C01

DIFFERENT BOLD TRANSIENTS IN SPIN ECHO AND GRADIENT ECHO EPI SIGNAL TIME COURSES DURING A SIMPLE MOTOR TASK

A. Ferretti[1], M. Caulo[1], A. Tartaro[1], G.L. Romani[1], C. Del Gratta[1]

[1]*Dip. di Neuroscienze ed Imaging, Università di Chieti; ITAB - Fondazione Università "G.D'Annunzio", Chieti.*

There is an ongoing debate on the physiological origin of the transient overshoot after stimulus onset and the post-stimulus undershoot in the BOLD fMRI signal, with possible explanations ranging from neuronal to vascular origin. In this study we measured the BOLD time course in different brain areas activated during a motor task using spin-echo (SE) and gradient-echo (GE) sequences, that are known to have specificity toward the microvasculature (SE) and both microvasculature and macrovasculature (GE), in order to investigate which compartment is mainly involved in the signal transients.
FMRI was carried out on a 3T Achieva Philips scanner using SE and GE EPI sequences (TR 2s, flip angle 80°, matrix 96x96, SENSE factor 1.8, voxel size 2.4x2.4x3mm^3, TE: 35ms (GE), 75ms (SE)). Subjects (n=16) performed a finger tapping task according to a block paradigm (30s task, 30s rest). Four task-rest cycles were used for each fMRI run, acquiring two GE and SE runs in a randomized order. After standard preprocessing, statistical activation maps were obtained using the general linear model and the BOLD response was expressed as relative signal change with respect to the baseline. Significance of transients amplitude with respect to the plateau response was assessed by means of a t-test.
Results showed a different activation amplitude and time course for the two sequences. As expected, the amplitude of the positive BOLD response in the GE acquisition was larger with respect to the SE acquisition. Moreover, a significant ($p<0.02$) transient overshoot following the task onset was observed for the GE but not for the SE signal time course, whereas the post-stimulus undershoot showed the same amplitude for the two sequences and was observed only in the primary motor area.
BOLD transients are often explained as being due to a temporal mismatch between CBV and CBF changes or between CMRO2 and CBF changes. These results showed that a BOLD transient overshoot is observed only for GE sequences, suggesting that this mismatch should arise mainly from the macrovasculature, whereas the post-stimulus undershoot showed the same behaviour for the two sequences, indicating that this transient should arise mainly from the microvasculature.
Poser BA et al., Hum Brain Mapp 2011(32):141-53.

C01
BIPLANAR LINKED GRADIENT COILS FOR MRI

A. Borceto[1], A. Viale[1], L. Bertora[2], F. Bertora[1]
[1]*IIT- Istituto Italiano di Tecnologia*
[2]*Paramed Medical System*

In a MRI system gradient coils must satisfy a great number of different requirements. Many MRI applications need the gradient fields to be strong and rapidly switched on: this implying the necessity of high efficiency and low inductance. It is also desirable to decrease the resistive energy, in order to allow the use of low power drivers and to minimize ohmic heating. The field linearity and uniformity are fundamental to avoid image distortions. In addition, shielded system are strongly recommended, because switched gradients induce eddy-currents in the surrounding conducting structures. The problem is that all these requirements are in conflict, hence the necessity of compromises that lead to a satisfactory solution. The art of gradient coil design is an inverse optimization process, in which all the requirements have to be weighted depending on the application. Here we present some examples of biplanar shielded gradient coils in which varying the optimization weighting factor heavily affects the wires distribution of the coil system.
Shielded systems usually consist of a primary coil, which produces the linear field over the region of interest (ROI), and a secondary one which shields the field produced by the first in the region of shielding (ROS). Conventionally the primary and the secondary coil are not connected together, but lie on two different parallel surfaces. Here, in the case of biplanar coils, we heuristically demonstrate that linking together the primary and the secondary coils is convenient since it conduces to lower resistive and inductive energies, compared to the traditional shielded arrangements. The Inverse Boundary Element Method (IBEM) has been used [1], where the solution is found by meshing a current carrying surface into a number of elements and optimizing a cost function that takes into account all the requirements described before.
References:
[1] M. Poole and R. Bowtell, "Novel Gradient Coils Designed Using a Boundary Element Method,"
Concept In Magnetic Resonance , vol. 31, pp. 162-175, 2007.

C01

CONFRONTO TRA LE TECNICHE DI RIEMPIMENTO DEL K-SPACE CONVENZIONALE CARTESIANA MULTISHOT E NON-CARTESIANA MULTISHOT PER LA RIDUZIONE DEI MOVIMENTI

S. Chiti[1], L.N. Mazzoni[2], S. Busoni[3], G. Belli[4], G. Roselli[1], R. Brugnoli[1], M. Moretti[1]

[1]*Dipartimento di Diagnostica per Immagini, °SOD 1, ^SOD 4, ^SOD DEA, °SOD NeuroRX - AOUCareggi, Largo Brambilla 3, 50134 Firenze*

[2]*Centro Interdipartimentale di Risonanza Magnetica, Viale Morgagni 85, 50134 Firenze*

[3]*SOD Fisica sanitaria - AOUCareggi, Largo Brambilla 3, 50134 Firenze*

[4]*Fisica sanitaria – Azienda USL 8 Arezzo, Via Curtatone 54, 52100 Arezzo*

Motivazioni: I movimenti volontari ed involontari dei pazienti durante l'esecuzione di esami di risonanza magnetica fa nascere l'esigenza di implementare tecniche che riducano il più possibile queste cause di artefatto nell'immagine.
Metodo: A differenza della tecnica cartesiana, nella tecnica non-cartesiana i dati sono raccolti nel k-spazio in N strisce o "Blade", ognuna delle quali consiste di un numero L di linee parallele che corrispondono a diversi valori della codifica di fase. Le linee centrali vengono campionate per ogni striscia e questo permette di correggere inconsistenze spaziali in posizione, rotazione e fase tra le strisce; correggere movimenti through-plane; diminuire gli artefatti da movimento in-plane attraverso una media tra le basse frequenze.
Per essere ricostruiti con la iFFT 2D i dati acquisiti con tecnica non-cartesiana vengono redistribuiti in forma di griglia con tecniche di re-gridding. Questa tecnica di riempimento del K-space può essere utilizzata con molte sequenze di acquisizione come le SE, GRE, EPI e con la MP.
Il confronto tra le due tecniche è stato eseguito acquisendo immagini di un phantom e di soggetti collaboranti di diversi distretti anatomici, facendo prima una valutazione tecnica di risoluzione di spaziale e di contrasto, poi una valutazione in base ad esigenze cliniche.
Risultati: la tecnica di riempimento non-cartesiana multishot per le caratteristiche menzionate, è in grado di ridurre gli artefatti da movimento in-plane di roto-traslazione in grado di alterare l'immagine acquisita con la tecnica cartesiana multishot.
Conclusioni: si ritiene, per le caratteristiche di riempimento e di ricostruzione, che il K-space non-cartesiano non debba essere utilizzato di routine come sostitutivo della tecnica convenzionale. Se ne consiglia, pertanto, un uso limitato ai casi in cui gli artefatti da movimento risultino troppo marcati per una corretta diagnosi.
Bibliografia
[1] James G. Pipe*. MRM - Magnetic Resonance in Medicine 42:963–969 (1999)
[2] Konstantinos Arfanakis1 et all. MRM - Magnetic Resonance in Medicine 58:1257–1265 (2007)
[3] Nicole Seiberlich1 et all. MRM - Magnetic Resonance in Medicine 63:1648–1658 (2010)
[4] Arvidas Cheryauka et all. 0-7803-7636-6/03/$17.00 ©2003 IEEE.

C01
Parallel transmitter for improved RF distribution in high field MRI scanners

P. Sebastiani[1], M. Alecci[2], C. Del Vecchio[3], A. Galante[2], A. Sotgiu[1]
[1]*Imaging Technology Abruzzo srl, Zona Industriale di Pile, SS17,L'Aquila*
[2]*Dip. Scienze della salute, Università dell'Aquila, Via Vetoio, L'Aquila*
[3]*Selex Communications, Zona Industriale di Pile, SS17, L'Aquila*

In a MRI experiment the RF transmitter section has the purpose of generating a rotating magnetic field B_1 in the sample region. The RF signal is generated in a synthesizer included in the console and can be modulated in phase and amplitude. These tasks are performed by units which are usually provided by the scanner manufacturer. The RF signal generated by the synthesizer it is delivered to a RF power amplifier which provides a power in the range of 5-10 kWatts to the RF coil. Following the development of parallel imaging, interest has been drawn towards parallel transmission, which describes the use of multiple RF transmit coils. It has been shown, particularly for applications to the head, that, the use of a plurality of RF transmitters (4 to 8) in a specially designed transmitter coil structure, provides a much better RF field distribution on the whole head volume. To obtain this improved RF distribution, on each channel the transmitted signal must be independently amplitude and phase modulated requiring a sophisticated transmitter that is substantially different from the units used in commercial MRI scanners.
We have developed an 8 channel parallel transmitter which will operate in the 3-7 T units and which will allow independent modulation of each channel at a rate of 1 MHz allowing to obtain the required excitation profile. The apparatus constitutes an add on system and does not require any modification of the original console. It has as an input the clock reference signal generated by the original console and the pulse start signal. It will not interfere in any other way with the original apparatus allowing use of the original receiver channels for the detection of the signal and for the image reconstruction.
The parallel transmitter consists of 8 units each composed of a VCO, a DirectDigital Synthesizer, a DAC and a RF amplifier. The design is completed by 8 RF power amplifiers operated between 125 and 170 MHz (just changing few components) for 4T and 3T systems. A substantial effort will be done to design these amplifiers in such a way to make it possible to put them near to the magnet to avoid losses in the connecting cables. A similar unit for the 7 T units is under development.

C01
RF Coils Design: A Comparison of Analytical, Numerical and Experimental Methods for RF Field Mapping

N. Fontana[1], A. Monorchio[2], G. Manara[2], R. Stara[3], A. Retico[4], A. Del Guerra[5], M. Tosetti[6], G. Tiberi[7], M. Alfonsetti[8], A. Galante[9], A. Vitacolonna[9], A. Marcello[9]

[1]*Dipartimento di Ingegneria dell'Informazione, Università di Pisa*

[2]*Dipartimento di Ingegneria dell'Informazione, Università di Pisa and Istituto Nazionale di Fisica Nucleare*

[3]*Dipartimento di Fisica, Università di Pisa*

[4]*Istituto Nazionale di Fisica Nucleare, Pisa*

[5]*Dipartimento di Fisica, Università di Pisa and Istituto Nazionale di Fisica Nucleare*

[6]*Department of Developmental Neuroscience, Stella Maris Scientific Institute, Pisa and Istituto Nazionale di Fisica Nucleare*

[7]*Fondazione Imago7, Pisa*

[8]*Dip. Scienze della Salute, Università dell'Aquila*

[9]*Dip. Scienze della Salute, Università dell'Aquila and Istituto Nazionale di Fisica Nucleare*

Introduction

Several clinical MRI/MRS applications at 1.5T and higher fields require a careful selection of the RF coil, to optimize the RF spatial distribution [1]. A number of analytical and numerical methods are reported in the literature to simulate the RF fields of volume/surface coils [2-3]. In this work, we have used a range of computational methods (Biot-Savart, FEKO®, CST Microwave Studio 2010®) to model a transverse field RF surface coil (figure-of-eight, FO8) [4]. Field measurements obtained on the workbench and with a 2.35T scanner are used to validate theory.

Methods and Results

A 2-elements circular FO8 coil (dia=10 cm, separation between elements=1cm) was simulated and built at 64 MHz [4]. The CST and FEKO software solve the Maxwell equations with the Finite Integration Technique (FIT) and the Method of Moments (MoM), respectively. The Matlab program simulates the B1 field by solving the Biot-Savart equation in the quasi-static approximation. A prototype FO8 coil matching the dimensions of the model was built and tested on the workbench. The B1 field distribution was measured on the workbench with the method of perturbing spheres and also by means of GE images acquired in the presence of an oil sample at 2.35T (100 MHz) (Bruker Biospec). The measured RF field along the coil z-axis was compared against the simulated distributions. A good agreement was obtained with all methods. The computational times for the B1 field numerical evaluation were: 40 minutes with CST analysis (Intel Core Duo i7@2.65GHz, 12GB RAM and OS Windows7 @64bit), 10 min with FEKO analysis (i7980 Xtreme 3.3GHz; 12GB DDR3 1600 MHz triple channel); 30 min with Biot-Savart (Pentium III, 1.2GHz, 500MB RAM).

Conclusions

The results presented here show that along the coil z-axis, the RF field distribution of the transverse field FO8 RF coils is spatially selective [4]. Several simulation methods and workbench measurements are used to validate the results. The FO8 coil can be useful to optimize the sensitivity in a particular region of interest (ROI) located in close proximity of the surface.

References

[1] Meyerspeer M et al, MRM 49:620-625 (2003)
[2] Jin J. Boca Raton, FL: CRC 1999
[3] Giovannetti G, et al, MAGMA 2002;15:36-44
[4] Alfonsetti M et al, MAGMA 18:69-75 (2005)

C02

JOINT ANALYSIS OF STRUCTURAL AND QUANTITATIVE MAGNETIZATION TRANSFER MRI FOR CLASSIFICATION OF ALZHEIMER'S DISEASE AND NORMAL AGING

G. Giulietti[1], M. Bozzali[1], V. Figura[1], R. Perri[2], C. Marra[3], M.G. Vita[3], F. Giubilei[4], M. Cercignani[1]

[1]*Neuroimaging Lab., Santa Lucia Foundation, Rome*

[2]*Dep. of Clinical and Behavioural Neurology, Santa Lucia Foundation, Rome*

[3]*Institute of Neurology, Cattolica University, Rome*

[4]*Dep. of Neurology, Sapienza University, Rome*

INTRODUCTION

Preliminary studies [ref], based on region-of-interests, suggest that quantitative Magnetization Transfer (qMT) provides complementary information to conventional MRI techniques in the characterisation of Alzheimer's disease (AD). Aim of this study was to extend these findings to the whole brain using a voxel-wise approach, and to determine the joint contribution of GM atrophy and qMT for the classification of AD using a multimodal image processing.

METHODS

We recruited 19 AD patients (F/M=10/9; mean [SD] age=70.0 [7.7] years] and 11 healthy subjects (HS) (F/M ratio=4/7; mean [SD] age=63.9 [9.5] years]. All subjects had a neuropsychological examination and an MRI acquisition at 3.0T including: MDEFT, 12 MT-weighted volumes for qMT, and the acquisition of T_1 and B_1 maps.

The MDEFTs were processed in SPM8 to yield maps of GM, while the other sequences were used to compute the qMT parameters on a voxel-by-voxel basis. Normalized and smoothed qMT maps were separately compared between groups (AD vs HS) using SPM8. Only the qMT maps that showed significant group differences were retained for a voxel-wise logistic regression analysis, designed to differentiate between the contribution of GM atrophy and qMT parameters to the classification of subjects as either AD or HS.

RESULTS AND DISCUSSION

Our results indicate that the forward exchange rate (RM_{0B}) is the most sensitive qMT parameter to AD, being the only parameter showing group differences. The logistic regression analysis found several areas of reduced GM volume and reduced RM_{0B} that were significantly predictive of AD diagnosis: the former were mainly subcortical (left (L) and right (R) putamen, L and R pallidus, R thalamus), while the latter were mainly cortical (L and R hippocampus, L and R posterior cingulate gyrus, L and R parietal cortex). This study suggests that an RM_{0B} reduction in the aforementioned cortical areas is more predictive of AD status than a reduction of GM volume in the same areas. An intriguing interpretation, supported by a PET study on AD, is that RM_{0B} might reflect, through the measurement of the efficiency of MT exchange, some metabolic information. [ref.: Kiefer C, et al. Neuroimage. 2009; 48(4):657-67]

C02
MULTI-FIBER RECONSTRUCTION TECHNIQUES FROM DWI DATA FOR BRAIN ANATOMICAL CONNECTIVITY EVALUATION

M. Campanella[1], E. Molinari[1]
[1]*Dip. Robotica, Scienze Cognitive e del Cervello, Istituto Italiano di Tecnolgia*

Diffusion weighted MRI (DWI) is one of the promising techniques to explore neural connectivity and reconstructing white matter fibre structure in vivo. The diffusion model conventionally used is the diffusion tensor (DT), of which the first eigenvector is assumed to align with the fiber orientation. It is based on Gaussian diffusion assumption, which implies that there can only be a single fiber population per voxel, enabling to trace only the major tracts in the brain, where anisotropy is high with a poor approximation where fibres cross, diverge or have high curvature. Alternative models and algorithms that aim to recover more detailed information about the orientations of fibres from diffusion MRI measurements nowadays are used. In the current study High Angular Resolution Diffusion Imaging data (64 directions, b-value = 1000 s.mm-2) were acquired. A comparison between the classical single tensor model and the newer q-space methods, such as ‘q ball’ and persistent angular structure (PAS)–MRI[1] in terms of tractography performances was developed. In particular a deterministic streamline tracking algorithms was performed to identify tracts between cortical areas of interest. Stopping criteria, based on voxel classification, anisotropy and curvature, were applied. For PAS-MRI a reduced encoding approach was followed evaluating the best number of encoding directions able to maintain a compromise between computation time, and good performances. Besides, in order to isolate the fiber bundles that connect the two areas of interest and estimate the degree of connections between them, an appropriate exclusion mask for the tractography analysis was created, taking into account the connectivity values over neighbourhood for each voxel.

[1] K. M. Jansons, D.C. Alexander, Persistent angular structure: new insights from diffusion magnetic resonance imaging data, Inverse Problems 19, 1031–1046, 2003

C02

ANOMALOUS DIFFUSION STRETCHED EXPONENTIAL IMAGING TO MEASURE MICROSTRUCTURE SIZES BY MEANS OF LOCAL INTERNAL GRADIENTS

M. Palombo[1], S. De Santis[2], S. Capuani[3]

[1]*Physics Department Sapienza University of Rome, Rome Italy.*

[2]*Cardiff University Brain Research Imaging Center (CUBRIC), Cardiff, UK*

[3]*CNR-IPCF Sapienza Roma, Physics Dpt. Sapienza Univ. of Rome, Rome Italy*

The departure from mono-exponential decay (S(b)=S(0)exp(-bD)), due to PFG (Pulse field gradient) signal as a function of the b-value increasing observed in biological tissues, prompted the search for alternative models to characterize anomalous dynamics of water diffusion. Several approaches have been proposed in the last years, such as anomalous diffusion stretched exponential model, in which γ is the stretching parameter arising from fitting the stretched function $S(b)=S(0)\exp(-(bD)^{\#})$ to PFG data. However, the exact meaning of the γ parameter still needs to be fully understood.

In this work we investigated the γ parameter by means of Imaging version of Pulse gradient Stimulated Echo (PGSTE) sequence in controlled phantoms comprised of micro beads (characterized by mean diameters of 6.0,10,15,20,30,40,80 and 140 μm) in water solution. Specifically, we tested the influence of the internal gradient (G_{int}) due to the magnetic susceptibility difference (ΔXm) between diffusing water and obstacles, with respect to the capability of the γ parameter to discriminate between structures characterized by different geometrical dimensions.

All measurements were performed at 9.4T using a micro-imaging probe (10mm internal diameter bore). An imaging version of PGSTE sequence with Δ/δ=40/4.4ms, diffusion gradients along x,y,z axis, TR=3s, STH=1mm, FOV=8 mm, and 10 values of g (b values range 500 - 6500 s/mm^2, plus b=0) was used to obtain Mγ maps.

Moreover, Spin Echo (SE) sequence (TR=1.5s, NS=8) with N=64 data points was used to extract G_{int} from SE decay as previously described [1].

Our results show that Mγ strongly depends on G_{int} measured by SE sequence. Specifically the higher the G_{int}, the lower the Mγ value. Moreover Mγ values strongly depend on bead size. Experimental results demonstrate, that γ value depends on G_{int} which are present at the interface of regions with different ΔXm. Specifically, as γ value quantifies the departure from the purely monoexponential decay of water diffusion in heterogeneous systems, our findings highlight a strong correlation between the increase of G_{int} strength and the increase of anomalous diffusion behavior of diffusing protons.

[1] De Santis et al. Phys Med Biol 2010;55(19):5767-5785.

C02
AN ACCURATE T2* MAPPING METHOD IN THE HUMAN BRAIN AT 3T

A. Sciarra[1], A. Oros-Peusquens[2], K. Reetz[2], M. Alecci[1], N.J. Shah[2]
[1] *Università dell'Aquila, Dipartimento di Scienze della Salute, L'Aquila, Italy*
[2] *Inst.Neuroscience & Medicine,Research Cen. Jülich,Fac of Medicine,Dept Neurology, RWTH Aachen University, Germany*

Introduction:T2* relaxation times are closely related to the local magnetic #eld inhomogeneities[1]. Apart from dipole-dipole interactions, a variety of other relaxation mechanisms may be operative, and relaxation in biological tissues is complicated even further due to compartmentalization[2,3].In this work we have developed an accurate 3T methodology that uses both T1-w and T2*-w images for the quantitative analysis in small neuro-substructures.
Materials and methods.Subjects:10 patients with PD and 10 healthy controls.Data Acquisition: 3T, Siemens Trio. Sequences: 4 scans with 3D-MPRAGE[3-5] for the anatomical characterization and 3 scans with 3D-GRE[3] to obtain T2*-w images.Image processing: for each sub ject, #rst were co-registered and realigned the MPRAGE scans and then calculated the average. The T1-w images were segmented followed by manual identi#cation of the key brain structures. From the GRE scans, after co-registration and realignment, a #tting procedure was used to obtain T2*-w images. Finally, the T1-w images were co-registered and realigned to the GRE images, 1_echo time,
thus overlapping anatomical images and quantitative T2*-w images to analyze the neuro-substructures in the human brain [6].
Results and Discussion
In vivo direct observation of the particular neuro substructure in the human brain is one of the most sought-after goals for many neurodegenerative diseases, and it has the potential to lead to non invasive diagnosis. Using a 3T clinical scanner, we obtained a better SNR than standard clinical acquisition and about 7 minutes acquisition time. The results showed an appreciable variation for T2* data between volunteers and PD subjects. The resolution of T2*-w images is still limited (0.96 pixels/mm), and the segmentation remains to be done manually. With the same data it will be also be possible to do susceptibility images, allowing the use of both images to quantify di#erent kinds of parameters in small ROIs.
References
[1]EM Haacke,Mag. Res. Imaging Wiley-Liss, 1999.[2]RA de Graaf. In Vivo NMR Spectroscopy Wiley 2007.[3]MA Bernstein,Handbook of MRI Pulse Sequences. Els.Acd.Press,2004.[4]Brant-Zawadzki,Rad. 1992;182:769-775.[5]JP. Mugler,JMRI 1991; 1:561-567.[6]IN Bankman,Handbook of Medical Imaging,AcademicPress,2000

C03
FUNCTIONAL AND PHARMACOLOGICAL MRI IN ANIMAL MODELS OF DRUG ADDICTION

A. Gozzi[1], M. Tessari[2], R. Ciccocioppo[3], M. Massi [3], A. Bifone[1]
[1]*Istituto Italiano di Tecnologia, Center for Nanotechnology Innovation, IIT@NEST , Piazza San Silvestro, 12, 56127 PISA*
[2]*GlaxoSmithKline Medicines Research Centre, Verona, Italy*
[3]*Department of Experimental Medicine and Public Heath, University of Camerino, MC, Italy*

Chronic drug abuse produces long-lasting neurobiological changes that are thought to underlie the loss of control over drug intake that defines drug addiction. Human neuroimaging studies have greatly enhanced our understanding of the neural substrates of addiction, by revealing a number of functional alterations which can be related to specific behaviors and symptoms. More recently, the combination of genetic analysis and neuroimaging techniques has started to shed light on the role of altered functional states as putative predisposing factors for the development of addiction. A strong rationale exists for the extension of this approach as a translational tool in animal research. Drug addiction is often modeled in experimental paradigms where rodents learn to self-administer the drug. However, the extent to which these models replicate the functional alterations observed in human imaging studies remains unknown. Moreover, no attempts have been made to image functional brain alterations in animal lines with high propensity for addictive behaviors. Here we used a multi-parametric functional and pharmacological MRI approach to assess basal and evoked brain function in rats subjected to a prolonged cocaine self-administration scheme. Consistent with human findings, cocaine-exposed rats exhibited marked hypo-frontality and blunted striatal dopaminergic reactivity, an effect that was significantly correlated with total cocaine intake. Moreover, functional connectivity analysis revealed an altered inhibitory interplay between thalamo-frontal regions involved in attentional functions. The same approach was applied to naive Marchigian–Sardinian alcohol-preferring rats, a line of animals widely used to study genetic predisposition for alcoholism. The study revealed substantial functional alterations in a coordinated network of limbic brain regions, with a clear involvement of the extended amygdala, a brain circuit that is thought to mediate the negative motivational state that drives addiction. Taken together, our findings support the translational value of fMRI as a tool to investigate the neuro-biological substrates underlying the behavioral expression of compulsive drug-intake and predisposition to addiction in laboratory animals.

C03

Macromolecular transport quantification in tumor by Magnetic Resonance Imaging of protein binding contrast agent

G. Valbusa[1], L. Miragoli[1], C. Cabella[1], F. Tedoldi[1], S. Colombo[1], E. Reitano[1]

[1]*Centro Ricerche Bracco, Bracco Imaging s.p.a*

A potentially serious flaw of novel anticancer strategies is their reliance on macromolecular drugs that could fail to penetrate the tumor interstitium. Although the importance of this type of “physiological resistance” is recognized no widespread in vivo diagnostic methods are available to identify penetration-resistant tumors. The potential of the albumin-binding contrast medium B22956/1 (Bracco Imaging S.p.a) to assess the macromolecular transport in tumors has been investigated by Dynamic Contrast-Enhanced MRI (DCE-MRI) in an experimental cancer model. Macromolecular vascular permeability was modulated using a potent VEGFRs inhibitor. PC-3 cells, a human prostate cancer line, was implanted in 16 NCR athymic nude mice. The transendothelial permeability (kTrans) to B22956/1 and the fractional plasma volume (fPV) were estimated from the analysis of dynamic MR data using a pharmacokinetic model and the Initial Area Under the Curve (IAUC) was calculated in several time windows, from 1 to 30 minutes, after contrast agent injection. Macromolecular penetration in tumors was probed by fluorescently labelled Bovine Serum Albumin (BSA) administered via tail vein after the last MRI session. The BSA is a prototypical non-binding macromolecule and B22956/1, because of its strong affinity for albumin, is expected to follow the same pharmacokinetic fate. The local microvessels permeability was measured by microscopy quantifying the extravasated fraction of BSA whether the blood vessel density was computed as the percentage of images area stained over an optimized threshold. Several DCE-MRI parameters were affected by the antiangiogenetic treatment, significant differences between treated and control group were observed for kTrans and for IAUC provided that the MRI session lasted at least 5 minutes post contrast agent injection. Very notably, kTrans, IAUCE5 and IAUCE10 showed a statistically significant linear correlation with the albumin extravasated from the vessels quantified histologically. In summary, with the use of B22956/1 the therapeutic effects of a VEGFRs inhibitor in an hypovascularized tumour can be monitored by DCE-MRI. These preliminary results suggested its potential clinical application for the characterization of macromolecular delivery in tumors.

C03

METABOLOMICS ANALYSIS OF MALIGNANT AND NORMAL PROSTATE TISSUES USING ^{1}H-NMR SPECTROSCOPY

L. Casadei[1], M. Valerio[2], V. Panebianco[3], A. Sciarra[4], C. Manetti[1]

[1]*Dip. di Chimica, Università "La Sapienza", Roma, Italia*

[2]*Area di Medicina Molecolare, Direzione Scientifica, Istituto Nazionale Tumori, Regina Elena, Roma, Italia*

[3]*Dip. di Scienze Radiologiche, Università "La Sapienza", Roma, Italia*

[4]*Dip. di Urologia, Università "La Sapienza", Roma, Italia*

The survival of patients with prostate cancer (PrC) depends on early diagnosis and the ability to monitor the progression and regression of malignancy. Up until now, the standard method for early PrC detection relies on serum prostate-specific antigen (PSA) measurement followed by histological analysis of biopsy specimens. Indeed, diagnostic limitations are associated with these clinical parameters. In fact, elevated serum PSA levels can be also caused by benign prostatic diseases which are mainly prevalent in older men. Moreover, due to the heterogeneous and frequent multifocal nature of prostate cancer, biopsy methods may not include an adequate specimen sampling of the prostate, originating likely false negatives. These considerations suggest that the identification of novel diagnostic and prognostic biomarkers is needed.
In this work, to identify novel diagnostic and prognostic biomarkers and guide the design of targeted drugs, healthy and cancerous prostate tissue samples (n=40), obtained from 19 prostate cancer patients after prostatectomy, were analyzed.
The metabolite compositions of hydro-alcoholic and lipophilic phases of the tissue extracts were investigated using 1H-NMR spectroscopy (11.7 T). To interpret this comprehensive metabolic information, the data were subjected to a multivariate statistical analysis. The most discriminant metabolites contributing to the multivariate model were selected and the metabolic correlations among them were identified using correlation maps. Furthermore, the extracted Principal Components (PC) from multivariate model were then correlated with clinicopathologic features acting as probes to afford some useful insights into the different metabolic pathways that underlie malignancy grading.

Our results show clearly distinct ^{1}H-NMR spectral patterns between benign and malignant prostate tissue. Although the paucity of the considered data set, the identification of metabolic patterns associated with different prostate tissue types is a proof-of-concept of the possibility of improving the malignancy grading systems. Moreover, the analysis of the most important metabolites for discriminating between benign and malignant prostate tissue and the metabolite correlation maps allowed to reconstruct the phenotypic disease network.

C03
INVESTIGATION OF ADIPOSE TISSUES IN ZUCKER RATS USING IN VIVO AND EX VIVO MAGNETIC RESONANCE SPECTROSCOPY

E. Mosconi[1], M. Fontanella[1], D.M. Sima[2], S. van Huffel [2], S. Fiorini[1], A. Sbarbati[1], P. Marzola[3]
[1]*Magnetic Resonance Lab., DSNNMM, Section of Anatomy and Histology, University of Verona, Verona, Italy*
[2]*Dep. of Electrical Engineering (ESAT-SCD), Katholieke Universiteit Leuven, Leuven, Belgium*
[3]*Dep. of Computer Sciences, University of Verona, Italy*

Introduction
In vivo, single Voxel, Magnetic Resonance Spectroscopy (MRS) at 4.7T and ex vivo, high resolution, Proton Magnetic Resonance Spectroscopy (HR-NMR) at 500 MHz were used to study the composition of adipose tissues in Zucker obese and Zucker lean rats(1). Lipid composition was characterized by unsaturation and polyunsaturation indexes and mean chain lengths. In vitro experiments were conducted in known mixtures of triglycerides and oils in order to validate the method. MRS peak quantification was performed by using the QUEST algorithm.
Methods and Materials
Oil standard samples for HR-NMR were prepared by diluting 20 uL of oil in 600 uL of deuterated chloroform (CDCl3) and placed in 5-mm NMR tubes. Plain oil was used for MRS.
Male, adult, Zucker obese (fa/fa) rats (n = 8) and Zucker lean rats (n = 8) were obtained from Harlan, UK. A reduced number of them (n=5 obese and n=4 lean) were used for Folch's extraction protocol and HR-NMR measurements. MRS experiments were carried out using a 4.7T Biospec System (Bruker, Germany) equipped with a birdcage coil and a flat surface coil. HR-NMR spectra were acquired using a Bruker DRX spectrometer operating at 500.13 MHz for 1H nuclei, with a 5-mm TXI probe.
Results
Albeit with different sensitivity and accuracy, both in vivo MRS and ex vivo HR-NMR revealed that white adipose tissue is characterized by lower unsaturation and polyunsaturation indexes in obese rats compared with controls. HR-NMR revealed that similar differences occurs also in brown adipose tissue. The present findings confirm the hypothesis that obese and lean Zucker rats have different adipose tissue composition. It remains to be investigated whether similar differences exist in human fat deposits and their potential diagnostic usefulness.
Conclusions
Proton MRS in lipid tissue is technically simple thanks to high signal and no need for water suppression and provide a non-invasive, painless method for obtaining lipid composition in animals and humans. MRS can be used in longitudinal studies aimed at monitoring changes in lipid composition in response to diet, exercise, and disease(2).
References
(1)Mosconi, Fontanella et al. Journal of Lipid Research 52:330 (2011)
(2)Ren et al.,Journal of Lipid Research 49:2055 (2008)

C03

A COMBINED INVESTIGATION OF THE BRAIN STRUCTURE AND METABOLISM IN THE APP/PS1 TRANSGENIC MOUSE MODEL OF ALZHEIMER'S DISEASE ON AGEING BY MEANS OF MRI AND ^{1}H MRS

M. Filibian[1], E. Micotti[1], A. Paladini[1], M. Marizzoni[2], L. Venturi[2], A. Caroli[3], C. Balducci[1], C. Caffarra[1], L. Buccarello[1], E.A. Irving[4], G. Frisoni[2], G. Forloni[1]

[1]*Department of Neuroscience, Istituto di Ricerche Farmacologiche "Mario Negri", Milano, Italy*

[2]*Laboratory of Epidemiology and Neuroimaging, IRCCS Fatebenefratelli, Brescia, Italy*

[3]*Biomedical Engineering Department, Istituto di Ricerche Farmacologiche "Mario Negri", Bergamo, Italy*

[4]*GlaxoSmithKline, Gunnels Wood Road, Stevenage SG1 2NY,*

In recent years the availability of transgenic models mimicking the hallmarks of Alzheimer's disease (AD) has boosted the impact of the translational study of its neurodegenerative processes and the research of novel potential biomarkers. We present a comprehensive study of the TASTPM APP/PS1 mouse model of AD [1], affected by early ß-amyloid (Aß) deposition, by means of both Magnetic Resonance Imaging (MRI) and Spectroscopy (MRS). By combing the two approaches we extensively characterize in vivo the progression of the structural and neurochemical changes occurring with age.

MRS and MRI data were collected with a 7 Tesla Bruker Biospec system in both the TASTPM (TG) and the wild type (WT) C57BL/6 mice from 4 to 25 months of age. We performed high resolution (146x117x146 µm voxel size) MRI by means of a 3D RARE sequence. The volume measurements in structural MRI images were segmented either manually or using a custom software. ^{1}H spectra were acquired by means of a PRESS sequence (TR=2500 ms, TE=10 ms) in two single voxels positioned in the dorsal hippocampus (4.2 µL) and in the thalamus (7 µL) respectively.

From MRI we inferred that a general atrophy in all the brain regions develops in the TG mice with respect to the WT mice. We report a reduction of the hippocampus of the TG mice and a strong enlargement of the ventricles volume with age, and also a general progressive atrophy of the olfactory bulb, the cortex and the caudato-putamen. From MRS we estimated in the TG mice significantly decreased N-acetyl-aspartate (-16%) and Glutamate (-23%) levels and a dramatic increase of myo-Inositol (+40%) after 20 months of age, while these levels don't change in the WT mice.

Since similar structural and metabolic alterations have been observed in AD subjects, our findings suggest that the TASTPM mice model is potentially relevant in the translational study of the effects of progressive Aß deposition in the brain. The research leading to these results was conducted as part of the PharmaCog consortium funded by the European Community's Seventh Framework Programme for the Innovative Medicine Initiative under Grant Agreement n°115009. For further information please refer to www.alzheimer-europe.org.

[1] C. Balducci and G. Forloni, NeuroMol. Med. (8 Dec 2010)

C03

EFFECTS OF A TREATMENT ACTIVATING RHO GTPASES ON BRAIN METABOLISM AND MORPHOLOGY IN THE MECP2-308 TRUNCATED MOUSE MODEL OF RETT SYNDROME BY IN VIVO 1H MRS AND MRI

R. Canese[1], B. De Filippis[1], C. Fiorentini[2], A. Fabbri[2], L. Ricceri[1], G. Laviola[1]

[1]*Cell Biology and Neurosciences Dept. Istituto Superiore di Sanità, Rome, Italy*

[2]*Therapeutic Research and Medicine Evaluation Dept. Istituto Superiore di Sanità, Rome, Italy*

Rett syndrome (RTT) is a pervasive developmental disorder caused by a mutations in the gene encoding methyl-CpG -binding protein 2 (MeCP2). Here we investigated the effects of Cytotoxic Necrotizing Factor 1 [(CNF1), a bacterial toxin that selectively activates Rho GTPases, thus reshaping actin cytoskeleton, enhancing neurotransmission and synaptic plasticity] administration to contrast the RTT phenotype in MeCP2-308 truncated mice, by in vivo 1H MRI and MRS.

Fully symptomatic adult MeCP2-308 male mice were intracerebroventricularly (icv) treated with CNF1 and evaluated in behavioral tests focused on RTT symptomatology. At the end of behavioral testing, animals underwent MRI and MRS scanning to evaluate genotype- and treatment- induced differences in morphology and metabolism.

MR examinations were performed on a VARIAN Inova MRI/MRS system operating at 4.7 T, by using a volume coil as transmitter and a surface coil constructed for mouse head as receiver (RAPID Biomedical). Single voxel localised 1H MR spectra (PRESS, TR/TE = 4000/23 ms, ns = 256) were collected from: prefrontal cortex (PFC), 6.8 μl; dorsal striatum (STR), 16 μl and hippocampus (Hip), 11.7 μl. Spectra were analysed by using LCModel fitting program. The unsuppressed water signal and water T2 analyses were used for metabolite quantification. Multislice fast spin echo axial images (TR/TEeff = 3200/60 ms, ns = 2, slice thickness 1 mm, 24 slices, matrix 256 x 256, FOV =25 x 25 mm^2) were acquired for volumetric analyses. Statistical analysis was performed by using ANOVA (2 x 2 genotype and treatment).

MRI analysis revealed a significant reduction of total brain, corpus callosum and motor cortex in mutant mice, in agreement with MRI results in RTT patients. Brain MRS analysis detected in vivo changes of metabolites involved in glial integrity and bioenergetics, and point to improved mitochondria functionality in CNF1-treated mice. These results clearly indicate that direct modulation of brain RhoGTPases may constitute a new therapeutic strategy for RTT.

C03

MRI VISUALIZATION OF RELEASE FROM Gd-LOADED LIPOSOMES TRIGGERED BY PULSED LOW FREQUENCY ULTRASOUND

E. Terreno[1], P. Giustetto[1], D. Delli Castelli[1], C. Boffa[1], D. Durando[1], S. Aime[1]

[1]*Dipartimento di Chimica IFM e Centri di Imaging Molecolare e Preclinico dell'Università di Torino*

- Introduction

In vivo visualization of drug release triggered by endogenous or externally-applied stimuli is an emerging topic in molecular medicine.[1] As far as US is concerned, most of the reported studies were performed using gas-filled nano- or micro-bubbles. However, there is a great interest to combine the peculiar properties of acoustic waves with other imaging modalities, especially MRI.

Liposomes are successfully used in clinic as drug delivery nanocarriers and they are also under intense scrutiny as theranostic MRI agents. The motivation of this study was to explore the possibility of inducing release from water-filled liposomes by acoustic pressure, and demonstrate the potential of MRI to visualize this process.

- Methods

Liposomes encapsulating the clinically approved MRI agent ProHance™ were prepared using the thin lipidic film method and insonated using an US apparatus operating at 27.6 kHz. The release of the MRI agent was monitored by relaxometric measurements performed at 0.47 T. MRI experiments were carried out at 7 T. In vivo experiments were performed using xenografted melanoma B16 tumor on mice.

- Results and Discussion

Release of the MRI probe from liposomes was observed under US exposure, and it was not induced by heating. As expected, the release was directly correlated with the insonation time and it was extremely sensitive to several variables like the duration of the ‘on’ phase of the pulsed US cycle, size, shape, and chemical composition of the nanovesicles membrane. The release occurred only during the US exposure, thus allowing a real control of the process. After insonation, the size of vesicles was not significantly affected, thus suggesting that the release mechanism was likely due to the formation of transient pores in the vesicles membrane. The in vivo potential of these findings were preliminarily assessed by injecting the paramagnetic liposomes into a melanoma B16 tumor xenografted on mice.

- Conclusion

The results obtained offer the opportunity to selectively trigger the release of imaging reporters (and drugs) from a mixture of different nanocarriers, thus opening new improved imaging-guided therapeutic schemes.

[1] S. Ganta et al., J.Control. Rel., 2008, 126, 187-204.

C03

GAUSSIAN AND ANOMALOUS DIFFUSION IN SPONGY BONE: Mγ AS A NEW POTENTIAL MARKER TO DETECT OSTEOPOROSIS

S. Capuani [1], S. De Santis[2]

[1]*CNR-IPCF Sapienza Roma, Physics Dpt. Sapienza Univ. of Rome, Rome, Italy*

[2]*Cardiff University Brain Research Imaging Centre (CUBRIC), Cardiff, UK*

In MR diffusion measurements, the signal is recorded by diffusion-sensitized sequences as a function of chosen b-values range. Apparent diffusion coefficient (ADC) can be extracted using a mono-exponential curve decay. However, the mono-exponential decay inherently assumes diffusion to be Gaussian which means that there are no obstruction or chaotic travel paths of water molecular displacement. This is clearly erroneous in biological tissues as demonstrated by some experiments performed in the last few years which underlined the inadequacy of the mono-exponential curve to fit diffusion data acquired in heterogeneous tissues. Using a stretched exponential model, the signal decay vs b, is modelled as a stretched exponential where the stretching exponent γ, that quantifies non Gaussian (or Anomalous) diffusion, is linked to the tissue heterogeneity in which spins diffuse. Recently we have developed a method for measuring the γ parameter as a rotationally invariant quantity Mγ(1).

Here, Anomalous diffusion (AD) measurements based on the evaluation of Mγ to quantify diffusion processes in bone marrow (BM) were proposed. BM is characterized by different relative percentage of water and fats. BM in femoral epiphysis fills pores generated by the trabecular bone network (TBN), while BM in femoral diaphysis is not forced in pores. Ex-vivo specimens extracted from calves were investigated at 9.4T. AD experiments, MRS and conventional ADC measurements were performed in samples characterized by different percentage of water and fat, and by different TBN. Mγ of water component shows a decreasing trend as bone marrow water decreases in spongy-bone specimens. Conversely Mγ values in diaphysis BM do not depend on the water percentage. ADC does not discriminate nor water in diaphysis and epiphysis, or spongy-bone characterized by different TBN, while Mγ does. Moreover, water in BM is dominated by AD while fat component is characterized by a Gaussian diffusion in the range of b-values and diffusion time Δ used. Experimental results show a dependence of Mγ on magnetic susceptibility differences between bone and water suggesting potential applications of water Mγ for the diagnosis of spongy-bone pathologies such as osteoporosis.

(1) De Santis et al. MRM 2011 in press.

C03

VALUTAZIONE NON INVASIVA, STRUTTURALE E QUANTITATIVA DEL PROCESSO DI DANNO/RIPARAZIONE DEL MUSCOLO SCHELETRICO IN MODELLI ANIMALI MEDIANTE RISONANZA MAGNETICA

T. Canu [1], L. Campana[1], A. Esposito[1], A. Palmisano [1], C. Colantoni [1], F. De Cobelli [1], P. Rovere-Quirini[1], C. Tacchetti [1], A. Manfredi [1], A. Del Maschio [1]

[1]*Ospedale San Raffaele di Milano*

Obiettivi:
Messa a punto e validazione di un protocollo di studio finalizzato al monitoraggio RM delle modificazioni del muscolo scheletrico durante il processo di degenerazione/rigenerazione.
Materiali e metodi:
24 topi C57BL/6N sono stati monitorati mediante RM, prima e ad 1, 3, 5, 7, 10, 15 e 30 giorni dall'induzione di danno acuto del tibiale anteriore mediante iniezione di cardiotossina, utilizzando un magnete 7T (Bruker, BioSpec70/30 USR, Gradients strenght 675mT/m, time rise 140#s; Paravision 5.0) e una bobina Heart Phased Array a 4 canali.
Il protocollo RM messo a punto comprendeva: mappe T2 Multi-Slice-Multi-Echo con soppressione del grasso (TR=1938ms; TE=10,73/171,68ms); diffusion tensor imaging con codifica in 30 direzioni (TR=3750ms; TE=33ms) e mappe di diffusione (TR=3000ms, TE=30ms, 6 b values). A ogni time-point 3 topi sono stati sacrificati e i dati istologici confrontati con i risultati RM.
Risultati:
Il protocollo ottimizzato consente il monitoraggio dell'andamento dei parametri di T2rt, FA e ADC con buona riproducibilità. Il protocollo ha una durata di circa 50 minuti. Aspetti fondamentali per la buona qualità delle sequenze acquisite si sono rivelati il corretto posizionamento e l'omogeneizzazione del campo magnetico mediante tecnica MAPSHIM. I valori di T2rt e FA del muscolo sano sono rispettivamente 16,06±0,562ms e 0,31±0,063. L'andamento del T2-rt e della FA si sono rivelati correlati con il numero di leucociti infiltranti e la percentuale di fibre rigeneranti documentati istologicamente.
Conclusione:
Le modificazioni di T2-rt correlano con l'infiltrato leucocitario. FA sembra essere un valido parametro per la valutazione delle modificazioni presenti durante il processo di danno/riparazione muscolare.
Riferimento bibliografico:
Radiology 2007 May; 243(2): 413-21.

C04

COMBINATION TRAINING IN AGING SUBJECTS INCREASES COGNITIVE PERFORMANCES, MODIFIES THE BRAIN RESTING STATE ACTIVITY AND IS AFFECTED BY DOPAMINE-RELATED GENES

R. Esposito[1], V. Pieramico[2], F. Cilli[1], D. Mantini[3], A.P. Mattei[1], V. Frazzini[1], V. Gatta[4], A. Tartaro[1], G. Romani[1], S. Sensi [5]

[1]*Department of Neuroscience and Imaging, University "G. d'Annunzio" Chieti-Pescara, Italy*

[2]*Molecular Neurology Unit, Center of Excellence on Aging, University "G. d'Annunzio"*

[3]*Institute of Neuro-psychophysiology, Catholic University of Leuven, Belgium*

[4]*Department of Biomedical Science, University "G. d'Annunzio*

[5]*Department of Neurology, University of California-Irvine, Irvine, CA, USA*

Aim: Aging is a major co-risk factor in many neurodegenerative diseases. In this study, we evaluated whether an exposure to 6 months of structured activities (Combination Training) can increase the cognitive functions as well as the brain plasticity in healthy elderly subjects. We also evaluated whether specific dopamine receptor (DRD1-5) genotypes could affect the response to the combination training.

Experimental procedures: Healthy elderly (65-75 years old) subjects were evaluated before and after the Combination Training by employing neuropsychological and occupational tests as well as functional magnetic resonance imaging (fMRI). The subjects were randomly divided into two groups of which only one received exposure to structured activities.We studied the plastic reorganization of the of the Default Mode Network (DMN) and Dorsal Attention Network (DAN). Cortical thickness was also studied using masks for these two networks. Dopamine receptor (DRD1-5) genotyping was used as a covariate in analyzing group differences.

Results: The trained group showed a statistical significant improvement in prose memory test and OT-Evaluation scores. Both groups showed a decreased integration in the Precuneus/Retrosplenial Cingulate, Right Angular Gyrus e Posterior Cingulate Cortex of the DMN; however, this reduction was significantly lower in the trained group. DAN analysis showed an increased activation of the Left Frontal Eye Field in the trained group. Analysis of different dopamine related genotypes showed that carriers of the DRD3 ser9gly polymorphism were the ones who benefitted the most from the combination training. Cortical thickness differences were found in the Orbitofrontal cortex, Hippocampus and Precuneus.

Conclusions: Our findings indicate that the combination training can counteract the age-related neural and cognitive decline and that significant levels of cerebral plasticity are maintained even in elderly individuals. Our data also indicate that the presence of a specific dopamine receptor maximize the beneficial effects of the combination training.

References:

Boyke, J., Driemeyer, J., Gaser, C., Buchel, C., and May, A. (2008). Training-induced brain structure changes in the elderly. J Neurosci 28, 7031-7035.

C04

TBSS TO ASSESS WM CHANGES IN PGRN MUTATION CARRIERS AT A CLINICAL AND PRECLINICAL STAGE OF FTLD

V. Battistoni[1], M. Bozzali [1], M. Cercignani[1], G. Giulietti[1], A. Alberici[2], E. Premi[2], C. Cerini[2], S. Archetti[3], R. Gasparotti[4], C. Caltagirone[5], A. Padovani[2], B. Borroni[2]

[1]*Neuroimaging Laboratory, Santa Lucia Foundation IRCCS, Rome*

[2]*Centre for Ageing Brain and Neurodegenerative Disorder, Neurology Unit, University of Brescia*

[3]*III Laboratory of Biotechnology, Brescia Hospital*

[4]*Neuroradiology Unit, University of Brescia, Brescia*

[5]*Department of Clinical and Behavioural Neurology, Santa Lucia Foundation IRCCS, Rome*

AIM. Pathogenetic mutations in the Progranulin (PGRN) gene have been identified as a major cause of Frontotemporal Lobar Degeneration (FTLD) (1), although their effects on brain tissue dysfunction still remain to be clarified. In this study, we investigated the microscopic effects of PGRN Thr272fs mutation in the white matter (WM) of FTLD patients. The WM abnormalities were evaluated through fractional anisotropy (FA), an index derived from diffusion tensor imaging (DTI), that reflects microstructural properties of WM. Tract-Based Spatial Statistics (TBSS) was used to perform a voxelwise analysis in an unbiased way, using FA as index of WM integrity.

MATERIAL AND METHODS. We recruited 23 patients (F/M=9/14 mean (SD) age=66.1 (6.8) years; 6 mutation and 17 non mutation carriers), 10 presymptomatic young carriers (F/M=2/8 mean (SD) age=40.8 (11.6) years) and 26 healthy subjects (F/M=20/6 mean (SD) age= 49.5 (13.7) years). All subjects underwent a genetic assessment and an MRI scanning at 1.5 T including a dual-echo turbo spin echo (TSE) and a DTI. DTI data were processed using the FMRIB software library (www.fmrib.ox.ac.uk/fsl/). TBSS was performed to assess the effects of the 2 factors (mutation and disease) on mean FA of the WM, adjusting for age and gender. Statistical analysis was based on permutation tests, and p-values were corrected for multiple comparisons using the threshold-free cluster enhancement method (TFCE). The significance level was set at $p<0.05$.

RESULTS. FTLD patients revealed a widespread reduction of FA compared to healthy subjects. A decrease of FA was found in the frontal areas (particularly on the left side) of patients mutation carriers compared to patients non mutation carriers. Moreover, TBSS was also performed to identify the WM areas of interaction between mutation and presence of symptoms. The interaction was significant only in the frontal areas, particularly along the corpus callosum fibres.

DISCUSSION. This study attempts an investigation of the effects of PGRN mutation in patients. The FA reduction in mutation carriers and the interaction between mutation and disease suggest that the PGRN mutation contributes and modulates the abnormalities of the WM in FTLD.

Ref.:1.Rabinovici and Miller(2010)CNS Drugs 24:375-398.

C04

PRONOUNCED STRUCTURAL AND METABOLIC BRAIN DAMAGE PREDICTS SHORT-TERM DISEASE EVOLUTION IN PATIENTS WITH CLINICALLY ISOLATED SYNDROME SUGGESTIVE OF MULTIPLE SCLEROSIS

E. Sbardella[1], V. Tomassini[2], M.L. Stromillo[3], N. Filippini[2], M. Battaglini[3], S. Ruggieri[4], L. Ausili Cefaro[4], E. Raz[4], C. Gasperini[5], P. Pantano[4], C. Pozzilli[4], N. De Stefano[3]

[1]*Dpt of Psychology, University "Sapienza" (Rome, IT)*

[2]*FMRIB centre, University of Oxford (Oxford, UK)*

[3]*Neuroimaging Lab (QNL), Dpt of Neurological and Behavioral Sciences, University of Siena (Siena, IT)*

[4]*Dpt of Neurology and Psychiatry, University "Sapienza" (Rome, IT)*

[5]*Azienda Ospedaliera San Camillo-Forlanini (Rome, IT)*

Background: In patients with clinically isolated syndrome (CIS), conventional magnetic resonance imaging (MRI) measures have important prognostic implications for conversion to multiple sclerosis (MS). Conversely, the role of quantitative MRI methods in detecting prognostic markers is still debated.

Objective: To evaluate in CIS patients measures of brain atrophy and brain metabolite levels as predictor of one-year disease evolution.

Methods: 49 CIS patients (21 men; mean age 32±7 years) and 25 sex- and age-matched healthy volunteers were recruited. At baseline all subjects underwent conventional and spectroscopy MRI. T1 gadolinium enhancing lesions (Gd-L) and T2 lesion number and volume (T2-LN and T2-LV) were evaluated in patients; normalized brain volumes (NBV), using SIENAX(1), and metabolic ratios (NAA/Cr and Cho/Cr) were measured in both patients and controls. According to the occurrence of relapses and new T2-LN over the subsequent year, patients were divided in “active” and “stable”.

Results: NBV was significantly lower in patients than in controls (p=0.001), whereas no difference was found in NAA/Cr (p=0.12) and Cho/Cr (p=0.62) levels. “Active” patients had lower baseline NAA/Cr and NBV (p=0.008 and p<0.001, respectively), and higher T2-LV (p=0.012) than “stable” patients. Moreover, baseline NAA/Cr, NBV and T2-LV independently predicted subsequent disease activity, but the multivariate logistic regression showed a significant effect for NBV (p=0.004) and NAA/Cr (p=0.05) only. At the ROC analysis, the area under the curve was 0.74 for NAA/Cr and 0.84 for NBV, with a slight but significant increase to 0.87 when the two measures were combined.

Conclusions: CIS patients with lower NBV and NAA/Cr levels at presentation have higher risk of disease progression in the subsequent year. Quantitative MR measures of brain atrophy and axonal damage may predict short-term disease evolution in CIS patients, particularly when used in combination. If confirmed in larger studies, these findings may have important therapeutic implications.

Reference

1.Smith SM, Zhang Y, Jenkinson M, et al. Accurate, robust, and automated longitudinal and cross-sectional brain change analysis. Neuroimage 2002;17:479-489.

C04
ALTERATIONS OF BRAIN RESTING STATE NETWORKS IN THE EARLY STAGES OF MULTIPLE SCLEROSIS

F. Tona[1], N. Petsas[2], M. Carni[3], L. Prosperini[1], L. Leonardi[1], F. Lafavia[1], M. Carmellini[1], F. D'Ambrosio[4], C. Pozzilli[1], P. Pantano[1]

[1]*Dept. of Neurology and Psychiatry, Sapienza - University of Rome*

[2]*Dept. of Psychology, Sapienza - University of Rome*

[3]*UOC Fisica Medica e Sanitaria - Policlinico Umberto I, Rome*

[4]*Dept. of Sense Organs, Sapienza - University of Rome*

Task-related fMRI studies have shown an increase in cortical activity in multiple sclerosis (MS), which has been interpreted as an expression of neuronal plasticity in order to compensate for tissue damage. These studies, however, explore only a small fraction of the overall brain activity and are influenced by the variability in the task execution due to different degrees of disability.
The aim of this study was to explore the brain activity at rest, that is in the absence of external stimuli, assuming that, in the early stages of MS, modifications of the brain resting state networks (RSNs) may be present, as already demonstrated in patients with clinically isolated syndrome*. For this purpose, we included 28 MS patients (mean age: 36 ± 10) with mild disability (EDSS median: 2), absence of cognitive impairment and short disease duration (mean 28 ± 22mesi) and 26 healthy controls (mean age: 31 ± 6). The resting state fMRI data, obtained using a 3T scanner, were preprocessed using SPM8. Using the GIFT software for independent component analysis, we identified the eight main RSNs. The group analysis was performed by SPM8 in order to evaluate differences in functional connectivity in each RSN between patients and healthy controls. In patients we found an increased connectivity in two of the eight RSNs (auditory/language and left fronto-parietal) and a reduced connectivity in the default mode network.
The increased functional connectivity of some networks may be interpreted as a compensatory phenomenon of cortical reorganization occurring in the early stages of MS. The reduced connectivity of the default mode network, which is usually associated with complex cognitive functions, may indicate a subclinical alteration anticipating the development of cognitive impairment in the later stages of disease.
*Roosendaal et al. Resting networks change in clinically isolated syndrome. Brain 2010; 133:1612-21.

C04
High-field MRI of the white matter in temporal lobe epilepsy.

L. D'Incerti[1], R. Garbelli [2], C. Marras [3], G. Mazzoleni [4], G. Milesi [2], M. Morbin [4], F. Villani[2], I. Zucca[5], M.G. Bruzzone[1], R. Spreafico[2]

[1]*U.O di Neuroradiologia, Istituto Neurologico C.Besta, Milano*

[2]*U.O di Epilettologia clinica e neurofisiologia sperimentale*

[3]*U.O. di Neurochirurgia III*

[4]*U.O di Neuropatologia*

[5]*Direzione scientifica*

Obbiettivo.
Correlazione tra dati RM ex vivo a 7T, istopatologia e microscopia elettronica nell'epilessia temporale farmaco-resistente.
Materiali e metodi.
32 pazienti operati per epilessia temporale farmaco-resistente con evidenza alla RM di sclerosi ippocampale, sono stati suddivisi in due gruppi secondo il riscontro o l'assenza di "blurring", cioè perdita di definizione del passaggio tra corteccia e sostanza bianca e sfumata iperintensità in T2 della sostanza bianca: gruppo 1(18 pazienti); gruppo 2(14 pazienti).
4 prelievi chirurgici di ciascun gruppo sono stati sottoposti allo studio di correlazione anatomica-radiologica.
I pezzi operatori, dopo fissazione in PF4%, sono stati sezionati in fette di 5mm di spessore con tagli coronali. Una fetta per ogni caso è stata sottoposta a RM 7T. Sono state acquisite sezioni T2-pesate (TR:4300ms, TE:50 ms, NA:36, ST:0.7 mm, FOV 30x30mm).

Successivamente, le fette sono state tagliate al vibratomo in sezioni seriate da 50μm e sottoposte a colorazioni con tionina, con Black-Gold per la mielina, e a inclusione per microscopia elettronica (ME).
Risultati.
Nei 4 casi con blurring, le sezioni sottoposte a colorazione per la mielina (Black Gold) hanno evidenziato aree di ridotta colorazione nella sostanza bianca a cui, nelle sezioni RM, corrispondeva una sfumata iperintensità di segnale. La ME dimostrava riduzione della densità assonale e numerosi vacuoli.
Nei casi senza blurring la sostanza bianca appariva omogenea sia alla colorazione per la mielina, che alla ME e alla RM 7T.
L'esame retrospettivo dei dati clinici di tutta la popolazione, mostrava nei pazienti con blurring esordio dell'epilessia più precoce e maggiore durata di malattia.
Discussione e conclusioni.
La correlazione tra RM ad alto campo,istopatologia e ME appare consistente.
Il blurring osservato alla RM clinica, di cui non esistono descrizioni di correlati istologici, appare legato al ridotto numero di fibre mieliniche ed al conseguente aumento di acqua nel tessuto.
I nostri dati suggeriscono inoltre una significativa correlazione tra le alterazioni RM, sia in vivo che ex vivo, e aspetti degenerativi della sostanza bianca legati all'età d'esordio e alla durata di malattia.

C04
PERINATAL BIOMARKERS OF ADVERSE NEUROPSYCHOLOGICAL OUTCOME IN PRETERM NEWBORNS

M. Caulo[1], R. Navarra[1], G. Perrucci[1], C. Sestieri[1], C. Briganti[1], A. Tartaro[1]
[1]*DEPARTMENT OF NEUROSCIENCE AND IMAGING, Chieti, Italy*

Introduction: Preterm newborns represent a high risk population for brain damage and neurodevelopmental disabilities. Since both axonal ingrowth and elaboration of synaptic connections occur in the third trimesters, microstructural changes in connectivity could be responsible neurocognitive deficits. We investigated whether the pattern of brain structural and functional connectivity of preterms, as assessed by diffusion tensor (DTI) and resting-state functional-MRI (rs-fMRI), is related to subsequent neuropsychological outcome.
Methods: 35 preterm newborns (range: 28+4 weeks) were studied at term-corrected age using DTI and rs-fMRI at 3 Tesla. Neonates were sedated for imaging. MRI included conventional sequences followed by two consecutive DTI (6 diffusion gradient directions) and 5-minute resting state BOLD scan. DTI was analyzed using FSL to produce fractional anisotropy (FA) and mean diffusivity (MD) maps. BOLD data was preprocessed using SPM8 and analyzed using the Group ICA toolbox. A neurological examination and Griffiths Mental Developmental Scale were performed at 6 months corrected age. A two-tailed T-test assessed the presence of significant differences in the measure of functional and structural connectivity according to the presence/absence of neurological deficits and periventricular lesions. The Pearson's correlation assessed the presence of significant correlations between measure of functional and structural connectivity and score obtained at the Griffiths subscales.
Results: Significantly lower measures of dorsal somato-motor network (dSMN) functional connectivity were associated with the presence of both neurological deficits and periventricular lesions at MRI. Furthermore, a robust correlation between dSMN functional connectivity and general Griffiths's score and each subscale was observed. In addition mean white matter FA and internal capsule MD were specifically correlated to the motor subscale.
Conclusions: A significant relationship between the pattern of structural and functional connectivity, especially involving the motor system, and the degree of neuropsychological development was observed. These results expand our understanding on the alterations in brain maturation that eventually lead to neurodevelopmental disabilities of preterm newborns.

C04

Lesion-method in low-grade gliomas: language evaluation with fMRI, Diffusion Tractography and neuropsychology

V.E. Contarino[1], S. Nava[1], F. Ferrè[1], S. Piacentini[1], D. Aquino[1], G. Castelli[1], M.G. Bruzzone[1], A. Bizzi[1]

[1]U.O. di Neuroradiologia, Fondazione I.R.C.C.S Istituto Neurologico Carlo Besta

OBIETTIVI

Nel presente lavoro sono state esaminate alterazioni morfologiche, funzionali e cognitive prodotte da neoplasia gliale infiltrante il lobo frontale sinistro, allo scopo di indagare i rapporti tra variabili istopatologiche, sede ed estensione della lesione e correlati funzionali e cognitivi del linguaggio.

PAZIENTI & METODI

In questo studio prospettico sono stati reclutati 19 pazienti con diagnosi di glioma infiltrante la parte ventrale del lobo frontale sinistro. I tumori sono stati divisi in due gruppi secondo la sede anatomica: anteriori, infiltranti il giro frontale inferiore (IFG) inclusa l'area di Broca; posteriori, infiltranti la circonvoluzione precentrale ventrale (VPCG). I pazienti prima dell'intervento chirurgico e 10 volontari sani sono stati sottoposti a test di Aachen (AAT) per l'afasia, RM convenzionale, trattografia con Diffusion Tensor Imaging e RM funzionale con 3 compiti: fluenza verbale, generazione di verbi e comprensione di frasi.

RISULTATI

Solo un paziente su 8 con glioma nell'IFG aveva afasia (transcorticale mista). Sei pazienti su 11 con tumore nel VPCG avevano afasia: di conduzione (3), transcorticale (2) e deficit di fluenza semantica (1).

La fMRI evidenziava riduzione dell'attività nelle corrispondenti aree eloquenti infiltrate dal glioma. Ciò nonostante la fMRI dimostrava lateralizzazione per il linguaggio a sinistra in 16 su 19 pazienti. La trattografia mostrava alterazione del fascicolo arcuato nei 7 pazienti con afasia, minimo coinvolgimento o integrità nei pazienti senza afasia.

CONCLUSIONI

Lesioni infiltranti la parte ventrale del giro precentrale si associano ad una maggiore compromissione del linguaggio rispetto alle lesioni dell'IFG (area di Broca).

Nel caso di lesioni infiltranti la corteccia è possibile che meccanismi di plasticità perilesionale preservino la funzione linguistica, mentre sembra che lesioni coinvolgenti il fascicolo arcuato siano più frequentemente associate copn afasia.

BIBLIOGRAFIA

BENZAGMOUT M, GATIGNOL P, and DUFFAU H. Neurosurgery, 61: 741-52; discussion 752-3, 2007.

BIZZI A. In Pia Sundgren M. (Ed.) Advanced imaging techniques in brain tumors: Elsevier, 2009, pp. 573-596.

C04

Prognostic value of ^{1}H-MRS and DTI after hypothermic treatment in newborns with perinatal asphyxial encephalopathy

C. Testa[1], C. Tonon[1], D. Manners[1], E. Malucelli [1], S. Grandi [2], F. Bravati[2], G. Faldella [2], G. Ancora[2], R. Lodi[1]

[1]*U.O. Diagnostica con Spettroscopia RM, Dip. di Medicina Interna, dell'Invecchiamento e Malattie Nefrologiche, Università di Bologna*

[2]*U.O. di Neonatologia, Dip. Salute della Donna, del Bambino e dell'Adolescente, Università di Bologna*

Introduction.
Brain cooling (BC) in term neonates with hypoxic-ischemic encephalopathy (HIE) has been shown to reduce mortality without increasing major disability in survivors [Jacobs S 2007]. As previous studies have demonstrated that brain MRS and DTI provide accurate prognostic markers in non treated neonates with HIE [Hunt RW 2004, Ancora G 2010] we investigated whether these markers are altered by the metabolic effect of BC.
Methods.
Twenty infants with moderate-severe HIE were treated with BC within 6 hours of life. All neonates underwent conventional MRI and single-voxel ^{1}H-MRS (PRESS,TR/TE=1500/40 ms) localized within basal nuclei, parieto-occipital cortex and fronto-parietal white matter (WM) at a mean of 8.3 (±2.8) days of life. DT imaging (15 directions, b-value=900 s/mm^{2}) was acquired in 15 infants. Peak area ratios and concentrations of N-acetyl-aspartate (NAA), creatine, choline (Cho), myo-inositol (mI), and Lac+Lipids were calculated. DTI analysis was performed using FSL. ROIs were drawn on study specific FA and MD templates covering: supratentorial region, posterior cranial fossa, genu and splenium of corpus callosum, thalamus, caudate, posterior limb of internal capsula (PLIC), optic radiation, lenticular nuclei and areas from the occipital, frontal, frontoparietal WM. ROIs were back-projected to each subject, checked and if necessary manually corrected. MD, FA and metabolites values were compared between the group of patients with benign and pathological outcome (PO) assessed by neurological standardized scales at 24 months of age ($p<0.05$).
Results.
PO (death or cerebral palsy) was observed in 6/20 newborns. The most significant results of MRS were diminished [NAA], [mI], NAA/Cho and mI/Cho in the basal ganglia. Patients with PO had significantly lower MD in the whole supratentorial region, in all ROIs of deep gray matter, in those of fronto and fronto-parietal WM. FA was significantly lower in the PLIC and in the fronto-parietal and parietal WM.
Conclusions. BC does not affect the early prognostic accuracy value of MRS and DTI, performed in the subacute phase of HI insult, suggesting that the metabolic and microstructural evaluation in targeted brain structures should be feasible during routine examination of HIE patients, treated or not with BC.

C04
STUDIO DELLA CONNETTIVITA' CEREBELLARE NELLE ATASSIE

M. Quarantelli[1], F. Saccà[2], E. Tedeschi[3], A. Prinster[1], C.V. Russo[2], B. Carotenuto[2], E. Salvatore[2], A. Filla[2], A. Brunetti[3]
[1]*Ist. Biostrutture e Bioimmagini - CNR, Napoli*
[2]*Dip. Scienze Neurologiche, Università Federico II - Napoli*
[3]*Dip. Scienze Biomorfologiche e Funzionali, Università Federico II - Napoli*

SCOPO Valutare i pattern di connettività funzionale tra il cervelletto e le aree corticali sovratentoriali in pazienti con atassia.
METODOLOGIA 20 pazienti con atassia (15 con Atassia Spino-Cerebellare di tipo 2, 5 con variante cerebellare di Atrofia Multi-sistemica, 14maschi, età 50±16 anni) e 14 volontari sani (8 maschi, età 46±19 anni) sono stati studiati a 3 Tesla mediante esame RM funzionale a riposo (resting state fMRI, RS-fMRI).
Gli studi RS-fMRI (EPI, TR/TE 2500/40ms, voxel: 3x3x4mm3, 128 time points) sono stati analizzati con FMRI Expert Analysis Tool (FEAT, www.fmrib.ox.ac.uk/fsl) per valutare le fluttuazioni di attività corticale a riposo [Worsley 2001], evidenziando i cluster di significativa correlazione con una singola regione di interesse posizionata in corrispodenza di entrambi gli emisferi cerebellari (si e' utilizzata una regione singola data la notevole correlazione del segnale dei due emisferi cerebellari evidenziata ad un'analisi preliminare, e in accordo con la letteratura).
Sono state poi considerate significative le differenze tra i due gruppi con p<0.05, FWE-corretto a livello di cluster alla second-level analysis, effettuata con SPM5, dopo normalizzazione delle mappe Z utilizzando come "proxy" la media delle acquisizioni di ciascuno studio RS-fMRI.
RISULTATI Nei pazienti si è evidenziata una significativa riduzione della connettività con il cervelletto bilateralmente in corrispondenza della corteccia prefrontale dorso-laterale, dorso-mediale e rostrale (aree di Brodmann 8, 9 e 10).
In nessuna regione si e' evidenziata una connettività aumentata nei pazienti rispetto ai soggetti normali.
CONCLUSIONI Le alterazioni strutturali sottotentoriali in corso di patologia neurodegenerativa a prevalente interessamento cerebellare determinano una riduzione della connettività funzionale cerebellare evidenziabile a carico delle componenti frontali di alcuni dei network nei quali e' coinvolto il cervelletto (controllo esecutivo, default-mode e salience [Habas C 2009]).
Bibliografia
 Smith S. Human Brain Mapping 2002;17:143 - Woolrich MW NeuroImage 2001;14:1370 - Worsley KJ. in FMRI: An Introduction to Methods OUP, 2001 - Habas C. J Neurosc 2009;29:8586

C05

DIFFUSION-WEIGHTED MRI OF THE PANCREAS: CORRELATION WITH SECRETIN-ENHANCED MAGNETIC RESONANCE CHOLANGIO-PANCREATOGRAPHY (S-MRCP) FINDINGS IN PATIENTS WITH CHRONIC PANCREATITIS

G. Restaino[1], F. D'Argento[2], M. Missere[1], S. Costanzo[3], M. Occhionero[1], G. Paolantonio[2], M. Ciuffreda[1], G. Sallustio[1]

[1]*Dip. Immagini, U.O.C. di Radiodiagnostica, Università Cattolica del Sacro Cuore, Campobasso, ITALY*

[2]*Dip. Bioimmagini e Scienze Radiologiche, Università Cattolica del Sacro Cuore, Roma, ITALY*

[3]*Laboratory of Genetic and Environmental Epidemiology, Università Cattolica del Sacro Cuore, Campobasso, ITALY*

Purpose

To evaluate the correlation between apparent diffusion coefficient (ADC) values of the pancreas on diffusion-weighted imaging (DWI) and severity of chronic pancreatitis and pancreatic exocrine function determined by S-MRCP.

Material and Methods

Mean ADC values (b=0, 700) derived from 3 or 2 manually drawn region of interest of the pancreas on DWI were measured in 15 healthy volunteers and in 50 patients with known or suspected pancreatic diseases referred for S-MRCP. S-MRCP images of the patients were evaluated for the diagnosis of chronic pancreatitis (Cambridge score) and assessment of pancreatic exocrine function (Matos score). Correlation between ADC values in volunteers and patients was performed using t-test for unpaired data. ADC values in patients were compared to Cambridge score and Matos score with ANOVA test.

Results

Mean pancreatic ADC value was 2.71x10-3mm^2/s in healthy volunteers and 2.21x10-3mm^2//s in the patients' group, with a significant statistical difference in the two groups ($P < .0001$), even after adjusting for sex and age ($P = .0033$). There wasn't any significant correlation between pancreatic ADC values and Cambridge classification or Matos score in patients with chronic pancreatitis, even after adjusting for sex and age.

Conclusion

Pancreatic ADC values were significantly lower in patients with known or suspected chronic pancreatitis than in healthy volunteers. We didn't find any significant correlation between pancreatic ADC values and Cambridge classification or Matos score in patients with chronic pancreatitis.

Balci NC, Smith A, Momtahen AJ, et al. MRI and S-MRCP findings in patients with suspected chronic pancreatitis: correlation with endoscopic pancreatic function testing (ePFT). J Magn Reson Imaging. 2010 Mar;31(3):601-6.

C05

Left bundle branch block: usefulness of MRI in the evaluation of regional left ventricular dyssynchrony and in the detection of previous myocardial infarction with Late Enhancement

M. Di Girolamo[1], C.N. De Cecco[1], G. Muscogiuri [1], M. Maurizi Enrici[1], V. David[1]

[1]*Dip. di Radiodiagnostica, Azienda Ospedaliera Sant' Andrea di Roma, Seconda facoltà di medicina e chirurgia*

PURPOSE:

Aim of this study was to evaluate the mechanical left ventricular dyssynchrony with high temporal resolution cine MRI and to evaluate the presence of late-enhancement (LE) in order to diagnose previous myocardial infarction.

MATERIALS AND METHODS:

We retrospectively evaluated 38 patient with LBBB underwent cardiac MRI using a 1.5 T magnet (Magnetom Sonata, Siemens). The MRI protocol consisted of a left ventricular functional study (4-chamber, vertical long axis, short axis)(TR:3.09ms,TE:1.3ms, FA:80,thick:8mm) followed by late enhancement data set acquired 10-15 minutes after iv administration of 0.2 mmol/kg of Gd contrast agent. Late enhancement was evaluated on Inversion recovery Turbo-Flash sequences (TR:8ms,TE:4ms,TI:250-340ms,thick:8mm) as an area with ¬¬SI ¬¬>2 SD from normal tissue.

RESULTS:

We detected a characteristic dyssynchronous ventricular contraction with septal flattening during early ventricular systole in all patients, tenting of mitral valve apparatus in 5 patients and functional mitral regurgitation in 2 patients. In 1 patient we found the characteristic functional features of dilated cardiomyopathy with no myocardial area of LE. In 8 patients we found areas of LE (3 patients transmural and subendocardial in 5 pts) with typical patterns of myocardial infarction (MI). The location of MI was septal in 4 patients, infero-septal in 2 patients, lateral in 1 patient, and superior in 1 patient. In 30 patients we found a reduction of the ejection fraction (75%).

CONCLUSIONS:

According to our results, many studies show relevance of cardiac MRI in myocardial infarction to detect ventricular dissynchrony [1] in patients where the assessment of ventricular dyssynchrony on echocardiography is not technically possible and when the area of previous myocardial infarction cannot be determined.

REFERENCES:

1) Rutz AK, Manka R, Kozerke S et al. (2009). Left ventricular dyssynchrony in patients with left bundle branch block and patients after myocardial infarction: integration of mechanics and viability by cardiac magnetic resonance. Eur Heart J; 30(17):2117-27.

C05

PREOPERATIVE LOCOREGIONAL (T AND N) STAGING OF GASTROESOPHAGEAL JUNCTION CANCER (GEJC) AND GASTRIC CANCER (GC): MAGNETIC RESONANCE (MR) INCLUDING DIFFUSION WEIGHTED SEQUENCES (DWI) VERSUS ENDOSCOPIC ULTRASOUND (EUS)

M. Cellina[1], F. De Cobelli[1], F. Giganti[1], S. Kusamura[2], L. Albarello[3], P. Arcidiacono[4], E. Orsenigo[2], P. Gazzetta[2], C. Losio[1], C. Staudacher[2], A. Del Maschio[1]

[1]U.O. Radiologia, IRCCS Osp. San Raffaele - Università Vita - Salute di Milano

[2]U.O. Chirurgia Gastro-enterologica, IRCCS Osp. San Raffaele - Università Vita - Salute di Milano

[3]U.O. Anatomia Patologica, IRCCS Osp. San Raffaele - Università Vita - Salute di Milano

[4]U.O. Gastroenterologia, IRCCS Osp. San Raffaele - Università Vita - Salute di Milano

The most critical aspect in pts with GC is the accuracy of imaging staging: pts with localized lesions (T1-2) may be treated with radical surgery; pts with locally-advanced lesions (T3-4) or with adenopathies (N+) are treated with neoadjuvant therapy. EUS is regarded as the most reliable technique for locoregional staging of GC, but besides a variable range of accuracy*, it has some limitations: invasiveness, operator-dependence, restricted field of view. Therefore there's a need for alternative imaging techniques.

Aim of this study was to evaluate diagnostic accuracy of MR, included DWI, in the preoperative locoregional staging (T, N) of GEJC and GC, compared to EUS.

From November 2009 to December 2010, 30 pts affected by 5 GEJC and 20 GC underwent presurgical MR. All pts were examined with a 1.5 T MR system, using a 5-elements-phased-array-surface coil. The MR protocol included DWI, acquired using a SSEPI sequence with b values of 0 and 600 s/mm^2. MR images were evaluated by 1 experienced radiologist; apparent diffusion coefficients (ADC) of primary tumor and lymph nodes were calculated. All pts also underwent EUS, performed by 3 experienced gastroenterologists. We classified T stage in stages T1-T2 (organ-confined neoplasia) and T3-T4 (infiltrating neoplasia) and lymph nodes status as negative (N-) or positive (N+). Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) were calculated for T and N status. Regarding T status, we considered as positivity the presence of infiltrating tumors (T3-T4). EUS and MR assessments were compared with histopathological findings.

Sensitivity, specificity, PPV, NPV calculated for T stage were for MR: 50%, 83%, 66%, 71%, while for EUS: 75%, 72%, 64%, 81%; for N status, for MR: 83%, 89%, 83%, 89%; for EUS 66% 66% 57% 75%. Mean ADC of primary tumors was: 1,53x10^{-3}mm^2/s±0,47; of lymph nodes was: 1,42x10^{-3}mm^2/s±0,46.

In staging gastroesophageal cancer: EUS is superior to MR for T evaluation, while regarding N stage, MR is superior for N evaluation, maybe for the added value of DWI and for the panoramic view. Therefore it's possible to hypothesize an association of these 2 techniques for locoregional staging of GEJC and GC.

*Power DG et al; J Am Coll Surg 2009, 208: 173-178.

C05
MISURA QUANTITATIVA DI DIFFUSIONE E PERFUSIONE DEL PARENCHIMA EPATICO PEDIATRICO

M. Esposito[1], A. Ciccarone[2], S. Savelli[2], G. Zatelli[1], C. Fonda[2]
[1]*S.S. Fisica Sanitaria, Azienda Sanitaria Firenze*
[2]*U.O. Radiologia, Azienda Ospedaliero-Universitaria Meyer*

Lo studio del decadimento del segnale RM pesato in diffusione, in funzione del valore di b, permette la misura sia del coefficiente di diffusione (D) che di parametri di perfusione (D*, f). Lo scopo di questo lavoro è quello di studiare la variabilità di questi parametri sia in un singolo parenchima che in una classe di pazienti in età pediatrica, che hanno una funzionalità normale del fegato.
Sono stati arruolati 15 pazienti pediatrici con sospette disfunzionalità epatiche. Lo studio DWI è stato effettuato prima della biopsia, su uno scanner RM da 1,5T, ed è consistito in una sequenza con 13 valori di b (b=0,5,10,20,30,40,60,100,200,300,500,700,900,1200), ottimizzata per la riduzione degli artefatti da eco planare tramite uno studio su fantoccio. I parametri D, D* ed f sono stati calcolati attraverso un fit bi esponenziale:S(b)=S(0)((1-f)*exp(-b*D)+f*exp(-b*(D+D*))) , dove il decadimento del segnale è stato misurato su ROI di circa 2 cm^2, distribuite in modo da coprire tutto il fegato, escludendo i grossi vasi e gli artefatti visibili sull'immagine. Tutti i pazienti hanno riscontrato l'assenza di fibrosi epatica allo studio bioptico. Sono state generate le distribuzioni statistiche dei valori quantitativi misurati, sia in ogni singolo fegato, sia in tutti i pazienti.
In ogni fegato, le distribuzioni dei parametri D ed f sono risultate simmetriche e con deviazione standard intorno al 10% del valor medio. La distribuzione di D* all'interno del fegato è asimmetrica e con deviazione standard pari al valor medio. I valori medi e le deviazioni standard all'interno del gruppo di pazienti studiati sono: $(916\pm95)x10^{-6}mm^2/s$ per D, 0.25±0.06 per f e $(82000\pm44000)x10^{-6}mm^2/s$ e per D*.
I valori di D ed f esibiscono una bassa variabilità, sia a livello di singolo fegato che nel gruppo di pazienti, il parametro D*, invece è caratterizzato da una grande variabilità di valori sia in un singolo fegato sia nel gruppo di pazienti selezionato. Non è stata riscontrata nessuna correlazione fra i parametri studiati e l'età e il sesso dei pazienti.
[1] B. Taouli D.M. Koh January 2010 Radiology: 254: 1 48-66
[2] Luciani et al. December 2008 Radiology, 249, 891-899.

C05

QUANTIFICATION OF LIVER FAT CONTENT: COMPARISON OF TRIPLE-ECHO CHEMICAL SHIFT GRADIENT-ECHO IMAGING AND LIVER BIOPSY IN PATIENTS WHO UNDERWENT LIVER TRANSPLANTATION

M. Di Martino[1], R. Di Miscio[1], V. Lombardo[1], G. De Filippis[1], M. Del Monte[1], M.L. Mennini[1], V. Forte[1], S. Santinelli[1]

[1]*Dip. Scienze Radiologiche, Oncologiche ed Anatomo Patologiche "Sapienza" - Università di Roma*

PURPOSE: To validate a triple-echo gradient-echo sequence for measuring the fat content of the liver, by using liver biopsy as the reference standard

METHOD and MATERIALS: This prospective study was approved by our IRB. Twenty consecutive liver transplanted patients underwent liver MRI at 3T (Discovery, General Electric) to evaluate liver parenchyma after liver transplant. MR examinations were performed within 1 month from surgery (mean 45 days; range 16 – 60) Liver fat fraction was computed from triple-echo (consecutive in-phase, opposed-phase, and in-phase echo times) breath-hold spoiled gradient-echo sequence (flip angle, 20°), by estimating $T2^*$ and relative signal intensity loss between in- and opposed-phase values, corrected for $T2^*$ decay. Liver biopsy was performed within two weeks from surgery. Linear regression analysis and the Pearson correlation coefficient (r) were used for the statistical analysis

RESULTS: Mean fat fractions calculated from triple-echo sequence was 14% (range, 0%-90%).

Mean $T2^*$ time was 14.7 msec (range, 5.4-25.4 msec). Pearson correlation coefficient was 0.90 ($p<.0001$)

CONCLUSION: A breath-hold triple-echo gradient-echo sequence with a low flip angle and correction for $T2^*$ decay is accurate for quantifying fat in liver

C05

The relevance of diffusion-weighted MR-imaging at 3T with different b value for the detection of prostate cancer (500,1000,3000).

T. Mazza[1], D. Lisi[2], V. Panebianco[2]

[1]*GE healthcare*

[2]*Dept. of Radiological Sciences,Policlinico Umberto I "La Sapienza" University of Rome*

PURPOSE

To prospectively determine the accuracy of diffusion-weighted (DW) magnetic resonance (MR) imaging for identifying cancer in the prostate peripheral zone (PZ) in association with T2-weighted and DCEMR imaging before biopsy.

METHODS AND MATERIALS

The institutional review board approved this study and all the patient subscribed an informed consent. Twenty-seven patients underwent endorectal MR at 3 T magnet (Discovery M750, GE Healthcare) equipped with surface phased array and endorectal coil. Scan protocol included morphologic imaging with TSE T2-weighted sequences on the axial, sagittal and coronal planes, DWI sequences at different b value (500, 1000, 3000) and dynamic contrast enhanced imaging using FSGRE 3D T1-weigthed sequence. Image cluster analysis was performed on voxels within the suspected tumor regions. Post processing method included ADC value calculation was done. Two readers in consensus recorded the presence of prostate cancer at magnetic resonance imaging and rated the imaging quality of DWI.

RESULTS

For all the patients, the DWI sequence images were suitable for the evaluation of the zonal anatomy of the prostate gland and the tumor localization. In the prediction of prostate tumor foci, we noticed an improvement for tumor detection with a b value of 3000 in comparison with other b value (500 and 1000) with 89% and 87% respectively for sensitivity and specificity, and was crucial especially in cases with negative or borderline pattern at DCEMR.

CONCLUSION

DWI is a feasible technique that can be used for the differentiation of malignant and benign tissues in the prostate gland tissue. We obtained a significant improvement using high value of b (1000-3000).

C05

BREAST VOLUME, DENSITY, AND VASCULARITY AT MAGNETIC RESONANCE IMAGING (MRI): WHAT CORRELATION?

N. Verardi[1], R.M. Trimboli[1], L.A. Carbonaro[2], G. Di Leo[2], F. Sardanelli[3]

[1]*Scuola di Specializzazione in Radiodiagnostica, Università degli Studi di Milano*

[2]*U.O. di Radiologia, IRCCS Policlinico San Donato*

[3]*Dip. Scienze Medico-Chirurgiche, U.O. Radiologia; Università degli Studi di Milano, IRCCS Policlinico San Donato*

Purpose: To propose a semiquantitative method for estimating breast density at MRI and to evaluate the correlation among breast volume, density, and vascularity.

Methods: We reviewed a consecutive series of 59 negative examinations of 57 women (aged 48±11 years) who underwent 1.5-T breast MRI. The imaging protocol included a dynamic study performed using T1-w 3D FLASH sequences before/after injection of 0.1 mmol/kg of gadobenate dimeglumine. Using unenhanced images of each breast, we selected the axial and the sagittal planes passing through the nipple and the coronal plane at the mid-point between the pectoral muscle and the nipple. For each plane, we assigned a 5-point score to the breast density as: 0=nearly absent gland; 1=fat prevalence; 2=equal representation of gland and fat; 3=gland prevalence; 4=nearly absent fat. We defined a breast density index as the sum of the scores over the 3 planes (range from 0 to 12). On axial and coronal images we measured anterior-to-posterior, medio-lateral, and cranio-caudal sizes in order to obtain a breast volume related product (BVrP). Using maximum intensity projection reconstructions, we counted the total number of detectable vessels within each breast. Each breast was considered as a single statistical unit and Spearman coefficient was calculated for correlations.

Results: The breast density index ranged from 0 to 12 (median 6); BVrP ranged from 122 cm^3 to 2,256 cm^3 (median 791 cm^3); the total number of vessels ranged from 0 to 13 (median 5). The density index negatively correlated with the total number of vessels for women aged 30-50 years ($r= -0.328$, $p=0.004$), for women aged >50 years ($r= -0.322$, $p=0.037$), and overall ($r= - 0.282$, $p=0.002$). The density index negatively correlated with BVrP ($r= -0.561$, $p<0.001$). The total number of vessels positively correlated with BVrP ($r=0.243$, $p=0.008$).

Conclusion: Contrary to possible assumptions, the portion of gland tissue is not positively correlated with breast vascularity. The larger the breast, the higher the number of vessels, and the lower the breast density. Breast density can be estimated using a fast semiquantitative score distributed on 13 density levels. Large breasts should be expected to have high vascularity, independently from the gland/fat ratio.

C05
BREAST MRI IN PRONE VERSUS SUPINE PATIENT POSITION: WHAT IS THE DIFFERENCE?

L.A. Carbonaro[1], N. Verardi[2], R.M. Trimboli[2], F. Cartia[1], G. Di Leo[1], F. Sardanelli[3]
[1]*U.O. di Radiologia, IRCCS Policlinico San Donato, San Donato Milanese*
[2]*Scuola di Specializzazione in Radiodiagnostica, Università degli Studi di Milano*
[3]*Dip. Scienze Medico-Chirurgiche, U.O. Radiologia; Università degli Studi di Milano, IRCCS Policlinico San Donato*

Purpose: Breast MRI examinations are usually performed with the patient in prone position, while surgery in supine position. Our aim was to measure the lesion spatial displacement when shifting from the standard prone to the supine patient position at breast MRI.
Methods: Eleven women presenting with 10 lesions underwent contrast-enhanced 1.5-T MRI. Patients were firstly prone positioned in the gantry. In this position, a dynamic 3D T1-weighted axial FLASH study (TR/TE=11/4.8 ms, matrix 512×512, FOV 384 mm, 0.1 mmol/kg of gadobenate dimeglumine) was acquired using a dedicated 4-channel breast coil. Ten minutes after contrast injection patients were supine positioned, and a fat-saturated VIBE sequence (TR/TE=4.8/2.2 ms, FA 10°, matrix 334×512, FOV 400 mm) was acquired using a surface coil. For each lesion, the followings were measured:
A. the minimal antero-posterior distance from pectoral/intercostal muscle;
B. the distance from a coronal plane tangent the sternum;
C. the medio-lateral distance from the median sagittal plane;
D. the cranio-caudal distance from the tracheal bifurcation.
These same measurements were repeated for each nipple. Limiting to lesions, the minimal distance from the skin (E) was measured. The spatial displacement of lesions and nipples observed when shifting from prone to supine position was measured. Data were presented as mean±standard deviation and median in parenthesis.
Results: The lesion displacements were as follows:
A. 32±31 mm (27 mm);
B. 60±38 mm (55 mm);
C. 39±27 mm (41 mm);
D. 41±33 mm (34 mm);
E. 6±5 mm (7 mm).
The nipple displacements were as follows:
A. 48±20 mm (48 mm);
B. 84±44 mm (91 mm);
C. 54±24 mm (56 mm);
D. 27±15 mm (24 mm).
Conclusion: Changing the patients' position lesions displace for at least 3 cm in each of the three spatial axes. Radiologists and surgeons should be aware of this when planning the best treatment.

C05
Whole-body MRA in Takayasu arteritis: systemic assessment of arterial stenosis and related mural involvement

C. Zini[1], A. Napoli[1], G. Cartocci[1], L. Molisso[1], L. Di Mare[1], C. Catalano[1]
[1]*Department of Radiological Sciences, Sapienza, University of Rome*

Purpose: to assess vessel involvement and activity of Takayasu arteritis (TA) with whole-body MRA (WB-MRA).
Methods and Materials: 23 patients with TA diagnosis underwent WB-MRA with Gadobenate dimeglumine (Gd-BOPTA); according to the Birmingham Vasculitis Activity Score (BVAS) 16 (70%) patients were classified as active/persistent disease (AD) and 7 (30%) patients as remissive disease (RD).
The arterial system was divided into 32 segments and 5 regions. Image quality, wall thickness (WT) and signal intensity of wall (SI) were evaluated in the unawareness of clinical data. Quality analysis was performed using Wilcoxon's rank test; statistically significant difference in SI values of AD and RD were tested using an unpaired t-test on a per region analysis.
Results: A total of 736 arterial segments were assessed with good to excellent image quality. In 12 patients WBMRA depicted a vessel involvement that could not be assessed by mono-station MRA; 5 extra-vascular findings were identified at MRA data set. Vessel wall thickness of AD group (4.2±1.9 mm) was thicker than RD group (2.9±2.4 mm; $p < 0.05$); post-contrast signal intensity ratio was significantly different between two groups (active/persistent vs remissive, 1.8±0.6 vs 1.1±0.5; $p < 0.05$); a per region analysis showed an higher wall intensity in carotid and subclavian regions ($p < 0.05$) in both groups.
Conclusion: WB-MRA allows a comprehensive assessment of vessel involvement. MRA could be useful for TA activity evaluation, mandatory for therapy management.

P01
Metabolite Quantification in 1D and 2D COSY Spectra from Rat Brain at 9.4T

A. Palma[1], S. Grande[1], A.M. Luciani[1], V. Viti[1], A. Rosi[1], E. D'Amore[2], L. Guidoni[1]
[1]*Dipartimento di Tecnologie e Salute , Istituto Superiore di Sanità and INFN, Roma*
[2]*Servizio Biologico e per la Gestione della Sperimentazione Animale, Istituto Superiore di Sanità, Roma*

Two-dimensional (2D) proton-proton experiments are increasingly used to compare the global metabolic profiles. Acquisition of 2D data allows to obtain comprehensive metabolic profiles with a robust metabolite identification, thus removing ambiguities in peak assignments. In fact, 1D NMR spectra have overlapping resonances that may affect both peak assignment and accurate quantification of metabolite levels.
Aim of this study is to compare intensities of signals from 1D and 2D spectra in order to provide quantification of selected metabolites in the experimental set-up that may be used for needle biopsy evaluation. The 1mm microprobe operating on digital Avance spectrometer (Bruker, Karlsruhe, Germany) at 9.4T was used.
Rat brain samples clearly showed NAA, total choline-containing compound (t-Cho), Creatine/Phosphocreatine (Cr/PCr), Myo-inositol (MI) and Macromolecule (M) resonances in 1D spectra. Signals from many minor metabolites were also detected. The 2D spectra showed, besides the two characteristic GABA cross peaks, NAA, Asp, MI and Lys cross peaks as most relevant signals.
The same resonances in pure compound spectra were examined, showing specific scaling factors for the 2D compared to the 1D spectra. Effects of pH changes were also considered.
Measurements were then performed in a number of spectra from healthy rat brain and findings are compared to different tumour samples from rat brain.

P02

METABOLIC VARIATIONS AND METABOLITES POTENTIALLY INVOLVED IN BYSTANDER SIGNALLING STUDIED BY 1H MRS

S. Grande[1], V. Dini[1], G. Esposito[1], L. Guidoni[1], A.M. Luciani[1], A. Rosi[1], M.A. Tabocchini[1], V. Viti[1]

[1]*Dip. di Tecnologie e Salute, Istituto Superiore di Sanità, and INFN, Rome*

MRS can be used to obtain a better understanding of radiation induced alterations in intracellular metabolism. Particularly 1H MRS has been exploited: i) to analyse metabolic variations in bystander AG01522 fibroblasts, with respect to their corresponding sham samples, and ii) to investigate the presence in the medium of metabolites potentially involved in bystander signalling.

AG01522 fibroblasts were treated with medium collected from 0.5Gy alpha or gamma irradiated fibroblasts (Irradiated Cells Conditioned Medium, ICCM), and their corresponding sham samples, i.e. AG01522 treated with medium collected from sham irradiated fibroblasts (Sham Cells Conditioned Medium, SCCM).

In addition, direct damage experiments were performed on AG01522 fibroblasts. Spectra of cells irradiated with either 0.5, 1.0, or 10 Gy were compared with those of their corresponding sham irradiated samples.

Two main groups of 1H MR signals have been examined: i) the Glu signals inside the GSH molecule and the signal of free Glu; ii) signals from mobile lipids, mainly triglycerides, present in actively proliferating cells. Both these groups have been demonstrated to be affected by irradiation [1, 2]

1H MR spectra were run at 400.14 MHz on a digital Avance spectrometer (Bruker, Germany) equipped with a 1 mm microprobe.

The main result is related to variations observed on GSH signal intensity in bystander cells. These variations are small, but reproducible. An activation of transport systems that determines an increase of GSH content can be hypothized. This is supported by similar data obtained in directly irradiated cells, although only at high doses, where the GSH activation prevails on its depletion due to its activity as antioxidant.

As far as the data from lipid signals are concerned, the observed effects point to a role of MRS in the study of the metabolic response to alpha and gamma rays. The relationship between unbalanced phospholipids synthesis, apoptosis and MR spectral data can be exploited.

[1] Rosi A et al. Radiat Res. 2007; 167 (3): 268-82.

[2] Luciani AM et al FEBS Journal 2009; 276: 1333-46.

P03

^{1}H NMR Spectroscopy of Cancer Stem Cells from Human GBM

L. Guidoni[1], S. Grande[1], A. Palma[2], A.M. Luciani[1], V. Viti[1], A. Rosi[1], L. Ricci Vitiani[3], S. Di Martino[4], R.M. De Maria[3]

[1]*Dipartimento di Tecnologie e Salute, Istituto Superiore di Sanità and INFN, Roma*

[2]*Dipartimento di Tecnologie e Salute, Istituto Superiore di Sanità, Rome, Italy*

[3]*Dipartimento di Ematologia, Oncologia e Medicina Molecolare, Istituto Superiore di Sanità, Roma*

[4]*Scuola Superiore di Catania, University of Catania, Catania*

Cancer stem cells (CSC) refractory to the usual therapies are responsible for maintenance of a subset of self-renewing cells producing cancer recurrence. Many studies are currently performed to understand the CSCs characteristics in order to provide more effective therapies. 1H MRS is used here to gain information on metabolism in CSC lines derived from primary GBM grade IV (WHO classification). Ten CSC lines are characterised and compared with T98G cells, grown as neurospheres, and MCF-7 cells (human breast cancer) grown as spheroids. CSCs deriving from primary glioblastoma were isolated and kept in culture as exponentially growing neurospheres according to [1]. The criteria used to check the stem cell phenotype of CSCs [2], were i) formation of primary spheres in vitro; ii) capacity of self-renewal on clonogenic and population analysis; iii) ability to differentiate both into GFAP-positive astrocyte-like cells and into neurofilament expressing neuron-like cells; iv) generation of tumors closely resembling parent tumor histology upon orthotopic (intracerebral) and subcutaneous transplantation in immunodeficient mice; v) maintenance of the chromosomal aberrations of the parental tumor. T98G cells were grown as neurospheres in the same culture medium. The MCF-7 spheroid samples were grown as in [3]. 1H MR spectra were obtained at 400.14 MHz with a 1mm microprobe. Signals were acquired under water suppression conditions. The neurospheres, despite the hypoxic environment, host viable and metabolically active cells showing neuronal markers such as GABA and glial markers such as gln. Lipid signals are clearly detected in the spectra, with different intensities depending on the observed CSC line. On the other hand the spectra from T98G neurospheres and MCF-7 spheroids are dominated by lipid signals. The high lipid signal intensity is not simply related to neurosphere formation. The overall picture points to a role for 1H MRS in the study of CSCs metabolism. Moreover, comparison of ten CSCs suggests the presence of metabolic variability that may be related to inherent GBM heteroogeneity.

[1] Pallini R. et al. Clin Cancer Res, 2008; 14 (24): 8205-8212. [2] Ricci-Vitiani L. et al. Cell Death and Diff, 2008; 15: 1491–1498. [3] Rosi A. et al. NMR in Biomedicine, 2004; 17: 76–91.

P04

Glutathione protects cells from apoptosis after irradiation with a therapeutic proton beam: a ^{1}H MRS study

A. Palma[1], S. Grande[1], G. Cirrone[2], G. Cuttone[2], C. Giovannini[3], L. Guidoni[1], A.M. Luciani[1], A. Rosi[1], V. Viti[1]

[1]*Dipartimento di Tecnologie e Salute, Istituto Superiore di Sanità and INFN, Roma*

[2]*Laboratori Nazionali del Sud - INFN, Catania*

[3]*Dipartimento Sanità Pubblica Veterinaria e Sicurezza Alimentare, Istituto Superiore di Sanità, Roma*

According to many studies, radiosensitivity and onset of apoptosis can be reasonably associated to low levels of Glutathione (GSH). The relationship between apoptosis induced by gamma radiation and role of GSH was evidenced by us in two human cancer cell lines, namely HeLa from cervix carcinoma, and MCF-7 from mammary carcinoma [1].
Proton therapy treatments offer several advantages in selected tumors, such as prostate and ocular tumors, due to the high-dose delivering to the tumor volume with a concomitant sparing of surrounding normal tissues. We have examined the tumor lines MCF-7 and HeLa cells after irradiation with 10 Gy of proton beams at the first Italian proton therapy facility (INFN-LNS, Catania, Italy).
Irradiation of HeLa cells with proton beams induced relevant apoptosis after proton irradiation, similarly to what observed for gamma irradiated cells [1]. On the contrary, the same treatment failed to induce significant apoptosis in MCF-7 cells, as expected [1]. On the other hand, treatment of MCF-7 cells with BSO to decrease GSH level through inactivation of γ-glutamylcysteine synthetase, inhibited protective function of GSH. In fact, relevant apoptosis and cell killing were observed after irradiation with proton beams compared with non-BSO treated MCF-7 cells.

1D and 2D COSY ^{1}H MR spectra were run at 400.14 MHz on a digital Avance spectrometer equipped with a 1mm microprobe to observe GSH signals before and after proton irradiation in HeLa and MCF-7 samples. A strong intensity decrease of GSH signals appeared in proton irradiated MCF-7 samples with respect to controls. The effect could be attributed to GSH consumption, thus testifying its protective effect towards reactive oxygen species generated by the irradiation. On the contrary, no effects could be revealed after similar irradiation treatments in HeLa cells where GSH concentration is much lower.

Present data show that GSH concentration, ^{1}H MRS detected, can be utilized as marker of radiosensitivity also for proton irradiated cells.

[1] Rosi A. et al. Radiat Res., 167, 268-282, 2007.

P05

ALTERATION OF BRAIN METABOLISM END MOTIONAL RESPONSES IN ADULT MICE SUBMITTED TO PRENATAL STRESS AND PHARMACOLOGICAL ACTIVATION OF THE ENDOCANNABINOID SYSTEM DURING ADOLESCENCE

R. Canese[1], S. Macrì[1], C. Ceci[1], G. Laviola[1]

[1]*Cell Biology and Neurosciences Dept. , Istituto Superiore di Sanità, Rome, Italy*

The central endocannabinoid system (ECS) and the hypothalamic-pituitary-adrenal-axis mediate individual responses to emotionally salient stimuli. Their altered developmental adjustment may relate to the emergence of emotional disturbances. Prenatal stress (PNS) has been shown to upregulate stress and fear responses in adult rodents. Here, we investigated whether PNS – maternal exposure to corticosterone in the drinking water (100 mg/l during the last week of gestation) – combined with a pharmacological activation of the ECS during adolescence (daily fatty acid amide hydrolase URB597 i.p. administration - 0.4 mg/kg - during postnatal days 29-39), influenced adult mouse emotional behaviour and brain metabolism. PNS adolescent mice showed reduced locomotion and were insensitive to the acute effects of URB597 administration. Adult PNS mice showed increased behavioural anxiety and reduced locomotion in the elevated plus maze. Magnetic resonance spectroscopy (VARIAN Inova system operating at 4.7 T) revealed that adult brain metabolism was significantly altered by PNS (hippocampal increased glutamate and reduced taurine; hypothalamic reduced inositol and N-Acetyl-Aspartate) and by early URB597 exposure (reduced prefrontal cortex inositol and taurine). Present data further corroborate the view that stress during gestation and pharmacological ECS activation during adolescence persistently regulate brain metabolism and emotional responses in adult mice.

Funding support: ECS-EMOTION, Dept. of Antidrug Policies c/o Presidency of the Council of Ministers, Italy (to G.L. and S.M).

P06

IN VIVO DETECTION OF EARLY REDUCTION OF ADC AFTER CISPLATIN TREATMENT IN A PRECLINICAL MODEL OF OVARIAN CANCER

R. Canese[1], M.E. Pisanu[1], A. Ricci[1], L. Paris[1], E. Surrentino[1], M. Venditti[1], M. Giannini[1], D. Mezzanzanica[2], S. Canevari[2], E. Iorio[1], F. Podo[1]

[1]*Istituto Superiore di Sanità, Rome, Italy*

[2]*Fondazione IRCCS, Ist. Nazionale Tumori, Milan, Italy*

MRI combined with MRS has demonstrated its utility in in vivo tumour diagnosis, prognosis and treatment evaluation of several pathologies, because of its non invasiveness and repeatability. Due to recent developments in fast imaging techniques, DWI is nowadays established as a useful functional imaging tool for abdominal and pelvic applications. DWI enables quantification of ADC, which can monitor and predict treatment response. In the present work we investigated the effect of cisplatin treatment on ADC of a human ovarian carcinoma xenograft (SKOV3.ip) implanted in the dorsum of SCID mice.

In vivo MRS measurements were performed on a Varian Inova system operating at 4.7 T. MRI/MRS analyses were carried out on tumour xenografts before and after three doses of treatment (cisplatin, 5 mg/kg i.v., weekly). MRI evaluation was performed by T1-weighted, T2-weighted and proton density multislice spin echo images. ADC measurements were obtained by acquiring diffusion gradient images (b ranging from 123 to 1105 s/mm ^{2}). 1H MRS analyses were performed, according to a quantitative protocol, by using a PRESS sequence (TR/TE = 4000/23 ms). Tumour water content was measured by a termogravimetric analyzer on tumour samples. LCModel was used for the spectral fitting. Histological analysis of SKOV3.ip tumor sections following hematoxylin/eosin staining was performed according to standard methods.

In vivo examinations showed tumour growth inhibition in the treated group. No significant differences were detected in in vivo xenografts in total choline or in lipid signals during treatment.

A significant reduction in the mean ADC value, a parameter related to cellularity and water compartmentalization, was detected in the treated tumours 24-48h after the first dose with respect to the pre-treated ones and to the control tumours.

These results are in agreement with the swelling of SKOV3.ip cells examined by optical microscopy after in vitro incubation with cisplatin and demonstrate the possibility to monitor an early treatment effect in an in vivo preclinical model of ovarian cancer.

P07

DIFFERENT GLYCOLYTIC PHENOTYPES IN EXPERIMENTAL MODELS OF OVARIAN CANCER CHARACTERIZED BY 1H MRI AND MRS

R. Canese[1], G. Nardo[2], M. Crescenzi[2], E. Iorio[1], S. Indraccolo [2]

[1]*Cell Biology and Neurosciences Dept., Istituto Superiore di Sanità, Rome, Italy*

[2]*Medical Oncology 2 Dept., Istituto Oncologico Veneto - IRCCS, Padova, Italy*

Various intensities of the Warburg effect have been observed in tumor cell lines and in patients affected by different tumor entities or among individuals affected by the same tumor type. These differences could reflect their genetic heterogenicity. Proper animal models would greatly contribute to evaluate the significance and biological role of these and other alterations during tumour growth or following treatment in ovarian cancer.

In this work we characterized by in vivo 1H MRI/MRS and in vitro MRS two experimental models of ovarian cancer with different glycolytic phenotypes based on measurements of glucose consumption and lactate production rates in vitro as well as on the expression levels of glycolysis-associated genes.

In vivo MRS measurements were performed on a Varian Inova system operating at 4.7 T. MRI/MRS analyses were performed on tumour xenografts 11-35 days following s.c. implantation of OC316 and IGROV-1 cells in the dorsum of SCID mice. MRI evaluation was performed by T1-weighted, T2-weighted and proton density multislice spin echo images. ADC measurements were performed by acquiring diffusion gradient images (b ranging from 123 to 1105 s/mm^2). 1H MRS analyses were performed, according to a quantitative protocol, by using a PRESS sequence (TR =4000 ms, in order to minimise T1 relaxation losses and TE ranging from 23 to 272 ms) and assuming 80% of tumour water content. LCModel was used for the spectral fitting. Histological analysis of OC316 and IGROV-1 tumor sections following hematoxylin/eosin staining was performed according to standard methods. In vitro MRS measurements were performed on a Bruker system operating at 9.4 T.

Metabolic differences have been detected between the two cell lines as well as the two in vivo models, notably in the lactate content. These differences were associated with tumour morphology and internal composition detected by MRI and ADC. Differences in the spectral profiles could reflect changes in tumor environment (i.e. pH) and/or altered metabolism. These results could highlight a link between the Warburg effect and the response to anti angiogenic therapy in ovarian cancer.

Acknowledgements We acknowledge Dr. Franca Podo for stimulating and encouraging this work.

P08

THE PI3K INHIBITOR LY294002 DOWNREGULATES AKT PHOSPHORYLATION AND REDUCES CELL PROLIFERATION WITHOUT DECREASING THE PHOSPHOCHOLINE LEVEL IN OVARIAN CANCER CELLS

E. Iorio[1], A. Tommasetti[2], A. Ricci[1], M.E. Pisanu[1], C. Alberti[2], P. Alberti[2], P. Pinciroli[2], S. Canevari[2], F. Podo[1]

[1]*Cell Biology and Neurosciences Dept, Istituto Superiore di Sanità, Roma, Italy*

[2]*Fondazione IRCCS Istituto Nazionale dei Tumori, Milano, Italy*

Studies have recently been addressed in our laboratories to gather objective evidence regarding the evolution of aberrant phosphatidylcholine (PC) metabolism in the tumor progression from epithelial ovarian non tumoral (EONT) to epithelial ovarian cancer (EOC) cells. In particular, we found a 3- to 8-fold increase in the phosphocholine (PCho) level in human EOC compared with EONT cells (Iorio et al. Cancer Res 2010). Purpose of the present study was to investigate the contribution of PI3K/AKT pathway activation (hallmark of cancer progression including EOC pathogenesis) to the increased PCho content in EOC cells, by incubating cell lines showing distinct phenotypes to the PI3K inhibitor LY294002 (LY). We selected three in vitro human cell lines at different steps of the EMT-like process occurring during tumor progression: OAW42 (with an epithelial phenotype), IGROV1 (epithelial-like with unstable adherens junction) and SKOV3 (a more frankly mesenchymal phenotype). The selected EOC cell lines showed different sensitivity to increased concentration of LY in a proliferation assay. PI3K inhibition was associated with strong and stable decrease in the phosphorylation of the PI3K downstream effector AKT in the LY-sensitive IGROV1, but not in the resistant SKOV3 cells, while OAW42 cells showed intermediate P-AKT levels. 1H MRS quantification revealed no significant changes in the levels of PCho content between untreated cells and cells exposed to LY for either 4h or 24h nor between LY-sensitive and LY-resistant cells, in spite of the differences in their proliferation activity. The level of PCho does not appear to represent a simple indicator of activation of the PI3K/AKT pathway, which is however confirmed to have a pivotal role in the proliferation of EOC cells. A more comprehensive characterization of the network of involved intracellular signaling pathways can probably lead to a better understanding of ovarian epithelial carcinogenesis and clearer elucidation of the molecular mechanisms responsible for MRS-detected changes of PCho levels in EOC cell lines, providing an opportunity to more effectively interfere with signal transduction targets involved in EOC growth, survival, and progression.

P09

EFFECTS OF DOWNMODULATION OF CHOLINE KINASE ON MRS CHOLINE PROFILE AND TRANSCRIPTOME IN OVARIAN CANCER CELLS

E. Iorio[1], M.E. Pisanu[1], A. Ricci[1], A. Granata[2], M. Comito[2], Z. Bhujwalla[3], D. Mezzanzanica[2], M. Bagnoli[2], S. Canevari[2], F. Podo[1]

[1]*Istituto Superiore di Sanità, Roma, Italy*

[2]*Fondazione IRCCS Ist. Nazionale Tumori, Milano, Italy*

[3]*John Hopkins University, Baltimore, MA, United States*

Epithelial Ovarian Cancer (EOC) remains the leading cause of death in women with gynecologic malignancies, due to late diagnosis and early relapse associated with development of chemoresistance. Detection of the abnormal phosphatidylcholine (PC) metabolism in EOC by analysis of MRS profile, showed a significant increase in phosphocholine (PCho) content in EOC cells compared with non tumoral counterparts (Iorio E et al, Cancer Res 2010), associated with an altered activity profile of some PC-cycle enzymes, including 12-to 25-fold activation of choline kinase (ChoK), responsible for PCho production, following choline phosphorylation in the PC biosynthetic Kennedy pathway. The alpha-isoform of ChoK (Chok-alpha) has an essential role in growth control and signal transduction and has been implicated in carcinogenesis. Aims of the present study are to evaluate the biological relevance of ChoK expression and activity in EOC and to define the possible role of MRS profiles in providing non invasive biomarkers to monitor the effectiveness of agents selectively targeted against ChoK-alpha activity. Inhibition of ChoK-alpha mRNA expression was associated with a significant reduction of overall ChoK protein expression and an about 70% drop in PCho content. We observed a 20% inhibition of cell growth associated with a consistent increase in cells blocked in the G1-phase of cell cycle. Comparative evaluation of the global transcriptome, showed 440 genes differentially expressed (FDR<0.25, P<0.05) in CHKA-silenced compared with controls cells, equally distributed among induced and repressed genes. Interestingly, among the most relevant co-repressed genes we found CyclinA1, related to regulation of cell cycle progression and cytokines genes (IL6 and IL8) related to inflammation and EOC aggressiveness, whose functional role is currently under further investigation.Our observations, confirming a main role for ChoKα in deregulated choline metabolism in EOC tumors, warrant further investigations on the upstream and downstream signaling and metabolic alterations associated with ChoK activition and suggest this enzyme molecule as a promising target for alternative therapeutic approaches.

P10

METABOLISM OF HER2-OVEREXPRESSING OVARIAN CANCER CELLS: COMPARATIVE EVALUATION OF THE EFFECTS OF CYSPLATIN AND PC-PHOSPHOLIPASE C INHIBITION

M.E. Pisanu[1], L. Paris[1], A. Ricci[1], R. Canese[1], E. Surrentino[1], M. Bagnoli[2], D. Mezzanzanica[2], S. Canevari[2], E. Iorio[1], F. Podo[1]

[1]*Dept. Cell Biology and Neurosciences, Istituto Superiore di Sanità, ROME, Italy*

[2]*Dept. Experimental Oncology, Fondazione IRCCS Istituto Nazionale Tumori, Milan, Italy*

We focused attention on the significance of the MRS profile of choline-metabolites as indicator of tumor progression and response to therapy in epithelial ovarian cancer (EOC). We found a 3-8-fold increase in phosphocholine (PCho) content of EOC cells compared with non tumoral epithelial ovarian cells (EONT). Major contributions to PCho accumulation derive from activation of two enzymes involved in phosphatidylcholine (PC) biosynthesis and catabolism, choline kinase (Chok) and PC-specific phospholipase C (plc)(1). Plc was found over-expressed on the plasma membrane of HER2-overexpressing breast cancer cells, where the enzyme co-localized with the receptor; moreover, plc inhibition downregulated HER2 over-expression on plasma membrane of these cancer cells (2). Purposes of the study were to investigate the PC metabolism in in vivo passaged HER2-over-expressing EOC cells (SKOV3.ip) and to evaluate the effects of conventional or targeted therapies.
The SKOV3.ip presented an increase in HER2 protein content and about two-fold higher PCho content vs the parental cell line. The biochemical mechanisms responsible for PCho accumulation showed an increase in plc expression, associated with an increase in Chok and plc activity.
Cisplatin did not induce a change in PCho level but resulted in a significant reduction of plc activity, associated with a cell growth arrest and a decrease in the HER2 content. Selective pharmacological inhibition of plc also induced antiproliferative effects, and was associated with a reduction of PCho and HER2 protein level, as well as with an arrest in G0/G1 without apoptosis. Both treatments induced alterations in the lipid biochemical machinery, as shown by significant increases of mobile lipids in intact cells.
These results stimulate further investigations on the possible role of plc inhibition in enhancing the effects of anti-HER2 targeted therapies in HER2-overexpressing EOC cancer,for which clinical trials showed only limited antitumor effect of Trastuzumab. This work suggests the interest of using MRS approaches to explore, at the preclinical level, the usefulness of therapies targeted against PC metabolism, to reinforce the antitumor effects of conventional chemotherapeutics.
1Iorio et al Cancer Res 2010
2Paris et al Breast Cancer Res 2010

P11

Decrease in 1H-MRS-detected PCho and modulation of CXCR4 receptor induced by phosphatidylcholine-specific phospholipase C inhibition in human lymphoblastoid and glioma cell lines.

A. Ricci[1], S. Cecchetti[1], M.E. Pisanu[1], L. Paris[1], L. Portella[2], S. Scala[2], G. Carpinelli[1], E. Iorio[1], F. Podo[1]

[1]*Dep. of Cell Biology and Neuroscience, Istituto Superiore di Sanità, Rome.*

[2]*Dep. of Oncological Immunology, National Cancer Institute "G. Pascale" Foundation, Naples.*

The development of new pharmacological therapies requires identification of pharmacodynamic end-point and selective molecular markers of treatment effectiveness.
MRS is a powerful approach to detect metabolic alterations of phosphatidylcholine (PC) metabolism associated with tumor cell growth and progression. Recent studies have demonstrated that the PC-specific phospholipase C (PC-PLC) regulates both expression and function of some relevant membrane receptors (Paris et al, Breast Cancer Res 2010).
Inhibition of the CXCL12/CXCR4 axis is currently being investigated as a possible therapeutic strategy for anticancer treatment, because of its relevance on the metastatic homing of tumor cells. Purpose of this study was to investigate the effects of a selective inhibition of PC–PLC on 1H MRS spectra profiles, expression and localization of CXCR4 and cell proliferation in a human T-lymphoblastoid (CEM) and glioma (U87-MG) cells.
1H MRS experiments (Bruker Avance 400 spectrometer), confocal laser scanning microscopy (CLSM), molecular and cellular analyses were performed on CEM and U87-MG cells.
CXCR4 and PC-PLC were both overexpressed on the outer plasma membrane of CEM cells, where these molecules co-localized and were found to be physically associated at the level of raft domains. Inhibition of PC-PLC activity by tricyclodecan-9-yl-potassium xanthate (D609) induced a significant down-modulation of CXCR4 from the plasma membrane (up to 50% at 5 h of treatment), suggesting a linkage between PC catabolism and the CXCR4/CXCL12 axis.
1H MRS profiling of CEM cell extracts showed a significant decrease (by about 40%) in the PCho level after D609 treatment, indicating that this metabolite may act as a possible marker of simultaneous PC-PLC inhibition and CXCR4 down-modulation.
Similar studies performed on U87-MG glioma cells using CLSM, showed overexpression of both PC-PLC and CXCR4 on the plasma membrane surface, along with a strong down-modulation of the receptor after 48-72h of enzyme inhibition, confirmed by Western blot analyses.
Further elucidation of the mechanisms underlying the involvement of PC-PLC in the CXCR4 signaling may contribute to the development of noninvasive MRS approaches to monitor both PC-PLC and the CXCL12/CXCR4 pathway as potential therapeutic targets

P12

Impact of biospecimen handling on 1H MRS profiles in breast and ovarian cancer tissues.

A. Ricci[1], E. Iorio[1], L. De Cecco[2], M.E. Pisanu[1], R. Canese[1], M. Giannini[1], V. Cappelletti[2], D. Mezzanzanica[2], S. Canevari[2], F. Podo[1]

[1]*Dep. of Cell Biology and Neuroscience, Istituto Superiore di Sanità, Rome; Italy.*

[2]*Dep. of Experimental Oncology, Fondazione IRCCS Istituto Nazionale Tumori, Milan, Italy.*

A major interest is today focused on existing correlations between the levels of individual choline metabolites under the total choline (tCho) profile and the percentage of cancer cells in the specimen, their aggressiveness and response to therapy (Podo et al., Curr Med Imaging Rev. 2007; Sitter et al., NMR Biomed 2006).

Purpose of this study was to analyze the metabolic changes by 1H MRS occurring between cancer tissue dissection and freezing.

Carcinoma specimens, collected at primary surgery were sampled and frozen at different times after dissection. MRS spectra were recorded within 1 h at 4 °C on samples of 11.53 ± 2.94 mg.

It has been reported, by gene expression analyses performed under these conditions, that a high number of genes modulated only at times longer than 24 h after tissue resection (De Cecco et al., BMC Cancer 2009).

High Resolution Magic Angle Spinning (HR-MAS) spectra were acquired on four breast carcinoma specimens whose multiple samples were frozen within 10-40 min, at 2 h, 6 h, and 24 h after dissection, respectively. The most relevant changes (P=0.04) occurred in the choline (Cho) signal which showed average increases of 2-fold after 2 h, 4-fold after 6 h and 5-fold after 24 h. The phosphocholine (PCho) and glycerophosphocholine (GPC) resonances were practically unaltered within 6 h and decreased by 50% at 24 h. Parallel decreases were observed for taurine, while myo-inositol did not change appreciably.

A more detailed examination of tissues isolated (at 0, 15, 30, 90 min) from subcutaneous EOC xenografts implanted in SCID mice, revealed that significant 4-fold and 8-fold increases in the free Cho content already occurred at 30 and 90 min respectively, compared with the basal content.

Our results indicate that to preserve the metabolic integrity of the tissue and proceed to correct HR-MAS analyses, the specimens should be frozen as quickly as possible after dissection and the elapsed time before freezing should be accurately recorded. The high free Cho signals reported in several studies could be due to phospholipase-, phosphodiesterase- and phosphatase-mediated tissue degradation occurring in the surgical theatre.

P13

Morphological and metabolic changes in the nigro-striatal pathway of Synthetic Proteasome Inhibitor (PSI)-treated rats: an MRI and MRS study

S. Delli Pizzi[1], L. Bonanni [4], M. Caulo[1], C. Rossi [2], V. Di Matteo [3], E. Esposito [3], R. Franciotti[1], A. Thomas[4], M. Onofrj[4], A. Tartaro[1]

[1]*ITAB, "G. D'Annunzio University" Foundation and Department of Neuroscience and Imaging, "G. D'Annunzio University", Chieti, Italy.*

[2]*Aging Research Center, Ce.S.I., "G. D'Annunzio" University Foundation of Chieti, Italy.*

[3]*Laboratory of Neurophysiology, Istituto di Ricerche Farmacologiche Mario Negri, Consorzio Mario Negri Sud, Santa Maria Imbaro (Chieti), Italy.*

[4]*Department of Neuroscience and Imaging and CE.S.I. Aging Research Center, University G. D'Annunzio of Chieti, Italy*

Systemic administration of a Synthetic Proteasome Inihibitor (PSI) in rats has been described as able to provide a model of Parkinson's disease (PD), characterized by behavioral and biochemical modifications, including loss of dopaminergic neurons in the substantia nigra (SN), as assessed by post-mortem studies.

With the present study we aimed to assess in vivo by Magnetic Resonance (MR) possible morphological and metabolic changes in the nigro-striatal pathway of PSI-treated rats.

10 animals were subcutaneously injected with PSI 6.0 mg/kg dissolved in DMSO 10%. Injections were made thrice weekly (Mon., Wed., Fri.) over the course of two weeks. 5 more animals injected with DMSO 10% with the same protocol served as controls. The animals underwent MR sessions before and at four weeks after the end of treatment with either PSI or vehicle. MR Imaging was performed to measure SN volume and Proton MR Spectroscopy (1H-MRS) was performed to measure metabolites changes at the striatum.

Animals were also assessed for motor function at baseline and at 4 and 6 weeks after treatment.

Dopamine and dopamine metabolite levels were measured in the striata at 6 weeks after treatment.

PSI-treated animals showed volumetric reduction of the SN ($p<0.02$) at 4 weeks after treatment as compared to baseline. A reduction of N-acetyl-aspartate/total creatine ratio ($p=0.05$) and an increase of glutamate-glutamine-γ amminobutirrate/total creatine were found at spectroscopy ($p=0.03$). At 6 weeks after treatment, PSI-treated rats also showed motor dysfunction compared to baseline ($p=0.02$), accompanied by Dopamine level reduction in the striatum ($p=0.02$).

P14

A CORRELATION STUDY OF EARLY COGNITIVE IMPAIRMENT IN A PARKINSON'S DISEASE RAT MODEL OBTAINED WITH 2.35T MRI AND TH+IMMUNOREACTIVITY

T. Florio[1], G. Confalone[1], D. Minchella[1], A. Capozzo[1], E. Scarnati[1], A. Sotgiu[2], M. Alecci[3]

[1]*Dipartimento di Scienze e Tecnologie Biomediche, University of L'Aquila, L'Aquila, Italy*

[2]*ITA SRL, L'Aquila, Italy*

[3]*Dipartimento di Scienze della Salute, University of L'Aquila, L'Aquila, Italy*

INTRODUCTION

Early stage of PD lies on the unbalanced capability to manage self-paced versus externally driven movements, or automatic-associated movement with respect to the intended voluntary movement. Several MRI studies found that non-demented patients with PD had a significant rate of median/global brain volume loss, and these changes correlated with global measures of cognitive decline (1-3) strengthening the idea that both striatal DA depletion and regional or global brain volume loss contribute to cognitive decline in PD (4).

Here, we examined the effect of an unilateral DA depletion of the right striatum, on the switching of a well learned task, as revealed using tyrosine hydroxylase (TH) immunoreactivity and high-resolution 2.35T MRI in a rat PD model.

METHODS AND RESULTS

Male albino Wistar rats (n=18) were used. After completion of behavioural performances, the fixated whole brains were scanned with a 2.35T Biospec equipped with a TX-only volume coil and a RX-only surface coil. GEFI images (TR=3000ms; TE=40ms; FOV=1.5cm2; 256*256; slice thickness=1.1mm; NEX=18; TAQ=3h15min) were acquired covering the whole brain. Coronal sections containing the striatum and substantia nigra were processed with cresyl violet and TH immunohistochemistry.

The switching imposed after habit condition evidenced an interference action of EC cerebello-cortical circuitry upon the ID striatal-cortical circuit building that became exclusive with DA depletion of the striatal-cortical circuitry. We found a correspondence between visual evaluation of brain MRI scans, used as volumetric measurement in evaluating regional brain atrophy and the histological section, showing a lesion localized in the striatum with an evident shrinkage of the whole striatum and an enlargement of the ipsilateral ventricle. The nearly complete loss of TH+ immunoreactivity in the right striatum, corresponded to a significant retrograde dopaminergic denervation in the ipsilateral substantia nigra.

REFERENCES

1. Hu MT, et al, Brain Res Cogn Brain Res 2004;21:193-205.
2. Beyer MK, et al, J Neurol Neurosurg Psychiatry 2007;78:254-9.
3. Ibarretxe-Bilbao N, et al, Mov Disord 2009;24:S748-53.
4. Jokinen P, et al, Parkinsonism Relat Disord 2009;15:88-93.

P15
DTI AND MRS IN THE PRECLINICAL MODEL OF AGING

S. Tambalo[1], E. Mosconi[2], A. Daducci[4], S. Fiorini[1], M. Balietti[3], P. Fattoretti[3], A. Sbarbati[2], P. Marzola[1]
[1]*Dip. Informatica, Università di Verona*
[2]*Dip. Sci. NN.MM., Università di Verona*
[3]*I.N.R.C.A.(Italian National Centres on Aging), Ancona*
[4]*EPFL, STI IEL LTS5 ELD 232 (Bâtiment ELD), Lausanne*

Introduction: The proportion of older persons in the population has been increasing; so healthy aging is fundamental for physical and mental wellbeing. MRI studies in humans have shown that aging is accompanied by various alterations. In this work, two groups of male SD rats, 13 and 24 months old respectively, have been studied by DTI and MRS. Quantitative measurements have been performed over the whole brain.
Methods and materials: Experiments were performed on a Bruker BioSpec 4.7T scanner with actively decoupled coils. A Stejskal-Tanner sequence with EPI readout was used for DTI. Two groups (adult=8; elder=6) were imaged with the following parameters: TR=3800ms, TE=39.5ms, 30 diffusion directions, b=1000s/mm^2, b0 IMG=5. Images were processed using FSL and MATLAB. FA and ADC maps were registered to a digital Rat Brain Atlas and tested with unpaired T-test. A second batch of rats (adult=6; elder=8) was used for MRS. Three voxels in the brain were selected: hippocampus 7x1.75x3mm^3; temporal cortex 3.5x2x5mm^3; prefrontal cortex 3x3x4mm^3 (VAPOR and PRESS sequence with TR/TE=4000/11). Spectra were analyzed with LCModel. Absolute quantification values considering internal water standard and Cr+PCr peak; also relative quantification with respect to GPC+PCh group was considered.
Results: FA and ADC measured over hippocampus and cortex (prefrontal, temporal) are different ($p<0.05$) in elder rats with a decrease in FA and an increase in ADC when compared to adult subjects. MRS computations showed in the hippocampus a significant difference in Cr and PCr between groups: Cr is decreased in aged rats ($p<0.01$, U-test) while PCr increased ($p<0.01$, U-test); the sum of the two components remains stable in both groups. The result is confirmed both when computing absolute concentrations with respect to Cr+PCr and relative concentrations with respect to GPC+PCh.
Conclusions: Accordingly to clinical results available in the literature, we have shown that DTI and MRS can be potentially used as valid tools to study neurodegenerative processes in animal models.
References: Mandeville et al, MRM 39:615-624, 1998; Minati et al, J Geriatr Psychiatry Neurol 2007; 20; 3; Takao et al. MRI (2010) vol. 28 (1) pp. 65-9

P16
IN VIVO IMAGING OF LABELLED NEURAL STEM CELLS IN A MOUSE MODEL OF SPINAL CORD INJURY

A. Degrassi[1], L. Ottobrini[3], M. Russo[1], R. Lui[3], D. Merli[4], A. Gorio[4], E. Pesenti[1], G. Lucignani[2]
[1]*Pharmacology Dep., B.U. Oncology, Nerviano Medical Sciences, Nerviano, Milano*
[2]*Dep. of Biomedical Sciences and Technologies, University of Milan*
[3]*Centre of Molecular and Cellular Imaging - IMAGO, University of Milan*
[4]*Dep. of Medicine, Surgery and Dentistry, University of Milan*

Introduction: Recent discoveries describe the possibility to use neural stem cells (NSC) in cell-mediated therapeutic protocols, for the regeneration of damaged tissues. Treatment efficacy evaluation is generally based on functional recovery end points, skipping the evaluation of the distribution of injected cells, localization at the target organ, cell survival and differentiation. Here we tested a multiple labelling approach for in vivo visualization by MRI and Bioluminescence Imaging (BLI) of murine NSC in a mouse model of traumatic spinal cord injury [1].
Methods: NSC, isolated from the subventricular zone of the adult mouse brain, were labelled for 24 h with 200 mg Fe/ml of Endorem®, in presence of Protamine Sulphate and analyzed for iron content, viability, morphology and differentiation capability. Labelled cells were injected either locally, at the site of the injury, or systemically into the tail vein and followed by MRI (Bruker Pharmascan 7.0 T) for more than a month to visualize NSC localization at the lesion site. Cells distribution and viability were also analyzed in vivo by BLI (Xenogen IVIS 100) after injection of NSC infected with a viral vector expressing luciferase. After imaging, mice were perfused with PFA and spinal cords extracted to perform ex vivo MRI and histopathological analysis.
Results: Iron oxide labelling procedure did not significantly perturb viability and proliferation rate of NSC. The percentage of iron positive cells increased with the PS content in the medium, reaching 210 pg Fe/cell. NSC, infected with the viral vector, were detected by BLI at the site of the injury after intramedullary injection, and at the same site one week after i.v. injection. MRI showed on both RARE T2-W and FLASH images an hypointense signal due to Fe+ labelled cells at the injury site three weeks after i.v. injection. Iron presence was confirmed on ex vivo MR images and on histological sections of perfused spinal cords.
Conclusions: Adult NSC can be efficiently labelled without significantly perturbing physiological features and self-renewal capability. Labelled NSC were visualized in vivo by MRI and BLI providing information on their localization at the spinal cord injury site and survival.
[1] Gorio et al. PNAS 99: 9450-5 (2002)

P17

COMPARISON BETWEEN CARDIAC MRI AND HISTOLOGY FOR INFARCT SIZE QUANTIFICATION IN MICE WITH CHRONIC CORONARY ARTERY LIGATION

I. Russo[1], L. Staszewsky[1], E. Micotti[2], A. Soldo[1], A. Biondi[1], R. Latini [1]

[1]*Dept. of Cardiovascular Research, Mario Negri Institute for Pharmacological Research, Milano*

[2]*Dept. of Neuroscience, Mario Negri Institute for Pharmacological Research, Milano*

Background: Accurate quantification of infarct size (IS) is crucial in the evaluation of the efficacy of post myocardial infarction (MI) treatments or response to gene alterations of the heart. Myocardial tissue is not always available for histology, the gold standard for IS calculation, especially if concomitant molecular biology studies need to be performed [1].

Aims: As cardiac MRI is considered the current in vivo method with the highest accuracy for non-invasive analysis of left ventricular (LV) morphology and function, we aimed to verify in our MRI lab its accuracy for IS calculation when compared to histology in a mouse model of chronic coronary artery ligation (CAL).

Methods: Cardiac MRI (BioSpec 70/30, 7T Bruker BioSpin, Germany) was performed 5 weeks post-CAL in 15 SCIDBg male mice, BW 25±1.6g, anesthetized with 3% of isoflurane in O_2. A linear volume coil (inner diameter 72mm) and a mouse surface coil (inner diameter 10mm) were used. Consecutive 1mm distance slices were acquired in SAX view covering the whole heart and measurements were done off-line. Multi-frame capability was used to assess the regional LV motility and akinetic segments were considered as scar tissue. Cardiac function and volumes were also calculated. IS by histology was assessed in a section immediately below the ligation; MRI measurements were carried-out on a slice at an equivalent level. Values were shown as mean±SE. Pearson's correlation coefficient method and Bland-Altman (B-A) difference plot were employed for statistical analysis.

Results: LVEDV was 246±27.2µl, LVESV 170±23.9µl and LVEF 34±2.7% (sham-operated mice: 65±9.6µl, 13±3.1µl and 81±2.4%). IS by MRI was 42.8±2.3% (range 23 to 67%) vs. 42.3±3.13% (range 20 to 66%) by histology, P=0.90, Pearson's coefficient and B-A analysis were r=0.98 ,P<0.0001 and Mean of Difference=-0.56%, SD=2.58, 95% Limits of Agreement: -5.62-4.50 respectively.

Conclusion: In vivo cardiac MRI was strongly correlated and showed good agreement with histology in the quantification of IS in CAL mouse model.

Reference:

[1] S. Bohl, CA. Lygate, H. Barnes, D. Medway, L-A. Stork, J. Schulz-Menger, S. Neubauer, and JE. Schneider, Am J Physiol Heart Circ Physiol 296, 1200-1208 (2009).

P18
MULTIMODAL IMAGING IN AN ORTHOTOPIC MOUSE MODEL OF PANCREATIC CANCER

M. Russo[1], L. Mancini[1], G. Texido[1], W. Veronelli[1], E. Pesenti[1], A. Degrassi[1]
[1]*Pharmacology Dep., B.U. Oncology, Nerviano Medical Sciences s.r.l., Nerviano, Milano*

Background and aims: Pancreatic adenocarcinoma has a rising incidence and a poor survival rate. Reliable animal models are needed to develop new treatment strategies. Orthotopic models (1), where human tumor cells are implanted into the mouse pancreas, resemble the human disease more closely than subcutaneous models, but need non invasive imaging techniques to be monitored.
We report a magnetic resonance imaging (MRI) and bioluminescence (BLI) approach to characterize these tumors during growth and treatment. Furthermore, our study aimed at proving feasibility of studying this model using advanced MRI techniques, such as Contrast-enhanced MRI and Diffusion Imaging, despite the difficulties arising from movement of abdominal organs.
Methods: A 7T Bruker Pharmascan and a Xenogen IVIS Lumina were used for MRI and BLI respectively. Mice were implanted with two luc-positive human pancreatic adenocarcinoma cell lines, Capan (n=12) and MiaPaCa (n=11). Parental lines were also implanted in some animals (n=5+5). A device was used to minimize movement artifacts in the abdomen. T2-W RARE sequences, together with Gd enhanced T1-W RARE and Diffusion EPI were optimized to monitor tumor growth, study morphology and evaluate the effect of Irinotecan therapy. Histopathological analysis was used to validate imaging data.
Results: MRI and BLI could follow mouse pancreatic tumors during growth and revealed Irinotecan efficacy on both cell lines. Differences in growth rate and tumor morphology were found between Capan and MiaPaCa implanted models. MRI images could detect tumors as small as 1-2 mm in diameter and showed the mass being localized between liver, stomach and spleen. A device separated the abdominal area from the thoracic region, subject to strong respiratory movements, and allowed the use of Diffusion Imaging in this tumor model.
Heterogeneities within the tumors were detected during growth and treatment, and necrotic areas were confirmed by higher diffusion coefficients.
Conclusions: MRI and BLI serve as noninvasive and complementary imaging modalities to monitor and characterize mouse orthotopic pancreatic tumors. Even more challenging MRI sequences, such as Diffusion, could be optimized and used in therapy evaluation.
(1) Grimm J et al. (2003) Int.J.Cancer; 106:806-11

P19
Cronologia dei reperti RM in modello animale di ischemia colica acuta

F. Iacobellis[1], D. Berritto[1], F. Somma[1], S. Cappabianca[1], A. Rotondo[1], R. Grassi[1]
[1]*Istituto di Radiologia, Seconda Università degli Studi di Napoli, Napoli, Italy*

Background: La colite ischemica (CI) costituisce la più frequente patologia ischemica del tratto gastroenterico. La eziopatogenesi può essere di natura occlusiva o non occlusiva ad evoluzione acuta o cronica. Al fine di identificare i reperti precoci di tale patologia, si è proceduto alla caratterizzazione cronologica delle lesioni macroscopiche, radiologiche (micro-Risonanza Magnetica a 7 Tesla [μ-RM]) ed istologiche, conseguenti l'occlusione acuta della arteria mesenterica inferiore (AMI) in un modello animale di ratto. Materiali e Metodi: Sono stati utilizzati 8 ratti Sprague Dawley; divisi in due gruppi (Gruppo I e Gruppo II) e sottoposti a legatura chirurgica dell'AMI. I ratti del Gruppo I (n=4) sono stati monitorati macroscopicamente fino ad un tempo massimo di 8 ore; nei ratti del Gruppo II (n=4) il monitoraggio è stato effettuato mediante μ-RM a time-points stabiliti. Ad ogni time-points un ratto di ciascun gruppo è stato sacrificato, il colon è stato prelevato e sottoposto ad analisi istologica. Risultati: Il monitoraggio macroscopico ha documentato la comparsa delle prime alterazioni ad 1 h dalla legatura dell'AMI, rappresentate da: pallore del mesentere e successivo viraggio cromatico verso il bluastro della flessura splenica del colon. I reperti di μ-RM consistevano in una sottile falda liquida intraperitoneale e in una lieve iperintensità di segnale della parete colica, che esordivano ad 1h e si aggravavano progressivamente. Ad 8h dalla chiusura dell'AMI si assisteva a riduzione da riassorbimento del liquido intraperitoneale ed alla persistenza dell'iperintensità in sede parietale colica per imbibizione edematosa. Dall'analisi istologica emergevano prima diffuse e lievi alterazioni ischemiche della mucosa fino a quadri di necrosi con importante edema sottomucoso. Conclusioni: I nostri dati suggeriscono un ruolo rilevante dell'imaging RM nell'iter diagnostico dei pazienti con colite ischemica acuta perché consente l'identificazione precoce e non invasiva dei segni di malattia offrendo la possibilità di una diagnosi tempestiva e di un trattamento efficace.

P20
La micro-RM a 7 T nell'infarto intestinale ad eziologia venosa in un modello animale di ratto.

F. Somma[1], D. Berritto[1], F. Iacobellis[1], S. Cappabianca[1], A. Rotondo[1], R. Grassi[1]
[1]*Istituto di Radiologia, Seconda Università degli Studi di Napoli, Napoli, Italy*

Background: L'ischemia mesenterica acuta è una condizione patologica ad elevate mortalità e con incidenza registrata in aumento nel corso degli ultimi anni. La sua scarsa prognosi è imputabile soprattutto all'assenza in letteratura di segni, sia clinici che radiologici, che siano precoci e fortemente indicativi di tale patologia. L'obiettivo di questo studio è pertanto quello di individuare in un innovativo modello animale di ischemia intestinale di origine venosa reperti utili ai fini di una diagnosi precoce con l'ausilio di una micro-RM a 7T e di riscontri macroscopici e istologici.
Materiali e metodi: Lo studio è stato condotto su 12 ratti Sprague Dawley divisi in 2 gruppi: nel primo (n=6), l'ischemia è stata ottenuta per legatura della Vena Mesenterica Superiore (VMS) al punto della sua confluenza e si è quindi proceduto all'osservazione macroscopica e microscopica; nel secondo (n=6), è stato realizzato un innovativo modello chirurgico in due tempi per caratterizzare l'evoluzione dei diversi reperti descritti in letteratura, evitando artefatti dovuti alle procedure chirurgiche.
Risultati: Le sequenze RARE T2 utilizzate hanno consentito la corretta individuazione e caratterizzazione temporale dei diversi reperti descritti in letteratura tra i quali l'alterato enhancement e l'ispessimento di parete di alcune anse, l'infarcimento mesenterico, la pneumatosi parietale.
Conclusioni: L'analisi istologica ed il monitoraggio macroscopico delle lesioni hanno dimostrato l'efficacia del modello chirurgico innovativo nell'indurre l'ischemia mesenterica acuta ad eziologia venosa. La micro-RM a 7T ha consentito uno studio approfondito e dettagliato delle alterazioni morfo-funzionali tipiche di questa condizione patologica, nonché di identificare alcuni reperti etichettabili come precoci e quindi utili ai fini di una diagnosi radiologica precoce.

P21
La Risonanza Magnetica nell'ischemia mesenterica acuta ad eziologia arteriosa

D. Berritto[1], F. Somma[1], F. Iacobellis[1], S. Cappabianca[1], A. Rotondo[1], R. Grassi[1]
[1]*Istituto di Radiologia, Seconda Università degli Studi di Napoli, Napoli, Italy*

Background: L'ischemia mesenterica acuta (IMA) rappresenta un'emergenza vascolare ad elevata mortalità. La diagnosi precoce è imprescindibile per migliorare sopravvivenza e qualità di vita dei pazienti. Dai contributi presenti in letteratura non emerge né una definizione cronologica degli eventi conseguenti all'ischemia mesenterica acuta, né una chiara correlazione tra i reperti radiologici e l'eziologia del danno. Pertanto, obiettivo del presente studio, è individuare i reperti precoci di ischemia mesenterica arteriosa acuta (IMAA) e documentarne l'evoluzione temporale tramite micro-Risonanza Magnetica (μ-RM) a 7 Tesla in un modello animale di ratto.
Metodi: Dodici ratti Sprague-Dawley sono stati suddivisi in 2 gruppi (n=6): nel primo gruppo, dopo legatura chirurgica dell'arteria mesenterica superiore (AMS), si è proceduto al monitoraggio macroscopico delle lesioni fino a 8 ore; nel secondo gruppo, l'occlusione della AMS è stata ottenuta mediante trazione di un cappio posizionato all'emergenza del vaso nel corso di una seduta operatoria avvenuta 3 giorni prima; le lesioni sono state successivamente monitorate mediante μ-RM a 7 Tesla. In entrambi i gruppi, a time-points stabiliti, il pacchetto intestinale è stato escisso e sottoposto ad analisi istologica.
Risultati: Il monitoraggio macroscopico ha documentato la comparsa precoce di assottigliamento dei vasi mesenterici, un successivo ileo riflesso spastico transitato poi in ipotonico ed il viraggio cromatico di alcune anse. La μ-RM ha documentato la comparsa di liquido libero intraperitoneale, seguita da dilatazione luminale delle anse del piccolo intestino con livelli idroaerei, ed edema parietale. L'analisi istopatologica ha documentato reperti sovrapponibili nei due gruppi confermando l'ischemia con danno più precoce a carico dell'ileo medio.
Conclusioni: Il modello animale ha consentito di riconoscere i segni correlati all'ischemia arteriosa, e di documentarne la progressione temporale, suggerendo l'utilizzo della RM nella diagnosi precoce di questa patologia.

P22

High Field ^{19}F MRI: optimization of Rapid Acquisition with Relaxation Enhancement (RARE) sequences to improve the sensitivity on a preclinical 7T MRI scanner.

A. Mastropietro[1], E. De Bernardi[1], I. Zucca[2], M. Figini[1], R. Spreafico[3], G. Baselli[1]

[1]*Department of Bioengineering, Politecnico di Milano, Italy*

[2]*Scientific Direction Unit, IRCCS Foundation Neurologic Institute "C. Besta", Milan, Italy*

[3]*Clinical Epileptology and Neurophysiology Unit, IRCCS Foundation Neurologic Institute "C. Besta", Milan, Italy*

Purpose-Aim of this work was to perform an optimization of RARE sequence for fluorine magnetic resonance imaging (^{19}F-MRI) studies on phantoms containing fluorinated compounds, in order to improve the sensitivity of the experimental set-up on a 7T MRI scanner.
Methods-Phantoms of aqueous solutions of Potassium hexafluorophosphate (KPF_6, T1=2500msec; T2=700msec; estimated with RAREVTR pulse sequence) at different concentrations (0.1, 0.05, 0.01, 0.005 M) have been acquired by fixing the total acquisition time and exploring various combinations of the parameters (TR and RARE-factor, i.e. number of collected echoes). Images were acquired on a Biospec 70/30 USR 7T MRI system operating at frequencies of 300 MHz for 1H and 282 MHz for 19F nuclei. Different encoding methods were analyzed to reduce the total scan time (i.e. Partial-FT acceleration, Zero-Fill Acceleration).
Results-The Fast Recovery RARE pulse sequence has been studied and optimized. For low values of TR (<500 msec) the SNR decreases as the RARE-factor increases, because the longitudinal magnetization is low and the contribute of the transaxial magnetization becomes fundamental; for large values of TR (>500msec) the SNR decreases as the RARE-factor increases because the longitudinal magnetization recovery becomes dominant. Globally, for KPF_6, the best SNR/t is obtained for TR=1000msec and RARE-factor=16. The Partial-FT acceleration increases the SNR/t by 31%, while the Zero-Fill Acceleration can increase the SNR/t by up to 200% but reduces the effective resolution of the image (i.e. causes blurring).
Conclusion-General guidelines for the choice of the best parameters as a function of T1 and T2 of the fluorinated compound have been derived from these data. The results suggest that fast imaging sequences are necessary for improving sensitivity (SNR) in ^{19}F MRI studies. The use of restricted k-space acquisition is a useful tool for significantly reducing the acquisition time in order to increase the number of averages and thus to further improve the sensitivity of the technique. Finally, the parameters must be calibrated on the magnetic properties (i.e. relaxation times) of the specific compound.

P23
Experimental comparison of SNR performance in different MEG-MRI prototypes

A. Galante[1], N. Catallo[1], P. Sebastiani[2], A. Sotgiu[2], A. Manna[3], R. Sinibaldi[3], C. De Luca [3], S. Della Penna[3]
[1]*Dip. Scienze della salute, Università dell'Aquila, Via Vetoio, L'Aquila, Italy*
[2]*Imaging Technology Abruzzo srl, Zona Industriale di Pile, SS17,L'Aquila, Italy*
[3]*Istituto di Tecnologie Avanzate Biomediche, Università di Chieti, Via dei Vestini, 31, Chieti, Italy*

Introduction
The integration of magnetoencephalography (MEG) and nuclear magnetic imaging (MRI) can provide a new tool for brain study, increasing the spatial accuracy of MEG sources localization [1]. The peculiar MEG environment (magnetic shielded room, liquid He cryostat and SQUIDs) is not compatible with high magnetic fields and limits the MRI system in the mT range. A low field MEG-MRI system can improve the quality of functional brain studies, increase the group of patients for MEG clinical studies and have clinical impact in the follow up of stroke recovery and non invasive determination of surgical resection epileptogenic cortex areas in patients with pharmacoresistant epilepsy.
Methods
Existing implementation of MEG-MRI have adopted two different strategies. The first one is based on SQUID signal detection at ultra low fields (ULF, typically below 100 microT) using a prepolarizing field in the 10-30 mT range to increase the proton polarization. The second one is with a single static field and detection with resonant air coils or other field tolerant devices (mixed sensors).
We compare the image SNR of two small scale MEG-MRI prototypes. The first one, realized by Aalto University, is based on 8 channels SQUID signal detection at ULF (50 microT) using a 10mT prepolarization pulse. The second, by ITA srl and Chieti University, is a system with B_0=8.9mT and detection with resonant air coil.
Results
The SNR comparison has been based on 2D images of water phantoms acquired without slice selection. The Aalto system is still undergoing optimization process and noise reduction improvements but first SNR results indicate that, contrary to expectations [2], the more favorable geometry of the resonant air coil system in Chieti over performs the ULF approach in Aalto . We claim that, even for a full head system where ULF can benefit from many receiving channels (up to several hundreds) the more conventional approach can be a viable and competitive alternative.
[1] Hybrid MEG-MRI imaging system, FP7 HEALTH-2007-1.2-1 project
[2] W. Myers et al., J. Reson. Med., 186: 182-192 (2007)

P24
PROTOTIPO PER MEG-MRI INTEGRATE

A. Galante[1], N. Catallo[1], P. Sebastiani[2], A. Sotgiu[2], G. Romani[3], P. Vittorio[3], C. Dal Gratta[3], R. Sinibaldi[3], A. Manna[3], C. De Luca[3], S. Della Penna[3]

[1]*Dip. Scienze della Salute, Università dell'Aquila, Via Vetoio, 67100, L'Aquila*

[2]*ITA S.r.l., Zona Industriale di Pile, SS17, Località Boschetto, 67100, L'Aquila*

[3]*Istituto Tecniche Avanzate Biomediche, Università di Chieti , Via dei Vestini, 31, 66100 Chieti*

Scopo del progetto [1] è realizzare un prototipo che integri le modalità di imaging MEG (magneto encefalografia) ed MRI. Il prototipo è un test bench per le tecnologie da adottare in un futuro sistema full scale volto a ridurre l'errore di localizzazione della MEG grazie alla coregistrazione del segnale MRI ed a consentire la MEG e l'MRI a persone appartenenti a categorie a rischio.

Metodi

Nella realizzazione del prototipo occorre tener conto dei vincoli imposti dalla MEG: i dispositivi usati per rivelare il campo magnetico cerebrale (SQUID) possono lavorare in campi magnetici molto minori di quelli usati nella diagnostica MRI, sono raffreddati a 4.2K e devono operare all'interno di una cabina schermata magneticamente (MSR). Il prototipo MEG è composto da 6 gradiometri assiali accoppiati a SQUID che possono essere disattivati durante l'MRI. Per la ricezione del segnale MRI sono previsti due approcci: una bobina risonante di volume a temperatura ambiente ed un mixed sensor (GMR accoppiato ad un pick-up superconduttivo) contenuto nello stesso dewar della MEG. Il set-up MRI usa un campo di 9mT, il massimo consentito dallo schermo termico del dewar che taglia il segnale NMR a frequenze >410KHz. La compatibilità con la MSR è stata garantita da un magnete che limita il campo di induzione sulle pareti.

Risultati

Al momento è stato implementato il sistema di ricezione basato su bobina risonante a temperatura ambiente. Al fine di massimizzare il SNR si è utilizzato un sistema di ricostruzione basato su sequenze spin-eco 3D e sulla ricostruzione dalle proiezioni ottenendo immagini con una risoluzione nominale di 1x1x1 mm^3 ed uno scan time di 4min per singola acquisizione. Le immagini ottenute hanno qualità sufficiente per essere sovrapposte ad immagini MRI ad alto campo, e migliorare l'accuratezza nella localizzazione delle sorgenti MEG.

Conclusioni

Il sistema sviluppato è un'alternativa all'approccio sviluppato da altri gruppi basato sull'utilizzo di campi pulsati di prepolarizzazione e la rilevazione del segnale MRI con gli SQUID. A breve sarà possibile un confronto con le performances del sistema di rivelazione basato sui mixed sensor.

[1] Hybrid MEG-MRI imaging system, FP7 HEALTH-2007-1.2-1 project

[2] P.Volegov et al, MRM 2004, 52:467

P25
JIMRI – Java Interface tool for MRI

P. Martinenghi[1], P. Sebastiani[1], A. Galante[2], A. Sotgiu[1]
[1]*Imaging Technology Abruzzo srl, Zona Industriale di Pile, SS17,L'Aquila*
[2]*Dip. Scienze della salute, Università dell'Aquila, Via Vetoio, L'Aquila*

JIMRI (Java Interface for Magnetic Resonance Imaging) is a cross-platform software application for creating magnetic resonance imaging (MRI) sequences [1]. It allows interactive designing of pulse sequences and provides an easy-to-use programming interface for MRI console. The present implementation of the software is for a low-field (140 mT) multi-channel scanner controlled by a ITA srl hardware console. The console has four receive channels and the possibility to add more up to a maximum of thirty-two.
Due to the clear software design, the main pulse sequences can be created, loaded and executed within a short time. All the sequence parameters can be edited or modified interactively and the corresponding RF and gradient profiles are displayed simultaneously.
All steps, from generating the sequence to data acquisition, can be performed within a graphical user interface (GUI). With this object-oriented interface implemented in Java, the sequence programmer is able to build or modify pulse sequences that can be created using an interactive environment. The software creates a composition of reusable, self-consistent objects that can be combined freely to develop new experimental sequences. The suite includes a post-processing package that receives from console the acquired data and reconstructs the corresponding image. With small changes in the communication protocols it can be easily adapted to work with virtually any existing console.
JIMRI runs under 32/64-Bit Windows Operating Systems and the Java implementation guarantees a total platform independence [2].
References
[1] M.A. Bernstein, K.F. King, X.J. Zhou, "Handbook of MRI Pulse Sequences", Elsevier Academic Press, 2004
[2] B. Eckel, "Thinking in Java, 4th Edition", Prentice Hall, 2006

P26
A STUDY ON THE RF SPATIAL DISTRIBUTION OF A 4T DOUBLE TUNED 23Na-1H SURFACE RESONATOR

A. Vitacolonna[1], S. Romanzetti[2], J. Felder[2], A. Galante[1], A. Sotgiu[3], N.J. Shah[4]
[1]*Dipartimento di Scienze della Salute, University of L'Aquila, L'Aquila, Italy*
[2]*Institute of Neuroscience and Medicine, Research Centre, Juëlich, Germany*
[3]*ITA srl, L'Aquila, Italy*
[4]*Faculty of Medicine, Department of Neurology, RWTH Aachen University, Germany*

INTRODUCTION
Sodium MRI/MRS [1-2] benefits of improved SNR obtainable at high fields (3-12T). In recent works [3-5] a novel Double-Tuned (DT) surface resonator, made by three microstrip elements for 23Na/1H MRI at 4T was described. Here, we report workbench and 4T MRI data showing the optimization of the RF spatial distribution of the 23Na channel vs the relative distance between the external microstrips.
METHODS
We built and tested two DT surface resonators made by: a central copper microstrip (10*190*35E-3)mm3 for the 1H channel and two lateral microstrip (5*190*35E-3)mm3 for the 23Na channel, each connected to the ground plane by two end capacitors. The centre-to-centre separation between the 23Na strips was S=35mm for the first prototype and S=25mm for the second prototype. The ground plane is separated from the strip plane by two 16 mm thick PVC slabs and with an air gap of 29 mm in between. The resonators were tested on the workbench and in a 4T MRI scanner in TX/RX mode. We used a 3D gradient-echo sequences and a 1 litre phantom solution containing water, 1.25g of NiSO4-6H2O and 5g of NaCl.
RESULTS
The S11 spectrum shows that decreasing the separation between the 23Na elements results in an increased frequency sweep between the useful MRI 23Na mode (44.5 MHz) and its adjacent mode due to a stronger inductive coupling. The MRI testing shows that the S=25mm prototype presents a more homogeneous RF profile for the 23Na channel. The RF distribution of the 1H (f0=168.3 MHz) channel was practically unaffected.
CONCLUSIONS
We compared two DT surface resonators and demonstrated that approaching the external elements to the central one improves the RF field homogeneity of the 23Na channel. With S=25mm the axial RF homogeneity is about 150 mm and the transverse RF homogeneity is about 50 mm, these values should be useful for many in vivo applications as musculoskeletal diseases or subcutaneous tumours.
REFERENCES
(1) Schepkin VD et al, NMR in Biomedicine 19:1035-1042 (2006)
(2) Constantinides CD, et al Radiology 2000, 216: 559-568
(3) Alecci M et al, Italian Patent RM2007A000585 (2007)
(4) Vitacolonna A et al, Proc. ISMRM 17, 4751 (2009)
(5) Vitacolonna A et al, Magn. Reson. Mater. Phy. Vol. 22, Suppl. 1, pg. 355 (2009)

P27
DESIGN AND WORKBENCH TESTING OF A 9.4T DOUBLE-TUNED (1H/23Na) SURFACE RESONATOR

M. Polsoni[1], A. Vitacolonna[1], A. Galante[1], A. Sotgiu[2], N.J. Shah[3], M. Alecci[1]

[1]*Dipartimento di Scienze della Salute, University of L'Aquila, L'Aquila, Italy*

[2]*ITA srl, L'Aquila, Italy*

[3]*Institute of Neuroscience and Medicine, Research Centre, Juëlich, and Faculty of Medicine, Department of Neurology, RWTH Aachen University, Germany*

Introduction. Sodium imaging is useful for monitoring chemotherapeutic effects [1] and musculoskeletal diseases [2]. In previous works [3-4] a novel 4T surface resonator for 1H/23Na MRI, consisting of two microstrip elements for the 23Na channel and a centrally positioned microstrip for the 1H channel, was described.
In this work we designed and tested on the workbench a 9.4T DT surface resonator. It was realized with a segmented ground plane to reduce eddy currents.
Methods and Results. The novel DT surface resonator is based on the microstrip design and made by: a perspex substrate (150*180*150)mm3; a segmented copper ground (35μm thick) made by three etched axial segments connected by nine 10pF capacitors; two copper microstrip (180*7.9*35E-3)mm3 for the 23Na channel positioned at a mutual distance of 20mm; and one centrally positioned microstrip (180*12.7*35E-3)mm3 for the 1H channel. A second prototype with the same geometry and a continuous copper ground was also built and tested. The measured S11 spectra of the two prototypes did not show differences in the frequency spectrum comprising the useful resonant modes. The S11 of the segmented ground plane alone was measured with a 17cm diameter loop coil, showing three ground-plane "resonances" between 30-85 MHz. These do not interact with the 23Na (105 MHz) and 1H (400 MHz) resonances at 9.4T. The measured S21 spectrum of the DT prototype showed a good isolation between the 23Na and 1H channels, better than -35 dB. The measurement of the Q values for the two prototypes, when empty or loaded with 0.5L saline, showed no changes for the 23Na channel and a small reduction ($\leq$ 17%) for the 1H channel.
Conclusions. We realized a 9.4T DT TEM prototype with a segmented ground plane showing "parasitic" resonances far enough from the useful MRI frequencies and without a significant decrease of the Q value. This novel resonator will be used for 9.4T simultaneous acquisition of 1H and 23Na images.
References. [1] Schepkin VD et al, NMR in Biomedicine 19:1035-1042 (2006). [2] Constantinides CD, et al Radiology 2000, 216: 559-568, [3] Alecci M et al, Italian Patent RM2007A000585 (2007). [4] Vitacolonna A et al, Proc. ISMRM Pg 4751 (2009).

P28
Workbench Optimization of a 4T Double Tuned (23Na/1H) Volume TEM Resonator

A. Vitacolonna[1], A. Sotgiu[2], S. Romanzetti[3], J. Felder[3], N.J. Shah[4], M. Alecci[1]
[1]*Dipartimento di Scienze della Salute, University of L'Aquila, L'Aquila Italy*
[2]*ITA srl, L'Aquila, Italy*
[3]*Institute of Neuroscience and Medicine, Research Centre, Jülich, Germany*
[4]*Institute of Neuroscience and Medicine, Research Centre, Jülich and Faculty of Medicine, Department of Neurology, RWTH Aachen University, Germany*

Introduction
Double-Tuned (DT) TEM coils have been developed for high-field MRI and MRS. DT TEM resonators were designed with two sets of transmission line elements (TLEs) at the same radial position [1], each set showing a multiplicity of resonant modes related to the number of TLE's. However, the common design of the DT TEM might give a limited frequency separation (<1MHz) between the high range modes. This feature leads to a partial overlapping of the useful resonant mode (M=1) with the adjacent modes (M=0, M=2), particularly when the coil is loaded with the human head, producing shading artefacts. Solutions to this problem were recently proposed [2,3] and it was theoretically shown [3] that adjusting properly the radial position of the TLE's elements, the modes separation could be significantly increased.
In this work, we have experimentally shown the optimization of the DT TEM design by building and testing on the workbench a head-size volume TEM suitable for 4T 1H/23Na MRI.
Methods and Results
The DT TEM resonator is made by two concentric cylinders with air in between, comprising a total of 32 microstrip TLEs (N1H=N23Na=16). A copper shield is positioned on the external cylinder. The microstrip TLEs were made by copper tape (length 18cm) connected to the RF shield by chip capacitors. First, as with standard designs, the 23Na TLEs (width 10mm) and the 1H TLEs (width 15mm) were positioned on the inner surface of the smaller cylinder at the same radial distance R1=12.5cm, and the S11 spectrum was measured to establish the resonant modes. In a second configuration, to improve modes separations, the 1H microstrip TLEs were positioned, by means of plastic holders, toward the centre at a radial distance R2=11.5cm. We observed that in this condition the frequency separation between the high frequency modes increases from 2 MHz to 4 MHz. The sodium spectrum remains practically unperturbed.
We have built and tested on the workbench, a 4T volume DT TEM resonator suitable for 1H/23Na. We experimentally demonstrated the increase of the 1H frequency modes separation, without a significant perturbation of the 23Na modes.
References
[1] Vaughan JT et al, MRM 32:206 (1994). [2] Avdievich NI et al, Proc ISMRM 239 (2007). [3] Vitacolonna A et al, Proc. ISMRM 4751 (2009).

P29

Sensitivity and Selectivity of Transverse Field RF Surface Coils: A Theoretical and Experimental Study at 2.35 T

M. Alfonsetti[1], A. Sotgiu[1], M. Alecci[1]

[1]*Università degli Studi di L'Aquila, Dip. di Scienze della Salute*

Introduction. Several clinical MRI/MRS applications require a careful selection of the RF coil design to optimize the coil sensibility and/or selectivity in a particular region of interest (ROI) [1-2]. We analyse axial RF coils (square loop, SL) and transverse RF field surface coils (figure-of-eight coil, FO8; butterfly-coil, BC) to study the spatial selectivity along the coil axis [3-4] and the coils sensitivity in imaging applications.

Methods and Results. To investigate the B1 axial field distribution of the SL, FO8 and BC coils (dimension=10 cm), we have performed simulations with a Finite Element Method (FEM) by using a commercial software (HFSS,Ansoft) in the presence of a homogeneous tissue model. The simulated normalized B1 field distributions along the z-axis are show that the BC presents the most pronounced spatial selectivity in close proximity of the coil, while the FO8 exhibit a maximum at about 10 mm. The SL coil presents a B1 distribution with a slow decrease. We have built prototypes of the FO8 and SL coil matching the dimensions of the models. Axial GE images were acquired in the presence of an oil sample (75mmx75mmx120 mm) using a 2.35T (100.3MHz) animal scanner (Bruker Biospec) for a range of flip-angle values. The images show a more pronounced spatial selectivity along the coil z-axis with the transverse FO8 coil, as compared to the standard SL. The MR signal profiles along the coil z-axis are compared with the simulated distributions. A good agreement is obtained for both RF coils. To quantify sensitivity, a ROI ($5x5mm^2$) was selected on the central slice of the axial images at about 4 mm from the coil plane and the square of the MRI signal was obtained vs the nominal flip-angle. The results show that in the proximity of the RF coil plane the FO8 coil is about 5 times more sensitive than the SL coil.

Conclusions. Along the coil z-axis the RF field distribution of transverse field RF coils is spatially selective with respect to the SL coil, and it can be useful to optimize the sensitivity in a particular ROI located in close proximity of the surface.

References: [1]Zaniol P etal, Physica Medica 8:87-91(1992). [2]Meyerspeer M etal, MRM 49:620-625(2003).[3]Alfonsetti M etal, MAGMA 18:69-75(2005). [4]Alfonsetti M etal, Meas Sci Technol 17:N53-59(2006).

P30
PROTOTIPO PER NMR DI SUPERFICIE

A. Galante[1], A. Savini[1], M. Alecci[1], P. Sebastiani[2], A. Sotgiu[2], V. Di Miccoli[3]
[1]*Dip. Scienze della Salute, Università dell'Aquila, L'Aquila.*
[2]*Imaging Technology Abruzzo srl, L'Aquila.*
[3]*ITEL Telecomunicazioni, Bari.*

Obiettivo della ricerca è lo sviluppo di uno scanner NMR portatile multipurpouse in configurazione di superficie [1] in grado di effettuare, fino ad una profondità di circa 1 cm, misure di tempi di rilassamento, coefficiente di diffusione ed imaging unidimensionale.
Il magnete presenta una innovativa forma ellittica, è controllato in temperatura e con un peso complessivo di circa 3 kg [2]. Genera un campo parallelo alla sua superficie con una elevata omogeneità lungo una direzione. Nello spazio libero al suo interno ospita il sistema di bobine RF (Tx ed Rx separate con la seconda in configurazione gradiometrica per ridurre il rumore ambientale). Anche la console NMR è una nuova realizzazione e la sua interfaccia di comando è stata adattata per le applicazioni di questo prototipo.

I primi test hanno evidenziato la capacità dell'hardware di eseguire sequenze con tempi di eco pari o superiori a 100 μs. E' stato acquisito il segnale NMR impiegando tipiche sequenze di acquisizione basate sugli echi di spin sia singoli (Hahn-Echo) che multipli (CP, CPMG). Utilizzando le sequenze di saturation recovery ed inversion recovery, è stato misurato il tempo di rilassamento longitudinale della magnetizzazione T_1 di varie sostanze. Con l'impiego della tecnica delle ratio-function, basata su sequenze CMPG multiple con diversi tempi di eco, sono stati misurati il coefficiente di autodiffusione D sfruttando il gradiente intrinseco del campo statico ed il tempo di rilassamento trasversale della magnetizzazione T_2.

Con queste caratteristiche lo scanner può trovare applicazioni in campo medico in indagini non invasive di tessuti superficiali (pelle, nei, tendini) o, più in generale, nel campo della diagnostica non distruttiva su campioni di grandi dimensioni e/o inamovibili.
Gli sviluppi futuri prevedono l'implementazione delle capacità di imaging 1D mediante l'utilizzo di una bobina di gradiente ed, eventualmente, la ricostruzione di immagini 2D a partire da varie acquisizioni unidimensionali.

[1] B. Blumich et al, "Mobile single-sided NMR", Prog. Nucl. Magn. Reson. Spectrosc., vol. 52, pp. 197-269, 2008.
[2] M. Ciarrocchi et al, "Design of an Elliptical Permanent Magnet for Surface MRI", Meas. Sci. & Tech., vol. 20, pp. 017002, 2009.

P31
Gradient design on arbitrary surfaces

A. Galante[1], G. Placidi[1], G. Mancini[2], A. Sotgiu[2]
[1]*Dip. Scienze della salute, Università dell'Aquila, Via Vetoio, L'Aquila*
[2]*Imaging Technology Abruzzo srl, Zona Industriale di Pile, SS17,L'Aquila*

Introduction
A crucial ingredient in MRI hardware is the set of gradient coils. Several parameters define the quality of a gradient coil: uniformity of gradient, efficiency, inductance, resistance, torque and balance. The best coil is the result of an optimization process since the increase of performance of one parameter is usually associated to a decrease of one or more of the others. Other important features are related to the interaction with surrounding elements (eddy currents) and with the sample (noise, peripheral nerve stimulation). The overall performance of a gradient system is a crucial aspect in any MRI apparatus and the design of gradient systems optimized for specific applications is an emerging field [1].
Methods
Several analytical as well as numerical methods have been developed to help in the design of gradient coils starting from the discrete wire approach to the more modern solutions based on current density techniques. The latter include Monte Carlo approaches like simulated annealing and methods based on inverse boundary element methods (IBEM). The advantage of IBEM is the possibility to transform the problem formulation into a linear matrix equation whose solution yields the desired coil design on an almost arbitrarily defined surface [2]. An appropriate weight function can be defined including several constraints like inductance, torque or more complex ones useful to limit eddy currents on magnet cryostat or peripheral nerve stimulation.
Results
We implemented a IBEM code in Matlab that allows the design of gradient coils on arbitrary surfaces. It has been used to design a gradient system for a MEG-MRI prototype in a classical cylindrical surface geometry and for a new system with elliptical geometry.
References
[1] B. Aksel1 et al, "Local planar gradients with order-of-magnitude strength and speed advantage", Magnetic Resonance in Medicine 58, 134–143, 2007
[2] R.A. Lemdiasov. R. Ludwig; "A Stream Function Method For Gradient Coil Design"; Concepts in Magnetic Resonance Part B: Magnetic Resonance Engineering, 26B(1), 67-80, (2005)

P32
Evaluation of a Passive Shimming Method on Multipolar Permanent Magnet

D. Franchi[1], A. Sotgiu[1], F. Mario[1], A. Galante[2]
[1]*ITA srl, Zona Industriale di Pile, SS17, Località Boschetto, 67100, L'Aquila*
[2]*Dip. Scienze della Salute, Università dell'Aquila, Via Vetoio, 67100, L'Aquila, Italy*

Introduction
Magnetic Resonance Imaging requires static magnetic field with a high homogeneity. Even if the main magnet is carefully designed, the experimentally determined field homogeneity is generally much lower than the computed value. Therefore, a magnetic field fine correction (shimming) is necessary to bring the magnetic field homogeneity to an acceptable level (typically few PPMs). Two mains approaches exist: passive and active shimming. Active shimming uses dedicated coils while passive shimming uses metal (iron) pieces or small permanent magnets placed inside the magnet in order to correct the magnetic field within a predefined volume of interest (VOI). Passive shimming has advantage that no power is required, is a low cost solution and this makes it a good solution for low field permanent magnet scanners.
Methods
Passive shimming is usually performed using a method based on linear programming [1]. It was originally proposed for the determination of the number of small iron shimming elements to be placed in several fixed positions inside a superconducting solenoidal magnets. The method can be easily generalized to the case of small permanent magnets shimming elements. In case of permanent magnet scanners, where iron is usually present on the magnet pole, a problem arises, due to non linear effects, when the shimming elements have to be placed directly on the pole surfaces. We address this problem in a numerical simulation of the shimming procedure for a new multipolar permanent magnet design comparing the best attainable performances using iron or permanent magnet shimming pieces.
References:
[1] B. Dorri, M.E. Vermilyea, W.E. Toffolo; Passive shimming of MR magnets: algorithm, hardware, and results; IEEE transaction on Applied Superconductivity, Vol. 3, Issue 1, pp. 254-257, 1993.

P33
SEGMENTAZIONE SEMIAUTOMATICA PER LA MISURA DEL VOLUME DEL GRASSO ORBITALE

M. Comerci[1], R. Senese[2], D. Cardone[3], P. Bonavolontà[3], D. Strianese[3], A. Elefante[4], B. Alfano[1], A. Brunetti[2]
[1]*Istituto di Biostrutture e Bioimmagini, Consiglio Nazionale delle Ricerche, Napoli*
[2]*Dip. di Scienze Biomorfologiche e Funzionali, Università Federico II, Napoli*
[3]*Dip. di Scienze Oftalmologiche, Università Federico II, Napoli*
[4]*Dip. di Scienze Neurologiche, Università Federico II, Napoli*

Introduzione: la segmentazione può essere utile per determinare l'estensione o la progressione di una patologia. In letteratura sono riportati pochi metodi per segmentare i tessuti orbitali in acquisizioni TC o RM. Scopo di questo lavoro è presentare un metodo semiautomatico per la segmentazione di tali tessuti, applicabile al monitoraggio dei pazienti con morbo di Graves, e valutarne la ripetibilità tramite uno studio di simulazione su un fantoccio digitale da noi sviluppato. Materiali e metodi: sono state utilizzate 5 simulazioni in differenti orientazioni di studi RM cerebrali di un fantoccio digitale descritto in un precedente lavoro[1]. I tessuti intra- ed extra-cranici sono stati segmentati con l'algoritmo descritto in Alfano et al [2]. Le ROI 3-D sono state definite strato per strato sulle due orbite per le 5 simulazioni da due operatori di differente esperienza, per un totale di 20 ROI. Esse sono state utilizzate per selezionare il solo grasso intraorbitale. E' stato sviluppato un software che seleziona i voxel interni alla ROI 3-D presegmentati come grasso e divide automaticamente le orbite nei 4 quadranti superiore, inferiore, laterale e mediale. Per ognuno dei quadranti e per tutta l'orbita sono stati calcolati media e SD del volume di grasso. Risultati: il volume di grasso medio misurato per le due orbite è stato rispettivamente di 11,87±0,49 e 11,10±0,32 cc. I valori per i quadranti superiore, inferiore, laterale e mediale sono stati rispettivamente 3,39±0,17; 4,41±0,39; 1,94±0,05; 2,13±0,06 per l'orbita sinistra e 3,03±0,16; 2,37±0,02; 1,83±0,09; 2,37±0,02 per l'orbita destra. Il coefficiente di variazione medio per l'intera orbita è risultato del 3,3% e per i singoli quadranti del 4,3%. Discussione e conclusioni: dai risultati si evince che la variabilità del metodo è soddisfacentemente bassa, e può consentire il monitoraggio delle patologie che modificano la quantità di grasso orbitale. La bassa variabilità potrebbe dipendere dal fatto che l'unica operazione manuale consiste nella separazione del grasso orbitale da quello extraorbitale, che risultano contigui in zone molto limitate. Referenze: 1) Alfano B et al. Med. Image Anal. (2011), doi:10.1016/j.media.2011.01.004 2) Alfano B et al. Magn Reson Med 37 (1) 84-93, 1997

P34
A FULLY AUTOMATIC LESION DETECTION METHOD FOR DCE-MRI FAT-SUPPRESSED BREAST IMAGES

A. Vignati[1], V. Giannini[2], M. De Luca[1], L. Morra[3], A. Bert[3], L. Martincich[4], D. Regge[1]
[1]*Fondazione Piemontese per l'Oncologia, Candiolo, Italy;*
[2]*Politecnico of Turin, Department of Electronics, Turin, Italy;*
[3]*im3D SpA, Turin, Italy;*
[4]*IRCC, Institute for Cancer Research and Treatment, Radiology Dept., Candiolo, Italy.*

INTRODUCTION
Dynamic Contrast Enhanced MRI (DCE-MRI) has today a well-established role, complementary to routine imaging techniques for breast cancer diagnosis such as mammography. Despite its undoubted clinical advantages, DCE-MRI data analysis is time-consuming and Computer Aided Diagnosis (CAD) systems are required to help radiologists. We here present the preliminary results of a fully automatic CAD system, capable of dealing with fat suppression image acquisition sequences, which represents a challenge for image processing algorithms due to the low SNR.
METHODS
The image processing pipeline includes: a) anatomical segmentation to select the breast area. In this step an atlas, representing the main anatomical structures, is deformed, by applying rigid and elastic deformation, in order to match it with the unenhanced image; b) a rigid and elastic registration to correct global and local misalignment between the unenhanced image and all the enhanced ones; c) lesion detection to automatically extract the enhancement areas from the normalized mean intensity projection image. The normalization is obtained dividing by the contrast uptake of mammary arteries, which is related to the actual amount of contrast agent delivered to breast lesions. d) a false positive reduction step.
Data. DCE-MRI studies were acquired with a GE unit (fat-suppressed 3D axial VIBRANT® sequence). Testing set was composed by 20 studies with 38 lesions (6 benign and 32 malignant; median diameter 19 mm, range 5-62 mm, 15/38 $\leq$10 mm). Each study was reviewed by an expert radiologist who labeled each segmentation finding as either a true positive or mammary/extramammary false prompts (FPs). Detection rate was calculated for benign and malignant lesions, sensitivity for malignant lesions only.
RESULTS AND DISCUSSION
Detection rate was 74% (28/38, 95% IC 58-85%), while sensitivity was 81% (26/32, 95% IC 65-91%); the median number of mammary FPs per breast was 4. The automatic system here presented has shown promising results in detection of breast lesions on DCE-MRI, and it could be employed in clinical practice to reduce reading time and inter-observer interpretation variability. Such a system could be also used as a second reader in breast DCE-MRI screening programs.

P35
Sviluppo di un CAD basato sull'analisi multi-parametrica delle acquisizioni DCE-MRI per l'individuazione dei tumori alla prostata

S. Mazzetti[1], M. De Luca[2], C. Bracco[1], A. Vignati[2], V. Giannini[2], M. Stasi[1], F. Russo[2], E. Armando[2], D. Regge[2]
[1]*Fisica Sanitaria, Istituto per la Ricerca e la Cura del Cancro di Candiolo*
[2]*Radiologia, Istituto per la Ricerca e la Cura del Cancro di Candiolo*

Obiettivo del lavoro è sviluppare un CAD-RM basato sulle immagini di contrast enhancement (DCE) per costruire mappe di probabilità e definire le regioni della prostata con caratteristiche maligne.
Lo studio comprende 10 pazienti con carcinoma prostatico confermato da biopsia e sottoposti all'imaging
RM morfologico e funzionale. Le sequenze con mezzo di contrasto includono 28 acquisizioni, ognuna con durata di 13 secondi. Per ogni caso un radiologo esperto ha definito una regione d'interesse (ROI) maligna e una corrispondente ROI sana sulla base dei reperti patologici.
L'analisi delle curve dinamiche è stata condotta pixel per pixel, applicando 4 modelli di quantificazione: Toft, Weibull, le Universalità Fenomenologiche e model-free. I parametri estratti sono stati suddivisi in due classi, a seconda che appartenessero a una ROI sana (5168 curve) oppure maligna (5796 curve). A ogni pixel è stato quindi associato un vettore contenente 13 parametri, successivamente ridotti a 6 sulla base dei coefficienti di correlazione e dell'analisi ROC, in modo da selezionare i parametri che permettessero di ottenere la migliore separazione fra curve benigne/maligne.
I dati così ottenuti sono stati impiegati in un classificatore bayesiano, per stimare la probabilità di malignità di un dato pixel. Infine, per valutare le performance dell'algoritmo, è stato applicato il metodo "leave-one-out".
I risultati mostrano che il classificatore basato sull'analisi multiparametrica raggiunge un'area sotto la curva ROC pari a 0,899 (95%CI:0,893-0,905), con sensibilità e specificità dell'82,4% e 82,1% rispettivamente. I dati risultano migliori rispetto all'utilizzo dei singoli modelli applicati separatamente: il solo modello di Tofts raggiunge un'area di 0,879, quello di Weibull 0.896.
In conclusione il CAD-MR mostra buone performance nel discriminare le regioni sane da quelle maligne e raggiunge un'area sotto la curva ROC maggiore rispetto ai modelli tradizionali, migliorando la capacità di detection delle lesioni.
Bibliografia:
Langer DL, et al. "Prostate cancer detection with multi-parametric MRI: logistic regression analysis of quantitative T2, diffusion-weighted imaging, and dynamic contrast-enhanced MRI". J Magn Reson Imaging 30, 327-334 (2009)

P36

DIFFUSION-WEIGHTED MAGNETIC RESONANCE IMAGING AND APPARENT DIFFUSION COEFFICIENT ANALYSIS IN AUTOSOMAL DOMINANT POLYCYSTIC KIDNEY DISEASE PATIENTS

M.C. Carminati[1], C. Corsi[2], R. Mignani[3], E. Cavagna[4], L. Cagnoli[3], G. Santucci[4], S. Severi[2], E.G. Caiani[1]

[1]*Politecnico di Milano, Dipartimento di Bioingegneria*

[2]*Universitá degli Studi di Bologna, DEIS, Cesena*

[3]*Ospedale degli Infermi, Unitá di Nefrologia e Dialisi, Rimini*

[4]*Ospedale degli Infermi, Unitá di Radiologia, Rimini*

Purpose. Autosomal dominant polycystic kidney disease (ADPKD) is a common genetic disorder characterized by massive development of cystic tissue in kidneys, causing progressive loss of functionality. We propose new indexes, computed from diffusion weighted MR images (DW-MR), to discriminate between normal and polycycstic kidney.

Methods. DW-MR images (1.5 T) of 25 patients (11 males, age range 24-69) with b=0, 500, 700 and 900 s/mm^2 (slice thickness 9 mm) were acquired without contrast media, and apparent diffusion coefficient (ADC) maps were calculated.
The population was divided in 3 sub-groups: A) lack of cystic tissue, B) cystic tissue and normal renal function, C) cystic tissue and chronic renal failure (CKD stage 3-5). Renal function was evaluated as serum creatinine <1.2 mg/dl or e-GFR with Cockroft-Gault formule >90 ml/min.

The b=0 s/mm^2 DW images were segmented through semiautomatic analysis based on a variational formulation of the classical level set method in order to define kidneys boundaries in each slice. The contours were then superimposed on corresponding ADC maps, and the statistical distribution of ADC values inside kidneys was studied. In particular, mean, median, standard deviation and interquartile range of the ADC value distribution were computed. To assist the analysis of ADC maps a Graphical User Interface in Matlab was developed, which allows for instant viewing of calculated parameters.
Results. Statistically significant differences ($p<0.05$) were found in the proposed ADC indexes for all b-values, highlighting higher measures for populations B and C compared with population A, underlining higher ADC values and a greater ADC variability in kidneys with cystic tissue. Regression analysis between the ADC indexes and renal function parameters did not show a clear correlation.
Conclusions. The analysis of ADC maps, using the proposed statistical indexes, is automated and does not require tracing of cysts contours inside the parenchyma. Since the kidney is strongly characterized by fluid transport phenomena and MR is currently the only way to observe diffusion in vivo non-invasively, this analysis could be clinically useful to detect potential changes in diffusion in follow-up evaluation of ADPKD patients.

P37

ANNULOPLASTY RING ASSESSMENT FOR THE TREATMENT OF ISCHEMIC MITRAL REGURGITATION BY PATIENT-SPECIFIC COMPUTATIONAL ANALYSIS FROM MRI IMAGES

M. Stevanella [1], C. Conti[1], E. Votta[1], F. Maffessanti[1], C. Carminati[1], M. Sotaquira[1], A. Roghi[2], O. Parodi[3], A. Redaelli[1], E. Caiani[1]

[1]*Politecnico di Milano, Dip. di Bioingegneria, Milan, Italy*

[2] *Niguarda Ca'Granda Hospital, CMR Unit, Noninvasive Cardiac Imaging Laboratories, Milan, Italy*

[3]*Institute of Clinical Physiology of CNR, Pisa, Italy*

Purpose. Ischemic mitral regurgitation (IMR) is usually treated through restrictive annuloplasty via rigid rings, which constrain the annular shape, or flexible rings, which preserve annular dynamics. The choice between these options is still debated and several methodologies have been adopted to identify the best solution. Among those, finite element (FE) models have provided useful insight, but past models suffered of simplifications that limited and biased the conclusions. We aimed at analyzing the effects of ring's flexibility in restrictive annuloplasty through mitral valve (MV) patient-specific realistic FE models based on cardiac magnetic resonance (MR) imaging, thus overcoming previous limitations. Methods. 18 evenly rotated long-axis planes (one every 10°) along the left ventricular long-axis were acquired in 7 ischemic patients (55 time-frames/ cardiac cycle). In each plane during systole, MV annulus, leaflets, and papillary muscles were manually identified using custom software, and automatically reconstructed in the 3-D space to be used as input to the MV FE models. A physiological transvalvular pressure load was applied to the leaflets to simulate valve closure up to peak systole. For each patient, three conditions were simulated: (i) pre-operative, (ii) after insertion of a ring with closed profile and regionally varying bending stiffness (CV ring), and (iii) after implanting a rigid ring with partially open profile at saddle-horn (RO ring). Results. The RO ring restored MV competence in 7/7 patients resulting in higher coaptation length, while CV ring succeeded only in 5/7. Conversely, annular dynamics was lost with the RO ring, while CV ring partially preserved it. Both rings significantly reduced leaflets stresses and tensions on chordae tendineae and papillary muscles. Conclusions. While RO rings seem resulting in a good performance, flexible CV rings could not always guarantee to counterbalance the effect of leaflets tethering associated to IMR. Moreover, despite their flexibility, annular dynamics was not completely preserved. Our patient-specific FE approach could provide new insight in optimizing tuning of local stiffness, thus potentially improving the performance of new ring design, as well as help in surgery planning.

P38

THREE-DIMENSIONAL ASSESSMENT OF TRICUSPID ANNULUS MORPHOLOGY AND DYNAMICS FROM MAGNETIC RESONANCE IMAGES

F. Maffessanti[1], P. Gripari[2], G. Pontone[2], D. Andreini[2], G. Tamborini[2], M.C. Carminati[1], M. Sotaquirà[1], M. Pepi[2], E.G. Caiani[1]

[1]*Dip. Ingegneria Biomedica, Politecnico di Millano*

[2]*Centro Cardiologico Monzino IRCCS, Milano*

Despite standard cardiac magnetic resonance (CMR) imaging is the reference technique for the evaluation of RV volume and function, its use for assessment of the tricuspid valve morphology is still minimal, due to the intrinsic inaccuracy in evaluating a complex three-dimensional structure on the basis of 2D images. We proposed a novel way to study tricuspid annulus (TA) morphology and dynamics, by means of multiple CMR long-axis cine images, followed by 3D reconstruction. Our aim was to test the feasibility of this approach in 8 healthy subjects (age 30±10 years).

CMR imaging (GE Signa, 1.5 T) of 18 long-axis planes, evenly rotated of 10° along the axis ideally passing through the center of TA, was performed with a temporal resolution of 20 frames per cardiac cycle (spatial resolution 0.74 mm, slice thickness 6 mm). In each plane, TA points were manually identified by an experienced cardiologist on the end-systolic and end-diastolic images. Then, using custom software, TA points were automatically tracked throughout the cardiac cycle. Finally, a 3D recontruction of TA was automatically obtained in the 3D space for each frame, and from this model several parameters were computed: TA area, height, the two main diameters and the peak systolic excursion (TAPSE) along TA perimeter.

CMR imaging took about 3 minutes, while post-processing 10 minutes, including manual initialization and correction, when necessary. Analysis was feasible in all subjects, allowing not only to quantitatively assess the complex TA dynamics, but also to evidence the different pattern of motion of the TA itself, as depicted by the space-varying TAPSE, increasing from the antero-septal to the posterior region.

Quantitative information on TA function is feasible from CMR imaging when performed in multiple long-axis planes. The proposed approach could constitute the basis for in-depth evaluation of the TA morphology and dynamics, with potential benefits on patient evaluation, surgical planning, and also TA prosthetic design.

P39
FUNCTIONAL CONNECTIVITY MRI (FCMRI) IN PATIENTS WITH BRAIN GLIOMAS

C. Briganti[1], C. Sestieri[1], D. Mantini[1], E. Pravatà[1], A. Tartaro[1], M. Caulo[1]
[1]*Dipartimento di Neuroscienze ed imaging, Università G. D'Annunzio, CHIETI*

Purpose: Functional connectivity MRI (FCMRI) measures the spontaneous and synchronous fluctuations of the BOLD signal between spatially remote brain regions. The present study aims at investigate modifications of FCMRI within the language network in patients with a left hemisphere brain glioma.
Methods and Materials: We retrospectively evaluated FCMRI in 39 right-handed patients with a left hemisphere brain glioma and in 13 healthy subjects. Patients and controls underwent fMRI to lateralize language functions in the cerebral hemispheres. For each subject, whole-brain connectivity maps were created positioning a seeding in the left inferior frontal gyrus (left Broadman 45) using the region with maximum BOLD signal as reference and accounting for any eventual anatomical derangement due to the presence of the tumor. 5 seed regions (right Broadman 45, Superior Temporal Sulcus and Temporo-Parietal Junction of both the hemispheres) were derived from connectivity maps. Cross-correlation matrices of BOLD signals fluctuations were calculated for each subject. Group-level analyses were performed by independent-samples t-tests and ANOVAs. Differences in FC between aphasic and non-aphasic patients were evaluated using a two tailed t-test.
Results: The global FCMRI was significantly reduced in tumor patients compared to controls ($p < 0.001$). FCMRI was significantly reduced within seed regions of the affected hemisphere (left intra-hemispheric FC) and within the right hemisphere (right intra-hemispheric FC) ($p < 0.05$); inter-hemispheric FCMRI was also significantly reduced in patients ($p < 0.001$). Aphasic patients showed a reduced inter-hemispheric FC between the Broca regions.
Conclusion: the presence of a brain tumor in the left hemisphere significantly reduces the FC between language-related brain regions. Modification of the FC is not restricted to the area surrounding the tumor; remote and contralateral areas are also influenced. A decreased pre-operative inter-hemispheric FC is associated with a reduced language performance.

P40
STUDIO RM MORFO-FUNZIONALE DELLA CONNETTIVITA' INTEREMISFERICA NELL'AGENESIA DEL CORPO CALLOSO

M. Ferrajoli[1], M. Quarantelli[2], D. Grossi[3], E. Tedeschi[1], A. Prinster[2], E. Salvatore[4], B. Carotenuto[1], N. De Lucia[3], R. Cogliano[3], A. Brunetti[1]

[1]*Dip. Scienze Biomorfologiche e Funzionali, Università Federico II - Napoli*

[2]*Ist. Biostrutture e Bioimmagini, CNR - Napoli*

[3]*Dip. Psicologia, Seconda Università di Napoli*

[4]*Dip. Scienze Neurologiche, Università "Federico II" - Napoli*

SCOPO Valutare i pattern di connettività morfologica e funzionale tra gli emisferi cerebrali in presenza di agenesia del Corpo Calloso (ACC).
METODOLOGIA Due pazienti con ACC rispettivamente completa e parziale (mancanza dello splenio) e 4 volontari sani sono stati studiati a 3T mediante acquisizione del tensore di diffusione (DTI) per lo studio delle fibre associative di sostanza bianca, e mediante esame RM funzionale resting state (RS-fMRI), per lo studio della connettività interemisferica corticale.
Lo studio DTI (TR/TE 5000/83ms, 40 scansioni contigue, voxel 1.8x1.8.3mm3, 64 direzioni, B-factors: 0 e 1000mm/sec2) è stato analizzato con il software dedicato 3D Slicer (www.slicer.org), per definire la presenza di connessioni omotopiche attraverso il CC.
Lo studio RS-fMRI (TR/TE 2500/40ms, , voxel 3x3x4mm3, 128 time points) è stato analizzato con FMRI Expert Analysis Tool (www.fmrib.ox.ac.uk/fsl) per valutare le fluttuazioni di attività corticale a riposo, evidenziando i cluster di significativa correlazione con le regioni di interesse (ROI) posizionate separatamente nella corteccia sensorimotoria, temporale ed occipitale di destra e di sinistra (Z>2.3, P=0.05 corretto per confronti multipli).
RISULTATI Le aree corticali sensorimotorie e temporali mostravano significativa connettività omotopica funzionale nei soggetti normali e nel caso di ACC parziale, con regolare decorso delle relative fibre associative interemisferiche. Le ROI corticali omotopiche sensorimotorie e temporali nel caso di ACC totale invece non mostravano correlazione funzionale, in assenza di connessioni anatomiche allo studio DTI. Le ROI corticali occipitali in entrambi i casi di ACC risultavano invece funzionalmente correlate, pur in assenza di connessioni anatomiche allo studio DTI.
CONCLUSIONI La connettività funzionale tra le cortecce sensorimotorie e temporali dei 2 emisferi necessita della presenza delle fibre di associazione transcallose, mentre quella tra le cortecce occipitali appare conservata anche in assenza di connessioni interemisferiche dirette.
Bibliografia
Smith S. Human Brain Mapping 2002;17:143
Woolrich MW NeuroImage 2001;14:1370
Worsley KJ. in FMRI: An Introduction to Methods OUP, 2001

P41

PATTERNS OF BRAIN ACTIVITY ASSOCIATED WITH PASSIVE HAND MOVEMENTS IN DIFFERENT FORMS OF MULTIPLE SCLEROSIS

N. Petsas[2], E. Tinelli[1], D. Lenzi[1], F. Tona[1], V. Tomassini[3], E. Raz[1], V. Nucciarelli[1], F. D'Ambrosio[4], C. Pozzilli[1], P. Pantano[1]

[1]*Dept. of Neurology and Psychiatry, Sapienza - University of Rome*

[2]*Dept. of Psychology, Sapienza - University of Rome*

[3]*Oxford Centre for Functional MRI of the Brain (FMRIB) and Clinical Neurology, Nuffield Dept. of Clinical Neurosciences, Univ. of Oxford, Oxford, UK*

[4]*Dept. of Sense Organs, Sapienza - University of Rome*

Several studies have demonstrated altered patterns of brain fMRI activation and deactivation with active hand movement in patients with Multiple Sclerosis (MS). These patterns are thought to represent compensatory mechanisms to maintain function, in spite of widespread tissue damage*. Little is known, however, about brain fMRI patterns of activation and deactivation during passive hand movements in MS. Passive tasks are not affected by individual performance and can be used to overcome high levels of disability as well as reduce inter-subject heterogeneity. Purpose of this study was to characterise patterns of activation and deactivation during passive hand movements in patients with MS and increasing levels of disability.

We studied 13 patients with relapsing remitting (RRMS) (7 women, mean±SD age38±10, median EDSS 1.5), 18 patients with secondary progressive (SPMS) (12 women, mean±SD age 49±6; median EDSS 6.0) and 12 healthy controls (CL) (5 women, mean±SD age 40±9) who underwent a fMRI scan at 1.5 Tesla during the execution of passive right hand movements. Data were analysed using SPM8: contrasts Passive > Rest (activation) and Passive < Rest (deactivation) obtained in the three groups of subjects were entered into ANOVA.

During passive hand movements an activation of cortical motor areas (primary sensorimotor, premotor and supplementary motor cortices) was observed, with a progressive and significant extension to the ipsilateral hemisphere in relation to the clinical form (CL < RR < SP). Contralateral sensorimotor activation correlated positively with increasing whole-brain T2 lesion volume (LV). A significant deactivation of the cuneus, precuneus and posterior cingulate cortex was observed in CL with a progressive reduced extension in RR and SP (CL > RR > SP). Bilateral precuneus deactivation correlated negatively with increasing T2 LV.

Passive hand movements in MS patients engage similar patterns of activation as active movements. With the progression of the disease, a progressive increase of activation and a progressive reduction of cortical deactivation occur. These results are likely to reflect brain reorganization in response to damage.

*Pantano ea J Neuroimaging. 2006,16:104-14

P42
Is SWI brain vessel change suitable for enhance functional activation cortical maps?

M. Maieron[1], S. D'Agostini [2], M. Skrap[3], R. Padovani[1], B. Tomasino[4]
[1]*Department of Medical Physics AOU SMM Udine*
[2]*Department of Neuroradiology AOU SMM Udine*
[3]*Department of Neurosurgery AOU SMM Udine*
[4]*IRCCS Medea: Nostra Famiglia, Pasian di Prato, Udine*

Aim
A recent development of fMRI mapping is the use of spontaneous blood oxygen dependent fluctuations to identify functionally related regions (1,2) even without the execution of any task.
BOLD contrast relies on the changes of paramagnetic deoxyhemoglobin concentration, those changes in venous vessels can also be monitored using a high-resolution Susceptibility-Weighed Imaging (SWI)(3,4).
In the study we want to evaluate the possibility to obtain reliable cortical activation maps using functional SWI, conventional BOLD-fMRI and resting-state fMRI.
Materials and Method
MRI data were acquired on a 3T Achiva Philips system from four healthy subjects. For each subject 5 sequences were acquired: a resting-state (rs_fMRI) run was acquired while subjects were instructed just to lay in the scanner; two SWI gradient echo sequences were performed: one performing a finger tapping task and the second no task performing; a BOLD-EPI fMRI run while the subject was instructed to perform a finger tapping in a block design paradigm (15s-15s). The SWI acquisitions cover the same brain portion acquired with fMRI.
The fMRI and rs_fMRI runs were analyzed using FSL software (FEAT, MELODIC). The SWI post-processing phase filtering was performed on the Philips workstation.
Results and Discussion:
The cortical activation map assessed by analysing task-performing run and the cortical activation map related to motor network identified from resting-state run show a strong similarity with 85% of overlapping pixels. In the subtracted SWI image it was possible to identify changes in oxygenation vessel level. In a comparison between fMRI maps and the SWI image, small venous vessels could be identified close to the areas of activation detected by conventional fMRI showing clear coincidences of blood vessel changes with cortical activations.
Conclusions:
SWI technique allows a direct visualization of the BOLD-effect at high spatial resolution. In combination with conventional fMRI, this technique may help to separate the contribution of brain parenchyma and venous vessels
[1] Raichle ME, et at (2007), Neuroimage 37:1083–90.
[2] Raichle ME, et al (2001), PNAS 98:676–82.
[3] Haacke EM (2003), Proc. ISMRM., pp1731
[4] Haacke EM (2009), AJN, vol 30, no. 1, pp. 19-30

P43

AN INVESTIGATION OF IRON DEPOSITION IN PARKINSON'S DISEASE USING QUANTITATIVE T2* MAPPING: AN IN VIVO 3T MRI STUDY

A. Sciarra[1], A. Oros-Peusquens[2], K. Reetz[2], M. Alecci[1], N.J. Shah[2]

[1] *Università dell'Aquila, Dipartimento di Scienze della Salute, L'Aquila, Italy*

[2]*Inst. of Neuroscience and Medicine, Research Centre, Jülich, Fac. of Medicine, Dip. of Neurology, RWTH Aachen University, Germany*

Introduction

In the past years, an increasing number of studies were focused on the quanti#cation of brain iron metabolism in di#erent neurodegenerative disorders. In Parkinson's Disease (PD) iron deposition is considered a useful clinical marker [1,2]. Quantitative MRI o#ers a range of promising methods for the indirect iron content characterization in vivo.

Materials and methods.

Subjects: 10 patients with PD and 10 age-matched healthy controls.

Data acquisition: Aachen University Hospital, Germany, 3T scanner (Siemens Trio). Sequences: 4 scans with 3D MP-RAGE (T1-w) [3] for anatomical characterization and 3 scans with 3D GRE [3] with a read-out train of 12 echoes for T2* mapping. All scans had 1mm^3 resolution.

Data processing: for each subject, all scans were coregistered and averaged separately, and the resulting average volumes were coregistered to each other. 11 anatomical structures were manually delineated on the T1-w average volume, separately for the left and right hemisphere. An exponential #t was performed on the multiple-echo 3D GRE data.

Iron quanti#cation: the putative iron content for each of the 11 anatomical structures was calculated based on the compilation by Hallgren and Sourander[4].

Results and Discussion

The R2* values for the healthy volunteers showed a good linear dependence on the putative [Fe] content in the regions we have investigated. The T2* shortening in Parkinson's patients might thus be related to an increase in [Fe]. Considering the limitations of the evaluation method and the limited number of subjects that make up our sample, this study is to be considered preliminary. The segmentation process shows variability especially for small structures. Imaging at high magnetic #elds would be very bene#cial for such studies by improving SNR and/or resolution and contrast, but this is not yet applicable in standard clinical settings. However, the present methods coupled with the use of other methodologies, such as susceptibility imaging, should improve the characterization of iron deposition in PD.

References

[1]Haacke,MRI 23(2005)1-25, [2]Ke,Progr in Neurobiol. 83(2007)149-173,[3]Bernstein,Handbook of MRI Pulse Sequences. Els.Acad.Press,2004,[4]Hallgren,J.of NeurocheM,1958;Vol.3:41-51.

P44

GENETICALLY DEFINED HEREDITARY SPASTIC PARAPLEGIA: MR BRAIN MORPHOLOGY AT 3T WITH AN HIGH RESOLUTION 32 CHANNELS COIL

E. Brighina[1], M. Re[2], F. Arrigoni[1], S. Bonato[1], M.G. D'Angelo[1], A.C. Turconi[1], G. Reni[1], N. Bresolin[1], F. Triulzi[3]

[1]*IRCCS Eugenio Medea, Bosisio Parini (LC)*

[2]*IRCCS Eugenio Medea, Bosisio Parini (LC); Dip Bioingegneria, Politecnico di Milano (MI)*

[3]*IRCCS Eugenio Medea, Bosisio Parini (LC); U.O. Neuroradiologia, Ospedale dei Bambini Vittore Buzzi (MI)*

INTRODUCTION:Hereditary spastic paraplegia (HSP) is a group of inherited disorders characterized by progressive spasticity and weakness of the lower limbs. The diagnosis is primarily made by neurological examination and testing to rule out other disorders. Several genetic mutations at different loci (Spastic Paraplegia Gene SPG) have been identified up to now which underlie some of the forms of HSP. Brain and spine MR conventional study can be negative or exhibit corpus callosum hypoplasia and white matter abnormalities[1,2].

MATERIALS AND METHODS:We analysed 15 patients aged between 6 and 63 years, with a clinical history and a neurological examination suggestive of HSP. 3 patients were presenting with dominant trasmission form (SPG3A and SPG4) and the remaining with recessive form (SPG11, SPG7, SPG15, SPG5). All patients were clinically, neurophysiologically and neuropsychologically characterized and underwent functional evaluations (gait analysis, Gross Motor Function Measure, Functional Independence Measure). MR studies were carried out with a 3T (Philips) and a 32 channels head coil. For each patient MR protocol was: 3D T1 TFE (voxel size 1x1x1 mm), 3D FLAIR TSE (voxel size 1.2x1.2x1.2 mm), axial and coronal 2D T2 TSE (voxel size 3x0.4x0.5 mm), axial 2D FLAIR (voxel size 3x0.7x0.7 mm).

RESULTS AND DISCUSSION:A hyperintesity on 3D FLAIR at the level of superior cerebellar peduncles was detected in 8 patients. Increased hypointensity on T2 WI and FLAIR of lentiform nuclei was found in all patients, in 10 patients increase hypointensity was found in dentate nuclei as well. A different degree of cerebellar hypoplasia was found in 8 patients. Patients with SPG11 showed in all cases a diffuse alteration of subcortical white matter whereas in only 2 cases exhibited a corpus callosum hypoplasia.

CONCLUSIONS:This is, to our knowledge, the first 3 Tesla brain MR study in group of patients with HSP. Preliminary morphological analysis confirms the data previously observed with 1.5T studies. The 3T studies allow also to detect an abnormal decrease of T2 signal not only in lentiform nuclei but also in cerebellar dentate nuclei, as well as the presence of a hyperintense signal on superior cerebellar peduncles on 3D FLAIR images.

[1]Stevanin,Brain 2008[2]França,Mov Disord 2007

P45
Distribution of diffusivity changes in subcortical deep gray matter in prion diseases

D.N. Manners[3], R. Lodi[1], E. Malucelli[1], C. Testa[1], G. Rizzo[1], S. Capellari[2], G. Pierangeli[2], P. Cortelli[2], P. Montagna[2], B. Barbiroli[1], C. Tonon[1], P. Parchi[2]

[1]*MR Spectroscopy Unit, Dept of Internal Medicine, Aging and Nephrology. U Bologna*

[2]*Dept of Neurological Sciences. U Bologna*

[3]*Dept of Histology, Embryology and Applied Biol. U Bologna*

Objectives. To assess the relationship between mean diffusivity (MD) changes and prion disease subtypes in deep gray matter structures (DGM). The variable pattern of increased brain signal intensity on DWI in different subtypes may be linked to the distribution of spongiosis resulting in restricted diffusivity

Methods.

9 patients with probable/possible prion disease and 12 age-matched controls were recruited. CSF samples were analyzed for the presence of 14-3-3 protein, and a genetic study of the human prion protein gene was carried out in all patients. A post-mortem examination was performed in 5 patients.

MR studies were performed using a 1.5T clinical scanner. T1-weighted FSE and T2-weighted FLAIR axial images and DTI SE-EPI images encoded in 6 directions were acquired at 4 mm slice spacing.

Data analysis.

Diffusivity and FA maps were generated using FMRIB/FSL tools. Automatic segmentation of sub-cortical grey matter structures was performed using a completely operator-independent method. Group differences in MD for each ROI were determined by the Student t test for unpaired data. Differences in variance between patients and controls were tested using the variance ratio F-test.

Results.

A definite diagnosis of either sporadic CJD (sCJD) or genetic prion disease was made in 6 patientsincluding 4 with sCJD (2 VV2, 1 MV2, and 1 MM1 patient), one with Familial Fatal Insomnia (FFI) and one with Gerstmann-Sträussler-Scheinker (GSS). In three patients without post-mortem examination all were positive for 14-3-3 protein, and final diagnosis was of probable CJD.

MD values were significantly reduced only in the caudate and striatum. However, group variance was statistically different between patients and controls in the basal ganglia and thalamus. Increased variance is associated with different sub-types of prion diseases. FFI and GSS patients tended to have MD values above the normal range in DGM while all the sCJD subtypes showed reduced MD values in the caudate. Reduced MD values in the thalamus were mostly associated with the homozygous VV subtype.

Conclusions.

MD values were increased in subtypes where there is little or no spongiosis, but variably reduced in basal ganglia of different sCJD sub-types all characterized by the presence of spongiosis.

P46
Secondary involvement of optic radiation in Leber's hereditary optic neuropathy

E. Malucelli[1], G. Rizzo[1], D. Manners[1], C. Tonon [1], C. Testa[1], M.L. Valentino[2], C. La Morgia [2], P. Barboni[3], V. Carelli[2], R. Lodi[1]
[1]*Unità di spettroscopia RM, Dip. di Medicina Interna, dell'Invecchiamento e Malattie Nefrologiche, Università di Bologna*
[2]*Dip. di Scienze Neurologiche, Università di Bologna*
[3]*Studio Oculistico d'Azeglio, Bologna*

Introduction
Leber's hereditary optic neuropathy (LHON) is a mitochondrial disease characterized by the peculiar preferential involvement of the small axons serving central vision; these fibers form the papillomacular bundle [Carelli V 2004]. Mitochondrial optic neuropathies may also occur in more complex syndromes, in which a DWI study has demonstrated an involvement of the optic radiation (OR) [Fortuna F 2009]. Recently a voxel-based morphometry (VBM) study pointed toward OR impairment in LHON patients [Barcella V 2010]. Aim of study was to investigate OR in LHON patients and healthy carriers using DWI.
Methods
22 LHON patients (17 M, age 33±11) and 22 healthy controls (16 M, age 37±17) and 11 healthy carriers (5 M, age 45±15) were studied using axial DWI (b-values=300, 600 and 900 s/mm^2). ROIs were determined by segmentation of the left and right ORs on the T2-weighted EPI images and were copied on the ADC maps. One-way ANOVA followed by post-hoc LSD test was used for comparison between groups. We investigate the effect of gender, mutation, age at onset, disease duration, history of recovery of visual acuity on DWI data using a multiple regression.
Results Right- and left-side ADC values were not statistically different for OR ROIs and are reported as mean. ANOVA detected a group difference ($P<0.01$) and post hoc testing revealed an increase in OR ADC of LHON patients compared with both healthy carriers ($P<0.05$) and controls ($P<0.01$). Healthy carriers and controls did not differ. In LHON patients multiple regression analysis led to a significant model including only history of recovery of visual acuity (negative correlation) and disease duration (positive correlation)($P<0.05$).
Discussion
Our results confirm retrochiasmatic involvement in LHON patients. This alteration is evident only in a part of the affected subjects and not in healthy carriers. Furthermore, lack of recovery of visual acuity and longer disease duration are associated with the increase of ADC in ORs of LHON patients. We can conclude that ADC changes regard only the patients with longer disease duration and absence of recovery of visual acuity. Thus they may represent secondary alterations, reflecting a downstream effect rather than a primary effect of the mitochondrial dysfunction.

P47

EFFECT OF IRON BURDEN ON HEPATIC APPARENT DIFFUSION COEFFICIENT (ADC) IN PATIENTS WITH THALASSEMIA MAJOR

G. Restaino[1], A. Caulo[2], S. Roiati[2], M. Missere[1], M. Occhionero[1], S. Costanzo[3], M. Ciuffreda[1], A. Pepe[4], G. Sallustio[1]

[1]*Dip. Immagini, U.O.C. di Radiodiagnostica, Università Cattolica del Sacro Cuore, Campobasso, ITALY*

[2]*Dip. Bioimmagini e Scienze Radiologiche, Università Cattolica del Sacro Cuore, Roma, ITALY*

[3]*Laboratory of Genetic and Environmental Epidemiology, Università Cattolica del Sacro Cuore, Campobasso, ITALY*

[4]*Magnetic Resonance Laboratory, Fondazione "G. Monasterio", IFC-CNR, Pisa, ITALY*

Purpose

Hepatic ADC is commonly used for characterization of liver disease. DWI-EPI sequence is very sensitive to susceptivity effects. Aim of the present study was to assess the effect of hepatic iron burden on ADC values of liver measured with 3 different b-values (200,600 and 1000)

Purpose

Hepatic ADC is commonly used for characterization of liver disease. DWI-EPI sequence is very sensitive to susceptivity effects. Aim of the present study was to assess the effect of hepatic iron burden on ADC values of liver measured with 3 different b-values (200,600 and 1000)

Material and Methods

53 patients with thalassemia major (35,2 y/o; 27 F) underwent liver MRI with 1.5T scanner. Liver T2*, as expression of iron overload, was measured with multiecho GRE sequence and with a dedicated software (HyppoMIOT,ifc-CNR,Pisa-Italy). ADC was measured in the same hepatic region with EPI-DWI sequence with 3 different b-values (200,600 and 1000) and a dedicated software (Functool2,ADW 4.2,GEMS). The T2* and ADC values were compared with Pearson's test.

Results

Liver iron overload resulted absent in 9 patients, borderline in 24, slight in 8, moderate in 11, and severe in 1. ADC measured with b=200 showed no significant correlation to T2* ($p=0.44$) and weak correlation to logT2* ($p=0.0258$;$r=0.31$). ADC with b=600 showed significant linear correlation to T2* and to logT2* ($p<0.0001$; $r=0.60$ and, respectively, $p<0.0001$;$r=0.76$). ADC with b=1000 showed the strongest correlation to T2* ($p<0.0001$;$r=0.83$) and even stronger correlation to logT2* ($p<0.0001$;$r=0.91$).

Conclusion

Iron overload has strong influence on hepatic ADC values measured with b=600 and b=1000, with significant linear correlation between T2* and ADC values. This effect must be considered when measuring hepatic ADC in patients with known or suspected iron overload.

Taouli B, Koh DM. Diffusion-weighted MR imaging of the liver. Radiology. 2010 Jan;254(1):47-66.

P48
HEPATOCELLULAR CARCINOMA IN CIRRHOTIC PATIENTS:PROSPECTIVE COMPARISON OF US; MDCT AND MR IMAGING

M. Di Martino[1], R. Di Miscio[1], D. Geiger[1], G. De Filippis[1], V. Forte[1], S. Santinelli[1], C. Catalano[1], R. Passariello[1]
[1]*Dip. Scienze Radiologiche, Oncologiche ed Anatomo Patologiche "Sapienza" - Università di Roma*

PURPOSE: To intraindividually evaluate the performance of Ultrasound (US), Multidetector CT (MDCT) and MR Imaging with gadobenate dimeglumine in the detection and characterization of HCC in a surveillance study population.
METHOD and MATERIALS: One-hundred and fourty consecutive cirrhotic patients with 163 HCC nodules underwent US (Sonoline Antares, Siemens) MRI at 1.5T (Avanto, Siemens) and 64-slice CT (Sensation 64, Siemens) at a mean interval of 14 days (range, 10–20 days). Imaging results were correlated with histopathologic findings and imaging follow-up. MR acquisitions comprised unenhanced breath-hold T2W images and volumetric 3D Gd-BOPTA-enhanced (0.1 mmol/kg; MultiHance, Bracco®) T1W GRE images acquired at 25s, 60s, 180s (dynamic phase) and 90 min (hepatobiliary phase). 64-slice CT was performed with 0.6 x 64 mm collimation, 3-mm section thickness, 250 mAs, 120 kVp. A triple-phase protocol was started 18s, 60s and 180s after reaching a trigger threshold of 150 HU above baseline CT number of the aorta. Three sets of images were analyzed in consensus by two radiologists expert on liver imaging. Diagnostic accuracy was evaluated using the jack-knife alternative-free response receiver operating characteristic (JAFROC) method. Sensitivity, Specificity, with corresponding 95% confidence intervals were determined. Informed consent and ethical approval were obtained.
RESULTS: MR Imaging with Gd-BOPTA (0.89) reported the significantly higher diagnostic accuracy ; MDCT (0,80) was also significantly better than and US (0.71). On a lesion-by-lesion basis, the mean sensitivity of Gd-BOPTA MRI (87%) was significantly higher than that of MDCT (70%) and US (71%) (P<.0001). The mean specificity (90%) of Gd-BOPTA MRI was significantly higher than that of MDCT (87%) and US (58%) (P<.001).
CONCLUSION: Gd-BOPTA-enhanced MRI is significantly more accurate, sensitive and specific than MDCT and US for the diagnosis of HCC in patients with cirrhosis

P49

ADDED VALUE OF DIFFUSION MR-IMAGING IN THE DETECTION OF FOCAL LIVER LESIONS IN CIRRHOTIC PATIENT

M. Di Martino[1], C. Catalano[1], R. Passariello[1], G. De Filippis[1], R. Di Miscio[1], M.L. Mennini[1], M. Del Monte[1], V. Lombardo[1]

[1]*Dip. Scienze Radiologiche, Oncologiche ed Anatomo Patologiche "Sapienza" - Università di Roma*

PURPOSE: To evaluate the usefulness of the diffusion-weighted sequence for the detection and characterization of focal liver lesions in patients with cirrhosis.

.METHOD AND MATERIALS: Fifty cirrhotic patients with 47 HCCs underwent MR Imaging at 1.5 T. MR acquisitions comprised unenhanced breath-hold T2W images and volumetric 3D Gd-BOPTA-enhanced (0.1 mmol/kg; MultiHance®, Bracco) T1W GRE images acquired at 25s, 60s, 180s (dynamic phase) and 120 min (hepatobiliary phase). DWI was perfomed by a respiratory-triggered SSEPI sequence (TR=2028, TE=76, matrix=192x125, slice thickness 5,00 mm, GRAPPA, b-values 0, 50, 500, 800 sec/mm^2. ADC values were correlated with histopathologic findings and imaging follow-up Quantitative analysis was performed in order to establish significant difference of ADC values of benign lesions compared with HCC. Sensitivity, specificity, Positive Predictive Value (PPV) and diagnostic accuracy of two different protocols with and without DWI-MR Imaging were calculated and compared each other.

RESULTS: A good positive correlation was found between ADC value of liver lesions and reference standard (Spearman's rho=.62) The mean ADC Value of HCC was significantly lower than the mean value of benign focal liver lesions [0,95x10-3mm²/sec ± 0.18 vs ,62x10-3mm²/sec ± 0.54 (P< .0001)]. However, it was not possible to establish a cut-off point due to the wide variability into the benign lesion group. The two MR imaging protocols reported similar results, and the second protocol, that with MR diffusion sequence, reported greater values. Sensitivity (85.1% vs 87.2 %), Specificity (89% vs 92%), Az (0.87 vs 0.89). However no significant differences were found.

CONCLUSION: DWI MR Imaging did not add significant informations for HCC detection and characterization in cirrhotic patients.

P50

DCE-MR in the assessment of tumor response in metastatic renal cell carcinoma patients submitted to antiangiogenic therapy

D. Lisi[1], V. Panebianco[1], R. Iacovelli[2], E. Cortesi[2], V. Buonocore[1], R. Passariello[1]

[1]*Department of Radiological Sciences, Sapienza University of Rome*

[2]*Department of Oncology, Sapienza University of Rome*

PURPOSE

Tumor vascularity is a potential predictor of treatment outcomes in metastatic renal cell carcinoma (mRCC), and contrast enhancement of tumors in MR is correlated significantly with microvessel density. In this study, we investigated if tumor enhancement in MRP is useful for predicting outcomes in patients with mRCC who are receiving antiangiogenic therapy.

METHOD AND MATERIALS

Thirty-one consecutive patients, twenty eight males and three females, with a mean age of 63 years (49-72 years), with mRCC were enrolled. A total of 108 lesions were evaluated but we considered 31 lesions as target lesion (one for each patient). All patients underwent MR examination on 1,5 T scanner (Magnetom Avanto, Siemens, Germany) equipped with double surface phased array (abdomen and pelvis); sequences were acquired before and after i.v. contrast agent administration (10 mL of Gadobutrol, 1M). MR examination was performed before treatment and 4 weeks, 8 weeks and 12 weeks after treatment. Scan protocol included morphologic imaging with TSE T2-weighted sequences on the axial, sagittal and coronal planes dynamic contrast enhanced imaging using 3D FLASH T1-weigthed sequence.

RESULTS

Tumor size was reduced in 23/31 lesions (74 %), was increased in 6/31 lesions (19 %) and was stable in 2/31 lesions (6%).Tumor vascularization was reduced in 25/31 lesions (80%) and other 8 lesions showed marked disease progression.

CONCLUSION

Our data indicate that MR imaging provides a tool for early monitoring of antiangiogenic treatment and can identify lesion reduction in terms of volume and vascularization. MR is a radiation free modality useful in the evaluation of antiangiogenic treatment response in patients with mRCC and influences clinical decision for oncologic patients' management.

P51

DIFFUSION WEIGHTED IMAGING FOR QUANTIFICATION OF HEPATIC IRON DEPOSITION IN PATIENTS WITH THALASSEMIA MAJOR: COMPARISON WITH MULTI-ECHO T2*-WEIGHTED IMAGING

G. Restaino[1], A. Caulo[2], S. Roiati[2], M. Missere[1], M. Occhionero[1], S. Costanzo[3], M. Ciuffreda[1], A. Pepe[4], G. Sallustio[1]

[1]Dip. Immagini, U.O.C. di Radiodiagnostica, Università Cattolica del Sacro Cuore, Campobasso, ITALY

[2]Dip. Bioimmagini e Scienze Radiologiche, Università Cattolica del Sacro Cuore, Roma, ITALY

[3]Laboratory of Genetic and Environmental Epidemiology, Università Cattolica del Sacro Cuore, Campobasso, ITALY

[4]Magnetic Resonance Laboratory, Fondazione "G. Monasterio", IFC-CNR, Pisa, ITALY

Purpose

Multiecho MRI GRE sequence has been fully established in clinical practice for liver iron overload assessment in severe conditions like hemochromatosis and thalassemia major.

Diffusion weighted imaging (DWI) is very sensitive to susceptivity effects from iron deposits.

Purpose of the study is to determine the diagnostic performance of DWI for hepatic iron quantification in patients with thalassemia major.

Material and Methods

53 patients with thalassemia major and 20 healthy volunteers underwent liver MRI with 1.5T scanner.

Liver T2* was assessed with a multiecho GRE sequence. ADC values were measured in the same hepatic region with EPI-DWI sequence with 2 different b-values (600 and 1000).

Subjects were classified, according to liver T2*, in 4 groups: (I)no iron overload, (II)borderline, (III)slight, and (IV)moderate/ severe overload.

ADC values were compared in the groups with ANOVA with Dunnett's adjustment.

Results

All volunteers resulted in iron burden group I; amongst the patients, 9 were in group I, 24 in group II, 8 in group III, and 12 in group IV.

In both DWI acquisitions it was impossible to differentiate the group I from II and the group III from IV because of overlapping of ADC values.

Conversely, there wasn't any overlap between ADC values after grouping I-II groups and III-IV groups.

Conclusion

DWI with b=600 and b=1000 had excellent performance for differentiating subjects with absent or borderline iron overload from subjects with slight to severe iron overload.

1: Taouli B, Koh DM. Diffusion-weighted MR imaging of the liver. Radiology. 2010 Jan;254(1):47-66

P52

COMPARISON BETWEEN MULTISLICE CT AND HIGH FIELD MR IMAGING IN THE DIAGNOSTIC EVALUATION OF PATIENTS WITH PANCREATIC MASSES

M. Fusari[1], S. Maurea[1], M. Imbriaco[1], C. Mollica[2], G. Avitabile[1], L. Camera[1], M. Salvatore[1]

[1]Dipartimento di Scienze Biomorfologiche e Funzionali (DSBMF), Università degli Studi di Napoli Federico II (UNINA),

[2]Istituto di Biostrutture e Bioimmagini (IBB), Consiglio Nazionale delle Ricerche (CNR); Fondazione SDN (IRCCS); Napoli, Italy

To compare multi-slice CT and high-field MR imaging results for the diagnostic evaluation of pancreatic masses, 40 patients with clinical-echographic evidence of pancreatic masses were studied, of which the majority (78%; n=31) had proven pancreatic malignant tumors (ductal adenocarcinoma=24, mucinous cystoadenocarcinoma=6, intraductal papillary mucinous carcinoma=1) while in the remaining 9 patients (22%) benign lesion were demonstrated (chronic pancreatitis=8, syerous cystoadenoma=1). All patients underwent multi-slice CT and MR imaging studies. Imaging results were compared with biopsy (n=33) and/or histology (n=7) data to calculate diagnostic sensitivity, specificity, accuracy, positive and negative predictive value for the correct identification of tumors and the evaluation of potential resectability in case of malignancies. Both for tumor identification and resectability, CT and MR showed comparable diagnostic accuracy with no statistic significant differences; tumor identification CT/MR: accuracy=98/98%, sensitivity=100/100%, specificity=88/88%, positive predictive value (PPV)=97/97%, negative predictive value (NPV)=100/100%; tumor resectability CT/MR: accuracy=94/90%, sensitivity=92/88%, specificity=100/100%, PPV=100/100%, NPV=78/70%. MR imaging represents a valid diagnostic alternative to CT in the evaluation of patients with pancreatic masses, both for the correct identification and characterization of primary lesions and to establish potential surgical resectability in case of malignancies; the high-field intensity of new equipments allows to obtain good MR imaging quality with favorable contrast resolution in the evaluation of the superior abdomen.

Stroszczynski C, Grützmann R, Kittner T CT and MR imaging of pancreatic cancer. Recent results. Cancer Res 177:5-14

P53
CHARACTERIZATION OF DIFFERENT KIDNEY PATHOLOGY THROUGH MR-DTI (DIFFUSION TENSOR IMAGING): RESULTS AND STATISTICAL ANALYSIS

P. Berardi[1], E. Fabbri[1]
[1]*U.O. Fisica Sanitaria, Azienda Ospedaliero-Universitaria di Bologna*

Purpose of this work is to analyze the statistic trend of Apparent-Diffusion-Coefficient (ADC) and Fractional-Anisotropy (FA) values, to characterize diffusion of human kidneys, using ADC maps, DTI tensor and Fyber-Tracking to detect nephritic lesions and in vivo renal functionality evaluation: DTI can provide valuable information about microstructure and physiopathology of tissue. Three different Statistics Analysis have been applied: Roc Curves Analysis, t-test and p-value and ANalysis Of VAriance (ANOVA).
MR images were obtained with 1,5 Tesla MRI GE HDXSIGNA scanner unit, using phased array Head-Neck-Spine 16-channel coil (maximum gradient strength 33 mT/m, slew rate of 120 T/m/s), single-shot spin-echo planar imaging EPI sequence. Different b values (about 400-800 s/mm2) were applied with a diffusion gradient in 6 different directions. The study population consisted of 15 healthy volunteers (Group A age range 20-50y, 10 female 5 male), and 27 patients (Group B age range 30-65y, 14 female 13 male), a heterogeneous group with renal disease, renal artery stenosis, renal insufficiency, renal vascular disease and suspected renal masses.
As results, values obtained from signal intensity matching DTI-T2weighted images in left and right kidney are measured; mean ADC and FA values in cortex and medulla are compared with the creatinine value and GFR values calculated with MDRD method. Population was divided into five Chronic-Kidneys-Disease class, according to the guide NKFK-DOQI, for the nephropathy kidney staging and examined true T-test and ANOVA. In conclusion, the ROC Curves Analysis shows a good correlation between the ADC/FA values and the creatinine values and Glomerular Filtration Rate. The T-test gives discrete P-value for ADC cortex, ADC medulla, FA cortex and FA medulla. All test ANOVA and have given good P-level of significance in particular for ADC cortex and FA medulla. The ROC analysis is invariant to variation in class priors, while the variation due to prior class probabilities is incorporated into ANOVA.

P54

LA SEQUENZA RM CHEMICAL-SHIFT PER LA DIFFERENZIAZIONE TRA LESIONI SURRENALICHE ADENOMATOSE E NON ADENOMATOSE: CONFRONTO CON LE SEQUENZE STANDARD E POST-CONTRASTOGRAFICHE

M. Calabrese[1], S. Maurea[1], M. Imbriaco [1], C. Mollica[1], M. Salvatore[1]

[1]Dipartimento di Scienze Biomorfologiche e Funzionali (DSBMF), Università degli Studi di Napoli Federico II (UNINA), Istituto di Biostrutture e Bioimmagini (IBB), Consiglio Nazionale delle Ricerche (CNR); Fondazione SDN (IRCCS); Napoli, Italy.

Scopo:Valutare l'accuratezza diagnostica della sequenza RM Chemical-shift (CS) nella caratterizzazione degli adenomi del surrene

Sono stati studiati 36 pz (9M, 27F), età media 51.3±14.4 anni con masse surrenaliche mono (31) o bilaterali (5); sono state valutate 41 lesioni del diametro medio di 3.0±2.2cm e sono stati utilizzati come standard di riferimento per la diagnosi i risultati istologici (19), bioptici (3) o del follow-up clinico-strumentale (19) che hanno mostrato 29 adenomi, 5 feocromocitomi, 3 cisti e 4 carcinomi. Gli studi RM sono stati effettuati con un apparecchio di 1,5Tesla (Gyroscan Intera, Philips Medical Systems) con sequenze in apnea respiratoria FFE-T1 (TR/TE=236/4,6ms), TSE-SSh-T2 (TR/TE=831/80ms), DUAL-FFE-T1 (TR=236, double-TE=4.6/2.3 ms) e sequenze FFE-T1 dopo gadolinium-DTPA (Gd) ev. Gli studi sono stati acquisiti sui piani assiali e coronali con spessore di strato di 3-5mm. Le immagini RM sono state analizzate qualitativamente valutando l'intensità del segnale delle lesioni surrenaliche nelle sequenze T1, T2, CS e T1-Gd. Sono stati considerati criteri diagnostici per adenoma l'iso- o l'ipo-intensità sia in T1 che in T2, la " perdita" di segnale (netta ipo-intensità) "in opposizione di fase" rispetto alle immagini "in fase"nella sequenza CS e la precoce impregnazione di mdc in fase arteriosa con rapida dismissione di mdc. I valori di accuratezza, sensibilità, specificità, VPP e VPN per l'identificazione degli adenomi surrenalici con le sequenze T1-T2 sono stati di 80%, 72%, 100%,100% e 60% rispettivamente; i risultati dell'analisi qualitativa dell'intensità di segnale eseguita con le sequenze CS (in fase ed opposizione di fase) e T1-Gd hanno mostrato analoghi valori di accuratezza, sensibilità, specificità, VPP e VPN, rispettivamente di 93%,90% ($p<0.05$vs T1-T2), 100%,100% e 80% ($p<0.05$ vs T1-T2). La RM dei surreni con sequenza CS migliora la caratterizzazione delle lesioni surrenaliche paragonata con le sequenze convenzionali T1-T2, identificando accuratamente gli adenomi nella maggioranza dei casi; la sequenza CS deve ritenersi fondamentale nello studio RM dei surreni, evitando la necessità di utilizzare la sequenza T1 post-mdc.

Bibliografia:Blake MA, Cronin CG, Boland GW Adrenal Imaging. AJR 2010; 194:1450-1460

P55
USE OF FLAIR SEQUENCES FOR DETECTION AND LOCAL STAGING OF BLADDER TUMORS WITH MRI

M. Di Girolamo[1], A. Fegolino[1], I. Ruggiero[1], V.A. Vitale[1], L. Argnani[1], G. Muscogiuri[1], V. David[1]
[1]*Dip. di Radiodiagnostica, Azienda Ospedaliera Sant' Andrea di Roma, Seconda facoltà di medicina e chirurgia*

PURPOSE: To increase the diagnostic accuracy of MRI in the detection and local staging of bladder tumors by using Fluid-attenuated Inversion Recovery (FLAIR) sequences.
METHOD AND MATERIALS: 32 patients with bladder tumors detected by US underwent MRI using 0.5 and 1.5 T superconductive magnet (Philips Medical System). We performed SE T1-weighted (TR: 500ms, TE: 30ms), TSE T2-weighted (TR: 2500 ms, TE: 120ms, ETL: 40) and FLAIR sequences (TR: 6000 ms, TE: 150 ms, TI: 2000 ms, N.Ex.: 4; Acq. time: 7'30") on axial scans. The contrast to lesion ratio was evaluated in all sequences. All patients underwent cystoscopy with transurethral biopsy and 14 had subsequent cystectomy.
RESULTS: In comparison with other sequences, FLAIR sequence was more sensitive in the detection of bladder neoplasms. This sequence demonstrates the hyperintense signal of bladder neoplasms from the filled bladder lumen hypointensity. The sensitivity in the identification of bladder neoplasms was 100% with FLAIR sequences, 89.6% with TSE T2-weighted sequences and 86.2% with SE T1-weighted sequences. That was due to the higher signal to lesion ratio of the FLAIR sequences in comparison with the others. In fact on FLAIR sequences the mean value of contrast to lesion ratio of bladder neoplasm was 33.1 while on SE T1-weighted sequences and TSE T2-weighted sequences was respectively 15.2 and 29.2. FLAIR sequences allowed the detection of small papillomas (less than 2 mm). TSE T2-weighted sequences were more sensitive than other sequences in the study of bladder wall infiltration.

CONCLUSIONS: Matsuda H. [1] using FLAIR technique shows sensitivity of 78.6% and a specificity of 91.7% for pT1 or smaller lesions, while the values were respectively 91.7% and 78.6% for pT2 or worse lesions. Therefore FLAIR sequences were more sensitive than others in the detection of bladder neoplasms, thanks to their higher contast to lesion ratio and can be very helpful in the visualization of small papillomas, especially when multifocal.
REFERENCES:
1) Matsuda H, Ueshima S, Kurita T. (1996) MR imaging of bladder tumors using fluid attenuated inversion recovery (FLAIR) technique. Hinyokika Kiyo; 42(6):411-5

P56

VOIDING MR-CYSTOURETHROGRAPHY: A NEW DIAGNOSTIC IMAGING TECHNIQUE FOR THE EVALUATION OF MALE LOWER URINARY TRACT

M. Di Girolamo[1], S. De Santis[1], A. Fregolino[1], J. Sternberg[1], C.N. De Cecco[1], G. Muscogiuri[1], V. David[1]

[1]*Dip. di Radiodiagnostica, Azienda Ospedaliera Sant' Andrea di Roma, Seconda facoltà di medicina e chirurgia*

PURPOSE:
To evaluate the diagnostic accuracy of imaging technique called voiding MR- cystourethrography that allows the visualization of the male urethra.
MATERIALS AND METHODS:
10 normal volunteers and 86 male patients with documented bladder outlet obstruction underwent voiding MR-cystourethrography. MR examination was performed with an 1.5 Tesla (Intera, Philips Medical System) with supine patient. Filling of the urinary bladder with paramagnetic contrast agent was obtainded by the i.v. administration 20 mg of furosemide followed by the i.v. administration of ¾ of the normal dose of a paramagnetic contrast agent (Magnevist, Schering, Germany). An appropriate urisheath was placed at the tip of the penis in order to collect urine. During the micturition T1-weighted spoiled 3D gradient-echo acquisitions on sagittal plane were performed (TR: 12 ms; TE: 2,7 ms; flip-angle: 40°; slice thickness: 2 mm). Two consecutive MR acquisitions were performed and the 3D row images were post-processed with MIP algorithm.
RESULTS:
Ten patients were unable to perform the MR examination. All volunteers and patients studied (76 pts) we obtained a perfect evaluation of the male urethra with voiding MR-cystourethrography. Visualization of urethra with MIP reconstructed images was considered comparable to conventional cystourethrography but proximal portion of urethra was visualized better with MRI. We detected 24 cases of bladder neck obstruction, 36 cases of urethral stricture, 10 cases following TURP and TUIP procedures, 2 urethral papillomatosis and 4 cases of benign prostatic hypertrophy. Analysis of 3D sagittal scans and urethral virtual endoscopy allowed a better evaluation in comparison with conventional cystourethrography.
CONCLUSIONS:
According to Nolte-Ernsting [1] we demonstrate that voiding MR-cystourethrography can show morfology of bladder neck and urethra during the micturition and can substitute standard retrograde and micturating cystourethrogram. This novel technique avoids radiation exposure to the gonads and urinary catheterization.
REFERENCES:
1) Nolte-Ernsting CC, Glowinski A, Katterbach FJ, et al. (1998) MR-micturating cystourethrography using radical k-space sampling. Rofo.; 168(4):385-9.

P57

Diagnostic value of DWI in chronic pelvic pain of women: a comparison study using laparoscopy as standard of reference. Preliminary results

P. Lucchesi[1], P. Paolantonio[1], M. Rengo[1], M. Maceroni[1], E. Palombo[1], A. Laghi[1]

[1]*Department of Radiological Sciences "Sapienza" - University of Rome Polo Pontino, Latina*

Purpose:

To assess the feasibility of diffusion weighted imaging (DWI) to identify the appearance of deep pelvic endometriosis in patients with chronic pelvic pain.

Materials and Methods:

We included in the study 50 women (mean age 32 years) suffering of chronic pelvic pain. MRI was performed on a 1.5T scanner (Signa Hde;GE) equipped with 8-channel phased-array coil with parallel imaging capabilities. MR protocol included high resolution T2w TSE sequence acquired on axial and sagittal planes and T1W TSE sequence acquired on the axial plane using spectral fat saturation. We divided the pelvic region in various areas to provide accurate information to the surgeon for diagnostic laparoscopy. DWI images were reviewed by two radiologists in consensus in comparison with conventional T2W TSE images and laparoscopic results. Signal intensity of deep pelvic endometriosis were recorded.

Results

In 13 patients a multifactorial origin of pelvic pain was discovered. Uterine adenomyosis was founded in 25 patients, pelvic adhension in 12 patients, ovaric endometriosis in 34 patients. Final diagnosis was deep pelvic endometriosis in 29 patients. Deep pelvic endometriosis showed low signal intensity on T2W TSE images and high signal intensity on heavy DW images in 25 patients (82.7%). In 3 cases (6.8%) pelvic endometriosis showed high signal intensity on heavy-DWI and was not recognizable on conventional pulse sequence. DWI showed a sensitivity of 88% in the identification of deep pelvic endometriosis.

Conclusion:

In the majority of our cases, deep pelvic endometriosis showed high signal intensity on heavy DWI. This finding is probably related to restriction of water diffusion within fibrotic tissue surrounding ectopic endometrium. DWI has a potential role in increasing sensitivity of MRI in the identification of deep pelvic endometriosis in patient with chronic pelvic pain.

P58

3T DTI Fiber Tracking and 3D T2 FSE cube overlapping in the depiction of periprostatic nerve in patients submitted to nerve-sparing prostatectomy

D. Lisi[1], V. Panebianco[1], V. Buonocore [1], T. Biondi[1], A. Sciarra[2], R. Passariello[1]

[1]*Department of Radiological Sciences, Sapienza University of Rome.*

[2]*Department of Urological Sciences, Sapienza University of Rome*

Purpose

Aim of this study is to depict neuroanatomical distribution and relationship with capsular profile of periprostatic nerve in patients submitted to a bilateral nerve-sparing prostatectomy using DTI Fiber Tracking and 3D fast spin-echo cube at 3T magnet.

Materials and Methods

The study is performed on patients candidate to nerve-sparing prostatectomy (33 pts) at 3T Magnet ((Discovery M750, GE Healthcare) equipped with surface phased array and endorectal coil. Scan protocol includes morphologic imaging with TSE T2-weighted sequences on the axial, sagittal and coronal planes, DWI sequences at different b value (500, 1000, 3000) and 3D fast spin-echo T2 cube sequence; in addition DTI fiber tracking with b value 1000 and 16 directions (funtool protocol, version 7.4) is done.

Results

Overlapping 3D cube sequence and fiber tracking we can obtained a precise view of the NVB in terms of: thickening of nerve fibers, distance from nerve fiber to prostate capsule, integrity and course on each part of the prostate. Periprostatic nerve fibers reveal a relatively even distribution in both lateral and dorsal parts of the prostate, asymmetric course bylaterally.

Conclusions

DTI fiber tracking and 3D FSE T2 Cube overlapping proposed in this study, would provide an additional diagnostic tool in decision making process in the patient nerve-sparing prostatectomy management .

P59

INTRAOBSERVER REPRODUCIBILITY OF BREAST GLANDULAR DENSITY MEASUREMENT AT MRI USING A GROWING-REGION ALGORITHM

G. Di Leo[1], E. Ferruggia[1], D. Ntoula[1], T.V. Tien[2], F. Cartia[1], F. Sardanelli[3]

[1]*U.O. di Radiologia, IRCCS Policlinico San Donato, San Donato Milanese*

[2]*Scuola di Specializzazione in Radiodiagnostica, Università degli Studi di Milano*

[3]*Dip. di Scienze Medico-Chirurgiche, U.O. di Radiologia; Università degli Studi di Milano, IRCCS Policlinico San Donato*

Purpose: To estimate the intra- and interobserver reproducibility of the breast density measurement obtained using a new semiautomatic measurement method based on MR images and a not-dedicated image-processing software

Methods: We evaluated 15 MR examinations negative at follow up. Using a visual criteria, the following patient groups were selected:

- 3 women with scarcely glandular breasts (highly adipose)
- 3 women with certain breast density but prevalently adipose
- 3 women with a nearly balanced distribution of glandular and adipose tissues
- 3 women with breast with a prevalence of glandular tissue
- 3 women with breast highly glandular (scarcely adipose)

We acquired a coronal FLASH T1-w sequence with an isotropic voxel of 1x1x1 mm^3. For each breast, the volume between the pectoral muscle and the nipple was selected. Those images were processed using ImageJ software (http://rsbweb.nih.gov/ij/). For each slice, the following measurement protocol was applied: selection of window, segmentation of the breast, measurement of total breast area, delineation of glandular tissue and measurement of glandular area. The total glandular and breast areas were calculated adding the partial areas of each slice. Since the pixels were isotropic, breast density was calculated as the ratio between total glandular area and total breast area. This measurement was repeated once more after 10 days. The Bland-Altman method was used: the coefficient of repeatability was divided by the mean of the two datasets and the complement to 100% was considered as a measure of reproducibility.

Results: The mean breast volume resulted 576±299 cm^3, the mean glandular tissue volume resulted 49±35 cm^3, corresponding to a mean breast density of 10±6%. The intra- and interobserver reproducibility of the breast density measurement resulted 97% and 96%, respectively. The mean segmentation times for the first and the second measurements resulted 2h 52min and 2h 19min, respectively.

Conclusion: Quantitative measures of breast density based on MR images is highly reproducible. The time needed for data processing could be strongly reduced by implementation of our procedure directly in the acquiring console.

P60

Correlazione tra coefficiente di diffusione apparente e fattori prognostici istopatologici e moleculari nei carcinomi mammari: osservazioni iniziali in 53 pazienti

L. Bonello[1], G. Petralia[2], P. Summers[2], S. Raimondi[3], R. Di Filippi[2], L. Preda[2], M. Bellomi[2]

[1]*Scuola di Specializzazione Radiodiagnostica, Università degli Studi di Milano*

[2]*Div. di Radiologia, Istituto Europeo di Oncologia, Milano*

[3]*Div. di Epidemiologia e Biostatistica, Istituto Europeo di Oncologia, Milano*

Scopo: correlare il coefficiente di diffusione apparente (ADC) con i fattori prognostici istopatologici e molecolari nei carcinomi mammari (CM).

Materiali e metodi: Cinquantatre pazienti (donne, età media 48.1, range 28-81 anni) con diagnosi istologica di CM sono state sottoposte a risonanza magnetica convenzionale (incluse sequenze T2 pesate e T1 dinamiche dopo contrasto) e sequenze RM pesate in diffusione (DW) (valori di b = 0, 250, 500 e 1000s/mm^2). L' ADC del CM, calcolato definendo regioni di interesse (ROI) sulle immagini con valore b=1000 s/mm^2, e' stato correlato con fattori prognostici molecolari e istopatologici. I valori di ADC sono stati utilizzati per valutare eventuali differenze tra i diversi sottitipi genetici (Luminal A, Luminal B, HER-2, triple receptor negative) [1], invasione vascolare (presenza/assenza), grading (G1/G2/G3), espressione di ER / PgR / HER-2 (positivo/negativo), Ki67 (<14% o >14%) e stadiazione TNM utilizzando l'analisi della varianza (ANOVA). Il coefficiente di Spearman e' stato utilizzato per valutare la correlazione tra i valori di ADC e variabili continue (eta', percentuale di ER, PgR, HER-2, Ki-67).

Risultati: La media dei valori di ADC dei carcinomi mammari inclusi nello studio e' stata di 1.14±0.20 x 10-^{3}mm^2/sec. Il valore di ADC dei tumori positivi per HER-2 e' stato più basso rispetto agli altri sottotipi raggiungendo significativita' statistica quando paragonato con il triple receptor negative (p=0.055). Il valore di ADC nel sottogruppo T3 (n=8) e' stato più basso che negli altri gruppi di T, ma statisticamente significativo quando paragonato ai T1 (p=0.03). E' stata osservata una correlazione marginalmente significativa (Spearman r=-0.35, P<0.05) tra i valori di ADC e l'espressione di HER-2.

Conclusioni: I nostri risultati non hanno mostrato un a chiara correlazione tra i valori di ADC e i fattori prognostici molecolari e istologici esaminati. Fanno eccezione i gruppi che esprimono HER-2 e il sottogruppo di T3.

[1] Sorlie T . Proc Natl Acad Sci U S A 98:10869-10874, 2001.

P61

Correlation between left ventricular function and late-enhancement mass in patients with hypertrophic cardiomyopathy underwent cardiac magnetic resonance

C.N. De Cecco[1], G. Muscogiuri [1], M. Di Girolamo[1], S. Fierro[1], F. Mancuso[1], V. David[1]

[1]*Dip. di radiodiagnostica, Azienda ospedaliera Sant' Andrea di Roma, Seconda facoltà di medicina e chirurgia*

Purpose:

The aim of this work is to show correlation between left ventricular function and late-gadolinium mass in patients with hypertrophic cardiomiopathy.

Materials and methods:

We retrospectively evaluated 28 patients with HCM diagnosis and late enhancement underwent cardiac MR using a 1.5 T system (Magnetom Sonata, Siemens). The MRI protocol consisted of a left ventricular functional study (4-chamber, vertical long axis, short axis)(TR:3.09ms,TE:1.3ms, FA:80,thick:8mm) followed by late enhancement data set acquired 10-15 minutes after iv administration of 0.2 mmol/kg of Gd contrast agent. Late enhancement was evaluated on Inversion recovery Turbo-Flash sequences (TR:8ms,TE:4ms,TI:250-340ms,thick:8mm) as an area with ¬¬SI ¬¬>2 SD from normal tissue. Left ventricular volumes and myocardial mass were calculated with a dedicated software. LGE mass was measured by manual planimetry on short axis. For statistical analysis we used Spearman's correlation.

Results:

This study showed the following parameters: mean VTD volume 128±33 ml., VTS 38±20 ml., FE 71±10 ml., SV 90±24 ml. and LE mass 9.1± 8.8g. We observed statistical significative results about correlation between left telediatolic volume (p = 0,02), telesistolic volume (p = 0,02), ejection fraction (p = 0,04) and late gadolinium mass. Correlation does not significative for left stroke volume (p = 0,7) and late gadolinium mass. Increase of late gadolinium mass is correlated with a gain of telediastolic and telesistolic volumes and decrease of ejection fraction.

Conclusion:

According to other studies[12], extent of hyperenhancement is associated with progressive left ventricular dysfunction. Valuation of late gadolinium mass assume an important role in the management of patients with hypertrophic cardiomiopathy.

References:

1) Motoyasu M, Sukuma H, Uemura S et al (2004) Correlation between hyperenhancement on delayed contrast enhanced MRI and diastolic function in hypertrophic cardiomyopathy. J Cardiovasc Magn Reson 6:246.

2) Moon JC, McKenna WJ, McCrohon JA, et al (2003) Toward clinical risk assessment in hypertrophic cardiomyopathy with gadolinium cardiovascular magnetic resonance. J Am Coll Cardiol. 7;41:1561-7.

P62

Hypertrophic cardiomyopathy: Correlation between left ventricular mass and late-gadolinium mass in patients underwent cardiac magnetic resonance

C.N. De cecco[1], G. Muscogiuri[1], M. Di Girolamo[1], S. Fierro[1], F. Mancuso[1], V. David[1]

[1]*Dip. di radiodiagnostica, Azienda ospedaliera Sant' Andrea di Roma, Seconda facoltà di medicina e chirurgia*

Purpose:

The aim of this work was to find correlation between left ventricular mass and late gadolinium mass in patients with hypertrophic cardomyopathy underwent cardiac magnetic resonance.

Materials and Methods:

We retrospectively evaluated 28 patients with HCM diagnosis and late enhancement underwent cardiac MR using a 1.5 T system (Magnetom Sonata, Siemens). The MRI protocol consisted of a left ventricular functional study (4-chamber, vertical long axis, short axis)(TR:3.09ms,TE:1.3ms, FA:80,thick:8mm) followed by late enhancement data set acquired 10-15 minutes after iv administration of 0.2 mmol/kg of Gd contrast agent. Late enhancement was evaluated on Inversion recovery Turbo-Flash sequences (TR:8ms,TE:4ms,TI:250-340ms,thick:8mm) as an area with SI>2 SD from normal tissue. Left ventricular myocardial mass was calculated with a dedicated software. LGE mass was measured by manual planimetry on short axis. For statistical analysis we used Spearman's correlation.

Results:

The following parameters were obtained: mean LE mass 9.1±8.8g and mean left ventricular mass 200±79g. We observed that there is a strong correlation between increase of myocardial mass of left ventricle and gain of late gadolinium mass ($p = 0,0003$).

Conclusion:

This is the first study that shows late gadolinium mass, other study evaluated only percentage [1], and correlation with left ventricular mass. Late gadolinium is associated with an high risk to develop sudden death. This study demonstrated that an increase of myocardial mass is correlated with an increase of late gadolinium mass.

References:

1. Moon JC, McKenna WJ, McCrohon JA, et al (2003) Toward clinical risk assessment in hypertrophic cardiomyopathy with gadolinium cardiovascular magnetic resonance. J Am Coll Cardiol. 7;41:1561-7.

P63

Correlation between medium myocardial thickness wall of left ventricle and late-gadolinium mass in patients with hypertrophic cardiomyopathy underwent cardiac magnetic resonance

C.N. De Cecco[1], G. Muscogiuri[1], M. Di Girolamo[1], S. Fierro[1], F. Mancuso[1], V. David[1]

[1]*Dip. di radiodiagnostica, Azienda ospedaliera Sant' Andrea di Roma, Seconda facoltà di medicina e chirurgia*

Purpose:

The aim of this work was to establish correlation between medium myocardial thickness wall of left ventricle and late gadolinium mass in patients with HCM.

Materials and methods:

We retrospectively evaluated 28 patients with HCM diagnosis and late enhancement underwent cardiac MR using a 1.5 T system (Magnetom Sonata, Siemens). The MRI protocol consisted of a left ventricular functional study (4-chamber, VLA, short axis)(TR:3.09ms,TE:1.3ms, FA:80,thick:8mm) followed by late enhancement data set acquired 10-15 minutes after iv administration of 0.2 mmol/kg of Gd contrast agent. Late enhancement was evaluated on Inversion recovery Turbo-Flash sequences (TR:8ms,TE:4ms,TI:250-340ms,thick:8mm) as an area with SI>2 SD from normal tissue. To extract medium myocardial thickness wall of left ventricle we measured thickness of inferior, septal, anterior and lateral wall in basal, medium and apical part of ventricle and we averaged all values. LGE mass was measured by manual planimetry on short axis. For statistical analysis we used Spearman's correlation.

Results:

The following results were obtained: mean medium thickness 10±2 mm. and LE mass 9.1±8.8g. We observed a statistical significative correlation between medium myocardial thickness wall of left ventricle and LGE mass ($p = 0,01$). No significative correlation was observed between the mean wall thickness when was analyzed the single section (basal, medium, apical) and late gadolinium mass of same areas. We observed that an increase of medium wall thickness of left ventricle is correlated with a gain of late gadolinium mass.

Conclusion:

Yamada M.[1] showed that LGE was mainly detected in the hypertrophied areas of the myocardium.

Our result show a correlation between mean whole heart wall thickness and late enhancement mass so evaluation of medium wall thickness of left ventricle could be an important preditictive index to develop late gadolinium areas.

References:

Yamada M, Teraoka K, Kawade M, Hirano M, Yamashina A. (2009). Frequency and distribution of late gadolinium enhancement in magnetic resonance imaging of patients with apical hypertrophic cardiomyopathy and patients with asymmetrical hypertrophic cardiomyopathy: a comparative study. Int J Cardiovasc Imaging; 25 Suppl 1:131-8.

P64

Right ventricular function, late-gadolinium mass and left ventricular mass correlation in patients with hypertrophic cardiomyopathy underwent cardiac magnetic resonance.

C.N. De Cecco[1], G. Muscogiuri[1], M. Di Girolamo [1], S. Fierro[1], M. Maurizi Enrici[1], V. David[1]

[1]*Dip. di radiodiagnostica, Azienda ospedaliera Sant' Andrea di Roma, Seconda facoltà di medicina e chirurgia*

Purpose:

To assess correlation between right ventricular function and late gadolinium mass in patients with hypertrophic cardomyopathy.

Materials and Methods:

We retrospectively evaluated 28 patients with HCM diagnosis and late enhancement underwent cardiac MR using a 1.5 T system (Magnetom Sonata, Siemens). The MRI protocol consisted of a left ventricular functional study (4-chamber, vertical long axis, short axis)(TR:3.09ms,TE:1.3ms, FA:80,thick:8mm) followed by late enhancement data set acquired 10-15 minutes after iv administration of 0.2 mmol/kg of Gd contrast agent. Late enhancement was evaluated on Inversion recovery Turbo-Flash sequences (TR:8ms,TE:4ms,TI:250-340ms,thick:8mm) as an area with SI>2 SD from normal tissue. Right ventricular volumes and myocardial mass were calculated with a dedicated software. LGE mass was measured by manual planimetry on short axis. For statistical analysis we used Spearman's correlation.

Results:

This study showed the following results: mean VTD 121±31ml, VTS 36±13 ml, FE 69±8 ml, SV 83±23 ml. A statistical significative correlation was not observed between right functionality and late enhancement. We obtained this results: correlation between late gadolinium mass and stroke volume (p = 0,9), ejection fraction (p = 0,6), telesistolic volume (p = 0,2) and telediastolic volume (p = 0,2).

Conclusion:

Generally study of right ventricle in HCM is neglected. Only one [1] analysed the usefulness of pulsed Doppler tissue imaging to detect impairment of right ventricular myocardial function and to provide evidence about ventricular interaction in forms of hypertrophic cardiomyopathy which involve interventricular septum. Our study analyses for the first time correlation of late gadolinium mass and right functionality. We show that right functionality in patients affected of hypertrophic cardiomiopathy doesn' t correlate with an increase of late gadolinium mass.

References:

1) Severino S, Caso P, Cicala S, Galderisi M, de Simone L, D'Andrea A, D'Errico A, Mininni N. (2000). Involvement of right ventricle in left ventricular hypertrophic cardiomyopathy: analysis by pulsed Doppler tissue imaging. Eur J Echocardiogr;1(4):281-8.

P65

MR DIFFUSION INVESTIGATION GIVES MORE INSIGHT ON SPONGY BONE QUALITY: RESULTS OBTAINED FROM FEMORAL AND CALCANEAL LOCATIONS OF HEALTHY AND OSTEOPOROTIC SUBJECTS

S. Capuani[1]

[1]*CNR-IPCF Sapienza Roma, Physics Dpt. Sapienza Univ. of Rome, Rome, Italy*

Bone Mineral Density accounts only for about 60% of the global risk of bone fracture. In particular, bone-marrow in spongy bones, also contributes in determining bone strength.
Spongy-bone is a porous system characterized by a solid trabecular network immersed in bone-marrow and characterized by a different relative percentage of water and fats. Recently (1), we demonstrated that water is more prevalent in the boundary zone while fats are rearranged primarily in the central zone of each pore. Moreover, differently from fat parameters, water ADC may be reliable marker to assess the status of spongy bone. Aim of this study was to combine Diffusion weighted imaging (DWI), Diffusion Tensor Imaging (DTI) and 1H-MRS data to obtain information in vivo on bone strength in humans. Two different investigation will be illustrated: 1) a DWI-1H-MRS study performed on calcaneus of fifty-four volunteers (nineteen osteoporotic, nineteen osteopenic and sixteen healthy women); 2) a DTI-1H-MRS study performed on femoral neck of forty-one volunteers (fifteen osteoporotic, fourteen osteopenic and twelve healthy subjects). All subjects underwent a DXA examination, to establish their T-score and their right feet, or their right femur were imaged at 3.0T. 1H-spectra (Single-Voxel-Spectroscopy) were collected from calcanei or from femoral neck of each subject and marrow fat-to-water ratio percentages (Mfc%) were extracted from each spectrum. DWI (b-values 0-8000 s/mm2, using a diffusion-gradient applied along the anterior-posterior direction) were collected from calcanei and ADC were extracted from DW-images. DTI (b-values 0, 200 and 2500 s/mm2, using diffusion gradient along 6 no-coplanar directions) was used to obtain Mean Diffusivity (MD) and Fractional Anisotropy (FA) maps from femurs of each subjects. FA, MD (or only ADC in investigation 1), T-score, Mfc% and age of each subject were correlate and compared. Our results indicate that calcaneal ADC in combination with 1H-spectroscopy is a sensitive measure to discriminate between normal and osteoporotic women and might contribute in a better determination of bone quality. Moreover FAvsMD graph obtained from femoral neck may be used to perform a single subject diagnosis of osteoporosis.
(1) De Santis, et al. Phys Med Biol 2010;55:5767.

P66

To evaluate the usefulness and the applicability to the study of joint knee cartilage of T2 and T2ρ maps obtained with a new sequence protocol on a dedicated open MRI system

C. Sirignano[1], E. Soscia[1], D. Iodice[2], G. Palma [3], S. Innocenti[4], D. Greco[4], B. Alfano[1], M. Salvatore[2]

[1]*I.B.B. Istituto di Biostrutture e Bioimmagini - C.N.R. Consiglio Nazionale delle Ricerche - Napoli - Italia*

[2]*Facolta' di Medicina e Chirurgia "Federico II" - Istituto di Radiologia - Napoli - Italia*

[3]*Esaote S.p.A., Napoli, Italy*

[4]*Esaote S.p.A., Genova, Italy*

Purpose:
To evaluate the usefulness and the applicability to the study of joint knee cartilage of T2 and T2ρ maps obtained with a new sequence protocol on a dedicated open MRI system.
Materials and Methods:
In 80 patients, two optimized 3D SSFP sequences (FOV: 200x200x120 mm3; Resolution: 1x1x2.5 mm3; overall scan time: 8') have been added to the standard knee acquisition protocol (Esaote G-Scan – 0.25 T). The related signal equations were inverted voxel-by-voxel to obtain quantitative PD, T1, T2 and T2ρ maps of the whole joint. T2 and T2ρ maps were evaluated in consensus by two radiologists at fixed range scales (T2 ranging from 0 to 150 ms; T2ρ from 0 to 300 ms) to find cartilage defects. The number of focal or diffuse cartilage alterations detected by means of each map was then compared to the number of anomalies in original SSFP images (SSFP-I). Also bone focal or diffuse anomalies were analyzed to test map sensitivity and correlation between cartilage and bone defects was evaluated.
Results:
In the evaluation of diffuse cartilage alteration SSFP-I were positive in 4 case, T2 map in 35 cases and T2ρ in 24. Moreover SSFP-I found 3 focal cartilage alteration, T2 map 48 and T2ρ 70. In the bone evaluation SSFP-I showed 3 diffuse bone signal anomaly, T2ρ 10. No diffuse bone alterations were evident in T2 map. SSFP-I showed 40 focal bone cortical/subcortical anomalies, T2 map 10 and the T2ρ 14. A correlation between cartilage and bone anomaly was found in 3 case with SSFP-I and T2 map, and in 25 cases with T2ρ map.
Conclusion:
The study of cartilage is one of the limits of dedicated systems; the possibility to obtain not only morphological information but structural data also is an important objective to achieve so to qualify dedicated system as practical and complete tool for the study of the knee. Our initial results show that both T2 and T2ρ maps are suitable to give extra information on the health status of knee cartilage, also in absence of morphological evidence of alteration on native 3D sequence; T2ρ map appeared more sensitive than T2 one. The sequences used not only gave structural information about the cartilage, but also allow to evaluate bone pathology; in pathologic cases T2 and T2ρ maps showed more and more clearly bone alteration if compared to SSFP-I.
Next step will be a double blind evaluation of our data with orthopedics' arthroscopy findings.

P67

NON-CONTRAST MRANGIOGRAPHY: ANALISI DELLE VARIABILI TECNICHE E DELLE SEQUENZE D'IMPULSO UTILIZZATE PER LA VISUALIZZAZIONE DEI VASI

S. Chiti[1], L.N. Mazzoni[2], S. Busoni[3], G. Belli[4], G. Roselli[1], R. Brugnoli[1], M. Moretti[1]

[1]*Dipartimento di Diagnostica per Immagini, °SOD 1, ^SOD 4, ^SOD DEA, °SOD NeuroRX - AOUCareggi, Largo Brambilla 3, 50134 Firenze*

[2]*Centro Interdipartimentale di Risonanza Magnetica, Viale Morgagni 85, 50134 Firenze*

[3]*SOD Fisica sanitaria - AOUCareggi, Largo Brambilla 3, 50134 Firenze*

[4]*Fisica sanitaria – Azienda USL 8 Arezzo, Via Curtatone 54, 52100 Arezzo*

Al contrario delle tecniche di angio RM TOF, PC ed in parte anche per le CEMRA 3D, dove ogni casa costruttrice di RM ha utilizzato la stessa sequenza d'impulsi (Rapid Aquisition GRE - FID imaging) la stessa tecnica per evidenziare il segnale dei vasi (TOF – inflow; PC – phase shift; CE – T1 contrast enhanced), le nuove sequenze di angio RM senza MDC oltre che nei nomi si distinguono soprattutto per la tecnica utilizzata per rendere il sangue iperintenso oltre che nelle sequenze d'impulso per acquisirne il segnale.

Questo lavoro nasce dalla necessità di una profonda conoscenza delle tecniche utilizzate dalle industrie leader nel settore, dovuta alla sempre maggiore diffusione della RM e della maggiore variabilità di scanner di marche diverse nei grandi centri ospedalieri e con una sempre maggiore necessità di lavorare su più scanner e con le conseguenti difficoltà tecniche nella gestione corretta dei parametri.

Viene riportata una valutazione delle tecniche di preparazione utilizzate per marcare gli spin (labeling) o sopprimerne il segnale (IR suppression) e di sottrazione (subtraction) e delle tecniche di saturazione del grasso (CHESS, CHESS-IR adiabatica. …) di sincronizzazione delle funzioni vitali (trigger cardiaco e respiratorio) e di riempimento del K-space (centrico e periferico) e delle sequenze di impulsi (Rapid Acquisition GRE: FID imaging, SSFP-FID+Echo) utilizzate per rilevare il segnale del sangue (bright blood)

Bibliografia:

[1] Kotaro Shimada, MD,* Hiroyoshi Isoda, MD, PhD, Tomohisa Okada, MD, PhD, Toshikazu Kamae, MS, RT, Shigeki Arizono, MD, Yuusuke Hirokawa, MD, Toshiya Shibata, MD, PhD, and Kaori Togashi, MD, PhD "Non Contrast Enhanced MR Portography With Time-Spatial Labeling Inversion Pulses". JMRI - Journal of Magnetic Resonance in Medicine 29:1140–1146 (2009)

[2] Ioannis Koktzoglou1,2* and Robert R. Edelman1,2 "STAR and STARFIRE for Flow-Dependent and Flow-Independent Noncontrast Carotid Angiography". MRM - Magnetic Resonance in Medicine 61:117–124 (2009)

[3] Ek T. Tan, John Huston, III, Norbert G. Campeau, and Stephen J. Riederer* "Fast Inversion Recovery Magnetic Resonance Angiography of the Intracranial Arteries". MRM - Magnetic Resonance in Medicine 63:1648–1658 (2010)

P68
DIFFUSION WEIGHTED IMAGING: SCAN PARAMETERS AND ARTIFACTS

C. Biagini[1], C. Biagini[1], L. Natale[2]
[1]*Centro Oncologico Fiorentino, Via A. Ragionieri 101, 50019 Sesto Fiorentino (FI)*
[2]*Centro Oncologico Fiorentino, Via A. Ragionieri 101, 50019 Sesto Fiorentino (FI); Dipartimento di Bioimaging e Scienze Radiologiche, Università cattolica "Sacro Cuore", Largo Francesco Vito 1, 00168 Roma*

Motivazione: In Risonanza Magnetica le acquisizioni pesate in diffusione [1] rappresentano un valido strumento per lo studio del sistema nervoso centrale e dell'encefalo in particolare [2,3]. Nell'ambito dell'imaging Body, la pesatura in diffusione ha ricevuto grande impulso negli ultimi anni, in particolare in applicazioni Whole-Body per la stadiazione delle neoplasie [4]. Purtroppo, le sequenze utilizzate hanno caratteristiche tecniche non comuni e le problematiche conseguenti sono di difficile approccio [5,6]. Il nostro lavoro affronta alcuni punti-chiave per l'implementazione di sequenze Dw-Whole body, fornendo alcune soluzioni volte a ridurre gli artefatti più comuni.
Metodo: Si è valutata la dipendenza da alcuni parametri di scansione (dimensione nominale del pixel, spessore di strato, fattore EPI, fattore SENSE) del rapporto segnale/rumore e degli artefatti più significativi (distorsione geometrica, Nyquist's ghosts, sfocatura da decadimento T2*, defasamento intra-voxel) su apparecchiature Philips Intera-Achieva e Siemens Aera da 1,5 Tesla.
Risultati: Gli artefatti sono classificati in base alla loro dipendenza. Se ne propone una valutazione critica per minimizzarne gli effetti.
Bibliografia:
[1] E.O. Stejskal and J.E. Tanner, "Spin diffusion measurement: spin echoes in the presence of a time-dependent field gradient", J. Chem. Phys. 42, 288-292 (1965)
[2] D. Le Bihan, "Intravoxel Incoeherent Motion Perfusion MR Imaging: A Wake-UP Call", Radiol. 248, 748-752 (2008)
[3] T. Moritani, S. Ekholm and P.-L. Westesson, Diffusion-weighted MR Imaging of the Brain (Springer, Berlin-Heidelberg, 2005)
[4] D.M. Koh and H.C. Thoeni (eds), Diffusion-weighted MR Imaging – Applications in the Body (Springer, Berlin-Heidelberg 2010)
[5] M.A. Bernstein, K.F. King and X.J. Zhou, Handbook of MRI pulse sequences (Elsevier Academic Press, New York, 2004)