip angle calibration. The correction for relaxation effect was performed through a weighting factor, depending on the relaxation constants of both sodium in tissues and in the reference vials, by the designed algorithm.Segmentation was carried out on $^{1}H$ turbo inversion-recovery images through SPM12 tool using MATLAB, obtaining binary tissue masks of gray matter (GM), white matter (WM), cerebrospinal fluid (CSF). A safety margin of one nominal scan resolution was subtracted from tissue masks to reduce partial volume effects (PVE). The [Na] of segmented GM, WM and CSF was compared to manual analysis. In addition, comparison between stroke and contralateral areas, mirrored to the brain midline, was performed.
Results and discussion: The applied weighting produced a 3%-decrease in [Na] for GM and WM areas, while an increase of 7% was observed in the CSF, leading to mean results within the literature ranges ($[Na]_{GM}$= 66.12 mM, $[Na]_{WM}$= 59.20 mM, $[Na]_{CSF}$= 139.97 mM inside the ventricles for segmented areas) thus supporting the adopted strategy for accuracy enhancement.Compared to manual analysis, in GM the [Na] showed no difference, while in WM an increase by 13% was found, probably due to the erroneous partial inclusion of pathologic tissue. In CSF, a large underestimation in mean [Na] (manual 161.27 mM vs automated 101.91 mM) led to the development of a semi-automatic procedure to extract and assess only ventricles from CSF mask, avoiding strong PVEs, resulting in $[Na]_{CSF}$= 139.97 mM.As attended, the [Na] in stroke ROIs were found in no physiologic range, higher than the correspondent contralateral areas (+36%), GM (+26%) and WM (+34%) while lower than CSF in ventricles (-42%).
Conclusion: The applied algorithm appears to be effective for GM and WM analysis, but further implementations are suggested for CSF analysis.The investigated strategies could be suitable to be included in the stroke assessment routine to enhance sodium images and potentially reduce the inter-observer dependence in computation of [Na].

**COD. P13**

**Characterization of intra- and inter- subject variability of functional connectivity estimates**

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Introduction: The interest in studying directed and undirected interactions between different regions in the human brain (i.e. the functional 'connectome') is growing exponentially, and the advent of graph theory applications to neuroscience has provided additional avenues to represent, analyze and interpret information contained in complex, possibly dynamic networks like the human connectome. Functional connectome estimates are often derived from resting state functional MRI (rsfMRI) data. While these data are known to exhibit significant inter- and intra-subject fluctuations, the impact of this variability on connectome measures has not yet been investigated. We quantify and compare intra- and inter- subject variability of both directed and undirected resting state functional connectivity in order to establish the reliability of such measures.
Methods:We employed rsfMRI data from 1003 subjects part of the Human Connectome Project (S1200 PTN release). Each subject underwent a total of 4 resting state scans (1200 volumes/scan, TR=0.72). We employed subject-wise node timeseries resulting from group independent component analysis (gICA) at dimensionality 15. Subject-wise undirected adjacency matrices were obtained though both Pearson and partial correlation, while directed adjacency matrices where obtained through multivariate Granger Causality (mGC) in its most recent state-space formulation [Barnett et al. PRL 2015]. Then, global and local graph-theoretical indices of functional connectivity (nodal strength, efficiency, clustering, betweenness centrality, eigenvector centrality, transitivity) were computed for each subject and each node (where applicable).
As a variability measure for matrix weights and all graph theoretical metrics, we employed the pairwise normalized difference (ND) [(a-b)/(a+b)] between any two sessions, both intra-subject (six unique pairs from 4 distinct sessions from the same subjects, for a total of 6018 unique values) and inter-subject (6 unique pairs build from 4 sessions sampled at random 1003 times from 4 different subjects without replacement). We then compared the intra- and inter-subject distributions of ND in each metric through nonparametric Mann-Whitney-U tests.
Results:In all matrix weights (Pearson Correlation, Partial Correlation and Granger Causality), intra-subject variability is significantly lower than inter- subject, with mGC exhibiting the largest difference. Surprisingly, this finding is not confirmed in global graph metrics, whose intra-subject fluctuations are indistinguishable from inter-subject fluctuations (Fig.1(B)). When looking at local graph metrics, an intricate, anatomically dependent pattern emerged where the difference between intra- and inter-subject fluctuations depend on the specific node, with some nodes exhibiting higher intra-subject (as compared to intra-subject) fluctuations.
Conclusions:While matrix weights exhibit a higher reproducibility (lower within-subject vs between-subject variability) as compared to more sophisticated methods like e.g. state space Granger Causality, this overall difference disappears when looking at global and local graphs-metrics values, where re-scanning the same subject results in the same statistical fluctuation as scanning a different subject. This warrants extreme caution in the interpretation of graph-based connectomics studies, serves as a benchmark for future investigations aiming to estimate the presumed variability in own directed and undirected connectomic databases, and can also be employed for prospective power calculations in planning functional connectomics experiments.

**COD. P14**

**Longitudinal Molecular Magnetic Resonance Imaging of endothelial activation in a mouse model of traumatic brain injury**

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Background: Traumatic brain injury (TBI) is one of the major cause of death and disability. Despite progresses achieved in neurosurgery and critical care, we still lack an effective neuroprotective treatment able to counteract or attenuate injury progression. Inflammation after TBI is increasingly recognized as a key modulator of injury progression and neurodegeneration. We have recently demonstrated that focal TBI in mice is associated with a persistent tissue inflammatory response and blood brain barrier dysfunction that spread from the site of injury to remote brain regions including the contralateral hemisphere at chronic stages (up to 1year post-TBI) [1] and can be targeted for therapy. The development of in vivo approaches to longitudinally study cellular and molecular post-traumatic inflammatory processes is pivotal for monitoring injury evolution/recovery and effectiveness of therapeutic approaches. Here we provide a longitudinal and spatial in vivo MRI characterization of endothelial activation/dysfunction after experimental TBI by targeting p-selectin expressing endothelial cells.

Methods: C57 adult male mice were anaesthetized with isoflurane and subjected to craniectomy followed by induction of severe (s)TBI by lateral controlled cortical impact. Micro-sized particles of iron oxide (MPIOs) with diameter of 1.08 µm and characterized by p-toluenesulphonyl (tosyl) reactive surface groups (Dynabeads® MyOneTM Tosylactivated, Invitrogen) were covalently conjugated to goat anti-mouse antibodies for p-selectin or IgG antibodies to assess the signal specificity. Before imaging and after anaesthesia induction, mouse tail veins were cannulated and connected to a p-selectin conjugated MPIOs solution at 10 mg Fe/kg. MRI images were acquired on a 7T Bruker Biospec (Ettlingen, Germany) running ParaVision 6.01 and equipped with a quadrature cryogenic surface coil as transmitter and receiver. MPIOs visualization was performed with a 3D T2*-weighted gradient echo imaging with flow compensation (GEFC) sequence with spatial resolution of $80\times80\times80\mu m^3$, echo time (TE) of 7,5ms, repetition time (TR) of 50ms and a flip angle (FA) of 14°. The acquisition time is 17min. A baseline GEFC image was acquired before the MPIOs injection and another one 10 minutes after. The two images were subtracted and the percent variation of the MRI signal computed. Experiments were carried out at five different time points after injury (from 1 to 7 days).

Results: Data show that MPIOs conjugated with antibodies for p-selectin are able to induce a strong MRI signal decrease in correspondence of the perilesional regions, including the cortex and the hippocampus. This signal alteration can be monitored longitudinally; is already detectable at 24 hours <!-- Forse solo perche non abbiamo fatto tempi piu' precoci -->after sTBI, peaks in terms of intensity and diffusion at 3 days post injury, than partially decreases but persist up to 7 days after injury. No signal is detected in sham mice. When MPIOs conjugated with IgG antibodies are infused in TBI mice no signal is ever detected supporting the high specificity of this method. This approach may represent a useful tool to evaluate in vivo the therapeutic response towards agents targeting vascular activation and permeability.

**COD. P15**

**Application of new diffusion MRI analysis on a rodent chronic multiple sclerosis model**

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Routinary scans in multiple sclerosis (MS) patients represent a challenge for neurologists as searching lesions and their outcomes across time remains a challenge. Moreover, diffusion MRI reveals high sensitivity to tissue changes, but still lacks of specificity within the plaques and near areas of gray matter affected. To evaluate diffusion weighted imaging technique, in the framework of unravelling new metrics for brain microstructure at high magnetic field (9.7T), a rodent model with inflammatory cerebellar lesions was analysed both in-vivo and ex-vivo. Mathematical model was evaluated in-silico by means of algorithms related to myelin content and fiber integrity. In particular, spherical mean transform calculated new reconstructed images, formerly maps of free-water, intra and extra-axonal volume fraction, and diffusivity direction, parallel and perpendicular to fiber tracts. Here we used a T cell adoptive experimental autoimmune encephalomyelitis (EAE) mouse model, where myelin-specific T cells were differentiated into pro-inflammatory Th17 cells. Adoptive transfer of those Th17 cells lead to severe inflammation and demyelination in the brain, particularly in the cerebellum. This model shares many clinical and histological features with MS as EAE mice showed symptoms of ataxia, locomotor impairment (typical of cerebellar lesions), as well as mild-severe paralysis (typical of spinal cord lesions). Histologically, it is characterized by inflammatory cell infiltrates, axonal damage and demyelination of the central nervous system. C57BL/6J EAE and control mice were analysed with ex-vivo MRI at high resolution.. Additional T1 and multi echo T2 weighted images were acquired to obtain useful T1 and T2 maps. In-vivo brain acquisitions of 3D-MPRAGE, MEMS were used to assess disease progression at two temporal points (day zero and the day of disease peak) and optimize parameters in pulse sequences, while ex-vivo DWI and multi echo T2 were processed for myelin pre-tested algorithms. After acquisitions, all subject brains were dissected for histology. Inflammation load in tissues and number of lesions were evaluated by means of different stainings in two sections per cerebellum, and region of interest were subsequently traced in DWI maps as region of interest for analysis. Results showed that myelin disruption is correlated with disease score in mice with severe cerebellar EAE signs, while changes in water content in lesions well correlated with inflammatory load. Algorithms used in this study are promising as new ways of contrast to highlight the different patterns of damage in EAE plaques occurring in brain and can be further adapted for in-vivo scan or ex-vivo higher resolution images in preclinical research.

**COD. P16**

**The underestimation rate of atypical ductal hyperplasia percutaneously diagnosed under MRI guide: systematic review and meta-analysis**

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Background: Atypical ductal hyperplasia (ADH) is a high-risk breast lesion and an independent risk factor for invasive breast cancer, but its management is still a matter of discussion.Objectives: To estimate the pooled underestimation rate (UR) of atypical ductal hyperplasia (ADH) percutaneously diagnosed under MRI guide, compared to the other imaging techniques. Methods: A systematic search was performed in October 2018 using MEDLINE and EMBASE for studies reporting the UR of pure ADH cases diagnosed at percutaneous biopsy. The study was registered on PROSPERO and written following the PRISMA statement. The pooled-UR (pUR) was calculated using the fixed or random-effect model; subgroup and meta-regression analyses were used for the assessment of potential UR-predictors. Study quality was judged using the Newcastle-Ottawa scale and publication bias with visual inspection of the funnel plot and Egger test.Results: Of 521 articles, 9 were analysed totalling 296 ADHs on 5899 MRI-guided percutaneous biopsies, 259 surgically excised. Mean age 50–57 years; all the studies used vacuum assisted biopsy. Heterogeneity was high ($I^2$ =56%). The pUR was 31% (95% CI 22%–41%). Quality of studies was low to medium; no risk of publication bias (p=0.103).Conclusions: A pUR of 31% was calculated from 296 ADHs surgically excised after MRI-guided percutaneous biopsy. At the present, before more reliable pathological methods are developed, for example with the use of second expert opinion, this meta-analysis demonstrates that conservative management is not to be recommended in these patients, while makes open surgical excision mandatory.

**COD. P17**

**Fast thoracic MRI as an alternative to chest X-ray radiography: a retrospective evaluation of 287 patients**

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Purpose: The aim of this study was to compare the distributions of chest cardiac and non-cardiac findings detected at magnetic resonnce imaging with the only use of the Half-Fourier acquisition single-shot turbo spin-echo (HASTE-MRI) and chest X-ray (CXR) in patients undergoing both examinations.

Material and methods: All patients who underwent both chest 1.5-T HASTE-MRI and CXR performed no more than seven days apart, were analyzed. Two independent radiologists, blinded to the original reports, re-evaluated all images. For both examinations the presence of the following findings were reported: pulmonary nodules and infiltrates; pleural effusion; cardiac and aortic enlargement. McNemar test and weighted kappa were used respetively to compare finding's distirbutions and to calculate the agreement between the two readers.

Results: At the targeted re-valuation a total of 5 pulmonary nodules were found by both techniques with a lesion detection rate of 1.7% (5/287). The agreement between readers was modest for CXR ($k=0.393$, $p>0.001$) and perfect for MRI ($k=1.000$, $p<0.001$). Concerning the pleural effusion, the detection rate of CXR and MRI were respetively 40/287 (14%) and 55/287 (19%) with a significant difference ($p<0.001$), but an almost perfect agreement ($k=0.812$, $p<0.001$). Agreement for CXR and MRI was $k=0.773$, $p<0.001$ and $k=0.902$, $p<0.001$, respectively. The detection rate for pulmonary infiltrates of CXR was 22/287 (7.7%), while that of HASTE-MRI was 24/287 (8.4%), with a non-significant difference ($p=0.625$) and an almost perfect agreement between techniques ($k=0.905$, $p<0.001$). Agreement was moderate for both CXR ($k=0.554$, $p<0.001$) and HASTE-MRI ($k=0.639$, $p<0.001$). The detection rate of CXR for cardiac enlargements was 138/287 (48%), while that of HASTE-MRI was 130/287 (45%), with a borderline-significant difference ($p=0.057$) and an almost perfect agreement ($k=0.902$, $p<0.001$). The inter-reader agreement was substantial for both CXR ($k=0.744$, $p<0.001$) and HASTE-MRI ($k=0.798$, $p<0.001$). The detection rate for aortic dilations of CXR was 28/287 (10%), while that of HASTE-MRI was 51/287 (18%), with a significant difference ($p<0.001$) but a substantial agreement ($k=0.648$, $p<0.001$). The inter-reader agreement was moderate for both CXR ($k=0.346$, $p<0.001$) and HASTE-MRI ($k=0.724$, $p<0.001$).

Conclusions: Our results indicate that HASTE-MRI yields a performance at least comparable to that of CXR when assessing some among the most common chest findings, without exposing patients to ionizing radiations.

**COD. P18**

**Inter-reader agreement in the detection of supraspinatus tendon who need surgery intervention: comparison at 1.0, 1.5, and 3-T MRI examination**

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Background: magnetic resonance imaging (MRI) is widely used to diagnose shoulder pathology and supraspinatus tendon tears. Because of the enhanced signal-to-noise ratio and improved image quality at higher field strength, shoulder MRI equipment is shifting from 1.5 to 3.0 T. However, often claustrophobic and severe obese patients are not able to complete the examination delaying a depth evaluation of their shoulder.

Purpose: to evaluate the inter-reader concordance and agreement in the evaluation of supraspinatus tendon injuries using a 1.0-T open bore MRI compare to 1.5-T and 3.0-T MRI.

Methods: MRI of the shoulder of patients who underwent 1.0-T open bore MRI, 1.5-T MRI or 3.0-T MRI were retrospectively revaluated by two expert radiologists in blinded. Readers evaluated and subdivided these patients in two categories according to the Snyder scale: 1) patients with a score lower than A2B2; 2) patients with a score greater than A2B2 but lower than A4B4. The concordance between the two readers was calculated using the Weighted Cohen's k. The agreement expressed in percentage was also reported.

Results: a total of 60 patients underwent to an MRI of the shoulder from Jun 2018 to January 2019 were retrieved from our database. Twenty different patients for each group performed the 1.0-T, 1.5-T and 3.0-T MRI, respectively. Evaluating the examination performed using the 1.0-T open bore MRI, readers agreed in 85% of cases with a good (k=0.688) concordance. Their agree rose to 90% on the images evaluated using the 1.5-T and 3.0-T MRI with a good concordance of k=0.765 and k=0.783 respectively.

Conclusions: nevertheless, the better image resolution of 1.5-T and 3.0-T MRI examination, our results showed a good inter-reader concordance and agreement between on the images evaluated using the 1.0-T open bore MRI, suggesting the use unit as the ideal examination for claustrophobic or severe obese patients.

**COD. P19**

**Is DCE useless in early detection of prostate cancer? The analysis of quantitative parameters might help radiologists to decide if findings mildly restricted on ADC map should be sampled**

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Purpose: The aim is to evaluate whether the DCE can improve tumour detection, applying the quantitative analysis of pharmacokinetic parameters of lesions not having a clearly positive ADC map.

Methods and Materials: Among 1236 men who underwent mpMRI for PCa suspicion from 2015 to 2018, we retrospectively enrolled 86 patients treated with radical prostatectomy and 86 patients suspected of harbouring PCa with at least one negative systematic prostate biopsy, at least two negative mpMRI exams and a minimum follow-up of 48 months, as “control group” (Group C). Exams were performed at 3T with a PI-RADSv2-compliant protocol. Quantitative analysis was performed, computing both pharmacokinetic parameters (k-trans, k-ep and ve) and ADC values.

Results: Mean ADC value of 82,634$mm^2$/s (95%CI= 77,564 to 88,236), mean k-trans of 0,325$min^{-1}$ (95%CI= 0,278 to 0,372), mean k-ep of 0,568$min^{-1}$ (95%CI= 0,466 to 0,640) and mean ve of 0,77 (95%CI= 0,65 to 0,89). Results were stratified into two groups: lesions with a normalised ADC≤0,62 (Group A) 72% and lesions with a nADC>0,6 (Group B) 28%. The difference of Ktrans values of the groups was not significant (p=0,08), however a statistical difference was found comparing the normalised Ktrans (nKtrans) of healthy prostate tissue with the one of PCa lesions, both separately and together (p<0,05).

Conclusion: It seems reasonable to adopt the nKtrans in the decision-making process of performing a prostate biopsy, particularly for those radiologic findings having a nADC>0,6. The omission of DCE would decrease PCa detection, especially when the ADC map cannot be unequivocally interpreted.

**COD. P20**

**RM mammaria con gadoteridolo: valutazione del potenziamento ghiandolare di fondo (BPE) a due diverse velocità di flusso.**

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Obiettivo:
Lo scopo dello studio è stato di confrontare due velocità di somministrazione di gadoteridolo (ProHance), 3 ml/sec e 2 ml/sec, nella RM mammaria al fine di valutare eventuali differenze in termini di BPE e stablire quale sia la velocità di flusso più appropriata.

Materiali e metodi: Da Dicembre 2017 a Settembre 2018 sono state arruolate 80 pazienti che avevano in programma una RM mammaria, seguendo le linee guida dell'EUSOMA. Sono state escluse le pazienti in terapia con farmaci che hanno effetto sul BPE. Le pazienti hanno ricevuto, in maniera casuale, la somministrazione di 0.1 mmol/kg di gadoteridolo per via endovenosa ad una velocità di flusso di 3 ml/sec o di 2 ml/sec in bolo mediante iniettore automatico, seguita da 10-20 ml di soluzione salina. Gli esami sono stati effettuati su un magnete a 3T, acquisendo un protocollo standard per la mammella che includeva sequenze assiali T1 3D gradient-echo prima e dopo 0, 2, 4, 6 e 8 minuti dalla somministrazione di mdc. Le immagini sono state valutate in consensus da due radiologi con 4 e 15 anni di esperienza in RM mammaria, che hanno assegnato uno score da 1 a 4 per il grado di BPE valutando la seconda e terza immagine in sottrazione. E' stato anche valutato il profilo di sicurezza dei due gruppi.

Risultati:
I due gruppi di pazienti sono risultati sostanzialmente omogenei per caratteristiche anagrafiche e per il BIRADS finale assegnato. Il gruppo che ha ricevuto il gadoteridolo ad un flusso di 3 ml/sec ha riportato dei valori di BPE significativamente più bassi: 85% con BPE 1 e 15% con BPE 2, nessuna paziente con BPE 3 o 4. Il gruppo che ha ricevuto un flusso di 2 ml/sec ha, invece, riportato valori di BPE significativamente maggiori: 40% con BPE 1, 45% con BPE 2, 10% con BPE 3 e 5% con BPE 4. Non sono stati registrati eventi avversi.

Conclusioni:
Benché si tratti di dati preliminari, il nostro lavoro suggerisce che un flusso più alto di somministrazione di gadoteridolo, pari a 3 ml/sec, potrebbe offrire dei vantaggi rispetto ad un flsso di 2 ml/sec riducendo significativamente il BPE e migliorando l'identificazione delle lesioni mammarie e la loro caratterizzazione.

**COD. P21**

**Side of Contrast Injection and Breast Size Correlate with Motion Artifacts and Image Quality on Breast MRI**

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Objectives: To assess frequency and amount of motion artifacts (MA) in contrast-enhanced breast MRI, to evaluate their impact on image quality (IQ), to investigate potential correlations between MA, technical parameters, and patient characteristics.

Material and Methods: We devised a retrospective two-center study on consecutive contrast-enhanced breast MRI examinations. All examinations were performed on 1.5-T units with the patient in prone position and with dedicated breast coils, after the intravenous injection of 0.1 mmol/kg of gadobenate dimeglumine (Bracco Imaging, Milano, Italy) at a 2 mL/s flow rate and with subsequent injection of 20 mL of saline solution at the same flow rate. Two radiologists (4 and 8 years of experience in breast MRI interpretation) independently reviewed the first subtracted images and maximum intensity projections to define the breast side more affected by MA and to grade IQ in terms of MA, scored as 1 (optimal IQ), 2 (reduced IQ, without reduction of diagnostic power), and 3 (reduced IQ, with reduced diagnostic power). Correlations with side of injection, breast size (cup A or B versus cup C or D), patient age, clinical indication, MRI unit, and examination protocol were assessed using $\chi^2$ and Fisher exact statistics; p values lower than 0.05 were considered as significant.

Results: A total of 237 examinations were included. Contrast injection was performed in the right arm in 124 patients (52%), in the left arm in 113 patients (48%). MA were more frequent on the side ipsilateral to the injection (144/237, 61%, with a 95% confidence interval [CI] 54-67%) than in the contralateral side (93/237, 39%, with a 95% CI 33-46%) ($p<0.001$); IQ was scored 1 in 154/237 (65%), 2 in 63/237 (27%) and 3 in 20/237 (8%); patients with A-B cups showed stronger artifacts (score 1, 2 and 3 of 54%, 29%, 17%, respectively) than those with C-D cups (score 1, 2 and 3 of 70%, 25%, 5%, respectively) ($p=0.002$). No significant correlations were found between ipsi- or contralateral injection and right/left injection, breast size, age, indication, scanner, protocol ($p\geq0.106$), the same for IQ ($p\geq0.318$).

Conclusions: Only in 8% of patients MA impaired the assessment of enhancing findings, a relatively low rate likely due to the well-established breast MRI technique. MA occurred in all age groups, were more frequent in the breast ipsilateral to the injection site and stronger in small breasts.

**COD. P22**

**Machine learning classification of low-grade and high-grade chondrosarcomas based on magnetic resonance imaging-based texture analysis**

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Purpose

Reliable grading of bony chondrosarcomas is crucial for the clinical outcome, because treatment ranges from intralesional curettage for low-grade neoplasms (G1) to resection or amputation for high-grade tumors (G2-G3). We aim to evaluate the diagnostic accuracy of machine learning (ML) algorithms for discrimination between low-grade and high-grade chondrosarcomas based on texture analysis parameters extracted from unenhanced Magnetic Resonance Imaging (MRI).

Methods and Materials

Institutional review board approval and a waiver of informed consent were obtained. We conducted a retrospective analysis of a surgical database maintained over 10 years and enrolled 58 patients with histologically proven chondrosarcoma (26 low-grade and 32 high-grade tumors). Patients were randomly divided into training (n=42) and test (n=16) groups for classification model development and testing, respectively. All tumors were manually segmented on T1-weighted and T2-weighted images by drawing a bidimensional polygonal region of interest (ROI) on the slice showing the largest tumor area. ROIs were used for first order and texture feature extraction on dedicated software, Pyradiomics. For each tumor, different data subsets were obtained by six feature selection methods (C4.5 learner-based, gain ratio evaluator, information gain evaluator, Principal Component Analysis and subset evaluator) and analyzed using 9 ML classification algorithms, evaluating their accuracy for differentiation of low-grade from high-grade chondrosarcoma. Thereafter, an experienced musculoskeletal radiologist blinded to histological data qualitatively evaluated the cartilaginous tumors based on tumor size and signal characteristics and adjacent bone marrow, cortex and soft-tissue changes.

Results

A Support Vector Machine correctly classified 75% of chondrosarcomas as low or high grade based on the datasets obtained by the subset evaluator feature selection mode. Specifically, true positive rate was 80% and 67% for identification of high-grade and low-grade tumors, respectively. There was no statistical difference in the number of errors between the high-grade and the low-grade tumor groups (P=0.551). The area under the receiver operating characteristic curve was 0.77. The musculoskeletal radiologist correctly graded 69% of chondrosarcomas as low or high grade. There was no statistical difference in terms of diagnostic performance between the ML approach and the radiologist (P=0.694).

Conclusion

ML algorithms had good accuracy for low-grade and high-grade chondrosarcoma classification based on extraction of texture analysis features from unenhanced MRI examinations. Even though qualitative image assessment still plays a central role in the diagnosis, our ML approach did not show inferior diagnostic performance compared to an experienced radiologist and could prove a valuable aid in the preoperative tumor characterization.

**COD. P23**

**Risonanza magnetica nei tumori renali: predizione del grading istologico con Texture Analysis e Machine Learning.**

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Introduzione
L'incidenza del carcinoma a cellule renali (CCR) è in aumento nel mondo occidentale. Il tasso di mortalità relativamente elevato impone un'accurata stratificazione del rischio nei pazienti affetti da questa patologia, per garantire le strategie terapeutiche più adeguate. Tra i parametri correlati con la prognosi, ed in particolare con la recidiva di malattia dopo trattamento chirurgico, vi è il grading istologico, disponibile esclusivamente dopo l'intervento chirurgico. Scopo del nostro lavoro è stato valutare se un approccio combinato di Texture Analysis (TA) e Machine Learning (ML), applicato ad immagini di Risonanza Magnetica (RM), potesse consentire di predire il grading istologico in pazienti affetti da CCR.

Materiali e metodi
Un totale di 27 pazienti consecutivi, trattati con nefrectomia radicale e con diagnosi istologica di CCR, sono stati inclusi nello studio e suddivisi in due gruppi a seconda del grading istologico (17 pazienti con CCR di basso grado e 10 pazienti con CCR di alto grado). Tutti i soggetti erano stati sottoposti ad esame RM con MdC prima dell'intervento chirurgico. Un radiologo esperto ha posizionato delle regioni di interesse (ROI) bidimensionali sulle immagini assiali T2 e T1 Vibe post-contrastografiche, segmentando manualmente la lesione tumorale sulla sezione in cui era maggiormente rappresentata. Utilizzando le ROI così ottenute e le immagini corrispondenti sono stati estratti i parametri di TA. Successivamente, tali parametri sono stati sottoposti, attraverso un software dedicato per il data mining, ad un processo di riduzione e di selezione allo scopo di identificarne i più significativi nella predizione del grading. Molteplici algoritmi di Machine Learning sono stati impiegati alla ricerca del classificatore con la performance migliore. Una cross-validazione con 10 fold è stata impiegata per valutare l'accuratezza dei classificatori.

Risultati
In tutto, 172 parametri di TA sono stati estratti per ciascun paziente, 86 per ciascuna ROI su ciascuna sequenza. I processi di riduzione e selezione dei parametri ottenuti hanno rivelato che il parametro definito come Joint Energy estratto dalla Gray Level Co-occurence Matrix delle immagini post-contrastografiche è quello maggiormente correlato al grading istologico. Utilizzando tale parametro, il classificatore di ML (Locally Weighted Learning) ha raggiunto un'accuratezza del 78% nel predire il grading istologico, con 21 pazienti correttamente classificati su 27.

Conclusione
L'approccio combinato TA e ML su immagini RM si è dimostrato promettente nella predizione del grading istologico in pazienti con CCR. Ulteriori studi con maggiore numerosità campionaria sono tuttavia indispensabili per stabilire il possibile ruolo di questa strategia nella pratica clinica.

**COD. P24**

**Safe Follow-up after EndoVascular Aortic Repair (EVAR) with Non-contrast Magnetic Resonance Imaging (NCMRI): the SAFEVAR Study**

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The aim of this study is to define the diagnostic accuracy of non-contrast MRI with CT as reference standard in the follow up of patients treated with endovascular aortic repair (EVAR).

Forty-two patients after EVAR for aortic and/or iliac arterial aneurysms were prospectively enrolled and underwent MRI and contrast-enhanced CT in the same day between 0,01 and 1,55 years after the implantation. MRI was focused on true fast imaging with steady-state free precession (TRUFI) and half-Fourier-acquisition single-shot turbo spin-echo (HASTE) sequences at the precise level of the vessel were EVAR was implanted. CT was performed before and after iodate contract injection. Two independent observers reviewed MRI to evaluate the presence of hyperintensity near the EVAR. Then, they evaluated in CT images the presence of endoleak and classified them according to the classification of Stanford in type I (a,b) and II.

MRI revealed that 11 patients had no hyperintensity, and no one of these had endoleak in CT images. 31 patients presented hyperintensity in MRI, and 19 of these reveled a presence of endoleak (6 type I, 13 type II). Sensitivity, specificity, positive predictive value and negative predictive value of both observers were 100% (19/19), 48% (11/23), 61% (19/31) and 100% (11/11) respectively. Positive likehood ratio was -1.9 and negative likehood ratio was 0.52.

The absence of hyperintensity near the EVAR in MRI images can exclude the presence of endoleak; nonetheless the hyperintensity can correlate with the presence of endoleak and require CT with iodate contrast to confirm it.

**COD. P25**

**Machine learning classification of soft tissue lipomatous tumors: preliminary results**

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The purpose of this study is to evaluate the diagnostic accuracy of machine learning (ML) algorithms to discriminate soft tissue lipomatous tumors based on texture analysis (TA) parameters from unhenanced Magnetic Resonance Imaging (MRI). We retrospectively enrolled 35 patients (n=18 atypical lipomatous tumours, n=13 lipomas and 4 liposarcomas) with pre-operative MRI. All lesions were histopathologically confirmed. Lesions were manually segmented by drawing a bi-dimensional polygonal region of interest (ROI) by a musculoskeletal radiologist on T1 and T2-weighted images, which were used for first order and texture feature extraction on a dedicated software (MaZda). Data were analyzed with Weka v3.8.2. Datasets were preprocessed by employing feature selection (one rule, correlation, information gain and C4.5 learner-based) and data reduction techniques was used (principal component analysis) to obtain different parameter subsets. For each lesion different data subsets obtained by four-feature selection methods were analyzed to evaluate their accuracy in identifying benign vs. malignant lypomatous tumours and Lypoma vs. liposarcoma vs. atypical lipomatous tumours. In absence of a dedicated test population, 10 iterations of 10-fold cross-validation were used to estimate the accuracy on a new population.

The Area Under the Receiver Operating Characteristic Curves for the best performing algorithm, a C4.5 tree, was 0.77 (0.21) and 0.87 (0.23) respectively for histopatological and benign vs malignant classification. Sensitivity and specificity in distinguish between benign and malignant were 85% and 86%, respectively, with 85% of tumors that were correctly classified. Algorithms show good accuracy in lipomatous tumors classification based on non-contrast MRI exams.

**COD. P26**

**T-staging del carcinoma della prostata: analisi della prevalenza e del valore predittivo dei criteri più utilizzati nella valutazione dell'estensione extracapsulare in risonanza magnetica.**

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Scopo: Valutare la performance dei criteri più utilizzati in risonanza magnetica (RM) per identificare l'estensione extracapsulare (ECE) del carcinoma prostatico (PCa).

Materiale e metodi: Retrospettivamente sono state valutate da 4 radiologi le RM pre-biopsia (T2WI, DWI, DCE con apparecchio 3 Tesla) di 67 pazienti (età media 63 anni, PSA medio 17 ng/ml) sottoposti sucessivamente a prostatectomia radicale tra il 11/2011 e il 12/2014. Di 8 criteri selezionati dalla letteratura sono stati calcolati la prevalenza e il valore predittivo positivo (PPV) utilizzando la media dei risultati dei quattro lettori, la cui concordanza è stata calcolata con l'agreement percentuale e con la K di Fleiss.

Risultati: Il contatto fra PCa e capsula prostatica è il segno con maggior prevalenza (56.9%) ma con il minor PPV (51.9%), sebbene esso aumenti con l'aumentare della lunghezza (57.9% se = 10 mm e 81.3% se = 20 mm). La prevalenza e il PPV degli altri criteri sono, rispettivamente: 18.6% e 69% per l'interruzione del segnale a livello capsulare, 11.8% e 75% per i margini sfumati, 14.7% e 75% per la protrusione capsulare, 8.8% e 85.7% per i contorni capsulari irregolari, 6.9% e 87.5% per l'infiltrazione dell'adipe periprostatico, 2.9% e 100% sia per l'obliterazione dell'angolo retto-prostatico che per la presenza di massa periprostatica. La concordanza fra lettori è compresa tra il 75% (per i margini sfumati) e il 94% (per la massa periprostatica e l'obliterazione dell'angolo retto-prostatico).

Conclusioni: L'ampio contatto fra capsula e PCa, i contorni capsulari irregolari, l'infiltrazione dell'adipe periprostatico, l'obliterazione dell'angolo retto-prostatico e la presenza di una massa periprostatica sono risultati i criteri associati a un maggior rischio di ECE da parte del Pca. Gli altri criteri sono più frequenti ma meno predittivi di ECE.

**COD. P27**

**Use of targeted prostate biopsy performed by fusion tecnique of multiparametric magnetic resonance (mpMR) and transrectal ultrasonography (TRUS): preliminary results**

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Aim

The aim of the study is to determine the diagnostic accuracy of the prostate biopsy (BX) MRI/TRUS guided performed with Fusion technique in the detection of malignant lesions compared to the systematic biopsy (SB) TRUS guided.

Material and methods

22 patients (pts), of whom 18 with a previous negative BX and 4 in active surveillance (AS), all with at least one MR suspected lesion (PIRADS score ≥3) were subjected to MR / TRUS fusion imaging by an electromagnetic tracking system (with BX of suspicious lesions). Subsequently in the same session a second operator blinded the guided SB TRUS (12 samples). Histological evaluation of biopsy samples was then performed.

Results

The total suspected areas of MRI were 26. The global detection rate per core was 38.9% (46/118) for the RM / TRUS targeted BX and 13.4% (29/216) for the SB. The global detection rate per pts was 59% (13/22) and 50% (11/22), respectively. The detection rate for clinically significant tumors was 92% (12/13) for targeted with fusion technique and 45% (5/11) for SB. In the 4 pts in AS, the SB was negative in 3, while the targeted biopsy identified 3 pts with clinically significant tumor and 1 pt negative.

Conclusions

There are no concordant results on what is the best technique for performing targeted MR prostate biopsy. Our data demonstrate that the targeted BX performed by MRI / TRUS fusion technique presents a superior detection rate of malignant lesions compared to the SB allowing to identify a greater number of clinically significant tumors with fewer samples and reducing any risks related to the maneuver. These results require confirmation on a larger number of pts.

**COD. P28**

**Mappatura rapida T1, T2, PD, T2* usando 2 sequenze a flip angle variabile spoiled gradient echo e SSFP**

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Obiettivi. La disponibilità di una mappatura rapida di T1 e T2 in pazienti interessati da glioblastoma, problemi cardiaci, renali ed epatici, suscita sempre più interesse per la sua valenza clinica. Le tecniche convenzionali di mappatura che utilizzano più tempi di ripetizione, di inversione e multi tempo di echo sono troppo lente, in particolare per applicazioni 3D. Il nostro lavoro sfrutta le sequenze spoiled gradient echo (SPGR) e SSFP con soli 2 flip angle per ottenere 4 diverse mappe: T1, T2, densità protonica (PD) e T2*.

Materiali e Metodi. Una sequenza SPGR è stata eseguita su un fantoccio ad acqua con una parte di cloruro di nichel, è stata acquisita una slice con 2 dinamiche a 2 flip angle diversi. La formula analitica dello stato stazionario SPGR si può linearizzare in modo da ricavare il T1 per ogni voxel. Una seconda scansione a stati stazionari SSFP anch'essa a 2 diversi flip angle, permette di ottenere il T2 conoscendo il T1. Sfruttando le espressioni del profilo del segnale si calcola una mappa in unità arbitrarie della densità protonica (PD) e una mappa assoluta del T2*.

Risultati. I valori di T1, T2 e T2* hanno una variazione entro il 10% da quelli misurati con le tecniche convenzionali di spin echo muti tempo di inversione, multi tempo di ripetizione e multi tempo di echo.

Conclusioni. La tecnica è molto rapida e accurata e può essere migliorata implementando una sequenza di mappatura B1 per la correzione del flip angle; in più può essere sviluppata per il suo utilizzo in 3D, dato che permette di mantenere un basso SAR.

**COD. P29**

**Cardiac MRI with Open 1.0-T versus Closed 1.5-T Unit: Image Quality Assessment**

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Background: Currently there is only one study regarding the use of an open 1.0-T MRI system (1.0T-Open) in patients with cardiac disease, and it is unclear whether the lower magnetic field allows for adequate assessment of these patients.

Purpose: To compare image quality of cardiac magnetic resonance (MR) examinations performed using a 1.0T-Open to that obtained with a closed 1.5-T system (1.5T-Closed).

Materials and Methods: We retrospectively evaluated two-hundred consecutive patients with cardiac disease undergone to 1.0-T (open magnet) and 1.5-T (closed magnet) MRI. For each sequence, the signal-to-noise ratio of blood (SNRb) and myocardium (SNRm), and their contrast-to-noise ratio (CNR) were calculated, and image quality was appraised using a 3-point (1=poor; 2=partial artefacts; 3=optimal) and 2-point (1=diagnostic; 2=not-diagnostic) Likert scale.
Mann-Whitney U test, Pearson $\chi^2$ and Cohen k were used.

Results: SNR and CNR in cine and short-tau inversion recovery (STIR) sequences resulted significantly lower ($p<0.001$) in 1.0T-Open compared to 1.5T-Closed. In late gadolinium enhancement (LGE) sequence, SNRm results significantly higher ($p<0.001$) in 1.0-Open than 1.5T-Closed, while CNR results significantly lower ($p<0.001$) at 1.0T-Open than 1.5T-Closed. The comparison of image qualities evaluated using the 3-point scale score showed an almost perfect agreement for cine ($k=0.963$), T1-weighted ($k=0.984$) and LGE ($k=0.981$), and a perfect agreement ($k=1.000$) for STIR. Using the 2-point scale, agreement was strong for cine ($k=0.886$) and STIR ($k=0.816$), almost perfect ($k=0.990$) for LGE, and perfect ($k=1.000$) for T1-weighted.

Conclusion: In cardiac imaging, although in 1.0T-Open the SNR and CNR are lower than in 1.5T-Closed, subjective quality of images between the two units is comparable. Thus, when certain contraindications are present, for instance obesity or severe claustrophobia, open MR may provide a helpful alternative without compromising quality.

**COD. P30**

**Late gadolinium enhancement in cardiac magnetic resonance with different doses of contrast material in patients with chronic myocardial infarction**

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Purpose: to determine if different dosages of gadolinium-based contrast agent provide the same quantitative image quality with regards to contrast-to-noise ratio (CNR) and signal-to-noise ratio (SNR).

Materials and methods: we retrospectively evaluated cardiac magnetic resonance (CMR) examinations of patients who had chronic myocardial infarction and had undergone gadobutrol-enhanced CMR. Patients with small infarctions (<50% of wall thickness) and with extensive artefacts were excluded. Regions of interest were drawn in T1-weighted inversion recovery gradient echo sequences for late gadolinium enhancement over the healthy myocardium, scarred myocardium, blood pool and air. SNR and CNR were subsequently calculated.

Results: our study population was composed by 94 patients, 37 of which had received 0.10 mmol/kg of gadobutrol, 26 0.15 mmol/kg, and 31 0.20 mmol/kg. Infarcted myocardium SNR was 50.8(interquartile range (IQR) 43.4#64.2) for the 0.10 group, 70.0(IQR 50.9#112) for 0.15 and 72.1(IQR 58.3-100.2) for 0.20. CNR between infarct and normal myocardium was 71(IQR 60.7#85) for 0.10, 96.5 (IQR 71.4#153.2) for 0.15 and 103.9(IQR 83.3#133.5) for 0.20. CNR between infarct and blood was 30.3(IQR 23.7#41.4) for 0.10, 32.7(IQR 17.6#62.5) for 0.15 and 29.6 (IQR 17.8#54) for 0.20. There were significant differences between 0.10 and 0.15 in SNR of the infarct (p=0.006) and in CNR between infarct and normal myocardium (p=0.001), while there were no significant differences in CNR between infarcted myocardium and blood (p=0.780). There were no significant differences between the 0.15 and the 0.20 group for SNR or any CNR (p=0.619,p=0.631,p=0.785 respectively).

Conclusion: gadobutrol dosages higher than 0.15 do not appear to provide quality benefits to CMR examinations and might thus be potentially avoided due to possible risks.

**COD. P31**

**MRI features of Breast implant-associated anaplastic large cell lymphoma.**

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Breast implant-associated anaplastic large cell lymphoma (BIA-ALCL) is a rare and new subtype of T cell Non-Hodgkin Lymphoma (NHLs) associated with breast implants.The mechanism involved in the development of this kind of lymphoma is still uncertain and its pathogenesis is currently under investigation.BIA-ALCL is generally an indolent disease localized to the breast implant and effectively treated with capsulectomy alone without chemotherapy. Clinically, BIA-ALCL may present as capsular contracture, seroma without spontaneous resolution, or peri-implant masses while radiologically as fluid within the intracapsular space or as an intracapsular or peri-implant mass. Magnetic resonance imaging (MRI) represents the best imaging technique to assess suspected cases of lymphoma and the state of the implants.

The main purpose of this poster is to illustrate the MRI signs of BIA-ALCL and correlate them with the corresponding ultrasound and pathology features in order to improve the knowledge of this type of lymphoma.

**COD. P32**

**Ottimizzazione di Bobine a Radio Frequenza di Volume Doppiamente-Tunate per Applicazioni di Risonanza Magnetica a 7 T**

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Introduzione

In questo studio si descrive un metodo innovativo che utilizza simulazioni Elettro-Magnetiche (EM) per ottimizzare bobine a radio frequenza (RF) di volume Doppiamente-Tunate (DT) per applicazioni di risonanza magnetica del sodio e del protone a 7 T. L'obiettivo è di ottimizzare l'omogeneità spaziale del campo a RF del protone a 7 T in un volume utile per imaging dell'encefalo umano. A tal fine, è stato scelto un modello non convenzionale di bobina RF DT, noto in letteratura come 'four-ring birdcage' [1], formato da tre strutture coassiali di tipo birdcage che hanno identico diametro. Il nostro studio ha richiesto l'analisi della omogeneità del campo magnetico a RF al variare dei gradi di libertà geometrici, cioè la lunghezza relativa della birdcage interna e delle due esterne. Il range delle variazioni geometriche è stato fissato in base all'applicazione finale prevista per la bobina, ossia l'imaging dell'encefalo umano.

Metodo

Le tre strutture del 'four-ring birdcage' hanno lo stesso diametro e condividono le cosiddette leg delle tre birdcage. La struttura più interna è una birdcage in configurazione passa-basso, sintonizzata alla frequenza di Larmor del sodio a 7 T ($^{23}$Na, 78.86 MHz) tramite dei condensatori posizionati sulle leg. Questa condivide in modo simmetrico i suoi due end-ring con le due strutture birdcage esterne, che sono invece due birdcage in configurazione passa-alto con i condensatori posizionati solo sui due end-ring esterni. Le strutture esterne generano il campo a RF del protone a 7 T ($^{1}$H, 298.03 MHz) in corrispondenza del proprio centro e la loro opportuna combinazione produce il campo a RF del protone nella regione centrale della bobina. La presenza di queste tre strutture risonanti comporta la necessità di scegliere in modo opportuno le lunghezze della birdcage interna e delle due esterne per ottimizzare l'omogeneità del campo a RF per $^{1}$H. A tal fine, i parametri geometrici legati alle lunghezze relative delle tre strutture risonanti sono stati variati e ad ogni variazione è stata valutata l'omogeneità del campo a RF mediante la polarizzazione circolare destra, $B_1^+$, valutata secondo il protocollo NEMA [2]. Le mappe del campo a RF sono state ricavate con simulazioni CST-MWS (Computer Simulation Technology – MicroWave Studio), che implementa il metodo FDFD. Nell'ambiente di simulazione è stato inserito un carico sferico con dimensioni (diametro=180mm) e parametri elettrici (permittività dielettrica=80; conducibilità=0.6 S/m) equivalenti a quelli dell'encefalo umano.

Risultati e Conclusioni

I risultati ottenuti mostrano che l'omogeneità del campo a RF, $B_1^+$, particolarmente critica a 7 T, può essere ottimizzata in funzione della lunghezza delle due strutture esterne. In particolare il valore percentuale maggiore per quanto riguarda l'omogeneità del campo a RF per $^{1}$H si ottiene con il birdcage interno di lunghezza 160 mm e ciascun birdcage esterno di lunghezza 36 mm. La dimensione totale di questa struttura ottimizzata (lunghezza 232 mm, diametro 180 mm) è compatibile con applicazioni a 7 T per l'imaging dell'encefalo umano.

Riferimenti

[1] Murphy-Boesch, R. Srinivasan, L. Carvajal, R. R. Brown, "Two configurations of the four-ring birdcage coil for $^{1}$H imaging and $^{1}$H decoupled $^{31}$P spectroscopy of the human head", J. Magn. Reson., B103, pp 103-114, 1994.
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**COD. P33**

**Radiomica basata su MRI per cordomi della base cranica trattati con ioni carbonio: risultati preliminari per la predizione di controllo locale**

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Motivazione.

Valutare il potere predittivo di features radiomiche rispetto al controllo locale in pazienti affetti da cordoma della base-cranio trattati con radioterapia con ioni carbonio (CIRT).

Materiali e metodi.

Dei pazienti affetti da cordoma della base cranica e trattati mediante CIRT (70.4 Gy(RBE)) presso il centro di adroterapia nazionale oncologica (CNAO, Pavia) tra il 2014 e il 2016, 56 sono stati selezionati retrospettivamente secondo le caratteristiche delle immagini di Risonanza Magnetica (MRI) acquisite prima del trattamento, lo stesso giorno della TC di pianificazione. Per ciascun paziente sono state acquisite sequenze 2D pesate in T1 (TE/TR=2.48-11/377-887ms, flip-angle=67-150°, risoluzione=0.47x0.47x3-0.97x0.97x3 mm) ed in T2 (TE/TR=76-104/2400-10951ms, flip-angle=80-150°, risoluzione=0.46x0.46x3-0.78x0.78x5 mm). La TC, a cui è associata una mappa di dose (risoluzione=2x2x2mm), è stata registrata rigidamente su ciascuna MRI per propagare il contorno del tumore delineato manualmente in fase di pianificazione. Il controllo locale è stato deifinito come variabile binaria, dove un valore positivo indica la mancanza di progressione di malattia all'ultimo esame di follow-up clinico (tempo mediano di follow-up: 34.5 mesi, controllo locale globale=68%).

Per compensare le variabilità dell'acquisizione MRI, sono state applicate la correzione di bias del campo magnetico e la normalizzazione di intensità, tramite matching di istogrammi. Quindi, sono state calcolate 107 features radiomiche (14 di forma, 18 del primo ordine, 75 di texture) 2D aggregate da ciascuna MRI e 3D dalla mappa di dose. Sono state selezionate le 10 features più rilevanti mediante un metodo di selezione supervisionato basato su mutua informazione per le features T1, T2, T1 e T2, e di dose. Infine, è stato utilizzato un algoritmo random forest per la classificazione. L'area sotto la curva ROC (AUROC) è stata calcolata sia per dati di training (media±deviazione standard, tramite cross-validazione 10-fold su 80% dell'intero dataset) che di test (20% del dataset) come indicazione del potere predittivo delle features rispetto al controllo locale. Un'AUROC di 0.500 identifica un classificatore random.

Risultati.

Le AUROC di training e test sono risultate essere rispettivamente 0.644±0.31 e 0.688 per features selezionate da T1, 0.628±0.31 e 0.641 da T2 e 0.634±0.31 e 0.875 dalla dose. Combinando features T1 e T2, è stato possibile ottenere AUROC di 0.684±0.30 per il training e 0.781 per il dataset di test.

Conclusioni.

Features radiomiche estratte da MRI sono state usate per predire il controllo locale in pazienti affetti da cordoma della base cranica trattati con CIRT. Da risultati preliminari si nota che features estratte dalla mappa di dose mostrano le migliori performance sul dataset di test. Inoltre, la combinazione di features estratte da T1 e T2 sembra fornire prestazioni migliori rispetto all'utilizzo di modalità di imaging individuali. Ulteriori analisi avranno l'obiettivo di migliorare la performance del modello e di effettuare una valutazione su un dataset più vario ed ampio.

**COD. P34**

**Scanner-dependence and software-dependence of magnetic resonance imaging (MRI) T1 and T2 relaxation times measurements at 1.5 T using an NMR spectrometer as reference.**

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Purpose

A new approach to the evaluation of standardization of nuclear relaxation times was proposed in order to take in to account the possibility of finding $T_1$ and $T_2$ mapping independence from the MRI scanners used.

Aim of this study was the assessment of the standardization in measuring nuclear relaxation times for $^1$H nuclei from post-processing of phantom images acquired with different vendor clinical magnetic resonance imaging (MRI) scanners and an NMR spectrometer.

Methods

Six vials of an Eurospin phantom (Diagnostic Sonar, UK), filled with agarose gels doped with gadolinium, were analysed with three different scanners: a nuclear magnetic resonance (NMR) spectrometer, used for the restatement of the gold standard $T_1$ and $T_2$ relaxation times values at 1.5 T with SR (Saturation Recovery), IR (Inversion Recovery), SE (Spin-Echo) and CPMG (Carr-Purcell-Meiboom-Gill) sequences; a Siemens Magnetom Aera and a General Electric Signa MRI scanners with which phantom images were acquired with body coils and by means of standard clinical sequences SE (Spin Echo, 3 images: $T_E$ from 20 ms to 100 ms; $T_R$ = 1500 s) and IR (Inversion Recovery, 8 images: $T_I$ from 100 ms to 3300 ms; $T_R$ = 5000 ms).

Images were processed by vendor independent software: Cvi42 (Circle Cardiovascular Imaging Inc.), an open source software, Segment (http://www.medviso.com). A manual computation of relaxation times was also performed using the gnuplot software (http://gnuplot.info).

Results

Results from Cvi42 and Segment maps were comparable with those evaluated with gnuplot (discrepancy below 1%).

Gnuplot manual fit procedure allowed the measurement of real fit errors of estimated relaxation times values obtained with mapping software (Cv142 and Segment).

$T_2$ values measured with the spectrometer Spin-Echo sequence were affected by a high diffusion, which suppressed the signal from the vials, and it shortened the relaxation of every scanned vials to a value near 20 ms. Thus, as reference values for the $T_2$ relaxation times, we considered the CPMG results.

In order to compare $T_1$ and $T_2$ values of MRI results with those estimated with the NMR spectrometer, which were standard reference values, the temperature difference of the various sites in which acquisitions were performed was considered: room temperature of spectrometer site was 23°C, Aera site was at 20°C and Signa compartment was at 21°C. The comparison was performed by reconducting values measured from cvi42 maps (Aera 20°C, Signa 21°C) at the same temperature of the standard reference values obtained by NMR spectrometer analysis (23°C), assuming a linear dependence.

Relaxation times calculated from data acquired with the three scanners showed a good agreement in the limits of experimental errors (on average, ± 3% for $T_1$ and ± 10% for $T_2$).

Conclusion

A good standardization level between different MRI and NMR devices and between different software for relaxation times estimation were shown. Results suggested that estimation methods are MRI diagnostic scanner-independent, but not sequence-independent. Gnuplot analysis helped in highlighting the importance of analysing both parametric maps and standard deviation maps associated to the first ones.

**COD. P35**

**ADC dependence on phase encoding direction: a multicentre intercomparison study**

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Purpose: To evaluate the dependence of Apparent Diffusion Coefficient (ADC) with respect to phase encoding direction, using a standardized spherical water phantom. Results may be used to characterize MRI scanner performance and may play a relevant role on quantitative imaging biomarker measurements. Preliminary results of a multicentre intercomparison are reported.

Methods and materials: twelve MRI scanners were enrolled in this study: four with 3T static magnetic field strength, eight with 1.5T. A custom PMMA spherical water phantom (14 cm diameter) specifically designed for Quality Assurance in Diffusion Weighted Imaging was provided to all participant centres. Phantom ADC value was certified as described in [1]. All the acquisitions were performed placing the phantom at isocentre of the scanner and using head coil.As described in [2], three DWI sequences with b-value ranging from 0 s/mm$^2$ to 1000 s/mm$^2$ (with 200 s/mm$^2$ steps), differing for the diffusion gradient direction (along the three main orthogonal axes), were performed. Axial plane images, with 5 mm slice thickness and 5 mm gap, were acquired. Acquisitions were repeated exchanging frequency and phase encoding directions.ADC maps were calculated for each gradient diffusion direction. Seven 2x2cm$^2$ ROIs were considered, one at isocentre and six in periphery (in left, right, superior, inferior, head and feet position with respect to isocentre). For each diffusion gradient direction and ROI, relative difference between two different phase encoding directions were evaluated.

Results: Maximum ADC relative difference between the two phase encoding directions, for all the three considered diffusion gradient directions, varies between -2% and +2.5% in peripheral ROIs, and is within 1% on central ROI. No differences were measured between 1.5T and 3T scanners performances.

Conclusion: A simple protocol for quantitative evaluation of ADC phase encoding direction dependence has been proposed. Dependence of ADC with respect to phase encoding direction should be consider in precision ADC measurements.

[1] Quality assurance multicenter comparison of different MR scanners for quantitative diffusion-weighted imaging; G. Belli et al. J Magn Reson Imaging. 2016 Jan;43(1):213-9. doi: 10.1002/jmri.24956. Epub 2015 May 26
[2] Dependence of apparent diffusion coefficient measurement on diffusion gradient direction and spatial position – A quality assurance intercomparison study of forty-four scanners for quantitative diffusion-weighted imaging; L. Fedeli et al. Physica Medica Volume 55, November 2018, Pages 135-141. doi: https://doi.org/10.1016/j.ejmp.2018.09.007

**COD. P36**

**Accuracy of T1 estimation in cardiac T1 mapping - Preliminary phantom test results.**

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Purpose: Basic protocols for quality assurance in magnetic resonance imaging (MRI) include performance assessment of MRI scanner at level of subsystems (static magnetic field, radiofrequency and field gradients), global system and a combination of subsystems and global system (AAPM Report N. 100 - 2010). However, these tests might be insufficient in assessing scanner performance when advanced clinical protocols are used. In the last few years quantitative imaging methods have evolved in cardiac applications, with T1 mapping being of great value in the assessment of changes of myocardial tissue composition (eg. myocarditis, amyloidosis and Anderson-Fabry). This work aimed at assessing the accuracy of T1 estimation in cardiac T1 mapping by using a phantom.

Methods: T05 Eurospin phantom, including 12 gel tubes with calibrated longitudinal relaxation times T1, ranging from about 200 ms to about 1300 ms, was scanned, using different imaging protocols, designed for T1 map calculation, while heart pace was simulated at 60 bpm. Nominal and estimated values of T1 were compared for Smart T1 map ARC, Smart T1 map ASSET, Molli T1 map ARC, Molli T1 map ASSET and corrected Molli sequences, run on a scanner GE Optima 450, 1.5T.

Results: Percentage differences ranged from 4% to 30%, depending on acquisition protocol and T1 values. In particular, the best agreement was achieved for Smart T1 map (ARC and ASSET) and Corrected Molli, with the percentage difference being about 5% for T1 values ranging from 300 to 1000 ms. Smart T1 resulted less accurate for long T1 (> 1000 ms), whereas Corrected Molli showed poorer accuracy for short T1 (< 300 ms).

Conclusion: We think that the assessment of the accuracy of the T1 quantification at Institutional level is relevant in clinical practice. The method described here is easy to apply and reproducible. Nonetheless, further investigations are required in order to accurately assess the performance of CARDIAC T1 mapping protocols.

References: Messroghli DR, Moon JC, Ferreira VM et al, Clinical recommendations for cardiovascular magnetic resonance mapping of T1, T2, T2* and extracellular volume: a consensus statement by the Society for Cardiovascular Magnetic Resonance (SCMR) endorsed by the European Association for Cardiovascular Imaging (EACVI), Journal of Cardiovascular Magnetic Resonance (2017), 19:75.

**COD. P37**

**Esperienza decennale di una procedura per la valutazione preventiva dei dispositivi medici impiantati in risonanza magnetica**

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Il DM 10-8-2018 riguardante la determinazione degli standard di sicurezza e impiego per le apparecchiature a risonanza magnetica obbliga la struttura sanitaria a predisporre un modello organizzativo specifico finalizzato a regolare l'accesso al SITO RM per i soggetti portatori di qualsiasi dispositivo od oggetto inamovibile dal corpo e di dispositivi impiantabili attivi. La procedura deve essere codificata in un documento, riportato anche nel Regolamento di Sicurezza, nel quale siano chiarite le competenze e le modalità di esecuzione della valutazione in tutta sicurezza del dispositivo medico in esame. Presso il Servizio di Radiologia dell'ICS Maugeri di Pavia è in uso una procedura finalizzata a discriminare i dispositivi medici che non possono essere esposti a campi magnetici da quelli che possono essere introdotti liberamente o nel rispetto di prestabilite condizioni. All'atto della prenotazione, il personale del CUP si accerta se il paziente è portatore di dispositivi impiantati, in particolare di protesi metalliche e dispositivi elettronici. In caso affermativo, viene richiesto al paziente di fornire la documentazione relativa al dispositivo, almeno per quanto riguarda marca, modello e anno di impianto. La documentazione viene quindi esaminata da fisici specialisti del Servizio di Fisica Sanitaria, i quali valutano la presenza di rischi per il paziente e prescrivono eventuali condizioni di sicurezza, anche sulla base delle informazioni richieste direttamente al fornitore o distributore in Italia. Queste indicazioni vengono quindi sottoposte al medico responsabile dell'esecuzione dell'esame il quale, in base alla propria esperienza clinica, alla valutazione delle condizioni del paziente e all'effettiva utilità dell'esame, decide sull'opportunità e sulle modalità di esecuzione dell'esame stesso. Vengono così fornite ai TSRM le corrette indicazioni a garanzia della sicurezza della prestazione e della salute del paziente.Dal 2006, anno di introduzione della procedura, sono stati analizzati circa 500 casi a fronte di 7500 esami RM all'anno. I vantaggi sono stati molteplici. Innanzitutto, è stato possibile intercettare in anticipo i pazienti portatori di pace-maker o di altre protesi dotate di circuiti elettronici, dispositivi controindicati per l'esame RM secondo la precedente normativa (DM 2-8-81). Sono state quindi garantite le condizioni di sicurezza per i pazienti portatori di protesi e impianti classificati "MR safe" e "MR conditional". Si sono infine ridotti i casi in cui si è deciso di precludere al paziente l'esecuzione dell'esame RM all'atto della visita anamnestica, garantendo così continuità alla programmazione giornaliera. Dal 2017, sulla base dell'esperienza acquisita, si è deciso di aggiungere all'atto della prenotazione la verifica della presenza di espansori per protesi mammarie, in quanto questa informazione veniva spesso omessa dalle pazienti e se ne aveva conto solo attraverso il questionario anamnestico, e, relativamente alle protesi metalliche, di restringere la valutazione solo a quelle impiantate prima dell'anno 2000, in quanto quelle successive sono risultate nella quasi totalità dei casi "MR safe".Questa procedura si è pertanto rivelata valida e affidabile, nonostante si renda necessaria una continua riqualificazione del personale coinvolto a tutti i livelli, ed è stata utilizzata per la codifica del comportamento organizzativo da applicare nei confronti di persone portatrici di dispositivi impiantabili attivi come richiesto dal DM 10-8-2018.

**COD. P38**

**Machine learning applications in cardiac magnetic resonance imaging: A systematic review**

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Introduction: Cardiac magnetic resonance imaging (MRI) is among the ones providing the largest amount of qualitative and quantitative data. In this setting, machine learning (ML) can play different roles, overcoming the limits of conventional statistics, or aiding the clinicians' work with the automation of different tasks. However, this technology is still evolving and has not reached a massive clinical adoption. In this scenario, our aim was to review the available literature on ML applications in cardiac MRI, focusing on spread, clinical applications and type of ML-based approach.

Methods: On October 2018, a systematic search was performed using MEDLINE and EMBASE for studies reporting on ML applications in cardiac MRI. A controlled vocabulary (EMBASE thesaurus in EMBASE and medical subject headings in PubMed) was used, focusing on the two main topics: "cardiac MRI" and "machine learning". Two independent readers performed the study selection and data extraction. For each article, year of publication, first author's affiliation country, study design, sample size, study aim, and ML methodology were recorded. Results: The search provided 162 studies potentially suitable for review and, from these, 34 articles were included, 31 (91%) of which with retrospective design. All the studies were published between 2004 and 2018 with an incremental publication trend over years. Europe (n=16, 47%) and North America (n=10, 29%) were the most active geographic areas. Steady state free precession cine-MRI were mostly used images for ML applications (n=16, 47%). In most of cases (22, 65%), 1.5-T scanners were used. Among addressed aims, image segmentation (n=18, 53%) was the most frequent followed by aided diagnosis (n=4, 12%), image quality improvement (n=3, 9%) and risk stratification (n=3, 9%). Among segmentation algorithm, 11 (58%) were applied to the left ventricle, three to right ventricle and three to scar tissues (16% each). Supervised learning approaches were used in most of cases (n=26, 76%), with artificial neural networks, support vector machine and random forest approaches accounting 66% of employed algorithms. Among unsupervised machine learning approaches (n=6, 18%), principal component analysis was the most frequent technique (n=4, 66%) followed by clustering approaches (n=2, 33%).

Discussion: There is a worldwide growing interest in the application of ML methods to cardiac MRI, but we are only at the beginning of this era. Despite the incremental trend of published paper on this topic, this systematic review provides a picture of a scenario that is expected to progress in the early future. Even if promising, ML-based application are still not ready for being fully translated in clinical practice. The multiparametric nature of cardiac MRI makes it particularly suitable for future ML-based applications and, from the result of this review, we can reasonably expect that aided diagnosis will be the task that will benefit the most.

Conclusion: Currently, image segmentation (of the left ventricle) on cine-MRI images represents the principal target application. Nevertheless, it is reasonable to expect that aided diagnosis will be the future focus of ML applications for cardiac MRI.

**COD. P39**

**Management of patients with implantable medical devices who are candidates for MRI examinations**

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For a long time, patients with active implantable medical devices (pacemakers, defibrillators, neurostimulators, etc.) were prevented from performing MRI exams. The introduction of Magnetic Resonance-conditional (MRconditional) devices has allowed the performance of this type of examinations under controlled conditions.The environment in which the MRI scanners are installed and used have to meet specific requirements to ensure safe use. Any other device introduced into such an environment must be compatible for the presence of the magnetic and electromagnetic fields generated by the MRI scanners.For several years, the scientific community has shown considerable interest in this topic, in an attempt to identify technological and organizational solutions capable of extending the benefits of MRI to patients with implantable medical devices. The results obtained from the research have permitted to identify the risks arising from the encounter of these technologies and to identify technical solutions to eliminate or reduce these risks.The Italian Government has published the DL August 10th, 2018 "Determination of safety standards and use for magnetic resonance equipment". This publication is placed in this context and it forced the health care facility to prepare a specific organizational model to ensure the safety of the performance and health of the patient. Recently, also the Lombardia Region - DG Welfare, in the "Operational Lines Risk Management in Health Year 2019", proposes the definition of organizational models / good practices to be followed, such as, for example, to submit to MRI examinations patients with pacemaker MRI conditional.Already in 2017, ASST Niguarda drew up a corporate procedure with the aim of identifying a codified path shared with the various professional figures involved in various capacities in the pre-peri-post MRI examination phases.It includes: the identification of the figures of responsibility in a multidisciplinary team; the articulation of the patient's path in the different phases ranging from the request for reservation of the MRI examination and acquisition of information elements (to the CUP), continuing with the assessments by the Radiologist, Electro physiologist, as well as the Medical Physics Expert, Technologist up to, if positive, the execution and subsequent reporting of the examination.To date, 57 patients with implantable medical devices (PM, ICD, Neurostimulators, etc.) have been evaluated. Only one patient should be examined because he or she has an incompatible device (MR-unsafe).The activities carried out have been taken care by the team of Electrophysiology and the technical indications for the execution have given by the Medical Physics Expert and by the Diagnostic Team which execute the exam. The NEXO [DOSE]® exposure monitoring software (Bracco, Italy) was then used to evaluate the different examination techniques performed in correspondence with what was described. For 11 patients of the 57 analyzed there was a discrepancy with the prescribed indications.

**COD. P40**

**PETER PHAN: An MRI phantom for radiomic studies on gynaecological cancers**

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The term “Radiomics” refers to a process of quantitative analysis of medical images to obtain data useful for the pathology assessment and treatment. Radiomic features are extracted from the images with mathematical algorithms starting from the numerical value associated to each voxel in the image and they can be an expression of the phenotype of the imaged tissue. The features could be integrated into predictive models useful for prognosis and the choice of treatment strategy, especially in clinical oncology.The application of radiomics on Magnetic Resonance (MR) images of patients with gynaecological malignancies is showing promising results: e.g. radiomic features were identified to be predictive of lymph-vascular space invasion and lymph node metastasis in cervical cancer patients evaluated preoperatively. Searching the literature, it is nevertheless evident that the methods employed vary widely. The variability concerns different steps of radiomic analysis, including the protocols used for images acquisition, the segmentation procedure, the technique used for features extraction and the statistical analyses. The lack of standardization makes the comparison between images challenging. As a matter of fact, some radiomic features were proven to be non-independent of variations of MR images acquisition parameters and, as a consequence, the reliability of the proposed predictive models could be compromised. To address this problem, methodological studies on the repeatability and robustness of the radiomic features extracted from MR images are needed. For this purpose, a dedicated pelvis phantom was developed to mimic the acquisition conditions of real patients. An abdomen-shape plastic container was filled with a solution of paramagnetic ions ($MnCl_2$) in order to obtain relaxation times similar to the muscle’s surrounding gynaecological malignancies. The relaxation times ($T_1$ and $T_2$) of the tissues - both normal and tumoural - of interest were measured in vivo with dedicated sequences on both healthy volunteers and gynaecological cancer patients. An NMR spectrometer was used to evaluate $T_1$ and $T_2$ of $MnCl_2$, aiming to find the proper concentration of the solution to match the values measured on human tissues. To simulate lesions with different texture, cylindrical phantom inserts were prepared by mixing agar and tiny polystyrene spheres with different diameters, in order to create different texture to be imaged. Finally, $T_1$ and $T_2$ mapping performed on the phantom showed the expected values for the relaxation times of both the inserts and the solution, validating the work.This kind of phantom will be imaged with the same sequences used for clinical imaging of pelvis district and radiomic features will be calculated on each insert, aiming to test the ability of radiomic features to distinguish between different patterns; this ability will be evaluated for regions of interest with different volumes. Repeated acquisitions in controlled conditions will be performed to test the short- and long-term repeatability of the radiomic features. The dependence of the features on the TR, TE and other MR sequence parameters will be evaluated as well. Lastly, comparisons between acquisitions performed on different scanner (vendor and/or centre) will be assessed.

**COD. P41**

**Predictive role of ankle MRI for tendon graft choice and surgical reconstruction**

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Purpose
To assess the correlation between anthropometric parameters and sizes of ankle tendons commonly used for surgical interventions to understand if specific MRI measurements could be tendon reliable predictors of tendons size.

Methods and Materials
One-hundred thirteen patients (57 males; mean age: 42±18) underwent ankle MRI at 1.5 T. We recorded gender, height, weight, body mass index (BMI) and ankle circumference of all patients. Ankle MRI measurements performed by a radiologist with six years of experience in musculoskeletal radiology were: axial shortest diameter of achilles (AT), posterior tibial (PTT), flexor digitorum longus (FDL), flexor hallucis longus (FHL), peroneus longus (PLT), and anterior tibialis (ATT) tendons, intermalleolar distance (ID) and talus width (TW). Mann-Whitney U test was used to compare the measurements of male and female patients. Pearson's correlation coefficient was used to determine the correlation between MRI measurements and anthropometric parameters.

Results
The mean measurements obtained were: height=169±9.8cm, weight=72.4±16.4kg, BMI=25±5.7, ankle circumference= 25.7±2.3 cm, AT=5.3±1.4mm, PTT=3.3±0.6mm, FDL=2.6±0.4mm, FHL=2.7±0.4mm, PLT=2.9±0.5mm, ATT=3±0.6mm, ID=62.9±4.5mm, and TW=28.8±2.5mm. All MRI measurements were significantly higher in males than in females ($p \leq 0.12$), except for PLT ($p=0.78$). All tendon sizes were significantly correlated with weight and TW ($r \geq .228$ and $p \leq .047$). Other significant correlations were: height with AT and ATT ($r \geq .226$ and $p \leq .066$), BMI with PTT and ATT ($r \geq .215$ and $p \leq .163$), ankle circumference with AT, PL and ATT ($r \geq .218$ and $p \leq .061$), ID with PTT, FDL and PL ($r \geq .248$ and $p \leq .001$).

Conclusion
Our data might help orthopedists in preoperative planning to identify the best graft and tendon size.

**COD. P42**

**Principi fisici e tecniche di RM: dove e come i radiologi e gli specializzandi cercano le loro informazioni?**

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Obiettivo
Lo studio si propone di indagare su quali fonti radiologi specialisti e radiologi specializzandi cercano informazioni tecniche e principi fisici di risonanza magnetica (RM).

Metodi
E' stato condotto un sondaggio online con 8 domande a risposta multipla. E' stato indagato quanto spesso i radiologi e gli specializzandi avessero dubbi su principi fisici di RM o su questioni tecniche, su quali supporti e quale tipo di informazioni cercassero, in quale lingua e su quali pagine internet. E' stato usato un test del chi quadro.

Risultati
Abbiamo ottenuto 122 risposte (40 radiologi, 82 specializzandi, da 6 diversi paesi europei). Radiologi e specializzandi cercano informazioni in primis in inglese piuttosto che nella loro madrelingua (75% vs. 68%, rispettivamente, p=0.761). Gli specializzandi riconoscono avere frequentemente (51%) o spesso (32%) dubbi su principi di RM mentre i radiologi solo a volte (45%) o raramente (25%), con una differenza significativa (p=0.002). Informazioni riguardo le tecniche di post-processing sono cercate nella stessa misura sia dai radiologi specialisti che dagli specializzandi (30%, p=0.953) così come tecniche avanzate e nuove tecniche (49% vs 40%, p=0.518). I protocolli di acquisizione sono cercati di più dagli specializzandi che dai radiologi (68% vs 35%, p=0.014) così come informazioni sulle tecniche di base (66% vs 10%, p<0.001). Riguardo alla fonte delle informazioni, gli specializzandi utilizzano maggiormente internet (90% vs 60% dei radiologi, p=0.005), libri (49% vs 20%, p=0.031) o chiedono direttamente ai colleghi della stessa età (32% vs 10%, p=0.065) o a colleghi più anziani (54% vs 40%, p=0.316). La valutazione dei siti internet quali fonti di informazioni descrive un quadro dominato da radiopaedia.org, sia per quesiti tecnici che clinici (75% e 46% rispettivamente), mriquestions.com (43% e 30%) e mrimaster.com (16% e 15%).

Conclusioni
Radiologi specialisti e specializzandi cercano informazioni sui principi fisici e sulle tecniche di RM con frequenze differenti. Differenze sono state descritte anche sui temi cercati, sul tipo di informazioni e sulle pagine web consultate.

**COD. P43**

**Qualitative (T2*w) and quantitative (QSM) imaging of cortical alterations in ALS patients with bulbar impairment**

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INTRODUCTION
Patients with amyotrophic lateral sclerosis (ALS) often experience impairment of the bulbar functions such as speech and swallowing, which affect quality of life and prognosis. To distinguish the contribution of upper and lower motor neuron compartments to signs and symptoms of bulbar impairment is challenging. Currently, there are not any imaging or neurophysiological tools recommended for diagnosing the UMN-related bulbar dysfunction. Recent studies suggested the T2*-hypointensity of the primary motor cortex (M1) as a marker of UMN impairment in ALS patients, but the cortical involvement in orofacial symptoms using this technique has not been explored yet. Therefore, we investigated the T2* signal intensity of the orofacial segment of the primary motor cortex (fM1) in ALS patients and its relationship with the bulbar impairment.

METHODS
Fifty-five ALS patients were enrolled. Bulbar functions were assessed clinically, using the items I-III of the ALSFRS-R, and with neurophysiological tests. All patients underwent a 3T-MRI of the brain including two 3D T2*-weighted sequences: one, with spatial resolution of $0.39\times0.39\times1mm^3$, targeted M1 and was used for visual inspection of fM1; the other, with spatial resolution of $0.94\times0.94\times1mm^3$, covered the brain from the vertex to the ponto-bulbar junction and was used for Quantitative Susceptibility Mapping (QSM) to measure the magnetic susceptibility ($\chi$) of fM1. Two neuro-radiologists visually assessed fM1 signal intensity using a score system (0=signal intensity similar to that of the postcentral gyrus; 1=mild hypointensity; 2=marked hypointensity). $\chi$ of the cortex was measured drawing ROIs on QSM images in representative segments of fM1.

RESULTS
Nineteen out of 55 patients had bulbar symptoms.
Fourteen patients had marked fM1 hypointensity and bulbar symptoms. The marked hypointensity involved the ventral part of fM1 that is the brain region in charge of the main bulbar motor functions. In 5 out of these 14 patients, a prolongation of the central motor conduction time and/or the absence of signs of denervation in the bulbar region were recorded. All patients with bulbar onset received score=2.
Ten patients received score=1 in fM1; only one had bulbar symptoms. The mild hypointensity was usually pale and close to the hand knob, without a significant involvement of the more ventral fM1 area.
Thirty-one patients received score=0; 4 of them had bulbar impairment.
Considering score=2 as pathological, T2* hypointensity in fM1 was 74% sensitive, 100% specific and 91% accurate in identifying patients with bulbar impairment. Intra-observer and inter-observer agreement were 0.95 and 0.76, respectively. $\chi$ was significantly higher in fM1 with score=2 (0.080±0.021 ppm) compared to fM1 with score 1 (0.062±0.014 ppm) and 0 (0.047±0.012 ppm) ($p\leq0.001$).

CONCLUSIONS
The marked hypointensity and the increased magnetic susceptibility of fM1 are frequent findings in ALS patients with bulbar symptoms, involve the middle and ventral part of fM1 and are usually bilateral. The relationship with clinical and neurophysiological data suggests those MR features as markers of UMN degeneration responsible for the impairment of voluntary bulbar motor functions rather than markers of bulbar impairment.

**COD. P44**

**Supra and infratentorial morphometric alterations in Multiple System Atrophy subtypes**

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INTRODUCTION

Multiple System Atrophy (MSA) is a neurodegenerative disease characterized by dysautonomia associated with a variable combination of parkinsonism and cerebellar dysfunction. According to the predominant motor features at time of evaluation a parkinsonian (MSA-P) or acerebellar phenotype (MSA-C) are distinguished [Wenning et al., 1994]. Few studies in limited populations examined the differences in brain morphology of MSA-P and MSA-C, and without conducting specific analyses of cerebellum and midbrain [Minnerop 2007, Yu 2015].Here we investigated the differences in atrophy between the two clinical sub-types and with respect to healthy controls using a supratentorial VBM analysis and an infratentorial VBM analysis using the Spatially Unbiased Infratentorial Toolbox, SUIT.

METHODS

We retrospectively analyzed 49 patients with probable MSA (age 61.7±9.1 years, 31/18 M/F), 23 MSA-P (age 62.1±9.2 years, 16/7 M/F), and 26 MSA-C (age 61.3±9.1, 15/11 M/F), and 49 age- and sex-comparable healthy controls (HC) (age 60.4±10.5, 31/18 M/F), who underwent brain MR scanning using a 1.5T GE scanner. The standardized protocol included a volumetric T1-weighted FSPGR images (1 $mm^3$ voxel). For supratentorial VBM analyses SPM12.0 was used. Whole-brain GM maps were non-linearly registered to MNI space and masked with a cerebellum mask. To preserve anatomical details of cerebellar sub-regions and get a more accurate inter-subject alignment at the infratentorial level, SUIT (Spatially Unbiased Infratentorial Toolbox, http://www.diedrichsenlab.org/imaging/suit.htm) was used. Voxel-wise non parametric testing was conducted on GM maps using the FSL tool randomize (https://fsl.fmrib.ox.ac.uk/fsl/fslwiki/Randomise) for comparisons between groups, considering $p<0.05$ corrected for multiple comparisons (family-wise error rate) as significant. After an ANCOVA with age, sex, total intracranial volume as covariates, post-hoc tests between groups were performed with analogous covariates.

RESULTS

Supratentorial analysis showed that, compared to HC, both MSA-P and MSA-C had lower GM density within the bilateral putamina and within the right caudate, the latter with a greater extent in MSA-P. The left putamen has lower GM density in MSA-P with respect to MSA-C; in both thalami GM density was extensively reduced in MSA-C with respect HC and MSA-P. Infratentorial specific analyses showed that MSA-P with respect to HC have atrophy in the midbrain and in the cerebellar regions Right I-IV, Left I-IV, Left V. MSA-C showed a diffuse atrophy in all cerebellum and brainstem. GM density in MSA-P was not lower than MSA-C in cerebellum.

DISCUSSION

The use of specific software to run supratentorial and infratentorial analyses has shown that both MSA subtypes have reduced GM density in putamina and right caudate, and that in MSA-P the putamen GM density is reduced with respect to MSA-C, indicating a supratentorial difference in brain atrophy severity between the two sub-types not previously detected. Further analyses correlating the degree of atrophy with clinical variables could clarify this finding.MSA-C, but not MSA-P, showed extensive atrophy in the whole cerebellum. The specific analysis for infratentorial structures has allowed exact localization of regions of atrophy correlated with sensorimotor impairment (lobules I-V) in MSA-P [Schoch B 2006, Schmahmann 2009].

**COD. P45**

**Joint effect of the "patterns" of grey matter atrophy and white matter microstructural damage in relapsing multiple sclerosis with mild disability**

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Introduction

Though few recent studies in multiple sclerosis (MS) have shown non-random "patterns" of either grey matter (GM) atrophy or white matter (WM) microstructural damage, as assessed by diffusion tensor imaging (DTI), using source-based morphometry (SBM), a novel multivariate MRI-based approach, it is currently unknown whether and to what extent in MS with mild disability such distinct GM and WM patterns may be inter-related and jointly associated with clinical outcomes.

Methods

To provide an answer to these topics, we assessed patients with relapsing-remitting (RR) MS with mild disability (n=41, age=35.6±10.4 years, median Expanded Disability Status Scale [EDSS]=1.5, cognitive impairment in 22% on the Rao Battery) and age-matched normal controls (NC, n=28). SBM was applied to high-resolution T1-weighted images (for GM volume) and DTI-derived fractional anisotropy (FA) images (for WM microstructure). Regional lesion volume (LV) was computed using a standard-space atlas approach. Multivariate linear regression analyses were used to explore the predictive ability of WM damage for the patterns of GM atrophy. A mediation analysis was employed to assess the combined effect of GM and WM patterns on clinical outcomes. Significance was set at $p<0.05$, corrected for multiple comparisons.

Results

Compared to NC, MS group showed GM atrophy in 3 of 6 patterns, including deep GM (DGM), sensorimotor and posterior GM. In addition, it also showed lower FA in 2 of 4 patterns, comprising callosal splenium/corticospinal tract (sCC/CST), mainly at the level of the normal appearing WM, and posterior corona radiata/thalamic radiations (PCR/PTR), overlapping with lesion areas. All patterns of GM atrophy and decreased FA were inter-related. On multivariate analysis, LV in the commissural WM resulted the best predictor for the DGM atrophy pattern ($R^2=0.687$, $p<0.001$) whereas decreased FA pattern in PCR/PTR best predicted the atrophy patterns in sensorimotor ($R^2=0.433$, $p<0.001$) and posterior GM ($R^2=0.309$, $p<0.001$). All GM atrophy patterns combined with all decreased FA patterns showed a mediation effect (effect size from -0.21 [small] to -0.374 [medium], $p<0.05$) on EDSS while DGM pattern and decreased FA pattern in the sCC/CST jointly contributed to abnormal test of visuospatial memory (effect size = -0.311 [medium], $p<0.05$).

Discussion

The patterns of GM atrophy and decreased FA in our group of RRMS with mild disability were all inter-related, showing a combined effect on physical disability. Lesion load in the commissural WM and decreased FA pattern at the level of PCR and PTR were the best predictors for, respectively, the atrophy pattern in DGM, and in sensorimotor and posterior GM. Finally, the patterns of DGM atrophy and microstructural damage in key regions of commissural and projection tracts jointly contributed to altered visuospatial memory.

**COD. P46**

**Investigating the contribution of interhemispheric disconnection to cognitive and motor disability in Multiple Sclerosis**

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Purpose Callosal damage and disconnection have been described across different multiple sclerosis (MS) phenotypes. Interhemispheric disconnection is usually inferred as a consequence of callosal atrophy or microstructural damage, but a direct quantification of the streamlines passing through the CC has never been attempted. Here, we decided to investigate the integrity of callosal subregions in MS through a tractography-based approach, and to explore the clinical impact of interhemispheric disconnection. Methods Fifty-five MS patients (35F, mean age 52.1±10.0years; 12 relapsing remitting-RR, 20 secondary progressive-SP 12, 22 primary progressive-PP) and 24 healthy controls (HC) (12F, mean age 46.5±10.6years) were prospectively enrolled. Patients were classified as: (i) cognitively impaired (CI) when showing z-scores≤-2 in at least 2 tests of the MACFIMS battery; (ii) motor impaired (MI) when showing a score≤6.33 seconds (median value) at the 25-foot walk test. All subjects underwent MRI on a Siemens Skyra 3T including: 3D T2-weighted sequence, T1-weighted MPRAGE sequence (1x1x1mm$^3$), DKI sequence with b-values of 1000, 2000s/mm$^2$and 30 directions each in addition to b=0s/mm$^2$images and voxel size of 2×2×2mm$^3$. Lesion filling was applied on T1-W images to perform tractography with ACT. DKI images were corrected for motion and eddy currents and used to perform tractography with iFOD2 algorithm implemented in MRtrix3. From the global tractography obtained, the streamlines passing through the CC were extracted using the FreeSurfer classical parcellation in 5 portions. The number of streamlines passing through these portions was used to perform between-groups ANOVA and to investigate their predictive role on motor and cognitive status. Age and gender and the volume of the considered CC portion were entered as covariates in all statistical analysis. Regression models were further adjusted for disease duration. Results were considered significant for p<0.01 (Bonferroni corrected). Results and Discussion When compared with HC, MS patients showed a significantly lower number of streamlines passing through posterior (p=0.003) and mid-posterior (p=0.010) CC. A post-hoc analysis showed significant differences between SPMS and HC in central (p=0.006), mid-posterior (p=0.002) and posterior (p=0.002) CC, and between PPMS and HC in posterior CC (p=0.001) and mid-posterior (p=0.006) CC. Comparing RR and HC, trends were present for posterior (p=0.031) and mid-posterior (p=0.047) CC. MI status was significantly predicted by the number of streamlines passing through central (p=0.007), mid-anterior (p=0.005) and anterior CC (p=0.011). A trend was present for the model including the number of streamlines passing through posterior CC and predicting CI status (p=0.028).Conclusion The analysis of CC integrity confirms the presence of an interhemispheric disconnection in MS, mainly affecting the splenium and the posterior portion of the CC body. Streamline loss pertains mainly to occipito-temporal regions, that are severely involved in PP and SP and show an initial involvement in RR. In SP disconnection also spreads to premotor regions. The reduced number of streamlines passing through the central and anterior portions of CC is reflected in motor disability while loss of streamlines in the posterior CC is related to cognitive impairment.

**COD. P47**

**Abnormal limbic system connectivity in borderline intellectual functioning: a network-based approach.**

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Borderline intellectual functioning (BIF) is characterized by both adaptive and intellectual abilities at the border between normality and disability. Due to cognitive and adaptive difficulties, BIF children are at high risk of school failure, social and behavioral problems, and are more vulnerable as adults to develop mental and physical health problems. A previous study (Baglio et al., 2014) showed abnormal development of the gray matter (GM) in areas involved in learning. To better understand the neural basis of BIF, their structural connectivity compared to tipically developing (TD) children was studied at the network level. Children with BIF (N=36), age 8.9±1.2 years, and age-matched TD (N=14), age 9.3±1.4 years, were enrolled. Inclusion criteria for BIF children were: Full Scale Intelligence Quotient (FSIQ) ranging from 70 to 85 determined with the WISC-III; presence of difficulties impacting on daily life as measured by Child Behavior Check List (CBCL). Images were acquired on a 1.5 T Siemens Magnetom Avanto Scanner. The scanning session included: 3D T1-weighted image acquired using a MPRAGE sequence (TR/TE=1900/3.37 ms, inversion time TI=1100 ms, resolution 1x1x1 $mm^3$, 176 axial slices); diffusion-weighted images (DWI) with echo planar imaging (30 directions, b-value=1000 $s/mm^2$, TR/TE=6700/100 ms, FoV=200x200 $mm^2$, resolution 1.6x1.6x2.5 $mm^3$, 40 axial slices). The 3D-T1 images were segmented into 163 GM cortical/subcortical parcels using FreeSurfer, according to the Destrieux atlas (Destrieux et al., 2010). After preprocessing of DWI (Laganà et al., 2019), networks were created by counting the number of fibers connecting each pair of nodes normalized for their volumes (NFn). The network-based statistic (NBS) toolbox (Zalesky et al., 2010) was used to detect sub-networks where NFn differed significantly between BIF and TD children (ANCOVA with age and sex as covariates) with threshold set to 3.3 and a FWER-correction using permutation testing (10000 permutations, p=.05). Bivariate correlations between FSIQ, mean NFn values of the identified sub-network (mNFnet) and CBCL were performed to select variables for the final regression model. The NBS analysis revealed significant lower NFn in the BIF group compared to the TD in a sub-network (p=.039) composed of 40 edges and 32 nodes comprising areas belonging to the limbic system (anterior and posterior cingulate, pericallosal sulcus, orbito-frontal areas, amygdala, basal ganglia, hippocampus), and visual areas (occipital pole, lingual gyrus) prevalently on the left hemisphere. The correlations showed a significant association between FSIQ and mNFnet and CBCL. Accordingly, mNFnet and CBCL were used in a multi-variable regression model predicting FSIQ whose results were significant only for mNFnet ($R^2$=.43, $\beta$=.54, p=.001).Our data demonstrate the presence of altered structural connectivity in BIF children in a sub-network connecting areas belonging to the emotion regulation and motivation, visual processing, and memory. These data are in line with the clinical manifestations of BIF children (Peltopuro et al., 2014). Moreover, the mNFnet predicted the FSIQ of children, suggesting a close relationship. Results underline the importance of early detection of BIF condition to implement effective interventions preventing poor outcome in the adult age.

**COD. P48**

**Altered connectomic measures in primary open angle glaucoma: a graph theoretical study**

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Introduction: Resting-state functional magnetic resonance imaging (rs-fMRI) is commonly employed to study changes in functional brain connectivity in neurodegenerative conditions such as Parkinson's disease or Alzheimer's Disease. Recently, the hypothesis of a brain involvement in primary open angle Glaucoma has sprung interest for neuroimaging studies in this pathology, with evidence for changes in regional homogeneity and low frequency fluctuations in fMRI signals from glaucoma patients as compared to controls. The purpose of this study is to evaluate a putative reorganization of brain networks in glaucomatous patients through graph-theoretical measures of integration, segregation and centrality.

Methods: Eighteen glaucoma patients and seventeen healthy control subjects (age: 50-76, mean 61 years) underwent MR examination at 3T scanner rs-fMRI data (voxel size: 3.31 mm^3 , TR (ms): 3000, TE (ms): 30, 200 volumes/subjects); a three-dimensional T1 weighted, magnetization prepared rapid gradient echo (MPRAGE) image was also acquired. rs-fMRI data was preprocessed in FLS v. 6.0 (motion and distortion correction and nonlinear coregistration to standard space via the high-resolution T1 weighted image), after which spatial averaging was employed within the regions defined through the automated anatomical labeling (AAL) atlas to obtain 116 time series per subject. Pearson correlation between all-time series was employed to generate subject-wise adjacency matrices, which were thresholded at 10% density. Successively, two local nodal measures (degree and betweenness centrality (BC)), one functional integration measures (global efficiency), four measures of functional segregation (local efficiency, clustering coefficient, transitivity and modularity), and one measure of resilience (assortativity) were calculated using the Brain Connectivity Toolbox. Local measures were analyzed through the disruption index k, which measures the degree of overall reorganization of specific property in the whole network. In addition, we identified hub regions using the BC of each node. Each region was classified as a hub when the BC was 1.5 times higher than the average BC across the whole brain. All local and global metrics were compared between groups using the Mann-Whitney U Test.

Results: We found no statistically significant differences in global graph measures between glaucoma and control patients. However, we found statistically significant group-wise differences in the disruption index in all local metrics (degree, BC, local efficiency, clustering coefficient and spectral measure of centrality). For all statistically significant comparisons, the k disruption index was lower in the glaucoma group as compared to the healthy control group, highlighting a complex functional brain network reorganization pattern in glaucoma patients. Accordingly, when comparing regions classified as hubs, we found that the left superior frontal gyrus and the homolateral crus I of cerebellar hemisphere appeared in the network of glaucoma patients, while on the other hand the left insula, left lingual gyrus, left inferior occipital cortex, right fusiform gyrus disappeared from the list of hubs in glaucoma patients as compared to controls.

Conclusions: The changes in local network measures highlight profound reorganization of brain networks in glaucoma patients, supporting the interpretation of Glaucoma as central nervous system disease, possibly part of the heterogeneous group of recently described disconnection syndromes.

**COD. P49**

**Connectivity changes induced by Agoraphobia within the vestibular cortex and motor output regions of the brain.**

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Introduction: Agoraphobia) was described in 1871 as a syndrome of altered spatial perception, cognitive distortions about safe locomotion, and fear-driven limitations of mobility, associated with dizziness and unsteadiness. In the modern era, agoraphobia is a psychiatric disorder defined solely by fear and avoidance of public places. Dizziness, unsteadiness, and difficulties with spacemotion stimuli are captured in the vestibular disorder of persistent postural-perceptual dizziness (PPPD) (Staab 2017). Agoraphobia and PPPD occur independently, but trait and state anxiety promote the development of PPPD and agoraphobia may co-exist with it. Imaging studies in humans (Indovina 2015; Riccelli 2017) identified networks that connect threat and visuo-vestibular systems in the brain. The central connectivity nodes of the visuo-vestibular system are located in the posterior perisylvian cortex including parietal opercula (Indovina 2018). In studies that controlled for anxiety-related variables, PPPD was linked to reduced activity, functional connectivity, and cortical folding within the parietal opercula (OP1-4) and a wider network of visuo-vestibular regions including posterior insula, posterior superior temporal sulcus, superior parietal cortex and motor vestibular regions (Indovina et al., 2015; Riccelli 2017). In contrast, state anxiety was linked to increased fronto-occipital connectivity in patients with PPPD (Lee 2018) and increased connectivity between motor cortex (Broadman area 4 – BA4) and orbitofrontal, fronto-polar, and anterior cingulate cortices in patients with PPPD plus phobic symptoms (Popp 2018). Here we tested the hypothesis that people with agoraphobia share some of the changes in brain networks previously identified in patients with PPPD, specifically reductions in visuo-vestibular connectivity. We compared resting-state functional MRI (fMRI) connectivity measures (Van Essen 2013) between 52 people with agoraphobia and 52 healthy individuals from the Human Connectome Project (HCP) by precisely matching groups on demographic, psychological, and personality variables.

Methods: We used rsfMRI data from the S1200 HCP data release, and specifically the individual connectivity matrices based on partial correlation coefficients between node timeseries, where the nodes were defined through group independent component analysis (gICA, dimensionality: 300). From the adjacency matrices, we calculated group medians of betweenness centrality for each node and compared them between groups (Mann- Whitney U test).

Results and Conclusions : Relative to controls, the agoraphobia group showed lower betweenness centrality in a node encompassing medial BA4 and BA5 bilaterally and parietal opercula region 2 (OP2).Parallels with patients with PPPD suggest that the vestibular cortex may not be fully integrated into networks involved in locomotion and spatial orientation in either condition. The OP2 sends vestibular inputs via the superior parietal lobule (BA5) to somatotopic parts of the primary sensory-motor areas (BA4-5) that control the lower limbs and trunk. It was hypothesized previously that connectivity changes in this network might underlie altered postural control in patients with PPPD. The current findings suggest that a similar process may contribute to spatial uneasiness in patients with agoraphobia, apart from the direct effects of anxiety. Future work will be needed to elucidate the brain 'fingerprints' of agoraphobia and PPPD and identify anxiety-related and anxiety-independent changes in brain function in both disorders.

**COD. P50**

**Conventional brain MRI findings and metabolic imbalance in MELAS syndrome**

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INTRODUCTION

MELAS (mitochondrial encephalopathy, lactic acidosis, and stroke-like episodes) is a rare multisystem disorder associated with typical m.3243A>G or atypical mutations in the MT-TL1 gene.Recently, there has been growing evidence that nitric oxide (NO) metabolism derangement play a role in MELAS pathogenesis. The main brain MRI features comprise stroke-like lesions (Tschampa 2013) as well as ventricular and/or parenchymal lactate (Lac) accumulation (Kaufmann 2011) and reduction of the neuro-axonal marker N-acetyl-aspartate (NAA) detected by proton MR spectroscopy (1H- MRS) within stroke-like lesions. The aim of the study was to describe the neuroimaging and neurometabolic features in a cohort of MELAS patients and to explore possible correlations with serum NO metabolism related markers.

METHODS

Twenty-three consecutive MELAS patients (9 on idebenone) (age: 42.2±12.1 years, 13M, 4 with atypical mt DNA mutations) and a group of sex- and age-matched healthy controls (HC) were were enrolled.Single voxel 1H MRS (1.5T, PRESS) was performed in regions without signal or morphological alterations: the medial parieto-occipital gray matter, POGM (TR/TE=4000/35 ms, volume= 18 ml), cerebellar hemisphere (4000/35 ms, 6 ml), parieto-occipital white matter, POWM (4000/35 ms, 8ml) and lateral ventricles (1500/288 ms, 3.7-8.2 ml). Relative metabolites content respect to Cr was evaluated for NAA, Cho and mI (LCModel 6.3). Serum concentrations of basal Lac and main NO metabolites related (alanine, glutamine, citrulline and arginine) were evaluated in patients within one year from the MR acquisition.

RESULTS

Six patients presented multiple stroke-like lesions, in areas not corresponding to vascular territories. Three of them showed: bilateral subcortical microcystic encephalomalacia (mut T10191C ND3), focal white matter microcystic encephalomalacia (mut T3271CmtDNA) and prevalently cortical respect to WM involvement (mut G10197A ND3). Compared to HC, MELAS patients showed: a) in the POGM lower NAA/Cr (1.24±0.16 vs 1.39±0.11, p=0.006,) that negatively correlates with basal serum [Lac] (r2=0.542, p=0.024) and lower NAA/mI (1.63±0.40 vs 1.91±0.23, p=0.008) that positively correlates with serum [alanine] (r2=0.889, p=0.005); b) In the cerebellum, lower NAA/Cr (0.96±0.15 vs 1.29±0.20, p<0.001), NAA/mI (1.37±0.29 vs 1.90±0.37, p=0.001) and Cho/Cr (0.24±0.03 vs 0.29±0.03, p=0.002); and NAA/mI correlates negatively with serum [alanine] (r2=0.734, p=0.014) and positively with [citrulline] (r2=0.674, p=0.023); c) In the POWM, lower NAA/Cr (1.62±0.23 vs 1.80±0.14, p=0.007), lower NAA/mI (1.56±0.53 vs 2.07±0.50, p<0.001), lower Cho/Cr (0.33±0.06 vs 0.37±0.04, p=0.005) and higher mI/Cr (1.13±0.33 vs 0.91±0.19, p=0.026). Ventricular lactate was present in 18/23 patients, and its content (relative to water) correlates with serum [Lac] (r2=0.334, p=0.024).

DISCUSSION

Stroke-like lesions in the chronic stage in MELAS patients with atypical mutations might show an atypical distribution and morphology. Both in typical and atypical MELAS mutations patients widespread metabolic alterations were detected in apparently normal posterior GM, WM and cerebellum. The correlation between the neurodegeneration and the oxidative deficit detected in vivo and the levels of serum Lac and NO-related metabolism markers confirm the interplay between NO-mediated and mitochondrial pathways and the neuronal and endothelial dysfunction. Our data suggest the use of in vivo MRS and NO related metabolites as surrogate markers of efficacy in future therapeutic trials.

**COD. P51**

**Echo-State Causality: a novel method for Directed Brain Connectivity**

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Introduction

While Granger Causality (GC)-based approaches, including the recent State Space Causality reformulation, have been widely employed to the estimation of information flow between brain regions (i.e. directed connectivity), they are based on linear multivariate autoregressive (MVAR) models. However, biological networks such as the brain are known to exhibit a high degree of nonlinear coupling. Additionally, given that the functional MRI (fMRI) signal is a result of convolving neural activity with a locally and time-varying haemodynamic response function (HRF), a linear MVAR approach is not suitable in reconstructing neither the nonlinear components of neural coupling, nor the multiple nonlinearities/time-scales which concur to the BOLD effect.

Methods

We define a novel approach to estimating nonlinear, directed network interactions based on a specific class of Recurrent Neural Networks (RNN) termed echo-state networks (ESN). Specifically, we modify the current ESN formulation to simultaneously model nonlinear, multivariate signal coupling while decoupling the internal model representations into separate, heuristically motivated orthonormal bases for network weights. We then reformulate the classical GC framework in terms of ESN-based models for multivariate signals generated by complex networks.We characterize the ability of ESNs to capture nonlinear causal relations by simulating multivariate coupling in a network of nonlinearly coupled, noisy Duffing oscillators. The ability of detecting true causal links while rejecting false causal links is quantified as the area under the ROC curve (AUC) as a function of the threshold in causality strength. We then explore the structure of ESN-based causality networks in the human brain in functional MRI (fMRI) data from 1003 healthy subjects scanned at rest at 3T (4 sessions,1200 volumes/subject, TR=0.72S) within the "HCP 1200-Subjects PTN Release" by employing the subject-specific time courses of 15 components resulting from spatiotemporal group independent component analysis (ICA).

Results

Synthetic validation shows a net advantage of the ESN approach in detecting nonlinear, causal links across different timescales. AUC has been employed as figure of merit to compare detection performances between employing the classical MVAR conditioned GC approach, the improved state-spaced formulation of GC and our novel ESN-based approach. Results of directed, between-component brain connectivity network derived in 1003 HCP subjects are presented.

Conclusion

We present validate a novel method for estimating nonlinear directed information flow between coupled multivariate time series, and apply it to the characterization of the directed functional interaction between brain areas defined by IC analysis in large-scale HCP data. Here, we disclose a strong bidirectional interaction between the Default Mode Network and the Salience network, a direct modulation of the fronto-temporal network by the fronto-visual network (but not vice versa) and a direct modulation of the striate-visual network by the sensory/motor-limbic-network. While these observations warrant additional validation through specific task-based investigation, in general we have shown that the ESN-based causality is able to detect in vivo functional interactions and causal dynamics across multiple neural networks while delivering superior performance as compared to both classical, MVAR-based Granger causality methods and latest developments in the field of Granger Causality (i.e. State Space Models).

**COD. P52**

**Single Subject Volumetry by VBM and ASHS Segmentation in Histologically-Confirmed Hippocampal Sclerosis**

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Background: The identification of a likely epileptic zone is important for decision-making prior to surgery in drug-resistant temporal lobe epilepsy (TLE), but a radiologically evident anomaly is absent in about 30% of cases. While voxel based morphometry (VBM) has proven successful in demonstrating group-wise differences, early reports regarding single-subject discrimination of structural alterations have achieved mixed results [1].

Methods: As a pilot evaluation for single-subject analysis in the 3TLE project*, we applied VBM and hippocampal segmentation in comparing pre-surgical MRI data from each of 7 patients with a reference set of 32 healthy controls (HCs). All patients had histopathologically-confirmed hippocampal sclerosis at resection of the hippocampus that was target of surgery. The VBM approach made use of MT maps generated using the hMRI protocol and software [2] as adapted to the temporal lobe [3]. The MT maps were preprocessed (segmentation, normalization, and smoothing) using the Computational Anatomy Toolbox for SPM12 [4,5]. The resulting individual grey matter probability maps were then subjected to a voxel-wise one-sample t-test between each individual TLE patient and the group of healthy controls ($p<0.001$, without FWE). Separately, the hippocampi were segmented on the basis of the R1 and T2 images using Automatic Segmentation of Hippocampal Subfields (ASHS) [6]. We report on the lateralization of significant hippocampal volume changes relative to histopathology, and the correlation observed between the two approaches to volumetric analysis.

Results: At histopathology, 3 patients had HS in the right temporal lobe and 4 in the left.

At VBM, volume reduction was seen within the target hippocampus in six of the seven patients, with one of the six also showing contralateral hippocampal volume reduction. The remaining patient lacked significant hippocampal volume reduction bilaterally.

As segmented by ASHS, all patients had significantly smaller hippocampi bilaterally (both absolute volume and normalized to intracranial volume) ($p<0.0005$) relative to HCs, with the target hippocampus being the smaller in all seven patients. In six patients, the hippocampal asymmetry (left to right hippocampal volume ratio) was significantly different from that seen in HC ($p<0.0005$) in favor of lower volume in the target hippocampus. The patient without significant asymmetry was not the one who lacked volume reduction at VBM.

The correlation between the number of voxels exceeding significance for reduction in content at VBM analysis and the segmented volume for each hippocampus was $r=-0.773$ ($p=0.043$).

Discussion: The VBM and segmentation techniques for evaluating alterations in the hippocampi volume provide moderately correlated indices of hippocampal sclerosis. The segmentation approach provided better agreement with histopathological findings in this small cohort, and may be able to detect smaller changes than the VBM approach. A further development will be to examine the hippocampal changes seen by VBM and segmentation at sub-field level.

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**COD. P53**

**Studio simulativo per valutare l'impatto del protocollo di acquisizione sulla sensibilità e sulla specificità delle metriche NODDI rispetto alla demielinizzazione e alla perdita assonale.**

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Lo scopo di questo studio è valutare l'impatto del protocollo di acquisizione sulla sensibilità e sulla specificità delle metriche che derivano dal modello di diffusione NODDI rispetto a due dei processi patologici più frequenti nelle lesioni demielinizzanti, ovvero la demielinizzazione e la perdita assonale. A tale scopo è stato costruito ad-hoc un nuovo modello sintetico di materia bianca cerebrale (una porzione di corpo calloso), in cui gli assoni mielinizzati sono tutti allineati tra loro e, nella condizione di integrità tissutale, sono caratterizzati da una certa densità e da una determinata funzione di distribuzione gamma dei raggi (i cui parametri sono determinati istologicamente). I tre compartimenti del tessuto sintetico (spazio intra-assonale, spazio intra-mielinico, spazio extra-cellulare) sono permeabili e ciascuno di essi è caratterizzato da una determinata diffusività e da un certo tempo di rilassamento spin-spin, come riportato in letteratura. La capacità di rivelare la perdita assonale e la demielinizzazione e quella di distinguere i due processi sono state testate valutando i cambiamenti delle metriche NODDI (la frazione volumica intra-assonale, la frazione volumica extra-cellulare e l'indice di dispersione delle orientazioni) al variare del grado di danneggiamento indotto nel tessuto sintetico, per 6 differenti protocolli di acquisizione. La demielinizzazione è stata simulata riducendo progressivamente il g-ratio, a partire dalla condizione di integrità g-ratiohealthy=0.7; la perdita assonale è stata simulata, invece, partendo da una condizione di integrità e selezionando un numero crescente di assoni da eliminare tenendo conto dell'osservazione sperimentale secondo cui vi è una selettività nella perdita assonale che riguarda gli assoni con raggio assonale <1$\mu$m. I risultati sono stati quantificati in termini di un indice di sensibilità e di un indice di specificità ed è stato valutato, quindi, l'impatto del protocollo di acquisizione sugli stessi. In generale, per ciascun protocollo selezionato, le frazioni volumiche sono sensibili sostanzialmente allo stesso modo sia rispetto alla perdita assonale che alla demielinizzazione, mostrando, entrambe, maggiore sensibilità alla perdita assonale; d'altra parte, l'indice di dispersione dell'orientamento non è sensibile alla demielinizzazione, né alla perdita assonale nei primi stadi della lesione. In ogni caso, per ciascuna metrica, sia la specificità che la sensibilità dipendono fortemente dal protocollo di acquisizione e in alcuni casi, in maniera differente da quanto si suppone in letteratura. I risultati delle simulazioni confermano, inoltre, le recenti osservazioni sperimentali secondo cui, la frazione volumica intra-assonale (metrica NODDI) stima con una buona accuratezza la reale frazione volumica intra-assonale. Concludendo, particolare attenzione va posta nella scelta del protocollo di acquisizione, il cui impatto sulla sensibilità delle metriche NODDI al danno tissutale non è trascurabile. In ogni caso, pur non essendo possibile distinguere tra demielinizzazione e le prime fasi della perdita assonale, è comunque effettivamente possibile rivelare la presenza del danno tissutale ed estrarre altre preziose informazioni sulla microstruttura cerebrale, utilizzando una tecnica di imaging non invasiva e un protocollo di acquisizione implementabile nella pratica clinica (tempo di acquisizione < 30 min; Gmax =< 63.8 mT/m). Questo studio simulativo suggerisce, infine, che la metrica NODDI frazione volumica intra-assonale potrebbe essere effettivamente un buon biomarcatore nelle malattie demielinizzanti.

**COD. P54**

**Test-retest reliability of pediatric brain MultiBand dMRI, with NODDI model GPU fitting**

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INTRODUCTION
Recently, Neurite Orientation Dispersion and Density Imaging (NODDI) has gained importance in diffusion modelling because of its ability to estimate neurites density and organization. Since it requires the acquisition of at least two shells, the acquisition time cannot be feasible in the clinical setting.
Pediatric studies are limited by acquisition-time as it leads to discomfort and moving artifacts in children. MultiBand acquisition is nowadays a very powerful tool to help reducing scan time even though at cost of less SNR.
On the other hand, fitting NODDI model is computationally expensive and fitting GPU-based implementations may be the solution.
There is still very little information on the robustness of NODDI model in children. This study aims then to assess the test-retest reliability for Multiband NODDI protocol when performing the fitting using GPU.

METHOD
7 pediatric subjects underwent MultiBand diffusion MRI protocol. A four shell protocol (b values: 300, 700, 1000, 2000 s/mm2) was used, and each subject was scanned twice, with a 20 minutes interval.
NODDI model was fitted with a GPU-based computation using two toolboxes, MDT (Microstructure Diffusion Toolbox, https://mdt-toolbox.readthedocs.io) and cuDIMOT (CUDA Diffusion Modelling Toolbox, https://users.fmrib.ox.ac.uk/~moisesf/cudimot/). In MDT, Powell's optimization algorithm was used, with both double (MDT-d) and single (MDT-s) precision computations, while in cuDIMOT the optimization followed the Levenberg-Marquardt algorithm and only used double precision. The GPU used is a P5000 from NVIDIA (8.9 TFLOPS) Orientation dispersion index (ODI), free water volume fraction (Viso) and intracellular volume fraction (Vic) from both toolboxes were the parameters used to assess the test-retest reliability.
A region of interest (ROI) was manually drawn for each subject in a white matter area, and the mean value of each parameter was calculated within that ROI. A variation factor between the two acquisitions was computed for each parameter, for each toolbox and for each subject. The mean and standard deviation have been computed.

RESULTS
Variation factor of Vic is lower than 1% (cuDIMOT) and lower than 3% (MDT); ODI shows a variation factor of 5 % (cuDIMOT), and lower than 12% (MDT); for Viso it is lower than 21% (cuDIMOT), lower than 21% (MDT-f) and lower than 36% (MDT-d).
The average fitting time was 16.6 min for cuDIMOT, 5.1 min for MDT-f and 6.6 min for MDT-d.

DISCUSSION AND CONCLUSIONS
Among the three computed parameters, Vic and ODI resulted the most reliable. Even though cuDIMOT performed slower than MDT, it showed better results. As seen in previous studies Viso reproducibility is very low as CSF contamination may be more difficult to separate from the other compartments.
No relevant differences between double and single precision computations were observed.
This study demonstrates that NODDI model can be acquired with Multiband protocol in children by keeping good reliability results. For any future study, Viso fitting results have to be treated cautiously and further investigations are necessary to draw conclusion.

**COD. P55**

**Impact of small parcellation changes on functional connectivity network measures**

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INTRODUCTION

There is growing interest in studying human brain connectivity and brain functional network structure. Brain network creation requires parcellation of cerebral cortex to define network nodes. Different methods of parcellations have been implemented. Parcellations might be affected by inter-subject variability as consequence of disease, age, physiological characteristics. This study investigates how parcellation changes as due to spatial variation may influence connectivity network measures. We identify graph measures that are robust to parcellation spatial error.

METHOD

We made use of two datasets: COBRE and ABIDEII ONRC, including MPRAGE sequences and Rs-FMRI data. COBRE consists of 73 healthy controls (HC) and 73 schizophrenic patients (SH); ONRC consist of 35 HC and 24 patients with autism spectrum disorder (ASD). Brain parcellation was implemented using Freesurfer with standard atlasDKT40 (64 Standard Macro Parcels: SMaP). In each subject 50 new parcellations (each of them consisting in new 64 Modified Macro Parcels: MMaP) were created by randomly modifying SMaP. Each of new parcellations were obtained by using freesurfer icosahedric4 parcellation (5124 Icosahedric Micro Parcels: IMiP). Each IMiP was mapped to determine which of the 64 SMaP was belonging to, then IMiP were randomly moved from one SMaP to the one nearby. Each of the random iterations consisted in modifying 38 SMaP and each SMaP modification was performed by moving 3 IMiP at the edge, resulting in mean SMaP area variation of 2.5%. All parcellations were mapped onto Freesurfer common template and were registered on each subject space. All fMRI data were filtered using Matlab R2017a to reduce the effects of drift with linear regression and physiological noise with CompCor method. For each parcellation, mean time series from each parcel were computed. Correlation matrices were calculated using Pearson coefficient as measure of the functional connectivity between pairs of regions. Adjacency matrices were constructed with 0.1,0.2,0.3,0.4 thresholds. 38 network measures were derived using BrainConnectivity Toolbox and Centrality Consistency functions. Brain connectivity measure variation-factor was defined as $v=(1/N)(1/P)\mathrm{sum}\{\mathrm{sum}\{[(x_{ip\_MMaP}-x_{ip\_SMaP})^2/(((x_{ip\_MMap}+x_{ip\_SMaP})/2)^2 )]\}\}$

whereby $x_{ip\_MMaP}$ and $x_{ip\_SMaP}$ were values of measure under investigation in subject i, for macroparcel p, in standard and new parcellation; N and P were number of subjects and parcels. The variation-factor was computed for each iteration, each analysed measure in HC, SH, ASD.

RESULTS

Variation-factor is lower than 1% in analysed groups in global-weighted/binary-efficiency, transitivity, neighbors-overlaps, short-cuts; lower than 10% in eigen-vector-centrality, Katz-centrality, Bonachic-centrality, degree, strength, local-wighted/binary-efficiency, clustering, path-length, density, pagerank-centrality, communicability, random-walk, topological-overlap, matching-index, modularity, rich-club-coefficient, core-ness-statistic, shortest-path-transitivity, search-information, k-coreness-centrality; it is between 10 and 50% in information-centrality, closeness-centrality, walk-length, subgraph-centrality, flow-coefficient, total-walk, Louvein-community, Newman-community and it is higher than 50% in betweenness-centrality, leverage-centrality, local-assortativity, global-assortativity. There are no significant difference among groups.

CONCLUSIONS

We studied inter-subjects parcellation variability to evaluate the impact of parcellation changes on graph metrics. Several studies analysed assortativity, betweenness-centrality, leverage-centrality to assess functional brain connectivity. The study points out the importance of paying close attention to parcellation spatial errors especially when reliability may be compromised.

**COD. P56**

**Study of brain networks through structural and functional connectivity using Magnetic Resonance Imaging**

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Purpose

The integration between structural and functional connectivity information is an open question in brain network research. Many studies suggest that the presence of a direct anatomical connection between two brain areas is associated with stronger functional interactions between these two areas [1, 2, 3]. Functional interactions have also been detected between brain areas without structural connections [1, 4]. However, how functional and structural connectivity are related each other is largely unknown. Here we report a new method of analysis for a brain networks and a way to integrate structural and functional connectivity in terms of groups analysis.

Methods

15 subjects (11 control subjects and 4 right-hand amputees, aged 10-50 years) underwent to the same protocol for the simultaneous study of structural and functional connectivity: a 3D T1-weighted structural sequence (FSPGR, TR= 11 ms, TE= 4 ms, 1 $mm^3$ isotropic voxel, matrix = 256 × 256, Flip Angle = 10°, acquisition time = 10 minutes), a Diffusion weighted sequence (DWI-EPI, 64 gradient directions, b value = 3000 , TR= 14 s, TE = 118 ms, 3 $mm^3$ isotropic voxel, matrix = 80 × 80, Flip Angle = 90°, acquisition times = 18 minutes) and a resting state acquisition EPI-GRE (TR= 3 s, TE = 50 ms, 3 $mm^3$ isotropic voxel, matrix = 64 × 64, Flip Angle = 90°, 120 volumes, acquisition time = 6 minutes).

We used an approach based on network measures (segregation and centrality), allowing a comparison between structural and functional networks. 3D T1 weighted images were segmented and parcelled by using the Desikan-Killany atlasand Freesurfer software. Diffusion and functional data were, at the first, coregistered with the anatomical images and then processed thanks to MRtrix and CONN software, so that to calculate connectivity matrices (containing number of tracks and correlation coefficients between nodes). On the basis of single subject networks, we averaged the connectivity matrices to construct a brain network representing the group; this method resulted to be reproducible in cases of a small number of subjects. Then, measurements of segregation were carried out on brain networks to look for modules in which networks splitting. On the results module we performed measures of centrality using a module degree z-score to identify hubs among nodes, and to classify them in provincial or connector ones. Finally, using structural connectivity unchangeability betweengroups, measurements of centrality were carried out with function data on the structural modules.

Results

The results clearly show that the developed method is able to point out the differences between control subjects and amputees, comparable with the disease under study. As expected, contrast to structural connectivity, functional connectivity in amputees was altered, finding differences with respect to controls in sensorimotor and linguistic networks. Lastly, the information obtained by structural and functional connectivity studies were integrated showing results comparable with the above analysis. These results strongly encourage to extend the implemented method to other types of pathology.

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**COD. P57**

**T1 gradient-echo and T1 spin-echo sequences detection of hypointense lesions in Multiple Sclerosis**

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Introduction

In Multiple Sclerosis (MS), hypointense areas on brain MRI T1 weighted images reflect severe tissue damage and axonal loss.The aims of this study are: to evaluate the performance of T1 spin-echo (T1SE) and T1 gradient-echo (FSPGR) images in detecting hypointense lesions to compare DTI microstructural parameters of tissue damage inside lesions detected on T1SE and FSPGR images.

Methods and materials:In this retrospective study, 3T MRI and clinical data of 18 patients with MS (pwMS) were analyzed. Diffusion Tensor Images were pre and post-processed to obtain Fractional Anisotropy (FA) and Mean Diffusivity (MD) maps. For each patient, axial 3D FSPGR, TSET2 and T1SE (3 mm slice thickness) were used for the analysis. Images were analyzed during multiple sessions by consensus of two experienced observers (one neuroradiologist and one neurologist). Lesion number (LN) on T1SE and FSPGR images and lesion volume (LV) on TSE-T2, T1SE and FSPGR images (resliced to 3 mm thickness), were obtained using manual segmentation technique (Jim version 7.0, Xinapse System). T1SE and FSPGR images were co-registered using a linear registration (NiftyReg package); by subtracting T1SE and FSPGR lesion masks between themselves, we obtained the lesion masks of the hypointense lesions detectable: both on T1SE and FSPGR images (a) exclusively on FSPGR images (b) exclusively on T1SE images (c)(a), (b) and (c) were co-registered using a linear registration (NiftyReg package) to b0 images.FA and MD values inside (a), (b) and (c) hypointense lesions were extracted. White matter, grey matter and cerebrospinal fluid (CSF) volumes, obtained by using SIENAX software on FSPGR images, were used to calculate the brain parenchymal fraction (BPF).LV, LN and FA, MD were compared between T1SE and FSPGR images by using a Student-t test.

Results:Compared to T1SE, FSPGR images showed a statistically significant higher LN ($p<0.005$). Hypointense lesions detectable on T1SE images had a statistically significant lower FA ($p<0.005$) and higher MD ($p<0.005$) values when compared with hypointense lesions detectable only on FSPGR images.

Conclusions:Compared to T1SE, FSPGR images were able to detect a statistically significant higher LN. FA and MD values inside T1SE lesions were suggestive of a more destructive tissue damage due to demyelination. Thus, compared to T1SE, FSPGR images could be able to show hypointense lesions characterized by less severe microstructural changes and this should be considered when using T1 “black holes” as a biomarker of tissue damage severity.Our data are still preliminary and an extension of patients' cohort is expected.

**COD. P58**

**Functional Quantitative Susceptibility Mapping (fQSM) of Brain Activity during Auditory Stimulation**

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Functional Quantitative Susceptibility Mapping (fQSM) is a recently established method that, based on the same acquisition technique as conventional functional Magnetic Resonance Imaging (fMRI), has two very appealing features: it is quantitative and it is considerably less affected by non-local effects than the Blood Oxygenation Level-Dependent (BOLD) signal. Here, for the first time, the response of the auditory cortex to the presentation of relatively short acoustic stimuli has been studied with fQSM. To obtain the timecourse of the fQSM response to stimuli, a data-driven approach based on signal deconvolution was used, to avoid any assumption regarding the response shape itself. The fQSM and BOLD responses showed, on average, very similar shapes. However, while the majority (82%) of fQSM responses described transient decreases in magnetic susceptibility (explainable by the same mechanisms underpinning the typical, positive BOLD responses), some voxels exhibited transient increments in magnetic susceptibility; since fQSM is void of the macroscopic blooming effects present in conventional fMRI, voxels with positive fQSM responses might be capturing, at least to some extent, spatial variations in the interplay among changes in fractional oxygen saturation, cerebral blood flow and volume. Statistically significant fQSM responses were observed not only in veins (which constitute the largest sources of magnetic susceptibility contrast) but also in gray matter tissue, suggesting that this technique might help to improve the localization of brain activity in a wide host of scenarios: for example, in pre-operative fMRI, fQSM might provide a more precise localization and interpretation of the sources of activation, and therefore assist the surgical planning in patients due to undergo brain surgery. In neuroscience, a more precise localization of brain activity might support the understanding of different functional properties in small spatial scales, ranging for example from topographic maps (e.g. retinotopy, tonotopy, somatotopy, etc) to cortical columnar and layer-specific functional architectures.

**COD. P59**

**Spine atrophy and sensory-motor disability in African Americans with Multiple Sclerosis**

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Background and aims: African Americans (AA) with multiple sclerosis (MS) present a more severe disease course than Caucasians with MS. Previous studies have suggested that the more severe course is associated with the higher white matter (WM) lesion load and diffuse microstructural damage in normal appearing WM, as well as cerebellar atrophy [1-4] but the contribution of cervical spinal cord (CSC) lesions and atrophy, which are independently correlated with physical disability in the general MS population [5], has never been explored specifically in AA. The main objective of the present study is to investigate the extent of CSC damage in AA with MS compared to age-, sex- and race matched healthy controls (HC).

Methods: Twenty-nine AA MS patients (23 females, mean age 38.8 ± 11.8 years, disease duration 4.08 ± 3.51 years, median extended-disability-status-scale (EDSS) 2.0, range [0-6.5]) and 21 AA HC (15 females, mean age 33.52 ± 10.15 yrs) were prospectively enrolled as part of an ongoing longitudinal study. Subjects underwent a brain and spinal cord 3T MRI (MAGNETOM Skyra, Siemens Healthcare, Erlangen, Germany). The brain was imaged using a 3D T2-weighted SPACE sequence (voxel size = 1x1x1 mm3; FOV = 256 mm, 176 sagittal slices, TR/TE = 3200/564 ms). The spinal cord was imaged using a 3D T2-weighted SPACE and a 2D T2-weighted TIRM sequences. Imaging parameters were: (i) 3D T2-weighted SPACE: voxel size = 0.9x0.9x0.9 mm3, FOV = 230 mm, 64 sagittal slices, TR/TE = 1000/123 ms; (ii) 2D T2-weighted TIRM sequence: voxel size = 0.4x0.4x3 mm3, FOV = 220 mm, 15 sagittal slices, TR/TE = 3120/45 ms. Cervical spinal cord volume was measured on the 3D T2-weighted SPACE images using the Spinal Cord Toolbox [6]. The CSC volume was normalized to the cranial cross-sectional area measured on the brain T2-weighted SPACE images using a semiautomated segmentation technique (JIM7, Xinapse Systems, Northants, UK) [7]. The CSC lesions count and extent were visually identified on the 2D T2-weighted TIRM images and labeled to the correspondind vertebra. An extensive sensory-motor evaluation was performed in AA MS subjects, including: 9-hole peg test (9-HPT), grooved pegboard test (GPT), 25-foot walk test (25-FWT), 2-minutes walk test (2-MWT), evaluation of upper and lower limbs strength, grip strength, vibration sensitivity and balance. Between-group comparison was performed with ANCOVA adjusted for age and gender. Partial correlations between MRI measures and clinical scores were also adjusted for disease duration. All statistical analyses were carried out using SPSS (v 19.0).

Results: A total of 33 CSC lesions were found in AA patients (median: 1, range: [0-5]). Sixty-nine percent of the lesions were limited in extension to one cervical level with the highest lesion frequency at C2 (22%), showing an anatomical extension and location similar to what reported in caucasions with MS. AA showed lower normalized CSC volume than HC (AA: 64.24 ± 5.64 mm3, HC: 68.41 ± 4.21 mm3, $p = 0.019$). Lesion count was correlated with hand vibration sensitivity ($r = 0.78$, $p = 0.003$), while normalized CSC volume was correlated with 2-MWT ($r = 0.47$, $p = 0.021$), grip strength ($r = 0.49$, $p = 0.016$) and lower limbs strength quantified as ankle plantar and dorsal flexion ($r = 0.61$, $p = 0.013$; $r = 0.50$, $p = 0.047$) and showed association trends with upper limb strength quantified as elbow flexion ($r = 0.38$, $p = 0.070$), feet vibration sensitivity ($r = -0.50$, $p = 0.080$) and balance test ($r = -0.43$, $p = 0.080$).

Conclusions: CSC damage in terms of both macroscopic lesions and atrophy significantly impacts motor and sensory performances in AA with MS.

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**COD. P60**

**Validation of probabilistic method of diffusion tensor imaging fiber tractography (DTI-FT): comparison between reconstructed tracts and evoked potential recorded in epileptic patients.**

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Purpose The aim of this study is to evaluate the accuracy of the probabilistic tracking method of diffusion tensor imaging fibertractography (DTI-FT), comparing to imaging-represented electrophysiology data in epileptic patients who underwent stereoelectroncephalography (SEEG). Methods Fourteen epileptic patients (mean age 28±9),who underwent DTI acquisition and other brain MR sequences used for SEEG plannig, were selected from "Claudio Munari" Epilepsy Surgery Center database. DTI sequences were collected using a 1.5T Philips Achieva scanner by using echo planar imaging and a receive coil head SENSE 8 channels. According to the implanted electrodes position, we recorded intracerebraltibial and median somatosensory-evoked potentials (SEP) in 7 patients and flash-visual evoked potential (VEP) in 8. The thalamocortical (THC) (separately considered as median and tibial THC) and optical radiation (OR) tracts were blindly reconstructed using a probabilistic algorithm implemented in FSL 5.0.6. The reconstruction of tracts was obtained using two ROIs corresponding to a seed-point and a way-point. The seed-point represents the starting region of the reconstructed tract, while the way-point is a region that is crossed by the reconstructed tract. In the reconstruction of THC bundle used the sensory thalamus as seed-point and the white matter (WM) lying underneath the somatosensory cortex as way-point. In the reconstruction of OR we use the lateral geniculate body as seed-point and the WM lying next to the calcarine cortex as way-point. The 3D tractographies were thencompared to the position of SEEG electrodes contacts, on which evoked potentials (EPs) were recorded. ResultsComparison between DTI-FT and EPs showed a satisfactory superimposition of the neurophysiological recording contacts and the reconstructed tracts. We obtained full superimposition in all median thalamocortical tracts. We observed a correspondence in 81% of tibial THC and in 81% of OR, considering a maximum distance of 3mm from the tract and the neurophysiological contact. In particular, we had full correspondence in the 52% of tibial THC and 70% of OR. ConclusionThis study is a preliminary one, suggesting that EPs recorded during SEEG monitoring can be considered as a valuable tool to validate the probabilistic tracking method in the reconstruction of THC and OR tracts.

**COD. P61**

**White matter hyperintensities volumetric burden in healthy adults: a systematic review and meta-analysis**

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Introduction

White matter hyperintensities (WMHs) are a common MRI radiological finding in middle-aged and elderly healthy subjects. They could constitute a useful
and reliable biomarker of the brain aging process. In order to use WMHs on this purpose, volumes of WMHs from different studies must be comparable
and a range of normality in their volumetric burden be established. In this light we performed a systematic review and meta-analysis of available studies
reporting WMHs burden in healthy adults, in order to inquire into current state of the art in WMHs volumetric assessment.

Methods

In September 2018 we performed a systematic search on EMBASE on the available literature published between 2008 and 2018 on the topic of WMHs
volumetric assessment in healthy adults. From each study we retrieved data about sample size, patients' age and WMHs burden. Using the random-effect
model, we calculated the pooled WMH burden, with 95% confidence interval (CI) and modelled standard deviation (SD). We performed subgroup/metaregression analyses for assessing age factor and Egger test and Kendall's tau for publication bias risk.

Results

Twenty-eight studies comprising 30 study parts were included in this systematic review and meta-analysis. Final samples comprised 6998 healthy
subjects: mean age 44.7- 84.1 years. Mean WMHs volume ranged from 0.27 ± 0.51 cm to 15.85 ± 14.57 cm , resulting in high heterogeneity ($I = 99.9\%$,
$p < 0.001$). Meta-analysis produced a pooled WMHs volume of 6.484 cm (95% CI 5.246-7.722 cm). Meta-regression analysis between WMHs volume
and age showed a positive correlation between WMHs volume and subjects' age ($y = 0.26x - 11.2$; $R2 = 0.41$). Visual inspection of funnel plot showed low
risk of publication bias, confirmed by the Egger- test ($p = 0.929$) and by Kendall's tau ($p = 0.089$).

Discussion

Results of our systematic review and meta-analysis showed large variability and heterogeneity in WMHs burden across the examined studies. We could
not perform a subclasses meta-analysis based on age subgroups due to the paucity of available studies and substantial overlapping age ranges among
samples. Age underpins only 41% of the observed heterogeneity in WMHs volumes, as shown by meta-regression. Several factors may explain the
remaining variability; the main of these could be the lack of an endorsed anatomical WMHs definition and non-standardised WMHs quantification
methods. Proper definition of WMHs anatomy and widely accepted guidelines for WMHs segmentation need to be outlined in the future, to allow a fully
reliable WMHs quantification. This would enable proper establishment of a range of normality for WMHs and would make their use as an aging biomarker
feasible.

Conclusion

The high heterogeneity in WMHs volumetric burden across the analysed studies has not allowed us to provide a range of normality for WMHs burden in
healthy adults. Supporting the impact of age as the main unmodifiable risk factor for WMHs development, a positive correlation between WMHs and age
was proved by meta-regression analysis.

**COD. P62**

**Evaluation of a Laterality Index for presurgical assesment of patients with drug-resistant epilepsy (DRE)**

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PurposeLanguage lateralization is an important factor for surgical choice on patients with drug-resistant epilepsy (DRE) to avoid serious problems, such as aphasia.The aim of this study is to establish a reliable coefficient, called Laterality Index (LI) based on functional magnetic resonance imaging (fMRI). MethodsfMRI offers a promising non invasive method to evaluate language lateralization. To determine a realiable LI, 98 patients with drug-resistant epilepsy (DRE) at "Claudio Munari" Epilepsy Surgery Center in ASST GOM Niguarda, who underwent fMRI exam, were analyzed. The images were acquired with a 1.5T Philips Achieva scanner. The comparison with the surgical outcome has been possible only for the 18 operated patients. This group is composed of 7 male and 11 female, with mean age of 26±11.A Laterality Index was estimated for each of the tasks given in fMRI exam (association, comprehension and fluency). The LI is obtained as the ratio between the difference of voxels activated in a specific area of left and right brain hemispheres and the sum of these two values; a LI=+1 means a left dominance, whereas LI=-1 implies a right dominance.In order to obtain these values, Broca's area (BA44 and BA45) and Wernicke's area (Superior Temporal Gyrus, posterior division) of Juelich and Harvard-Oxford Cortical Structural Atlases were fused with a standard T1 brain map. In the same way, activation blobs from fMRI was coregistered with T1 axial images for each patient. This two images are then compared, through FLIRT-FSL 5.0.6 software, in order to establish patient's activated voxels, exceeding a fixed threshold, within the areas of interest. LI values were compared with fMRI exam reports, Diffusion Tensor Imaging(DTI) exams, medical evaluations and psychological tests after surgery. ResultsLI values obtained with different language tasks were considered; the index calculated from association task was linked to Broca's area, the one from comprehension task with Wernicke's area. An appropriate threshold on LI values was chosen in order to categorize Broca's and Wernicke's hemisphere dominance as left, right or bilateral. A lot of bilateral cases were found, especially for Wernicke's area, pointing out the difficulties on determination of language lateralization.Preliminary results, obtained by comparing LI with fMRI exam reports, DTI exams and after-surgery evaluations, showed good a agreement in 70% of female and 80% of male patients. ConclusionsEvaluation of a reliable Laterality Index from fMRI studies, referred to different areas of the brain and supported by clinical data, is an important tool for planning surgery interventions. This preliminary study offers a valuable information that can help clinical routine, especially with patients at greater risk of aphasia.

**COD. P63**

**Hippocampal atrophy pattern in Subjective Cognitive Decline: a longitudinal study**

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Background:
Subjective cognitive decline (SCD) is a risk factor for mild cognitive impairment (MCI) and Alzheimer's disease (AD). Because this condition is very common among older adults and increases the risk for developing MCI and AD, many research studies have focused on SCD, trying to find a linkage between this condition and AD biomarkers.
Objective:
To test the hypothesis that SCD, compared to healthy elderly individuals without SCD, have a pattern of brain subfield atrophy in a longitudinal observation.
Methods:
Thirty-five (64.6 ±5.6 y, 15M/20F) community-dwelling elderly subjects underwent complete neuropsychological battery and a 3T Structural MRI examination (Philips Achieva X Series, Philips Medical System, Best, Netherlands). High-resolution structural images were acquired through a 3D magnetization-prepared rapid acquisition gradient echo sequence using the following parameters: matrix 256 × 256, field of view 240 × 240 × 170 mm, slice thickness 1 mm, no gaps, in-plane voxel size 1 mm × 1 mm, flip angle 12°, repetition time = 8.2 ms, echo time = 3.8 ms. Structural T1-weighted images were processed using FSL (https://fsl.fmrib.ox.ac.uk/fsl/fslwiki; version 6.0). Subjects were divided into two groups on the basis of their subjective cognitive decline Questionnaire (SCD-Q) score. Data collection was performed at baseline and after two years follow-up. VBM (voxel-based morphometry) analysis was completed.
Results:
A significant decreased of left hippocampal subfield was found at VBM analysis in SCD subjects after two years follow up. Clusters significant at P < 0 .05 (t-test, FDR corrected) were observed in the hippocampal region (SCD group) and frontal region (no-SCD group).
Conclusions:
According to the literature, hippocampal atrophy has been correlated to MCI and AD disease. Our results highlight selective hippocampal atrophy in SCD as a possible pre-clinical condition leading to degenerative dementia.

**COD. P64**

**Investigating proton-therapy induced brain microstructural changes through diffusion MRI and a bi-tensor model: a pediatric case study**

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Introduction: In brain cancer radiation treatments, the possibility to characterize tissue modifications during treatment is critical to possibly assess radionecrosis effects in target and surrounding structures. The use of proton-, rather than photon-beams, allows to focus irradiation to treatment target reducing dose exposition of surrounding areas[1]. Very few studies characterized microstructural changes associated with proton-therapy (PT)[2]. We evaluate longitudinal modifications occurring within treatment target and non-irradiated control areas during PT in a pediatric patient with diffusion MRI and a bi-tensor model. Characterizing acute tissue modifications might represent important advancements for patient management.
Materials and Methods: A 13-year-old male presenting a pilocytic astrocytoma, grade I WHO, in orbitofrontal cortex was investigated before, during, and at the end of his PT treatment (54Gy dose, fractionated in 30 sessions). A pre-treatment CT scan was followed by 5 brain MRI sessions, each included anatomical T1, FLAIR and diffusion (32 gradients, b=800s/mm$^2$, 1 b0 volume, TE=102ms) acquisitions. Diffusion MRI (dMRI) data were denoised, corrected for Gibbs ringing, eddy currents and motion, skull-stripped, and bias field corrected. At each time point we computed Fractional Anisotropy (FA), Mean Diffusivity (MD), Free-Water-Corrected tissue-FA (FAt)[3], and Free-Water (FW) maps[3]. Co-registered pre-treatment T1, CT, and a FLAIR image were used to draw tumor volume (TV) contours. Non-irradiated control areas were: Juelich-atlas-derived right visual area V1, as well as white matter (WM) regions of interest (ROIs) drawn in Middle Temporal Gyrus (MTG) and inferior parietal lobule/superior temporal gyrus (IPL-STG). dMRI data were aligned with pre-treatment T1. We eroded TV and co-registered V1 ($TV_{ERO}$, $V1_{ERO}$, respectively) to detect possible misregistration biases. Median and standard deviation diffusion scalars values were extracted from TV, $TV_{ERO}$, V1, $V1_{ERO}$, IPL-STG, and MTG ROIs. Combined effects of treatment and disease progression were assessed per each ROI through a Kruskal-Wallis test on voxel values. Post-hoc comparisons were run between pre- and end-treatment values (Wilcoxon-Rank-Sum tests).
Results: Significant changes between pre-treatment and last temporal point ($p<.05$) were observed for all ROIs before erosion for all scalars (FA, FAt, MD, FW). After erosion, changes of FAt and FA were not significant in $V1_{ERO}$. Post-hoc comparisons show significant end-treatment increases in FA in TV (1.6%, $p<.001$) and $TV_{ERO}$(8.8%, $p<.001$), while increases in FAt (6.4%, $p<.001$) and decreases in FW (-3%, $p<.05$) were observed only after erosion. Control areas show significant reductions in FW and MD, with WM-ROIs additionally showing reductions in FAt and FA ($p<0.05$).
Discussion: Brain diffusion changes were seen in both irradiated and non-irradiated structures. TV and V1 erosion allowed to potentially correct possible effects of ROI misregistration at structure interfaces. Further work is needed to better understand if the longitudinal effects in untreated WM-ROIs are dominated by misregistration effects or disease progression. As part of an ongoing project, this evidence suggests the feasibility of monitoring PT effects with dMRI, and the need to explore responses to PT in long-range structural connectivity.

1:Jones et al.(1998)
2:Hou et al.(2017)
3:Pasternak et al.(2009)

**COD. P65**

**Morphometric technique for cortical parameters estimation in neonates affected by congenital diaphragmatic hernia (CDH)**

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INTRODUCTION. Congenital Diaphragmatic Hernia (CDH) is a severe pediatric disorder with herniation of abdominal viscera into the thoracic cavity. Neurodevelopmental impairment constitutes one of the most common outcome. In this context, morphometric MR techniques allow to investigate cortical parameters like Cortical Thickness (CT) and Gyrification Index (GI), usually implicated in several neurodevelopmental disorders. However, the estimation of these parameters in children presents several limitations, mostly related to MR image quality (motion artefacts, inverted white matter-grey matter contrast, low resolution, low signal-to-noise ratio, partial volume effects). The purpose of this study is to elaborate a novel morphometric algorithm to evaluate CT and GI in neonates affected by CDH.

MATERIALS AND METHODS. 3D T2-w Turbo Spin Echo sequences were acquired on a 3T scanner (Siemens, Erlangen, Germany) of 13 CDH subjects (mean age = 39 d) and 13 age-matched Healthy Controls (HC) recruited at the Bambino Gesù Children's Hospital. Data were post-processed through a dedicated algorithm, consisting in a combination of voxel-based and surface-based morphometric techniques. The pipeline first produce a voxel-based segmentation, classifying the brain image in its main tissue (white matter WM, gray matter GM and cerebro-spinal fluid CSF) and then reconstruct inner and outer cortical surface by means of a largely diffused surface-based approach. CT was computed as the vertex-wise difference between the inner and the outer surface, while GI was measured as the amount of cortex buried within the sulcal folds, compared with the visible cortex in circular regions of interest. Statistical analyses were performed with Permutation Analysis of Linear Models (PALM) FSL package. We used PALM implementation of Threshold-Free Cluster Enhancement (TFCE) to identify areas on cortical surface where CT and GI of CDH significantly differed from HC. PALM correlation with TFCE was produced to evaluate the correlation between CT and clinical parameters. For statistical purposes and visualization, we used an infant surface template available on UCN website. All the analyses were performed in Matlab environment.

RESULTS. Mean distribution of CT and GI were computed for both hemispheres in CDH (CT: 2.11±0.31 mm; GI: 2.8±0.38) and HC (CT: 2.16±0.34 mm; GI: 2.83±0.42). Compared to HC, CDH CT resulted significantly reduced in parietal-occipital and frontal lobe of both hemispheres ($p < 0.05$), while no differences were found for GI. Correlation analysis demonstrated the presence of areas in the occipital lobe where CT significantly correlate to lung volume ($p<0.05$).

DISCUSSION AND CONCLUSIONS. Although the causes of neurodevelopmental impairment in CDH are still unclear, our results may suggest their link with altered CT and with reduced lung volume. Futture perspectives include a longitudinally evaluation of CT and GI, and their correlation with neurological outcomes, thus moving a step toward a better understanding of this severe disease.

**COD. P66**

**Probabilistic fiber-tracking in stereotactic radiosurgery planning with GammaKnife: a case report**

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INTRODUCTION

Stereotactic radiosurgery (SRS) is a technique in which small brain volumes receive high doses of radiation delivered in one or few number of fractions (i.e. 3). The aim of this paper is to describe the use of post-processing of Diffusion Tensor Images (DTI) for the reconstruction of fiber tracts as organs at risk (OAR) in SRS planning.

MATERIAL AND METHODS

A 69-year-old patient with tentorial meningioma was treated with SRS at the Gammaknife center of our hospital. The first step in SRS

planning was the mounting of the stereotactic frame for the immobilization of the patient and the definition of the sterotactic coordinates. Then, an acquisition of volumetric MRI images with T1 weighted sequences was performed with and without contrast agent (CA) on a Philips Achieva 1.5 T magnetic resonance imaging device. The Leksell GammaPlan V.11.1.0 treatment planning system (TPS) was used to contour target volumes and OARs on the axial images with CA reconstructed at 1 mm thickness, to elaborate the treatment

plan and to calculate the dose distribution. The dose prescription was 6.5 Gy at 50% of the maximum dose for 3 fractions delivered on

consecutive days with a Gamma Knife Perfexion unit. The target volume was in the region of the peduncle inside the brainstem, generally used as a region of interest (ROI) for cortico-spinal tract (CST) reconstruction. For this reason, seven days before the SRS treatment, it was scheduled a DTI acquisition with an Echo Planar Imaging sequence using a receive coil head SENSE 8-channel and to reconstruct the CST. For the post-processing of DTI images, the probabilistic algorithm PROBTRACKX (FSL v. 5.0.6) was used. The "seeds" and "way" ROIs were identified in an axial section of the peduncle and in the region of the motor area in the cerebral cortex.

RESULTS

The reconstructed cortico-spinal tracts for the hand and foot, after neuroradiologist and the neurosurgeon validation, were binarized using a threshold of 10% of the maximum value, coregistered with the MRI SRS planning images and imported into the TPS as neuronavigation images. The processing of the treatment plan took into account the information coming from the tractographic study to limit the hot spot in the volume occupied by the CST. The following parameters $D_{max}$, $D_{0.01cc}$, $D_{0.1cc}$ and $D_{1cc}$ were recorded from the Dose-Volume (DVH) histogram, respectively equal to 24.1, 20.5, 17.5 and 11.3 Gy.

CONCLUSIONS

Post-processing of DTI images has been proved to be useful to have a conservative approach during treatment planning and to evaluate the maximum dose at the Cortico-Spinal tracts. A patient follow-up is planned, which includes a new DTI acquisition and subsequent post-processing to assess any neurological damage or radiological changes.

**COD. P67**

**Integration of in vivo MRS/MRI and ex vivo MRS as new monitoring of the antitumor effects of NK cell-derived nanovesicles in a preclinical model of lymphoma**

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INTRODUCTION NK cells (NK) are the first effective barrier of body defense from tumor cells. Individuals with low NK activity display an increased risk to develop cancer (Vivier et al, 2008). Exosomes (EXO) and microvesicles (MV) are nanometer-sized secreted vesicles, 30-150 nm and 150-400 nm respectively, involved in numerous biological networks (Thery et al, 2009; Bakhshandeh et al, 2017). The in vivo immune regulatory properties and cell communication of these nanovesicles have been demonstrated in preclinical studies, supporting the possible use of exosomes in diagnosis and therapy of different disease, such as cancer (Xu et al., 2018). We have demonstrated that exosomes produced by NK cells (EXONK), isolated from blood of healthy donors, display a potent cytotoxic activity against tumors in vitro (Lugini et al, 2012).To date, it has been demonstrated that extracellular vesicles of NK (NKEVs) cells of tumor origin or genetically modified exert an antitumor effect towards murine melanoma (Lee et al, 2012), neuroblastoma (Neviani et al, 2018) and glioblastoma (Zhu et al, 2018).

AIM of this work was to monitor the effects of NKEVs treatment by integrating in vivo MRI/MRS and ex vivo MRS metabolomics in a xenograft model of lymphoma B.

METHODS Xenografts were derived from s.c. implantation of SUDHL4 cells in SCID mice, and treated twice per week with NKEVs=EXONK+MVNK (NK-derived extracellular vesicles, both exosomes and microvesicles ) or saline intra tumors. One group of animals (Co-NKEV) started to receive the treatment during the injection of cancer cells, another group (Post-NKEV) started to receive the treatment a week later.In vivo MRI/MRS measurements were performed on a Varian/Agilent Inova system (4.7 T) by adopting quantitative protocols (Canese et al, 2012). Ex vivo MRS analyses were performed on tissue extracts at 9.4 by using high resolution Bruker Avance spectrometer (Pisanu et al, 2014).

RESULTS We observed in vivo metabolic alterations in our xenografts after NKEVs treatment associated with a significant reduction of tumour growth [ANOVA repeated measurement, with treatment (saline, Co-NKEV an Post-NKEV) x time (7 points) design p=0.003] at all-time points starting from day 13 after the injection for the Co-NKEV group and from day 19 for the Post-NKEV group (Tukey post hoc analyses). Moreover, in the in vivo MR spectra we found a significant increase in the tumour lipid/lactate signal at 1.33 ppm (ANOVA one-way, p=0.0015) and a significant increase in taurine (ANOVA one-way, p=0.0018) in the Co-NKEV group with respect to controls and to the Post-NKEV group which could be attributed to cell apoptosis.

No differences have been observed in the ADC mean values and distributions (both in the vascular and tissue tumour component).

Ex vivo metabolomics as well as histopathology analyses are ongoing.

DISCUSSION and CONCLUSION In vivo MRI/MRS showed previously unexplored NKEVs induced metabolic changes in a model of human lymphoma B suggesting taurine and lipid signals as potential biomarkers of NKEVs response, providing evidence of altered lipid and redox metabolism following antitumor NKEV treatment.

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**COD. P68**

**Accuracy of computed tomography and magnetic resonance imaging to assess resection margins in primary malignant bone tumors having histology as reference standard**

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The purpose of this study is to evaluate the accuracy of MRI and CT in assessing the resection margins of primary malignant bone tumors. Forty-six patients' specimens of primary malignant bone tumors (27 males; mean age: 48±22 years) were imaged by MRI (fat-saturated proton density-weighted and three-dimensional fat-suppressed T1-weighted gradient-recalled-echo) and CT immediately after surgery. A radiologist and an orthopedist evaluated bone and soft tissue margins of the specimens on both examinations. Histological evaluation was performed by a senior orthopedic oncology pathologist. Margins were classified as R0 (safe margins), R1 (residuals between 0 and 1 mm), and R2 (macroscopic residuals). Cohen's k, Chi square, and McNemar's statistics were used.

Having histology as reference standard, reproducibility of the radiologist ranged from moderate (k=0.544) to substantial (k=0.741) for bone and soft tissue margins on CT, respectively, while that of the orthopedist ranged from fair (k=0.316) to moderate (k=0.548). When comparing R2 and R0+R1 scores, reproducibility of readers' evaluation of bone margins increased ranging from substantial (k=0.655) to perfect (k=1.000). Inter-reader agreement ranged from fair (k=0.308) to substantial (k=0.633). Accuracy of radiologist and orthopedist ranged from 76% to 83% and from 68% to 72%, respectively. When comparing R2 and R0+R1 scores, accuracy of both readers ranged from 83% to 100%. There was no association between local recurrence and margin scores of histology, MRI, and CT ($p \geq 0.058$).

MRI and CT may be useful for extemporaneous analysis of resection margins of primary malignant bone tumors, although wide accuracy variability between the different imaging modalities was observed.

**COD. P69**

**Investigations by MRI and MRS on brain metabolism and adipose organ composition in a transgenic mouse which over-expresses human hydrolase MTH1 which protects mouse tissues against the effects of oxidative stress**

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Introduction Oxidative stress, an imbalance in the production and detoxification of reactive oxygen and nitrogen species (ROS and RNS), is implicated in the pathogenesis of cancer, neurodegenerative disorders and in the aging process. Human MTH1 overexpression in hMTH1 transgenic (hMTH1-Tg) mice confers significant protection against neurodegeneration and motor impairment induced by the mitochondrial toxin 3-nitropropionic acid (3-NP) (De Luca et al., 2008). Moreover hMTH1 overexpression in the hMTH1-Tg mouse model protects several organs against oxidative DNA damage, prolongs life-span and enhances exploratory behavior (De Luca et al, 2013). Initial evidences have also shown reduced weight gain in the hMTH1-Tg mice with respect to controls following a 4-weeks high fat diet stimulus.

In this study, we used the hMTH1-Tg mouse model to investigate how oxidative damage to nucleic acids can affect brain metabolism and adipose organ composition and extension.

Aim To identify metabolic pattern which are characteristic of the brain and the adipose organ of hMTH1-Tg mouse in order to have a deeper view to the role of DNA damage in the inflammatory process which characterizes metabolic dysfunctions.

Methods 1H MRS experiments were performed in adult mice (male, 6-8 week old) on a VARIAN Inova MRI/MRS system operating at 4.7T. 1H localised MR spectra were collected from the hippocampus (HIP, 11.7 μl) and prefrontal cortex (PFC, 5.9 μl) using PRESS sequence (TR/TE = 4000/23 ms, ns 512). According to a quantitative protocol (Canese et al, 2012) which includes water T2 measurements, spectra were analysed by using LCModel fitting program and the unsuppressed water signal for metabolite quantification. A voxel of 3.4 μl was also selected in the interscapolar fat for water to lipid ratio determination and therefore to assess the brown fat amount in the region of the adipose organ which is reputed to be the richest).T1-weighted MRI was finally performed to the abdomen to quantify the volume of visceral fat depot in the two different mice groups. Visceral fat is known to be a risk factor for metabolic dysfunction which is related to obesity.

Results Alterations in brain metabolite concentrations have been detected between the two groups in both regions. In PFC we found a reduction of glutamate in hMTH1-Tg mice ($p<0.01$), in the hippocampus we detected an increase of inositol ($p=0.049$).In the interscapolar fat we observed a trend in the increase of the water/lipid signals ratio ($p=0.07$) in the hMTH1-Tg mice group, which is in accordance with increased presence of brown fat. Furthermore, T1-weighted MRI of the abdomen revealed a reduced amount of visceral fat for the hMTH1-Tg mice ($p=0.02$).

Discussion and conclusions In spite of similar body weight, adipose organ extension and composition is different in the two mice groups showing the hMTH1-Tg mice in accordance with a reduced risk to develop metabolic related disorders for the hMTH1 group. Moreover, brain metabolism alteration highlights a direct effect on brain functionality. The hMTH1-Tg mouse is a good model to investigate the role of oxidative stress in metabolic disorders.

**COD. P70**

**Potential Use of a Diluted High-relaxivity Gadolinium-based Intra-articular Contrast Agent for Magnetic Resonance Arthrography: an in-vitro study.**

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Purpose: To test in vitro different concentrations of gadobenate dimeglumine (Gd-BOPTA) to be potentially used to perform magnetic resonance arthrography (MRA).

Methods and Materials: Gd-BOPTA was diluted in saline (NaCl 0.9%) to achieve different concentrations (4mmol/l; 2mmol/l; 1mmol/l; 0.67mmol/l; 0.5mmol/l). Six sets of five sterile pipes were prepared with 5 ml of each solution, five sets added with 0.5ml of fresh synovial fluid. Two separate pipes were prepared with 5ml of gadopentetate dimeglumine (Gd-DTPA) at 2mmol/l, one pipe added with 0.5ml of synovial fluid. Pipes were imaged using a T1-weighted sequence at 1.5 T. For each pipe, signal intensity (SI) in arbitrary units (au) was measured.

Results: SI reproducibility range was 86%-99%. Mean Gd-BOPTA SI in pipes containing synovial fluid increased from 1236±8au (0.5 mmol/l) up to 1610±44au (1 mmol/l) and down to 1405±33au (4 mmol/l). Mean Gd-BOPTA SI in pipes without synovial fluid increased from 1184±29au (0.5 mmol/l) up to 1530±38au (1 mmol/l), and down to 1347±39au (4 mmol/l). SI of pipes without synovial fluid was lower than that of pipes with synovial fluid for both Gd-BOPTA and Gd-DTPA ($P \leq 0.002$). Regarding pipes with synovial fluid, mean Gd-DTPA SI at 2 mmol/l was 1246±27au. Compared with Gd-BOPTA, SI was not different at 0.5 mmol/l (-0.2%, P=0.587) while it was higher (P<0.001) at all other concentrations (range +13.3%[4 mmol/l]-+28.3%[1 mmol/l]). Regarding pipes without synovial fluid, mean Gd-DTPA SI at 2 mmol/l was 1275±56au. Compared with Gd-BOPTA, SI was lower at 0.5 mmol/l (-6.8%,P<0.001), while it was higher (P<0.001) at all other concentrations (range +6.1%[4 mmol/l]- +19.6% [1 mmol/l]).

Conclusion: In vitro, Gd-BOPTA at 1 mmol/ had a +28% SI increase in comparison to Gd-DTPA 2 mmol/l. SI similar to Gd-DTPA can be obtained using one fourth concentration of Gd-BOPTA.