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MYO-MRI+
IMAGING IN NEUROMUSCULAR DISEASE

Abstracts from the MYO-MRI+ 2023 | Imaging in Neuromuscular Disease Conference

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Dear colleagues,

We are happy to welcome you to the fourth International Imaging in Neuromuscular Disease Conference organised by the MYO-MRI+ consortium and held in Berlin from Sunday 5th to Tuesday 7th of November 2023.

The conference aims at promoting exchanges between radiologists, neurologists, biologists, physicists, engineers, and other scientists involved in neuromuscular imaging, particularly but not exclusively focusing on MR imaging and spectroscopy. The main topics selected for the 2023 edition are: emerging imaging approaches, other imaging modalities, dynamic imaging, and clinical research.

A good variety of high-quality abstracts have been submitted. 42 abstracts in the early round and 14 late breaking abstracts. The abstract book provides you with all abstracts ordered by oral and poster presenters.

We look forward to a varied and interesting scientific programme and fruitful discussions at the conference!

Pierre Carlier and Hermien Kan
– Chairs of the Scientific and Organising Committee –

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ORAL Presenters

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OP.01: Repeatability of muscle shear wave elastography and its association with age, sex and body mass index

Author/s: JLM van Doorn, J Wijntjes, N van Alfen and J Doorduin

Abstract

Background: Shear wave elastography (SWE) is an ultrasound technique to quantify tissue elasticity by perturbating tissue with acoustical energy and recording the propagation of the resulting wave-like motion. Valid measurement of tissue elasticity relies on the assumption of isotropy. Muscle tissue is not isotropic, although it could be described as unidirectional isotropic. Furthermore, every muscle has different architectural properties. These inherent limitations makes application of SWE in muscle less than straightforward. Moreover, anthropometric characteristics, such as age, sex and body mass index (BMI) influence muscle properties, but it is unknown how they affect muscle SWE.

Aims: To assess the repeatability of SWE in different muscles and provide associations between elasticity and anthropometric measurements.

Methods Healthy individuals across a wide age range were included. Three SWE measurements were obtained in the longitudinal direction from 4 different muscle groups: the biceps brachii (BB), flexor carpi radialis (FCR), rectus femoris (RF) and tibialis anterior (TA). A region-of-interest was placed within the SWE box in each image, the mode of the elasticity distribution was calculated, and elasticity averaged over the three measurements. The intraclass correlation coefficient (ICC) was used to determine intra-observer repeatability. Stepwise linear regression was used to assess the association between muscle elasticity and anthropometric measurements.

Results: 68 healthy individuals (age 43.0±21y, BMI 23.0±3.6kg/m2, 29 male) were included. The ICC of the BB was 0.90 (0.85-0.93), of the FCR it was 0.88 (0.83-0.93), TA 0.92 (0.89-0.95), and the RF 0.75 (0.62-0.84). Regression analysis showed that no association existed between muscle elasticity of the BB and RF with age, sex and BMI. However, muscle elasticity of the FCR was associated with age and sex, while muscle elasticity of the TA was associated with age, sex and BMI.

Conclusion: Reliability of SWE of the BB, FCR and TA was good to excellent, while for the RF it was only moderate to good. Normative elasticity depends on the muscle and normative data should be acquired for each muscle and each ultrasound system. These differences between muscles may be explained by differences in imaging depth, pennation angle and how parallel muscle fibres are organized.

OP.02: Compressed deep learning-based segmentation and fat fraction quantification in individual muscles of patients with muscle dystrophy

Author/s: Sandra Martin, Rémi Andre, Amira Trabelsi, Julien Wojak, Etienne Fortanier, Shahram Attarian, Maxime Guye, Marc Dubois, Redha Abdeddaim, David Bendahan

Abstract

Background: Fat fraction has been shown to be a relevant biomarker for monitoring Neuromuscular diseases. Quantitative Magnetic Resonance Imaging (MRI) is a technique able to provide fat fraction (FF) maps. However, calculating fat fraction values in individual muscles requires a segmentation step using anatomical images. This segmentation process is tedious and time-consuming when performed manually. Deep learning algorithms have been proposed as interesting alternatives for automatic segmentation. However, deep learning approaches yield complex models requiring onerous and energy intensive high- performance computing facilities. AIMS: This study intended to evaluate the impact of complexity reduction of 2D U-Net for muscle segmentation and FF estimation in thigh MRI images.

Methods: 54 dystrophic patients (CMT1A – CMT1B) and 10 controls volunteered to participate in the study. They were scanned at 1.5T MRI. The MRI database was composed of three-point Dixon 3D GRE scans (FF maps) and 2D T1-weighted fast spin echo (anatomical images). Several versions of 2D U-Net architecture were investigated by varying the number of parameters from 0.5M to 37M. Segmentation quality was assessed using DICE coefficient while FF estimation was assessed using relative mean squared error (MSE).

Results: The native U-Net (37M parameters) achieves an average DICE of 94.76 ± 1.70 while the best compressed U-Net (2M parameters) achieves 94.23 ± 2.27. Vastus Intermedius (VI) and Semi Membranous (SM) were the most challenging muscles to be segmented. Similar values were obtained using native and compressed U-Net architectures i.e. 92.44 ± 1.81% and 91.90 ± 1.91 % for VI and 94.06 ± 3.02% and 93.24 ± 3.73 % for SM. For each network, the average FF MSE was respectively 0.94 ± 1.90 and 0.82 ±1.20%.

Conclusion: DICE values were expected to increase with model parameters. Of interest, the results of the study indicate that preserving only 6.2% parameters of the original U-Net achieves comparable segmentation efficiency and FF estimation.
Significantly, segmentation errors mostly occurred in muscle borders. This type of error has a minimal impact on muscles surrounded by other muscles like SM. However, for VI the impact was larger given their vicinity to bone.

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OP.03: The motion study: Whole leg fully automated multiparametric qMRI processing and evaluation.

Author/s: Linda Heskamp, Lara Schlaffke, Martijn Froeling

Abstract

Background: Magnetic resonance imaging (MRI) is widely used to evaluate neuromuscular disorders. However, although sensitive, quantitative MRI (qMRI) parameters often lack specificity and are commonly not linked to muscle function.

Aims: In our ongoing study (MOTION) we aim to link qMRI and muscle architecture to function and lifestyle in a normal and healthy aging cross-sectional cohort. Secondly, we aim to develop and validate fully automatic full leg muscle data processing methods, and muscle architecture quantification. Lastly, we aim to identify critical confounding factors in multi-parametric qMRI evaluation. Here we present the results of the second aim, our data-analysis pipe-line.

Methods: We have acquired bilateral whole leg qMRI data from hip to ankle, lifestyle questionaries and Biodex muscle force measurements. The MRI protocol (45min) comprised of 6 overlapping continuous stacks with a combined FOV of 966 x 480 x 480 mm^3 using ME-GE (52s), ME-SE (1min48s) and SE-DWI (3min2s) acquisitions intended for water-fat imaging, T2 relaxometry and diffusion tensor imaging (DTI), respectively

Results: We have now included 25 out of 160 intended healthy subjects (13 female). Their age is between 21 and 58 (33 ± 11) years and average BMI is 23.8 ± 2.1 kg/m^2. Our developed data-analysis pipe-line comprises: 1) dicom to muscle-bids nifty conversion; 2) per stack data processing (iDEAL, EPG-T2, IVIM and DTI); 3) automated stack merging and registration to common ME-GE space and resolution; 3) UNET based segmentation (17 thigh and 14 leg muscles, and 4 bones per limb); 4) Full leg per muscle fibre tractography with; 5) Reporting of muscle qMRI parameters and muscle architecture parameters. Total processing time of the automated pipeline was around 3h per subjects and no user interaction was needed during the entire processing procedure.

Conclusion: In this work we have presented fully automated pipeline for bilateral whole leg multimodal qMRI processing and analysis. Although similar versatile pipelines exist, our pipe-line differentiates itself for the ability to process any number of overlapping stacks for multiple MRI contrasts for both uni- and bilateral data. Furthermore, it incorporates automated CCN-based muscle segmentation and full leg fibre tractography without user interaction.

OP.04: A minimal annotation pipeline for fully automatic segmentation of thigh muscles MRI

Author/s: Fabian Balsiger, Pierre-Yves Baudin, Lea Beck, Jean-Marc Boisserie, Benjamin Marty, Harmen Reyngoudt, Olivier Scheidegger

Abstract

Background: Automatic segmentation of muscles is a necessary step for automated analysis of quantitative outcome measures like fat fraction (FF) and water T2 (T2H2O).

Aims: To develop a thigh muscle segmentation method from Dixon imaging with minimal manual annotation effort, using an iterative approach in the training of a well-established convolutional neural network (CNN).

Materials and Methods: Iterative methodology: 1) thigh volumes are manually segmented and used for training a CNN; 2) the trained CNN is used to segment a batch of unseen validation volumes (n=20), which are subjectively graded by two raters regarding segmentation quality; 3) the worst graded volumes are manually corrected and added to the training volumes. Steps 2-3 are repeated until satisfactory segmentation quality is achieved based on the subjective grading.

Thirteen individual thigh muscles were segmented on out-of-phase volumes from 3pt-Dixon acquisitions from two sites. We used the nnU-Net (github.com/MIC-DKFZ/nnUNet) as CNN. A manually segmented testset (n=20) with FF and T2H2O maps was available for assessing the segmentation performance, covering a wide range of diseases and degrees of fatty replacement. A 5-point Likert scale was used for subjective grading of segmentation quality: very poor, poor, average, good, excellent.

Results: In the first iteration, 20 volumes were manually segmented. Five additional volumes were added after manual correction both in the second and third iteration, totaling 30 volumes of training data to achieve satisfactory segmentation quality. Most volumes in the validation set went from “average” or below to “excellent” over the iterations. The human annotation effort per volume went from 108 minutes for manual segmentation to 40 minutes for correction, using the iterative methodology. On the testing set, the Dice coefficient improved from 0.838±0.222 to 0.881±0.153 and the 95th percentile Hausdorff distance from 9.08±16.5mm to 6.51±12.5mm. FF and T2H2O values were automatically extracted with high agreement (bias of 0% and 0ms and 95% limits of agreement of ±5% and ±2.2ms in Bland-Altman analysis) to manual segmentation.

Conclusion: With only 20 volumes manually segmented, plus 10 more volumes manually corrected, accurate and robust CNN-based segmentation of individual thigh muscles in Dixon imaging was achieved using the proposed methodology.

OP.05: MYO-Guide: an automated approach to Neuromuscular Disease diagnosis with MRI and Artificial Intelligence

Author/s: Jose Verdu-Diaz, Carla Bolaño-Diaz, Alejandro Gonzalez- Chamorro, Gopi Veeranki, Sam Fitzsimmons, Jordi Diaz- Manera

Abstract

Background: Genetic Neuromuscular Diseases (NMDs) encompass a diverse range of disorders characterized by the progressive degeneration of muscle fibers, which are gradually replaced by non-contractile fat and connective tissue. This process leads to varying degrees of strength loss, mobility impairment, and reduced quality of life, affecting patients to different extents.

The diagnosis of NMDs has recently seen a breakthrough thanks to Next Generation Sequencing (NGS). However, NGS has some limitations and it's only available to most developed countries, while others still rely on the traditional Sanger sequencing

Muscle Magnetic Resonance Imaging (MRI) is useful in the study of NMDs, as it allows for muscle and fat differentiation and its non-invasive nature makes it appropriate for longitudinal studies. Over the last two decades, patterns of muscle involvement characteristic of different muscle diseases have been defined. The Mercuri score can be used to evaluate muscle involvement and identify these patterns. Therefore, MRI becomes a key tool for guiding NMD diagnosis and studying disease progression.

Despite these advancements, the use of this technique is not broad as patterns are complex and overlap with each other, there is no up-to-date atlas of patterns, and it requires both time and expertise.

Aims: Here, we present MYO-Guide, a platform aiming to push the role of MRI in the diagnosis of NMDs. The tool uses Artificial Intelligence to diagnose NMD patients using only the Mercuri scores. The platform also serves as a repository of fat infiltration patterns for different NMDs.Methods: Mercuri scores from 2674 patients and 31 different NMDs have been collected. A tree-based machine learning model has been trained to diagnose 15 different NMDs. The model has been deployed on a web platform, providing an easy-to-use visual interface for inputting Mercuri scores.

Results: The current model has achieved an overall 74.4% accuracy and a 88.23% Top-3 Accuracy. MYO-Guide keeps improving as new patients are obtained and used to train the model.

Conclusion: MYO-Guide closes the gap between experts and clinicians, offering an online and free tool for exploiting the diagnostic value of MRI without requiring field-specific expertise.

OP.06: Ultrasound-Guided Intramuscular Administration of a Non-Viral Gene Editing Delivery Technology for Intramuscular Treatment of Duchenne Muscular Dystrophy

Author/s: Özge Fındık Şener, Fanny G. Sage, Erik H. Niks, Marco, C. De Ruiter, Marten A. Engelse, Niels Geijsen, Mark C. Burgmans, Hermien E. Kan

Abstract

Background: Current gene therapy trials in Duchenne Muscular Dystrophy (DMD) focus on systemic delivery using viral vectors, but local gene editing therapies using non-viral delivery methods are being developed as well. These have the advantage of being unaffected by pre-existing immunity, have limited risk of adverse systemic effects and a good cost-benefit ratio. However, the optimal administration method of the gene editing therapeutic in muscle tissue, assuring maximal tissue distribution and therapeutic effect, is unknown.

Aim: To develop an optimal administration technique for local, intramuscular delivery of gene editing systems in a pre-clinical setting under ultrasound guidance in preparation for clinical trials.

Methods: Longitudinal versus perpendicular injections and different needle sizes were assessed in four isolated pig psoas muscles using cross-section visual evaluation after ink injection. Three different diameter needles (18G, 21G and 22G) were compared for ultrasonographic visibility, flexibility and ability to follow a needle trajectory parallel to the muscle fibers without large directional deviations.

In addition, extensor digitorum brevis muscles (EDB) of two pig hindlimbs were injected longitudinally under ultrasound guidance with an ink and gene editing solution (dilution 1/10). One EDB muscle was injected with a single-pass 2.5ml and a second EDB muscle was injected using two parallel insertions (2ml and 2.5ml). Ink distribution was evaluated visually (n=1) or quantitatively (Fiji ImageJ, (n=1)) in cross-sections of 2cm.

Results: Longitudinal injections visually had the best tissue distribution. Both the 21G and 18G needles allowed good directional control, while the 22G needle was prone to bending. Experiments in isolated muscle showed extensive fluid leakage attributed to the lack of fascia and skin, while this was not the case in pig limbs. The single-pass injection in the pig limb showed ink deposition in only one of the two heads of EDB muscle. The two injections approach showed an average distribution of 90% (range 72-98%) within the EDB muscle.

Conclusion: Our preliminary data suggest that ultrasound-guided longitudinal intramuscular administration using two parallel injections with a 21G Chiba needle provided up to 98% distribution of the gene editing or ink solution. Future experiments will investigate tissue biodistribution using Cas9-fluorescence in perfused limbs.

OP.07 Simultaneous creatine and phosphocreatine mapping of skeletal muscle by CEST MRI at 3T

Author/s: Licheng Ju, Kexin Wang, Michael Schär, Su Xu, Joshua Rogers, Dan Zhu, Qin Qin, Robert G. Weiss, Jiadi Xu

Abstract

For decades, researchers have been exploring non-invasive methods to detect phosphocreatine (PCr) or creatine (Cr) using MRI, given the important roles these compounds play in the body. While phosphorus (^{31}P) magnetic resonance spectroscopy (MRS) has been proven to be a specific method for assessing high-energy phosphates and mitochondrial impairment (1-9), it is not commonly used in clinical practice due to many practical challenges. In this study, we aim to obtain high-resolution ^{1}H MRI maps of amide, Cr, and PCr maps of skeletal muscle using a polynomial and Lorentzian line-shape fitting (PLOF) chemical exchange saturation transfer (CEST) at 3T (10-12).We used dynamic changes in PCr/CrCEST of mouse hindlimb before and after euthanasia to assign the Cr and PCr CEST peaks in the Z-spectrum at 3T and to obtain the optimum saturation parameters. Segmented 3D EPI was employed to obtain multi-slice amide, PCr, and Cr CEST maps of human skeletal muscle. Subsequently, the PCrCEST maps were calibrated using the PCr concentrations determined by ^{31}P MRS. A comparison of the Z-spectra in mouse hindlimb before and after euthanasia indicated that CrCEST is a slow-exchanging process in muscle. This allowed us to simultaneously extract PCr/CrCEST signals at 3T using the PLOF method. Fig. 1A displayed a typical ^{31}P MRS spectrum, showing well-defined PCr and ATP peaks, which determined an average of 39.58 mM PCr concentration in human calf muscle by the referring to the known ATP concentration (8.2 mM). (9,51-53). We evaluated the image quality of CEST images acquired using 3D EPI, and the results are presented in Fig. 1B, showcasing uniform and high-quality multislice images. Fig. 1B, C and D displayed the outcomes of CEST mapping (amide, PCr and Cr CEST maps) and quantification on the human calf muscle. Our study showed that in-vivo CrCEST is a slow-exchanging process. Hence, amide, Cr, and PCr CEST in the skeletal muscle can be mapped simultaneously at 3T by PLOF CEST.

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OP.08: Real-time MRI for characterization of respiratory dysfunction in Pompe disease

Author/s: Rachel Zeng, Leonie Töpert, Omar Al-Bourini, Leon Lettermann, Ulrike Olgemöller, Sabine Hofer, Matthias Boentert, Manuel Nietert, Jens Frahm, Martin Uecker, Ali Seif, Jens Schmidt

Abstract

Background: Respiratory dysfunction has a major impact on morbidity and mortality in patients suffering from neuromuscular diseases. Diagnosis of respiratory muscle weakness can be delayed due to compensatory mechanisms, which might conceal early symptoms of respiratory involvement.

Aims: The aim of this study was to characterize breathing patterns in patients with late-onset Pompe disease (LOPD), as well as healthy controls using real-time MRI and to compare this method to standard diagnostics.

Patients and Methods: 10 patients with LOPD and 11 matched controls participated in this study. 3 Tesla real-time MRI (RT-MRI) with acquisition times of approximately 40 ms enabled the assessment of natural breathing mechanisms and dynamic respiratory maneuvers. Segmentation and quantification of breathing patterns were performed both manually and semi-automatically via U-NET. MRI-assessments were compared to pulmonary function test and ultrasound of the diaphragm. Additionally, fast T1 mapping using a single-shot inversion-recovery method with serial acquisition of highly undersampled radial FLASH images was performed for tissue analysis of the diaphragmatic crura.

Results: Apart from the characteristically reduced diaphragmatic motion in patients with LOPD, RT- MRI enabled the exact quantification of compensatory increase of thoracic movements during different breathing maneuvers, and also unmasked paradoxical breathing movements during sniff maneuver in 9 out of 11 LOPD patients. Furthermore, the combination of RT-MRI and U-NET supported lung segmentation revealed new aspects to breathing mechanisms including diaphragmatic/thoracic synchronicity and breathing velocity during sniff maneuver. Additionally, our study showed a significant correlation between the degree of fatty involution of the diaphragm, as assessed by T1 mapping, with functional parameters from RT-MRI and pulmonary function test.

Conclusion: Real-time MRI allows for detailed evaluation of complex respiratory movements in patients with neuromuscular diseases. Quantitative T1-mapping provides a novel approach for the assessment of respiratory muscle involvement. These techniques yield promising potential in improving diagnosis and follow-up examinations of patients suffering from breathing disorders due to neuromuscular disease or other conditions.

OP.09: Dynamic MRI investigation for abdominal wall hernia repair

Author/s: Victoria Joppin, Thierry Bege, Catherine Masson, David Bendahan

Abstract

Background: The abdominal wall is a complex structure regulating the intra-abdominal pressure (IAP). Frequent pathologies are hernias resulting in a rupture into the abdominal strap. Although surgery can be used to repair, the recurrence rate is high [1] and the contributing factors have not been identified.

Aim: In the present study, we intended to use dynamic MRI in order to better understand the abdominal wall biomechanical behavior in patients with hernias. The ultimate goal was to determine accounting factors in the appearance and recurrence of hernias.

Patients and Methods: As a preliminary study, three patients (66yo±10) with hernia were investigated in supine position using dynamic MRI (VIDA, Siemens). 2D dynamic images were recorded in the axial plane with a 166ms time resolution, during audio-guided breathing, coughing and Valsalva maneuver. Breathing is passive in terms of abdominal muscle activity, whereas coughing and Valsalva recruit the abdominal muscles, especially the lateral muscles [2]. One patient had both pre and post-operative MRI. As previously described, a semi-automatic segmentation method [3] was used in order to delineate the abdominal muscles, the hernia sac (visceral contents passed beyond the neck of the hernia) and the dorsal zone. The radial displacement, strains [2], the distance between the rectus abdominis (RAM distance), the area of hernia sac and the visceral area were quantified.

Results: The hernia sac area changed more during active exercises as compared to passive exercises, as a result of the higher IAP generated by this type of exercise [4]. These results are supportive from those reported by Jourdan in healthy subjects cohort [2] . The surgery indicated a shortening of RAM distance (approximately 1cm).

Conclusion: Abdominal wall with hernia was biomechanically evaluated using dynamic MRI. The study will be conducted with more subjects so as to better understand the alterations and the effects of surgery.

OP.10: Exploring time-dependent diffusion in skeletal muscle of limb girdle muscular dystrophy R9 patients in a longitudinal study

Author/s: Susi Rauh, Pierre-Yves Baudin, Melissa Hooijmans, Tanya Stojkovic, Manon Granier, Sophie Olivier, Gustav Strijkers, Harmen Reyngoudt, Benjamin Marty

Abstract

Background: Limb-girdle muscular dystrophy (LGMD)-R9 is a slowly progressing muscle disease involving muscle wasting and fatty replacement, currently lacking effective therapy. Diffusion-tensor imaging (DTI) holds promise as a biomarker for monitoring disease progression and evaluating novel treatment efficacy in LGMD-R9.

Aim: To explore the potential of DTI at varying diffusion times to detect changes in muscle tissue among patients with LGMD-R9.

Methods: Eighteen LGMD-R9 patients (17f/1m, mean age 38.3y) and twelve healthy controls (11f/1m, mean age 37.4y) were included. MRI of the legs was performed at baseline, 1-year, and 2-year follow-up. The protocol included DTI of the right leg using a stimulated echo sequence with four mixing times (100-400ms), 6 gradient directions, b- values=0,400 s/mm² and 6 readouts, and a Dixon scan for fat fraction (FF) estimation. DTI processing involved denoising, fat-water separation using Dixon-based olefinic fat suppression (DOFS), and diffusion-tensor fitting. The outcome measures were FF, as well as mean diffusivity, diffusion-tensor eigenvalues, and fractional anisotropy at the varying diffusion (mixing) times. Muscle segmentations were manually drawn in the soleus and tibialis anterior. Muscles with signal-to-noise-ratio (SNR) < 15 were excluded. Outcome measures were compared among control subjects and patients, as well as within the patient group between baseline and follow-up assessments.

Results: All patients completed the baseline scan, with 16 and 14 undergoing the 1-year and 2-year follow-up, respectively. Time since diagnosis ranged from 1.5 to 17.9 years. No significant correlations were found between DTI parameters and SNR, age, FF, or years since diagnosis. No significant differences in DTI parameters were observed between controls and patients at various diffusion times. The majority of patients exhibited a low FF < 20% throughout the study duration, while a subset of four patients displayed higher FF (>20%). No temporal trend in DTI parameters was observed when comparing baseline and follow-up assessments in patients.

Conclusion: The application of DTI with varying diffusion times is feasible in patients with LGMD-R9. Our findings suggest that the diffusional changes in muscle in LGMD-R9 remain minimal over the 2-year follow-up. However, these changes might be subtle enough to fall below the sensitivity threshold of the method.

OP.11: Optimization of Skeletal Muscle Diffusion-Tensor Imaging Acquisition Protocol under Ultra-High Field

Author/s: Xingyu Zhou, Carly Lockard, Bradley Sutton, Melissa Hooijmans, Bruce Damon

Abstract

Diffusion-tensor MRI (DTMRI) is used to study skeletal muscle architecture in vivo. Ultra-high field MR has advantages of higher signal-to-noise ratio (SNR) and better image resolution, but has drawbacks including rapid T2 relaxation of tissue water protons, field inhomogeneity, limited RF coil availability, etc. With a single known exception (Foure et al., 2018), human muscle DTMRI has been limited to ≤3T. However, with increased use of 7T MRI in clinical and research imaging, skeletal muscle DTMRI protocols must be optimized for 7T.

Aims: To optimize 7T product sequences for skeletal muscle DTMRI, using the following goals: total acquisition time ≤10 minutes; with minimal image distortion, aliasing, ghosting and artifacts; voxel volume ≤6 mm3; and SNR ≥50.

Subjects These procedures were approved by our Institutional Review Board. Ten healthy persons (24-48 yrs., five male/five female) provided written informed consent to participate.

Hardware and pulse sequences MRI used a Siemens MAGNETOM Terra 7T scanner with a 28-channel receive, single-transmit knee coil. The EP2D and RESOLVE (readout-segmented EPI) product sequences were tested. Dielectric pads were placed around the region of interest.

Data acquisition MR images were acquired with a 192×192 mm2 field of view; acquired/reconstructed matrices of 96×96/192×192; sixteen 6 mm slices; b-values of 0 and 450 s/mm2, with number of excitations 4 (for b=0) and 2 (for b=450); 6-12 diffusion-encoding directions; TR=3600 ms (RESOLVE) or 3400 ms (EP2D); and minimum TE optimization.

Results: Phase-ghosting and image distortion were observed in EP2D images and were not eliminated through protocol adjustments. In RESOLVE images, there were no observable distortions, and signal voids were eliminated with sum of squares coil combination. Phase-ghosting occurred in RESOLVE images with acceleration factor ≥3. Adding readout segments increased scan time, but did not improve image quality. The mean SNR in the central slices was 82.3. The total scan time of the optimized RESOLVE sequence was 8:36.

Conclusion: For skeletal muscle DTMRI using the Siemens 7T Terra, we recommend using the RESOLVE sequence with 12 diffusion-encoding directions; parallel scheme, Slice Acceleration or GRAPPA with factor 2; sum of squares coil combination; and 5 readout segments.

OP.12: 3D MRF sequence optimization with undersampling artefacts simulation for water T1 and fat fraction mapping

Author/s: Constantin Slioussarenko, Benjamin Marty

Abstract

Introduction: In the field of neuromuscular disorders (NMD), fat fraction (FF) is an established biomarker of disease severity and water T1 (T1H2O) has been shown to be a potential biomarker of active muscle damages. The use of MR Fingerprinting (MRF) enables the simultaneous quantification of various parameters, including FF and T1H2O. In this work, we introduced an optimization framework that takes into account the longitudinal steady-state equilibrium of the MRF sequence with fat/water separation and simulates undersampling artefacts on a realistic numerical leg phantom. Through this framework, we optimized the echo times (TE), flip angles (FA) and recovery time of a shorter MRF sequence and compared its mapping accuracy and precision to the original implementation.

Methods: The optimization framework consisted of 5 blocks: i) a dictionary simulation block for steady- state MRF FLASH sequences with initial inversion pulse and variable TE,TR and FA, ii) a block simulating the time series of undersampled images based on a realistic leg numerical phantom iii) an MRF pattern matching algorithm, iv) a cost function and v) an optimizer.

We compared the original sequence (MRF T1-FF), the original sequence shortened to 760 spokes (MRF T1-FF 760) and the sequence obtained through the optimization framework described above (Fast MRF T1-FF) on a fat-infiltrated 3D numerical leg phantom and in vivo in the thighs of one healthy control (20 partitions, resolution 1x1x5 mm3, FOV 10x40x40cm3) acquired at 3T (PrismaFit, Siemens Healthineers).

Results: The Fast MRF T1-FF sequence was 30% faster than the original MRF T1-FF sequence. On the numerical leg phantom, T1H2O and FF estimation accuracy was better than the reference sequence (RMSE = 2.2% vs 2.4% for FF, RMSE= 48ms vs 65ms for T1H2O). For in vivo data, the optimization framework could reduce the streaking artefacts visible on the reconstructed maps from MRF T1-FF sequence and amplified on the MRF T1-FF 760 data.

Discussion & Conclusion: Using a novel optimization framework taking into account steady-state magnetization and undersampling artefacts, we designed a novel sequence (Fast T1-FF MRF) for fast quantification of T1H2O and FF, with reduced time and comparable results to those of the original sequence.

OP.13: Water T2 and IVIM MRI reveal alterations in muscle water compartmentation in GRMD dogs

Author/s: Ericky Caldas de Almeida Araujo, Yves Fromes, Inès Barthélémy, Stéphane Blot, Pierre-Yves Baudin, Harmen Reyngoudt, Benjamin Marty

Abstract

Background: Water-T2 (T2-H2O) is an instant and sensitive but non-specific marker of disease activity in neuromuscular disorders. The multi-exponential behavior of the T2-H2O reflects tissue water compartmentation and might increase T2-H2O specificity. The Golden Retriever muscular dystrophy (GRMD) dog is an animal model of Duchenne muscular dystrophy that presents much less fatty replacement.

Aims: Investigating alterations in tissue water compartmentation in GRMD by multi- exponential T2-H2O and intravoxel incoherent motion (IVIM), which is specifically sensitive to alterations in the vascular space.

Methods: The cohort consisted of 36 dogs (12 GRMD, 24 control) with single or multiple visits (56 CPMG, 41 IVIM data sets). Experiments were performed at 3T. Water
T2-relaxation data were acquired in the tibialis cranial using a fat-suppressed single-voxel (approx. 1x1x4 cm3) ISIS-CPMG (250 echoes, inter-echo-spacing = 2ms). A bi-exponential model was fitted to the data: S(TE) = A1.exp(-TE/T21) + A2.exp(-TE/T22). Diffusion- weighted images were acquired using a fat-suppressed spin-echo EPI (TE = 66ms, TR = 4s and b-values = 0, 400 and 900s/mm2). ADC, IVIM-weighted ADC (ADC-IVIM) and IVIM fraction (fIVIM) maps were analyzed in the tibialis cranial. Comparison between groups and correlations with age were evaluated using two-sample t-tests and Pearson's correlation analysis.

Results: In GRMD, T21 and the A2 were elevated ($p < 10\text{-}8$) and both decreased with age (R2/p = 0.49/2.7x10-4 and 0.4/1.5x10-3, respectively). The T22 was lower in GRMD ($p = 0.024$) and did not correlate with age. ADC was not different between groups. ADC-IVIM and fIVIM were elevated in GRMD ($p = 0.005$ and 3.7x10-5, respectively). In controls, ADC and ADC-IVIM decreased with age (R2/p = 0.44/2x10-4 and 0.35/1.5x10-3, respectively). fIVIM did not correlate with age in both groups.
Conclusion: Previous studies suggested that the 1st and 2nd T2-H2O components represent the parenchymal and vascular compartments, respectively. From this perspective, the CPMG results indicate an increase of the vascular compartment (higher A2) and the transendothelial exchange rate (lower T22), both suggestive of inflammation, while the elevated T21 is suggestive of tissue necrosis and interstitial edema. The IVIM results supported the CPMG findings, indicating an elevated vascular compartment in GRMD.

OP.14: Longitudinal follow-up of DMD patients with 1H and 23Na MRI

Author/s: Teresa Gerhalter, Lena Gast, Benjamin Marty, Pierre-Yves Baudin, Regina Trollmann, Frank Roemer, Michael Uder, Pierre Carlier, Armin Nagel

Abstract

In DMD, quantitative MRI studies commonly evaluated the fat fraction (FF) and water T2 (wT2) to assess disease severity and progression [1]. As both methods have their limitations, other NMR variables might overcome those and serve as early sensitive indicators for treatment monitoring. 23Na MRI has been previously proposed for follow-up of DMD patients as dystrophic muscles show increased total sodium concentrations (TSC) and intracellular-weighted 23Na signal (ICwS) [2,3]. This prospective case-control study investigates the relationship between TSC and FF in leg muscles over time.

Ambulant DMD boys (n=13, age 7.8±2.4y) were invited three times every six months for an MRI examination at 3T. The MRI protocol included FF measurements derived from the Dixon method and wT2 [4], as well as 23Na MRI to measure TSC [5] and ICwS [6]. Healthy age-matched boys (n=14, age 9.5±1.7y) underwent once the same protocol. For non- parametric statistical analysis, the following muscles were compared: gastrocnemius medialis, soleus, tibialis anterior and posterior of the right leg. A Wilcoxon rank sum test was used to compare controls to patient groups and a paired test for changes over time.

Compared to controls, patients with DMD showed significantly increased FF (all 4 muscles: 0.078±0.025 vs. 0.03±0.01), wT2 (all 4 muscles: 39.2±0.9 ms vs. 35.2±0.5 ms), TSC (all 4 muscles: 24.8±1.0 mM vs. 16.3±1.2 mM), and ICwS (all 4 muscles: 26.3±2.1 a.u. vs. 18.3±1.4 a.u.). Sodium anomalies were commonly observed in all four examined muscles - even in absence of fatty degenerative changes and water T2 increases. Between visit 1 and 2, FF increased by an average of 0.008, and significantly for GM (0.011±0.036) and SOL (0.015±0.023). Seven patients also returned for their third visit after one year, showing an average FF increase of 0.027±0.014. In the same time, wT2, TSC and ICwS did not show significant changes, thus remained elevated in comparison to the healthy control.

Although limited in the small number of subjects, the data supports that 23Na MRI could be used to characterize early dystrophic muscle alteration in a longitudinal fashion.

References: [1]Carlier_et_al (2016), [2]Weber_et_al (2012), [3]Gerhalter_et_al (2018), [4]Azzabou_et_al (2015), [5]Nagel_et_al (2009), [6]Nagel_et_al (2011)

OP.15: Dynamic MR spectroscopy to evaluate outcome of genetic therapies in Spinal Muscular Atrophy

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Abstract

Background: Deficiency of survival motor neuron (SMN) protein causes Spinal Muscular Atrophy (SMA), a progressive congenital neuromuscular disease characterized by degeneration of motor neurons leading to muscle weakness and atrophy. A major challenge is identifying responders of novel genetic treatments that boost intracellular SMN protein levels at an early stage, to minimize patient burden and maximize treatment cost-efficacy. Therefore, sensitive outcome measures that can detect the earliest effects of the treatment for SMA are needed. Here, we investigated the clinical utility of a novel diagnostic 7T MR upper-arm exercise platform to detect early treatment effects on motor function via 31P MR spectroscopy (31P MRS) readouts. We hypothesized that any metabolic consequences of positive treatment response at muscle level occur after 2 months and precede changes in muscle strength.

Methods: Twelve patients with SMA (seven non-ambulatory) starting SMN suppletion treatment were included. Patients were studied at three timepoints: baseline, 2 months, and 10 months after treatment onset. Dynamic 31P MRS data were collected from the biceps and triceps brachii muscles during concentric work at 80% of maximal voluntary contraction (MVC) force at baseline and after 2 months. Primary outcomes were changes in PCr, Pi, and pH during exercise and their recovery rate constant. MVC force was measured at baseline and after 10 months using isometric dynamometry.

Results: We collected 10 complete longitudinal datasets for the biceps muscle MVC force versus 8 for biceps MRS to conduct a preliminary test of our hypothesis. For weaker triceps muscle these numbers were 8 and 4, respectively. Median muscle strength of the biceps and triceps muscles remained stable in these patients over 10 months. Individual changes in muscle strength of the triceps after 10 months were positively correlated to changes in PCr recovery after two months ($r = 0.71$, $p = 0.03$). Associations between biceps muscle strengthand MRS parameters were not significant.

Conclusions: In conclusion, this first test of a novel diagnostic 7T upper-arm exercise platform in SMA patients suggests dynamic 31P MRS readout of muscle metabolic state variables may allow early detection of treatment response. Further validation of this platform will be necessary in a larger cohort study.

OP.16: Rapid quantitative assessment of sodium dynamics in response to exercise using 23Na-MRI of the tibialis anterior muscle

Author/s: Mary Neal, Carla F. Bolano-Diaz, Mark Richardson, Jassi Michell-Sodhi, Robert Muni-Lofra, Meredith K. James, Kieren G. Hollingsworth, Georgina Boyle, Heather Hilsden, J. Ian Wilson, Andrew M. Blamire, Volker Straub, Peter E. Thelwall, Jordi Diaz-Manera

Abstract

Background: The Jain Foundation Clinical Outcome Study (COS) of dysferlinopathy is an international study in genetically confirmed dysferlinopathy patients (DP). Dysferlin, expressed in the sarcolemma of skeletal muscle fibres, participates in cell membrane repair, and its absence or malfunction leads to muscle fibre death.

23Na-MRI presents a potential modality for non-invasive assessment of pathophysiological skeletal muscle function, due to the homeostatic mechanisms that take place to maintain Na+ concentration gradients across the cell membrane during muscle contraction.

Aims: This sub-study, undertaken at Newcastle COS site, aimed to determine the feasibility of performing 23Na-ISIS MR spectroscopy for high temporal resolution dynamic assessment of skeletal muscle sodium (23Na) content and relaxation properties post-exercise in healthy volunteers (HV) and DP.

Methods: 1 adult DP and 10 age and sex matched HV were scanned.
Imaging was performed on a Philips 3T Achieva scanner, with a 23Na birdcage coil (Rapid Biomedical) positioned centrally around the widest part of the calf of the stronger leg.

Pre-exercise MR-spectroscopy comprised a 23Na-ISIS acquisition (acquisition time=129s) and a 1H-PRESS T2 acquisition (acquisition time=45s), both with voxels placed within the tibialis anterior. Whilst in-situ, participants performed multiple, physiotherapist-guided isometric dorsiflexion contractions to achieve muscle exhaustion. Immediately subsequent to exercise completion, the 23Na-ISIS and 1H-PRESS sequences were alternately acquired serially for at least 35 minutes. HV underwent 3-point Dixon fat fraction (FF%) mapping of the calf. DP FF% had been measured previously.

Results: N=20 (4 male, mean age = 38±10 years). Baseline 1H-T2: 33.8±2.5ms (DP) and 29.3±1.0ms (HV), rising to 35.6±3.4ms and 36.3±3.3ms immediately post-exercise, respectively. Dynamic change in 23Na signal and 1H-T2 in the DP post-exercise was highly variable (contrary to HV) and FF% heterogeneous (R:5-52%). Notably, 23Na dynamics in a DP with normal FF% was altered with respect to the matched control. Biexponential analysis of 23Na-T2* showed elevated magnitude of both fast- and slow- decaying components in the DP , with an increase in the magnitude of the slow decaying component post-exercise.

Conclusions: Baseline 23Na signal was increased in DP, and post-exercise 23Na dynamics aberrated from HV, despite similar FF%. This reflects altered ion homeostasis beyond solely chronic changes.

OP.17: A fully SI-traceable test object for benchmarking performance in fat and iron content imaging

Author/s: Amy McDowell, Sarah Hill, Heidi Goenaga- Infante, Matt Cashmore, Cormac McGrath, Sian Curtis, Aaron McCann, Stephen Wastling, Nadia Smith, Alen Bošnjaković, Alessandra Manzin, Tugba Dispinar Gezer, Ilker Un, Lejla Gurbeta-Pokvic, Adriano Troia, Simone Busoni, Riccardo Ferrero, Elizabeth Cooke, Paul Tofts, John Thornton, Matt Hall, Cailean Clarkson

Abstract

Background and Aims: The iMet-MRI project has brought an international consortium together to create test objects, procedures, analysis tools, and best practice guidance for several quantitative MRI (qMRI) techniques and demonstrate them in an international multi-site trial. Although a powerful tool, MR can be inconsistent when comparing images acquired on different scanners or at different times. qMRI can provide additional consistency and clinical specificity but these measures need metrological support and validation.

Methods: The consortium has designed and produced a prototype analogue of fat to be combined with water percentages in a phantom (20%, 40% and 61% initially) which can be imaged alongside T1, T2 and T2* (Fe) vials to provide a reference for fat and iron content for muscle imaging. These will be produced by the National Measurement Laboratory (NML) based at LGC in partnership with the National Physical Laboratory (NPL). This prototype contains multiple peaks of fat similar to the clinical case but will be provided with a validated, traceable fat value provided by NML unlike current commercial phantoms. Tert- butanol fat fractions will also be included as a simple single-peak fat reference.

Results: The preliminary scan results show that 3-point Dixon, known to only include the major methylene fat peak in the calculation, is unable to detect the full fat percentage giving a 47.3(+/-1.6)% result for a 61% fat fraction for example. Although not a perfect replication, this is similar to the fat percentage known to be unaccounted for (calculated in Azzabou et al. for example) with in-vivo fat. Other more complex methods such as the 6-point Dixon or IDEAL-CPMG methods can be compared to a traceable reference using the phantom.

Conclusion: A prototype analogue fat fraction phantom has been produced with validation provided by NML. The results show that it reasonably mimics the clinical situation and can be used to link users' fat-fraction measurement methods to traceable standards for drug and clinical trials. Users will be able to scan the phantom on their site and send the results into NPL for processing and receive certification.

References

Azzabou, N. et al. (2015). J Magn Reson Imaging 41(3):645-653.

OP.18: Glycogen accumulation in the brain of classic infantile Pompe patients measured in vivo with 1H Magnetic Resonance Spectroscopy

Author/s: Chloe Najac, Vincent Boer, Ans van der Ploeg, Itamar Ronen, Hermien E. Kan, Nadine van Beek, Hannerieke van den Hout

Abstract

Background: Classic infantile Pompe disease is caused by abnormal lysosomal glycogen accumulation in multiple tissues including the brain due to a deficit in acid α-glucosidase (GAA). Treatment with recombinant human GAA (rhGAA) has dramatically improved survival. However rhGAA does not reach the brain and surviving classic infantile Pompe patients develop progressive cognitive problems and white matter (WM) lesions. Directly monitoring glycogen accumulation in the brain could allow to evaluate response to innovative therapies that will target the brain. Proton (1H) magnetic resonance spectroscopy (MRS) is a non-invasive technique used to quantify levels of endogenous metabolites (e.g. N-acetyl-aspartate (NAA) in neurons, myo-inositol (Ins) in glial cells, and glycogen). A previous study conducted at 1.5 T showed changes in NAA level which may suggest loss of neuronal viability. To the best of our knowledge, non-invasive in vivo assessment of glycogen in Pompe patients has not been reported.

Aims: We took advantage of the ultrahigh field MR scanner (7T) to increase our sensitivity/specificity compared to clinical scanners (1.5/3T). We used 1H MRS in a volume-of-interest (VOI) positioned in the periventricular WM (presenting lesions in patients) to assess the feasibility to monitor glycogen accumulation and other neurochemical alterations. In addition, we aimed at evaluating the spatial distribution of the neurochemical changes using 2D-MRS imaging (MRSI).

Methods: Four classic infantile patients (8-16 y) and 4 age-matched healthy controls (HC) were scanned on a 7T MRI scanner. The protocol consisted of (1) 3D-T1, (2) multi-slice 2D-T2 (3) SVS (VOI: 18x18x18mm3) and (4) 2D-MRSI scan.

Results: All patients had widespread WM lesions on T2-weighted images. SVS showed a clear shift in the neurochemical profile, particularly, a significant increase in glycogen/total creatine (Glyc/tCr; HC=0.09·104±0.03·104, patients=1.85·104±0.24·104, p=0.014) and decrease in NAA/tCr (HC=1.91±0.20, patients=0.95±0.22, p=0.014) in patients. MRSI results showed a widespread accumulation of Glyc/tCr (HC=0.42·104±0.27·104, patients=1.65·104±0.76·104, p=0.03) and a significant lower level of NAA/tCr (HC=1.65±0.42, patients=1.18±0.48, p=0.03) in patients.

Conclusion: We illustrated the potential of MRS, in SVS and in 2D-MRSI mode, to monitor glycogen accumulation and changes in NAA in Pompe disease. It could serve as a non-invasive readout to monitor disease progression and response to treatment.

OP.19: Multispectral optoacoustic tomography of muscle involvement in Pompe disease

Author/s: Roman Raming, Lina Tan, Jana Zschüntzsch, Adrian P. Regensburger, Frauke Alves, Jörg Jüngert, Ulrich Rother, Yi Li, Vera Danko, Werner Lang, Mathias Türk, Sandy Schmidt, Joachim Woelfle, Andreas Hahn, Alexander Mensch, Martin Winterholler, Regina Trollmann, Rafael Heiß, Alexandra L. Wagner, Ferdinand Knieling

Abstract

Introduction: Pompe disease (PD) is an ultra-rare autosomal-recessive glycogen storage disease caused by the deficiency of lysosomal acid α-glucoside (GAA) resulting in proximal muscle weakness and loss of respiratory function. While enzyme replacement therapy (ERT) is the only effective treatment, prospective biomarkers for disease monitoring are scarce.

Aim: In this study we aimed to investigate the potential of multispectral optoacoustic tomography (MSOT), a molecular-sensitive ultrasound (US) approach, for the non-invasive, rapid imaging of the muscle involvement in PD patients.

Methods: After *ex vivo* biomarker validation in a phantom study, an *in vivo* prospective clinical trial (clinicaltrial.gov ID NCT05083806) included n=10 Late-onset PD (LOPD) patients and n=10 gender- and age-matched controls. All subjects' biceps muscles were imaged using MSOT and results compared to standard clinical outcome parameters including muscle magnetic resonance imaging (MRI), ultrasound, spirometry, muscle testing, quality of life score (QOL). Study results were then further validated in n=3 PD subjects in a different clinical site with a different imaging system and investigators.

Results: Phantom experiments demonstrated the feasibility to image changes in tissue composition attributed to glycogen increase. In the clinical study, mean±SD age of participants in HV and PD was identical (41.2±14.2y vs. 40.6±12.1y), while PD patients had lower weight (73.9±11.9kg vs. 65.0±17.3kg), walking distance on 6-minute walking test (6MWT, 671±117m vs. 560±87m), and relative vital capacity of the lung (VC%, 105±10% vs. 63±21%). Using qualitative and quantitative US assessments (Gray scale level, P=0.11) and MRI-derived muscular fat fraction (9.7±2.2% vs. 14.3±14.1%, P = 0.38) it was not feasible to separate HV from PD patients. In contrast, MSOT showed altered optoacoustic spectral information and quantitative differences in unmixed parameters, eg. lipid (SpecL: 1267±357 vs. 2713±1732a.u., P<0.0001) and collagen (SpecC: 1727±556 vs. 2152±674a.u., P=0.0029). For external validation, the imaging findings and analytical approach was reproduced in n=3 subjects from a different medical center.

Conclusion: MSOT may allow for advanced and rapid disease phenotyping in human biceps muscles of LOPD patients providing correlation with clinical extend of disease.

OP.20: Disease initiation and progression in facioscapulohumeral muscular dystrophy identified by whole- muscle quantitative MRI

Author/s: Linda Heskamp, Augustin Ogier, Jack van Asten, David Bendahan, Arend Heerschap

Abstract

Background: Facioscapulohumeral dystrophy (FSHD), the second most common type of muscular dystrophy worldwide, is caused by release of suppression of the DUX4 gene. Subsequently, an unknown initiation process causes expression of the DUX4 transcription factor followed by a complex cascade of events that eventually leads to muscle cell death. In this study we determined the initiation site and progression profile of the disease in lower extremity muscles of FSHD patients by assessing fat infiltration and inflammation/edema along their full proximo-distal axis using quantitative MRI.

Methods: Nine patients underwent MRI of lower extremities to assess end-to-end muscle fat fractions (FFs) and inflammatory lesions using DIXON and TIRM pulse sequences respectively. Seven patients underwent the same MRI ~3.5 years later. Individual muscles (n=396) were semi-automatically segmented to calculate average FFs over all slices covering whole muscles. Disease progression was quantified from FF changes in 5 adjacent muscle segments.

Results: We provide evidence that fat replacement commonly starts at the distal end of affected muscles where the highest FFs occur ($p < 0.001$). It progresses as a reversed sigmoid shaped wave in the proximal direction at an increasing rate with the highest value (4.9 ± 2.7%/year) for muscles with baseline FFs of 30–40%. Thereafter it proceeds at a slower pace towards the proximal muscle end. In early phases of disease, inflammatory lesions preferentially occur at the distal muscle end in agreement with disease initiation at this location. Compared with whole-muscle analysis, the common FF assessments using only few MR slices centrally placed in muscles are significantly biased (~50% in progression rate).

Conclusions: These findings identify the distal end of leg muscles as a prime location forreversed sigmoid shape moving towards the proximal end, consistent with proposed disease mechanisms. End-to-end whole-muscle fat assessment is essential to properly diagnose FSHD and its progression.

OP.21: Skeletal muscle Mg2+, membrane permeability, and pH are altered in Becker muscular dystrophy: A 31P-MRS and DT-MRI study

Author/s: Esther Schrama, Melissa Hooijmans, Erik Niks, Hermien Kan, Donnie Cameron

Abstract

Background: Becker muscular dystrophy (BMD) is an X-linked disorder characterised by highly variable, progressive muscle damage and loss of function. MR-derived fat fraction is used as a marker for disease progression, but early markers are lacking. A reduction of intracellular ionised magnesium (Mg2+) and elevation of phosphodiesters (PDE) measured by phosphorus-(31P)-MRS indicate membrane leakiness and breakdown and may thereby reflect disease activity. Muscle permeability and fibre diameter measured with a random permeable barrier model (RPBM) using multi-diffusion-time diffusion-tensor-(DT)-MRI data, could also be early markers.

Aims: To compare intramuscular [Mg2+], 31P-MRS metrics, and RPBM membrane permeability between BMD patients and healthy controls and assess their correlations.

Methods: We included 13 BMD patients—age 20-59yrs—and 9 male controls—age 23-65yrs—who underwent both 7T 31P-MRS and 3T multi-diffusion-time DT-MRI in the left lower-leg. The 31P spectra were Hamming-filtered. Free-induction decays were output for the tibialis anterior (TA) muscle, where metabolite ratios, weighted pH, and [Mg2+] were calculated. In the DT-MRI data, TA ROIs were drawn on fat-water images, and radial diffusivities per diffusion time were fitted with the RPBM, producing membrane permeabilities and fibre diameters. Groups were compared via t-tests if normally distributed, or Mann-Whitney U-tests if not. Correlations were assessed via Pearson's r, and $p < 0.05$ was considered statistically significant.

Results: The 31P-MRS-derived [Mg2+] in the TA was lower in BMD versus controls: mean (SD)=0.63 (0.17) vs 0.86 (0.22)mM, respectively; p=0.022. PDE/γ-ATP was larger in patients versus controls: mean (SD)=0.36 (0.17) vs 0.22 (0.09), respectively; p=0.029. Comparing both metrics, [Mg2+] decreased with increasing PDE/γ-ATP: Pearson's r=–0.49, p=0.002. RPBM-DT-MRI showed similar permeabilities in patients versus controls—0.042 (0.033) vs 0.032 (0.021)μm/ms, respectively, p=0.410—though markedly high- and low-permeability outliers were evident in both groups. RPBM permeabilities did not correlate with [Mg2+] or PDE/γ-ATP, but RPBM fibre diameters were larger in patients, as reported previously.

Conclusion: We show reduced intramuscular [Mg2+] and increased PDEs and weighted pH in BMD patients versus controls, suggesting greater membrane permeability and possible applications as biomarkers of disease activity, while DT-MRI-measured permeability did not differ.

OP.22: Relationships between muscle quantitative MRI, 31P MRS and functional biomarkers in a placebo-controlled study of sirolimus in inclusion body myositis patients

Author/s: Harmen Reyngoudt, Damien Bachasson, Jean- Yves Hogrel, Pierre-Yves Baudin, Ericky Caldas de Almeida Araujo, Yves Allenbach, Pierre G. Carlier, Benjamin Marty, Olivier Benveniste

Abstract

Background: Inclusion body myositis (IBM) is the most frequent type of myositis in patients older than 50 years. The pathophysiology and the muscle response to treatment in IBM is not well understood. Two categories of histopathological features are characteristic of this disease suggesting inflammatory (myositis) and degenerative (inclusion body) mechanisms. The disease is slowly progressive and leads to severe muscle disability.

Aim: Here, we report the associations between the different quantitative MRI data including muscle fat fraction (FF) and contractile cross-sectional area (cCSA) and water T2, reflecting active muscle damage and 31P MRS indices, as well as the relationships between MRI/31P MRS and muscle function in the placebo-controlled phase 2b trial of sirolimus in IBM patients.

Methods: In the RAPAMI study (NCT02481453), quantitative MRI and 31P MRS data were obtained at 3 tesla in thigh and leg muscles of 45 patients (sirolimus vs. placebo) at baseline and year-1. FF, cCSA and water T2 values were assessed in leg/thigh muscles and 31P MRS indices (such as PME/γATP) in quadriceps or triceps surae. Functional assessments included the six-minute walking distance (6MWD). Spearman rank (ρ) correlation analyses were performed ($P < 0.05$).

Results: Significant correlations were found between baseline water T2 and change in FF, especially in hamstring ($\rho = 0.57$) and quadriceps ($\rho = 0.45$) muscles, with the strongest correlation in semitendinosus muscle ($\rho = 0.74$). This correlation was systematically stronger in the placebo group. Significant correlations were observed between baseline water T2 and change in cCSA for hamstring ($\rho = -0.55$) and quadriceps ($\rho = -0.52$). A significant correlation was found between baseline PME/γATP and change in FF in quadriceps ($\rho = 0.65$). At baseline, global leg FF, global leg water T2 and PME/γATP in triceps surae were significantly correlated to the absolute 6MWD value ($\rho = -0.74/-0.67/-0.58$, respectively). Change in global leg FF, baseline vastus lateralis water T2 and baseline quadriceps PME/γATP were significantly correlated to change in 6MWD ($\rho = -0.43/-0.51/-0.77$, respectively).

Conclusion: This study has demonstrated the predictive potential of water T2 and 31P MRS indices of future changes in FF and muscle function in IBM patients.

OP.23: Quantitative MRI of the upper arm in Duchenne muscular dystrophy

Author/s: Michel Cakici, Karin Naarding, Arina Prins, Menno Van der Holst, Erik Niks, Hermien Kan

Abstract

Background: In Duchenne muscular dystrophy (DMD), leg muscle MRI fat fraction (mFF) shows promise as surrogate endpoint in clinical trials, while the contractile Cross-Sectional Area (cCSA) seems less suitable due to higher inter-patient variability. It is unclear if MR parameters in the upper limb (UL) show the same variability. This is important to determine, as in more advanced stages of DMD, UL function is crucial for daily life activities.

Aims: To determine the sensitivity to detect change of several MR parameters and the Performance of the Upper Limb scale in non-ambulant patients with DMD. To explore their correlations.

Methods: Axial four-point chemical-shift-based fat-water separation gradient echo scans were acquired in non-ambulant DMD patients at 2 timepoints (v1:n=20) and 12 months (n=15) (33 slices, 1x1x10 mm). mFF, cCSA and contractile volume (CV) were determined for the center slice (CS, 40% humerus length from the elbow), 5 center slices (5S), 7 center slices (7s) and whole muscle (WM) for elbow flexors and extensor muscles.

A standardized response mean (SRM=(mean1-mean2)/(SD of the change)) was determined for all parameters where SRMs ≥ 0.8 indicate a large responsiveness to change, 0.5 – 0.8 a moderate and < 0.5 a low responsiveness. MR parameters with an SRM larger than 0.8 were correlated with PUL2.0 using Pearson's correlation and r reported if significant ($p < 0.05$).

Results: Median age was 13.3 (12.3–15.9 years) with median mFF WM of the flexors of 49.67% (40.5–68.0) and elbow extensors 45.26% (32.1–53.5) at visit 1. PUL2.0 had the highest SRM of 1.27. MR parameters with SRMs > 0.8 mainly contained mFF: flexors WM (1.20; correlation with PUL r 0.68), 7S (1.20; r 0.68), 5S (1.08; r 0.68). Extensors; WM (1.22), 7S (1.03), 5S (1.01), CS (1.08). For CV only flexor WM had a large responsiveness (0.97; r 0.84).

Conclusion: In these non-ambulant DMD patients responsiveness was always higher for mFF compared to cCSA and increased when analyzing a larger part of the muscle. Elbow flexors mFF showed a good correlation with UL function.

OP.24: Validation of genetic outcome by whole-body muscle MRI in early-onset childhood myopathies

Author/s: Rocio Garcia Uzquiano, Roberto Fernandez Torron, Amaia Guisasola Iñiguez, Teresa Iglesias Gaspar, Maria Itxaso Marti Carrera, Robert Ives Carlier, Susana Quijano Roy

Abstract

Background: Early onset neuromuscular diseases are often genetically determined. The availability of NGS (Next Generation Sequencing) techniques has contributed to improve their diagnosis, however, the interpretation of genetic variants is often complex.

Aims: to evaluate the usefulness of muscle MRI in the validation of the genetic result obtained by NGS techniques in patients with early onset myopathies.

Methods: Retrospective, observational, multicenter study of 50 paediatric patients with suspected early-onset childhood myopathy, studied by whole-body muscle MRI and presenting genetic abnormalities in a gene with a known muscle pattern.

Results: We present 50 patients, 16 have already been analysed (5 CAPN3, 2 RYR1, 2
COL6, 2 TTN, 1 DMD, 1 NEB, 1 DES, 1 DYSF, 1 LMNA). The identified genetic variants have been classified as pathogenic (3/16), probably pathogenic (11/16) and of uncertain significance (2/16), according to the ACMG Classification (American College of Medical Genetics and Genomics). In 75% (12/16) there is a complete consistency between the muscle pattern found by muscle MRI and the known pattern for the gene involved, and therefore the MRI supports the pathogenicity of the variant. In 18.7% (3/16) there is partial coherence: the muscle pattern is not very specific and does not support or rule out the pathogenicity of the variant. In 6.2% (1/16) there is a lack of coherence: the muscle pattern is not compatible with the genetic variant and points to another myopathy.

Conclusion: These preliminary results suggest that muscle MRI is a useful diagnostic tool in the interpretation of genetic variants implicated in early onset myopathies with a known radiological pattern.

OP. 25 Comparison of two corticosteroid regimens on brain volumetrics in patients with Duchenne muscular dystrophy

Author/s: Geuens Sam, Van Dessel Jeroen, Govaarts Rosanne, Ikelaar Nadine A, Meijer Onno C, Kan Hermien E, Niks Erik H, Goemans Nathalie, Lemiere Jurgen, Doorenweerd Nathalie, De Waele Liesbeth

Abstract

Background: Many patients with Duchenne muscular dystrophy (DMD) have neurobehavioral problems. Corticosteroids, the primary pharmacological treatment for DMD, have been shown to affect brain morphology in other conditions, but data in DMD are lacking.

Aims: This study aimed to investigate the impact of two corticosteroid regimens on brain volumetrics in DMD using Magnetic Resonance Imaging (MRI).

Methods: In a cross-sectional, two center study, T1-weighted MRI scans were obtained from three age-matched groups (9-18 years): DMD patients treated daily with deflazacort (DMDd, n=20, scan site: Leuven), DMD patients treated intermittently with prednisone (DMDi, n=20, scan site: Leiden), and healthy controls (n=40, both scan sites). MRI scanning was performed on a 3T Philips Achieva scanner with a 32-channel (Leuven) or an 8-channel head coil (Leiden).

Three voxel wise statistical analyses were performed with FSL-VBM to assess regional differences in gray matter between respectively the DMDd group and the control group, the DMDi group and the control group, and the DMDd group and the DMDi group.

The fsl_anat pipeline in FSLv6.0.5 was used to process T1-weighted images including bias-field correction, registration to standard space using a MNI152-template, brain extraction and tissue-type segmentation. Fslstats –V was used to compute each partial volume, which allowed us to calculate the global concentration of intracranial volume (ICV), total brain volume (TBV), gray matter volume (GMV), white matter volume (WMV) and cerebrospinal fluid (CSF). A MANCOVA was employed to compare global volumetrics between groups, with site as covariate.

Results: Both patient groups displayed regional differences in gray matter volumes compared to the control group. The DMDd group showed a wider extent of brain regions affected and a greater difference overall. This was substantiated by the global volume quantification: the DMDd group, but not the DMDi group, showed significant differences in gray matter, white matter, and cerebrospinal fluid volumes compared to the control group, after correction for intracranial volume.

Conclusion: Volumetric differences in the brain are considered part of the DMD phenotype. This study suggests an additional impact of corticosteroid treatment showing a contrast between pronounced alterations seen in patients receiving daily corticosteroid treatment and more subtle differences in those treated intermittently.

POSTER Presenters

MYO-MRI+ 2023 | Imaging in Neuromuscular Disease Conference

P.01: Phase contrast motor unit magnetic resonance imaging (PC-MUMRI) to investigate changes to muscle twitch dynamics in a healthy ageing cohort

Author/s: Matthew Birkbeck, Linda Heskamp, Ian Schofield, Julie Hall, Roger Whittaker, Andrew Blamire

Abstract

Background: Ageing results in slower muscle contraction and relaxation times. Current techniques to measure muscle twitch dynamics provide limited information about individual muscles and single motor unit twitch dynamics. We developed a phase contrast (PC) sequence which in conjunction with in-scanner stimulation can measure both whole muscle and single motor unit twitch dynamics.

Aims: Apply PC-MUMRI in a cohort of healthy ageing adults to assess the effect of age on whole muscle compartment, individual muscle and single motor unit twitch dynamics in the anterior compartment of the lower limb.

Methods: We included 47 healthy volunteers (mean age: 53±16; range 26–82 years). Participant's left foot was secured in an MR compatible force plate and stimulation electrodes were attached over the left common peroneal nerve. PC-MUMRI scans were acquired: field of view=160x160mm, in-plane resolution=1.5x1.5mm, slice thickness=8mm, number of slices=2, TR=500ms, TE=8.7ms, flip angle=25°, velocity encoding=15cm/s or 2cm/s for single motor unit scans, 100 dynamic acquisitions, acquisition time=3 min21s.
Velocity profiles from the PC-MUMRI scan along the main axis of the leg were used to estimate the contraction and relaxation times of the whole muscle compartment, individual muscles and single motor units respectively.

Results: Average contraction and relaxation times of the anterior compartment were 83±9 ms (range: 67-103 ms) and 196±36 ms (132-287 ms) respectively, and correlated with age (pcontraction=0.037 and prelaxation=0.004). Contraction and relaxation times of individual muscles all weakly increased with age, except the relaxation time of the extensor digitorum muscle (Tibialis anterior: pcontraction=0.061, prelaxation=0.004; Extensor digitorum longus: pcontraction=0.186, prelaxation=0.792, Peronus longus: pcontraction=0.168, prelaxation=0.0005). No differences in contraction or relaxation times were observed in single motor units (pcontraction= 0.462, prelaxation=0.534).

Conclusions: Contraction and relaxation times of the whole anterior compartment were significantly increased with ageing. Individual muscles demonstrated a mixed pattern of change with age, possibly due to the varied amount of type II and I fibres between these muscles. Single motor units demonstrated no change with age. PC-MUMRI has detected significant changes in muscle twitch dynamics with ageing and could be used as a tool to investigate how muscle twitch dynamics differ between healthy ageing and sarcopenia.

P.02: Quantitative muscle MRI depicts microstructural abnormalities but no signs of inflammation or dystrophy in Post COVID-19 condition

Author/s: Lara Schlaffke, Johannes Forsting, Marlena Rohm, Peter Schwenkreis, Martin Tegenthoff, Christine Meyer-Frießem, Elena Enax-Krumova

Abstract

Background: Patients with post COVID-19 condition (PCC) often suffer from musculoskeletal pain and premature exhaustion but the exact underlying pathophysiology is still unknown. Quantitative MRI (qMRI) techniques like Dixon fat fraction (FF), T2-imaging, and diffusion tensor imaging (DTI) are promising non-invasive tools in the evaluation of muscular pathology and inflammation and have been validated in several neuromusclular disorders.

Aims: To dissect the mechanisms of musculoskeletal complaints assessing muscular pathology of the lower limbs in patients with PCC using qMRI and to correlate these parameters with patient-reported outcomes and parameters of the clinical examination.

Methods: 20 PCC individuals and 20 age and gender matched healthy participated in this study. None of the controls reported a previous SARS-COV2 infection. All participants underwent a 3T MRI of both whole legs using a 16CH-Torso-XL coil including a Dixon sequence, a multi-echo spin-echo sequence for quantitative water mapping and a diffusion-weighted spin-echo EPI. Data were pre-processed to reveal parametric maps for FF, water T2 as well as diffusion metrics (FA, mean, axial and radial diffusivity). 30 muscles were segmented using an automated segmentation tool and subsequently further refined by an experienced rater. Furthermore, nerve conduction studies, electromyography and six-minute-walk-test was performed.

Results: An ANOVA revealed significant increased FF in PCC patients (Main Effect: $p < 0.001$), which disappeared when correcting for different BMI. No significant differences were found for T2-values.

A significant decrease of mean, axial and radial diffusivity was observed in PCC patients (Main effect: $p \leq 0.001$) while fractional anisotropy (FA) showed no difference between groups ($p = 0.325$, see Figure 3). Walking distance was significantly lower in PCC group.

Discussion: In conclusion, differences in diffusion metrics seem to be unspecific and could indicate fiber hypotrophy possibly due to deconditioning, as seen in sarcopenia, which would go along with the lower 6MWT performance. Importantly, inflammatory processed in the acute phase cannot be excluded by the used study design. However, qMRI did not reveal any signs of dystrophic process or inflammation in patients with long-lasting PCC, although it has been previously repeatedly shown to be sensitive to detect even subtle alterations in skeletal muscles.

P.03: Muscle diffusion MRI correlates with autophagic buildup in a Pompe disease mouse model

Author/s: Marlena Rohm, Gabriele Russo, Xavier Helluy, Martijn Froeling, Vincent Umathum, Nicolina Südkamp, Denise Manahan-Vaughan, Robert Rehmann, Johannes Forsting, Frank Jacobsen, Andreas Roos, Anne Schänzer, Matthias Vorgerd, Lara Schlaffke

Abstract

Background: Pompe disease is a hereditary glycogen storage disease where a defect in the lysosomal enzyme alpha-glucosidase (GAA) leads to progressive lysosomal glycogen overload predominantly in striated muscles and motor neurons. Patients with late onset Pompe disease develop muscular weakness of skeletal and cardiac muscles accompanied by irreversible fat infiltrations. Treatment strategies that reverse microstructural changes before fat infiltrations are desirable. Diffusion MRI in non-fat infiltrated leg muscles recently showed significant microstructural differences in Pompe patients of unknown origin.

Aim: To investigate the histopathology leading to these changes, a mouse model for Pompe disease was investigated using a quantitative MR protocol and correlating histopathology in a longitudinal study from presymptomatic to symptomatic state.

Methods: Pompe (Gaa6neo/6neo) and wildtype mice were scanned monthly from the age of 1-8 months using diffusion MRI, T2-mapping, and Dixon-based water-fat imaging with a 7T small animal MRI. Immunofluorescence studies on quadriceps muscles were analyzed for lysosomal accumulations (LAMP1) and autophagic buildup (LC3 and p62) at three timepoint and correlated with MRI findings.

Results: Fat fraction and water-T2 did not differ between groups. In Pompe mice, fractional anisotropy increased, while mean diffusivity (MD) and radial diffusivity (RD) decreased in all observed muscles. Significant changes were observed from the age of two months. Autophagic marker p62 and muscle fibre diameter revealed significant negative correlations with reduced RD ($r(7) = -0.77$, $p = 0.02$) and MD ($r(7) = -0.73$, $p = 0.03$). The autophagic marker LC3 correlated negatively (RD: $r(7) = -0.62$, $p = 0.07$; MD: $r(7) = -0.51$, $p = 0.16$), while lysosomal marker LAMP1 did not show any change or correlation ($p > 0.44$).

Conclusions: In non fat infiltrated muscles, diffusion changes were detected in presymptomatic Pompe mice. Correlations of MD and RD with p62 allow the conclusion that diffusion MRI reflects rather autophagic buildup than glycogen accumulations.

Therefore, our findings clearly support the concept that autophagic buildup is an important pathomechanism even in the early stages of disease progression and comprises a major component of disease modifications in Pompe disease.

P.04: mDTI captures microstructural changes in calpainopathy

Author/s: Johannes Forsting, Marlena Rohm, Martijn Froeling, Anne-Katrin Güttsches, Nicolina Südkamp, Andreas Roos, Matthias Vorgerd, Lara Schlaffke, Robert Rehmann

Abstract

Introduction: Clinical presentation of calpainopathies (Limb Girdle Muscular Dystrophy (LGMD) R1 and D4) is typically characterized by a progressive weakness of limb girdle muscles with variability in disease onset and severity related to the mutation type and gender. In recent years, different therapeutic options for LGMD have been emerged pre-clinically, varying from immunomodulation to genetic treatment. To assess those new therapeutic options, the development of non-invasive surrogate biomarkers is essential. Quantitative MRI (qMRI) is a promising non-invasive tool in the evaluation of neuromuscular diseases (NMD). Therefore, in this study we aimed to evaluate differences in qMRI parameters in leg muscles of patients with calpainopathy (LGMD R1/D4) compared to healthy controls, to correlate those findings to clinical parameters and to evaluate if qMRI parameters show muscle degeneration in not-yet fatty infiltrated muscles.

Methods: Eight thigh and seven calf muscles of 19 calpainopathy patients (10 females, mean age (m+f) 38.0 years) and 19 healthy age- and gender-matched controls were evaluated using a 3T MRI including a mDTI, T2w and mDixonquant sequence. The qMRI-values axial diffusivity (λ 1), mean diffusivity (MD), radial diffusivity (RD), fractional anisotropy (FA), water T2 time and fat-fraction were analysed.

Clinical assessment included testing for muscle strength with QMFT and manual muscle testing as well as NSS and ACTIVLIM for daily activities. Analysis was done with IBM SPSS V28.

Results: Average FF was significantly different between patient and control group in all muscles ($p < 0.001$). In muscles with less than 8% FF a significant increase of FA ($p < 0.005$) and decrease of RD ($p < 0.004$) was found in high-risk muscles of calpainopathy patients. Water T2 times were increased within the low- and intermediate-risk muscles ($p \leq 0.045$) but not in high-risk muscles ($p = 0.062$). Correlations between clinical assessments and qMRI values showed a differing degree of correlation based on the assessment.

Conclusion: Good correlation of FF but also diffusion metrics to clinical assessments were found. Diffusion metrics and T2 values are promising candidates to serve as sensitive early and non-invasive methods to capture early muscle degeneration in non-fat-infiltrated muscles in calpainopathies.

P.05: Towards patient-friendly arterial-spin-labeling MRI in muscle: Effect of exercise intensity and standardisation on perfusion parameters and signal-to-noise

Author/s: Donnie Cameron, Esther Schrama, Linde Boogaarts, Thom Veeger, Celine Baligand, Lydiane Hirschler, Matthias van Osch, Hermien Kan

Abstract

Background: In dystrophinopathies, impaired muscle perfusion is observed during exercise due to decreased vasodilation, leading to muscle damage through insufficient oxygen supply. Potential treatments could be evaluated via non-invasive arterial-spin-labelling MRI; however, patients are expected to show impaired post-exercise perfusion and reduced SNR. Further, exercise paradigms should be relatively low intensity, to minimise patient burden.

Aims: We compare three ASL exercise paradigms—two standardised, with different exercise intensities, and one non-standardised at a single intensity—to develop patient-acceptable ASL-MRI, reporting muscle blood flow (MBF), arterial transit time (ATT), T2*, and SNR.

Methods: We scanned 17 volunteers at 3T (Philips). Split-label pulsed-ASL MRI was applied in the lower leg, and consisted of single-shot three-echo EPI (TR/TE/ΔTE= 3000/14.0/17.4ms; FOV=190mm×190mm×86mm; voxel-size=3×3×8mm3; 2 slices, gap=70mm) with ten post-label delays (600:200:2400ms). SNR was determined via noise scans without RF. ASL-MRI was performed during 10mins post-exercise recovery. The non-standardised exercise (n=12) was self-guided. The standardised exercise (n=5) was guided by PsychoPy animations. Both paradigms comprised 5mins dorsiflexion with a load = 25% maximum voluntary contraction (MVC) for the non-standardised exercise, or 25% and 15% MVC for the standardised exercise. When testing both loads, one bout was performed per leg. ROIs were drawn in the tibialis anterior. MBF and ATT were fitted via the Buxton model per slice and dynamic. Post-exercise data were split into five, and medians and interquartile ranges were compared using two-way repeated-measures/mixed ANOVA.

Results: Standardised exercise data showed less dispersion than non-standardised exercise data, as did 25% versus 15% MVC data. MBF areas-under-the-curve did not differ between 25% and 15% MVC. T2* was higher for 25% MVC data; notably, participants reported cramps at 25% MVC. Perfusion was elevated for longer in 25% vs 15% MVC data; data acquired at 15% MVC did not achieve an SNR≥6, as recommended for ASL parameter estimation.

Conclusion: We investigated whether exercise standardisation improves ASL parameter estimates and whether exercise intensity can be lowered without compromising SNR. Less variability was observed with a standardised protocol or at 25% MVC. At 15% MVC, the SNR was too low for robust parameter estimation. Further improvements are required to develop patient-friendly exercise ASL-MRI.

P.06: Longitudinal Dixon Magnetic Resonance Imaging in dysferlinopathy patients has powerful potential for assessing outcomes of therapeutic interventions.

Author/s: Ian Wilson, Andrew Blamire, Jordi Diaz Manera, Carla Bolano Diaz, Ursula Moore, Heather Hilsden, Volker Straub, Ericky Caldas de Almeida Araujo, Pierre Carlier, Harmen Reyngoudt

Abstract

Background: Fat replacement in muscles measured by Dixon MRI provides an excellent marker for disease progression in dysferlinopathy patients. Although no specific therapies exist for dysferlinopathies, these disorders entail multiple pathways to muscle cell death, each of which is potentially a target for intervention; therefore, developing methods to measure therapeutic outcomes of novel drug trials is extremely important.

Aims: The aim of the study was to determine if longitudinal analysis of Dixon MRI scans could provide a feasible tool for monitoring disease progression as well as a non-invasive marker for therapeutic intervention in dysferlinopathy patients.

Methods: In this study, we looked at a cohort of 11 patients from the JAIN COS natural history study who had been scanned at least 6 times over a 10-year period. Fat fraction analysis to measure the quantity of fat in muscles was carried out for seven muscles in the lower leg and nine muscles in the thigh.

Results: In both lower legs and thighs, percentage fat fraction showed a steady increase over the years with lower legs regressing slightly faster (slope = 3.24 % per year, SD = 0.85, range 1.62-4.74%) than thighs (slope = 2.16 % per year, SD = 1.21, range 0.42-4.57%), this difference was significant (p=0.015). The R2 fit was almost linear with a mean of 0.94 (range 0.81 to 0.99); there was no sign of sigmoidal behaviour for FF progression in this subgroup of JAIN COS patients, which is commonly seen in other muscular dystrophies. Furthermore, certain muscles undergo disease progression early with gastrocnemius medialis and soleus in the lower leg, semimembranosus and adductor magnus in the thighs being most likely to show fatty transformation before other muscles.

Conclusions: Linear regression analysis may predict disease progression in individual muscles in individual patients. Such analysis may allow prediction of time to lose ambulation. Dixon MRI provides a valuable tool to capture any changes in disease progression following therapeutic drug intervention by measuring deviations in the slope of fat fraction percentage progression.

P.07: Incorporating Prior Knowledge on Fat Replacement in Deep Learning Models for Muscle Segmentation in MRI of Becker Dystrophy Patients

Author/s: Mohamed Kilany Hassan, Karin Naarding, Erik Niks, Hermien Kan, Berend Stoel

Abstract

Background: Automatic segmentation of MR-images of fat-replaced muscles has proved to be very challenging. Deep learning (DL)-based automatic segmentation of individual muscles in quantitative MRI is a promising approach. However, DL models encounter challenges due to limited training data, muscle size variability, and heterogeneous fat-replacement within muscles. Therefore, incorporating prior-knowledge of muscle size and fat-replacement level during training could enhance DL model performance.

Aims: To study the impact of incorporating muscle size and pathology severity into the training loss to enhance segmentation and fat quantification, particularly in severely fat-replaced muscles, in which anatomical information is obscured.

Materials and Method 2D multi-slice fat and water MR-Dixon-images of the upper leg were included from 21 patients with Becker muscular dystrophy at wide range of disease progression. We employed a V-net architecture with residual and attention blocks to segment 12 muscles. Two losses were introduced to optimize the DL model: volume-based weighted-Dice (VbWD) and fat-based weighted-Dice (FbWD). VbWD addressed muscle size variability, while FbWD addressed the heterogeneity in fat-replacement. The base V-net underwent 1500 iterations of training using VbWD, followed by 100 tuning iterations using FbWD (Fat-tuning). For a fair comparison between the two loss functions, the base-network underwent additional 100 iterations (Volume-tuning). The results were evaluated using 3-fold cross-validation.

Results: Each fold comprised 18 training and 2 testing subjects. To assess the impact of the introduced loss functions across different fat replacement levels, fat fractions were categorized into mild (fat fraction < 0.33), moderate ($0.33 \leq$ fat fractions ≤ 0.66), and severe (fat fractions > 0.66) replacement. Average Dice-score and fat-fraction estimation error were evaluated for each category.
The difference in Dice-scores between the Fat-tunned and Volume-tunned models were 0.5% for mild, -0.2% moderate, 0.6% severe categories. However, the fat-fraction estimation errors were almost similar in both models.

Conclusion: The Dice-scores indicated a potential influence of FbWD on segmentation quality specially in the severe fat-replacement muscles. However, this improvement did not significantly impact fat-fraction estimation error. The study showed that, in the current setting, adding fat-fraction as prior-knowledge has no significant improvement over prior-knowledge based on muscle size.

P.08: MRSI metabolite alterations in the putamen of patients with multiple sclerosis and positive-oligoclonal immunoglobulin-G bands

Author/s: Petra Hnilicova, Ema Kantorova, Marian Grendar, Daniel Cierny

Abstract

Multiple sclerosis (MS) is a multifactorial disease with expanding neuro-axonal degeneration in the central nervous system leading to progressive neuro-muscular dysfunctions. The causative pathology of MS involves autoimmune and inflammatory provenance and diffuse neuro-axonal degeneration evoked by various stimuli. Generally, the recognized accompanying sign of MS is the positive-oligoclonal immunoglobulin-G bands (OCB) examined in the cerebrospinal fluid and serum. Although positive-OCB is not a fully specific MS hallmark, its prognostic relevance is associated with a more aggressive disease course. Nevertheless, the exact pathological cascade eliciting MS progression and its effect on neuro-muscular projection remain unclear. Remarkably, several small and deep-seated brain structures, such as the putamen, were not extensively researched in context of MS; although its role in motion control and its involvement in various motoric disorders was proven.

This preliminary study evaluated putaminal metabolic alternations in patients with early MS (n=13, 7 men/6 women, 35±9 years of age) using the unique neurotransmitter-edited proton-1H magnetic resonance spectroscopy imaging (MRSI) performed at 3 Tesla MR scanner. This MRSI method with excellent resolution of ~3cc enabled the noninvasive assessment of biomedically relevant metabolites that can reflect neuro-axonal degradation (tNAA: N-acetyl aspartate/aspartyl-glutamate), ongoing gliosis (mIns: myo-Inositol), and neurotransmitter dysregulation (GABA: gamma-aminobutyric acid, Glx: glutamate/glutamine) in the selected brain area without needing a biopsy. In this study were quantified two voxels, bilaterally selected from the putamen area, with a goal to assessed especially the main excitatory (Glx) and inhibitory (GABA) neurotransmitters.

The MS patients with positive-OCB shoved significantly lower GABA levels in the putamen than negative-OCB patients, while Glx, tNAA, and mIns were unchanged. Furthermore, in the putamen of MS patients with positive-OCB was confirmed strong correlation of GABA with neurological disability (measured by the Expanded Disability Status Scale). According to our results, MS patients with potentially worse prognoses suffered from suppressed inhibitory neurotransmission, which might be critical for muscular weakness.

This study was supported by VEGA 1/0092/22, co-funded from EU sources.

P.09: Effects of diffusion tensor imaging b-value on the quantification of lower leg skeletal muscle fascicle architecture

Author/s: Zhenkai Zhao, Fiona Elizabeth Smith, Emma Hodson-Tole

Abstract

Background: The b-value reflects the strength and timing of the gradients used to generate diffusion-weighted images and is an important factor when considering skeletal muscle fibre tractography. Higher b-values can capture greater diffusion effects, but the signal-to-noise ratio (SNR) can be much lower and influences the architectural measurements.

Aims: To investigate the effects of different b-values on muscle fibre tractography in lower leg skeletal muscle.

Methods: Six healthy adults (3 male and 3 female (24-45y)) were recruited. Leg muscles were scanned using a 3T Siemens MR scanner and a torso-array surface coil. Diffusion Weighted Images (DWI) were acquired with six b-values ranging from 10 to 500 s/mm2 using 12 diffusion weighted gradient directions. Segmentations were completed manually with 3D slicer on T1-weighted images before registration to the diffusion images.
Tractography was performed using a deterministic tractography algorithm built into DSI studio (Yeh et al. 2013), and quantitively evaluated with the fascicle length (FL), pennation angle (PA), fascicle curvatures, fractional anisotropy (FA), and mean diffusivity (MD) for gastrocnemius medialis (GM), tibialis anterior (TA), and soleus muscles (SO).

Results: Higher FA and MD values were associated with lower b-values, especially for values lower than 100 s/mm2. MD was between 4-8 mm2/s at b = 100 s/mm2 compared to 1.3-1.5 mm2/s at b = 500 s/mm2; fascicle curvatures were greater for lower b-values, from
8.5/m to 15/m on average. There were no apparent changes for the fascicle length and averaged pennation angles for the same muscle across different b-values. However, reduced fascicle tract density occurred for higher b-values with the identical stopping criteria. It seems necessary to carefully consider the b-value for tractography across different types of muscles. For lower leg muscles, b-values lower than 250 s/mm2 are not sufficient to capture the diffusion effects and differentiate multiple fibres for GM, TA, and SO muscles, even though higher SNR can be achieved.

Conclusion: The b-value is not a determinant for the architectural properties across different muscles but does influence the architectural measurements in terms of diffusivity and curvature.

References: Yeh, Fang-Cheng 2013. PLOS ONE, 8: e80713.

P.10: Muscle Diffusion Tensor Imaging in Facioscapulohumeral Muscular Dystrophy

Author/s: Leonardo Barzaghi, Matteo Paoletti, Mauro Monforte, Sara Bortolani, Chiara Bonizzoni, Thorsten Feiweier, Niels Bergsland, Francesco Santini, Xeni Deligianni, Giorgio Tasca, Silvia Figini, Enzo Ricci, Anna Pichiecchio

Abstract

Introduction: Muscle diffusion tensor imaging (mDTI) have been applied on several myopathies such as Pompe disease, Duchenne muscular dystrophy and inflammatory myopathies. mDTI parameters have been shown to reflect the fat replacement grade in muscles rather than the myofiber architecture integrity. No application of mDTI, however, is reported in facioscapulohumeral muscular dystrophy (FSHD).

Aims: We aimed to assess diffusivity parameters in FSHD subjects compared to healthy controls (HCs), to investigate the correlation between mDTI metrics and fat replacement, even along the main axis of the muscle, and to study the ability of mDTI parameters to precede any fat replacement process in the muscle.

Methods: Ten FSHD subjects and fifteen age-matched HCs were enrolled in this study. From the 6-points Dixon and Multi-echo Spin-echo (MESE) sequences, three slices from proximal, medial and distal thigh levels have been semi-automatically segmented into eleven regions of interest (ROIs). The ROIs were co-registered to the DWI dataset which have been subsequently de-noised, registered to the b0 image and then corrected for eddy currents. We calculated for each ROI (left and right side averaged) the Fat Fraction (FF) from the 6-points Dixon sequence, the water T2 (wT2) from the 17-echoes MESE and the mDTI parameters from the DWI sequences, i.e. Fractional Anisotropy (FA), Mean Diffusivity (MD), Radial Diffusivity (RD) and Axial Diffusivity (AD).

Results: FF and wT2 were significantly higher in FSHD than controls whereas MD, RD and AD were significantly lower than controls (p < .05). No difference with controls was shown for FA. FF positively correlated with FA and negatively with MD, RD and AD. FF and FA showed significantly higher values distally than proximally. whereas wT2, MD, RD, AD showed lower values distally than proximally (p<.05). Muscles with no significant fat replacement or edema showed a significantly lower AD and FA than controls.

Discussion: Our results suggest that mDTI parameter changes may predominantly reflect fat replacement in FSHD and show disease involvement in muscles even before significant fat replacement occurs.

Funding: This research was funded by the Ministry of Health RC 2022-2024.

P.11: Longitudinal evaluation of a cohort of facioscapulohumeral disease subjects and evaluation of predictive power of fat fraction and water T2 on fat replacement over time

Author/s: Matteo Paoletti, Mauro Monforte, Leonardo Barzaghi, Giorgio Tasca, Niels Bergsland, Arianna Faggioli, Francesca Solazzo, Giulia Manco, Sara Bortolani, Eleonora Torchia, Beatrice Ravera, Xeni Deligianni, Francesco Santini, Elena Ballante, Silvia Figini, Enzo Ricci, Anna Pichiecchio

Abstract

Introduction: Quantitative magnetic resonance imaging (qMRI) has proven to be a valuable tool for assessing and monitoring the progression of facioscapulohumeral dystrophy (FSHD) for which there are still no effective clinical treatments.

Objective: We aimed to longitudinally monitor disease progression with a quantitative lower limb muscle MRI protocol in a cohort of patients with facioscapulohumeral disease (FSHD) over a total period of 24 months. We investigated the ability fat fraction (FF) and water T2 (wT2) at baseline to predict long-term disease involvement, i.e. fat replacement.

Methods: Thirty FSHD subjects with at least an edematous muscle at MRI were enrolled and scanned at baseline and at 6, 12 and 24 months of follow-up. FF and wT2 were calculated in twelve muscles of the thigh and six muscles of the lower leg. FF and wT2 were analyzed longitudinally at whole-thigh and leg level as well as at single compartment and single muscle level. FF and wT2 at baseline were also evaluated as predictors over fat replacement over the same time period. The standard clinical scores of 6 minute walking test (6-MWT), clinical severity score (CSS) and dynamometry tests were correlated with FF and wT2 using Pearson's r correlation at baseline, 12 and 24 months.

Results: Yearly, FF showed a mean increase of 2% whereas wT2 decreased on average by 1-2 ms. The compartments with intermediate and higher baseline FF showed the greater increase of FF at 24 months; those with higher baseline wT2 showed the greater FF increase at follow- up. FF and wT2 anticorrelated with 6-MWTand dynamometry and positively correlated with CSS.

Conclusions: Our results suggest that intermediate and higher FF and higher wT2 at baseline are strong predictors of higher fat replacement over time.

Funding: This work was supported by the Italian Ministry of Health (RF-2016-02362914)

P.12: MRI-based characterization of muscles in ageing mice fed on high-energy diet and sedentary lifestyle

Author/s: Béatrice Matot, Ericky Caldas de Almeida Araujo, Walha Taras, Pierre-Yves Baudin, Harmen Reyngoudt, Benjamin Marty, Yves Fromes

Abstract

Background: Ageing is a typical translational research topic. Strategies to improve the translation of ageing research laboratory findings to develop and implement interventions that directly benefit older people are crucial.

Aim: Our primary goal, in this longitudinal study, was to assess leg muscles' trophicity and structure by MRI and function in a cohort of mice exposed to a high-energy diet and a sedentary lifestyle.

Methods: Thirty-six C57Bl/6JRj male mice from 2.5 to 22 months of age were fed ad libitum with high-energy diet. Ten of these mice were scanned on a 7T MRI Bruker system with a surface transceiver cryoprobe positioned next to the anterior compartment of the legs. Maximal muscle cross-sectional area (maxCSA) and muscle T2 were evaluated by high-resolution gradient echo axial images (res= 50x50x200 μm3) and MSME sequence (30 TEs; inter-echo-spacing = 3.07ms), respectively. Muscle function was assessed on a second group of twenty-six mice by a grip test and a RotarodTM test. ANOVA and t-test were used to analyse MRI and functional data, respectively ($p < 0.05$ for statistical significance).

Results: A Kaplan-Meier curve pointed out an increased mortality in our cohort with a survivorship of 50% around 20 month whereas the life expectancy reported for this strain is around 24 months of age. In parallel, mice body weight increased in a normal range with age. Motor function and coordination did not change significantly over age, but mean and maximal grip force were negatively correlated with age. No significant effect of age on max_CSA of the anterior compartment muscles was observed. Finally, muscle T2 significantly increased with age (2.5m: 21.5 ± 0.2; 22m: 22.8 ± 0.1 ms), mainly during growth, up to 9 month (22.3 ± 0.4 ms).

Conclusions: High-energy diet and sedentary lifestyle have negative effects on life expectancy that could not be linked to overweight in our study. Leg muscle trophicity remained stable, but force decreased with age. Moreover, mouse leg muscles displayed age-related increase in T2 values, similar to humans.

P.13: Multi-contrast partially spoiled GRE for quantification of muscle fat fraction and water T2

Author/s: Eleonore Vermeulen, Pierre-Yves Baudin, Marc Lapert, Benjamin Marty

Abstract

Background: In clinical trials related to neuromuscular diseases, the intramuscular fat fraction (FF) and water-T2 (T2H2O) relaxation time are typically used as imaging biomarkers of disease severity and activity, respectively. Longitudinal assessments often require rapid 3D parametric sequences, where reproducible positioning is needed, as the muscle damage can be heterogeneously distributed. The reference approach for T2H2O measures, using a multi-spin-multi-echo (MSME) sequence, is only available in 2D. It has been shown that RF phase-modulated (or partially-spoiled) 3D gradient-echo (p-SPGR) steady-state signal could be sensitized to T2 by varying RF-phase increments, but no method has exploited this feature while accounting for the presence of fat in the tissue.

Aims: The goal of this study was to obtain 3D multi-parametric mapping sequence adapted to the study of skeletal muscles. In the present work, we optimized the parameters of a series of p- SPGR acquisitions, to extract simultaneously the T2H2O and FF in muscle tissues.

Methods: Acquisitions were performed on a 3T MRI scanner. The VIBE sequence was modified in order to control the phase increment. To limit the examination time, the number of acquired volumes was set to 10, TE and TR were set to minimum. The 10 flip angles and phase increments were optimized via EPG simulations and minimization of the Cramer-Rao bound. T2H2O and FF maps were obtained by exhaustive search of the acquired signals in a bi-component dictionary generated using EPG simulations. The proposed method was compared to reference methods for T2H2O (MSME 17-TE) and FF (GRE-VIBE 3-points Dixon) on the leg of a volunteer, before and after performing a calf extension exercise

Results: The mean relative T2 increase in the exercised muscle was 12.8 % with the proposed method, similar to that obtained reference sequence (12.4%). The fat fraction map was also in agreement with our reference method in the tested subject (bias: -0.9%, 95% limits of agreement: ± 19.8 %, Bland-Altman analysis).

Conclusions: The proposed method provided valid parametric maps for the characterization of muscle in healthy volunteers. Further studies on patients will be necessary to evaluate it on muscles with different levels of disease severity.

P.14: Muscle specific assessment of calf in Miyoshi muscular dystrophy by quantitative MRI

Author/s: Ivica Just, Petra Hnilicova, Radka Klepochova, Siegfried Trattnig, Monika Turčanová Koprušáková, doc Martin Kolísek, Martin Kršš̌ák

Abstract

Miyoshi myopathy is a rare type of muscular dystrophy caused by changes in the DYSF gene, being part of dysferlinopathic group of diseases. Weakness and atrophy affect mainly lower extremities, especially in calf muscles.

Aim of the study was to detect and quantify fat infiltration in calf muscles of individuals with symptomatic Miyoshi myopathy compared to asymptomatic disease carriers with mutation in the DYSF gene and healthy controls.

Methods: Study was performed at 3T MR system (Prisma Fit Siemens) using 15-Channel 1H Tx/Rx knee coil (Siemens). The calf muscles of four patients with symptomatic dystrophy (age 36.0 ± 5.1 y, BMI 21.9±2.9 kg/m2), three asymptomatic carriers of DYSF genetic mutation (age 35.0 ± 5.3 y, BMI 22.4±1.9 kg/m2) and four healthy volunteers (age 35.0 ± 2.9 y, BMI 21.7 ± 0.94 kg/m2) were examined. Measurement protocol consisted of multi-echo Dixon, T1-w and T2-w images. Nine muscles were segmented using 3D slicer and average fat fraction (FF) was calculated for each single muscle and as an average for all muscles as well.

Results: Fat fraction was significantly different in dystrophic patients in all calf muscles, with average 68.3 ± 12.6 % vs carriers (20.9 ± 4.0%) and healthy volunteers (14.1 ± 5.6%). Differences between asymptomatic carriers and healthy volunteers were not significant.
Highest FF in dystrophics were found in posterior group of muscles – gastrocnemius lateralis and medialis (85,3% and 78.5% resp.), soleus (79.5%) together with peroneus muscle (82.8%). The least affected was deep muscle compartment, especially tibialis posterior (34.8%), and extensor and flexors of the toes (range of 55.6 - 67.9%). Most different in comparison between symptomatic patients and healthy controls were tibialis anterior and gastrocnemius medialis muscle (13- and 9-fold, resp.). Carriers presented also slightly higher FF in all muscles, but the ratio to healthy volunteers didn't exceed 1.9.

Conclusion: Quantitative MRI revealed the posterior chain of calf muscles as most affected in Miyoshi myopathy. Deep compartment of the muscle is the most preserved.

P.15: Myosteatosis in aging muscles

Author/s: Alfredo Lopez, Béatrice Matot, Jean-Marc Boisserie, Sophie Jouan, Ericky Caldas, Pierre-Yves Baudin, Benjamin Marty, Harmen Reyngoudt, Yves Fromes

Abstract

Background: The typical adult will lose muscle mass with age; the loss varies according to sex and the level of muscle activity. Our primary goal was to assess leg muscle's trophicity, structure, function and biochemistry based on quantitative MR examination in a prospective open label study to benchmark various outcome measures. More specifically, is fat infiltration part of normal aging or a pathological feature.

Methods and patients: Inclusion criteria were based on clinical screening, absence of any chronic disorder, age "> 20 years". A 3T MRI scanner (Siemens Prisma) was used to assess skeletal leg muscles and extract various parameters. Thus, cross sectional area, fat fraction and water T2 were measured. Descriptive statistics express results as mean ± SEM. Group comparison was based on T test and ANOVA.

Results: We present preliminary results on N = 65, aged 20 to 81 years. Volunteers were stratified as young ("> 35yo"; N: 15), middle-aged (35-60yo; N: 25) and elderly ("> 60yo"; N: 18). Of our cohort, 84% were either active or very active. Based on Peronnet index, we found that young individuals displayed a significant gender difference (11.0 vs. 27.2, "$p < 0.01$"). Body composition changed towards higher fat content in both genders, with a faster increase in male and a decrease in gender imbalance (Fat mass index: 25.4 vs. 31.3, "$p < 0.05$"). More specifically at the level of skeletal muscles, cross-sectional areas of triceps surae slightly increased with age. Intramuscular fat fraction increased with age (0.037 ± 0.008; 0.053 ± 0.011; 0.066 ± 0.013, respectively). However, body composition seems only poorly linked to and muscle steatosis. Intrinsic T2 values (ms) increased with age (36.2± 1.6; 37.2 ± 1.7; 38.2 ± 1.6, respectively).

Conclusions: NMR provides interesting tools to assess not only structural aspects of the aging muscles, but our innovative set-up allows to investigate functional and biochemical aspects also. Fatty infiltration of skeletal muscles appears to increase with age without a strong link to body composition. Regular activity seems to preserve muscle mass and function, but more subtle changes can be observed by MRI.

P.16: Lower limb muscle-water T2 as a non-invasive imaging biomarker of disease severity and progression in amyotrophic lateral sclerosis

Author/s: Nick Zafeiropoulos, Uros Klickovic, Luca Zampedri, Stephen Wastling, Jasper Morrow, Tarek Yousry, Michael Hanna, Linda Greensmith, Pietro Fratta, John Thornton

Abstract

Background & Aims: Lower limb muscle-water T2 (T2m) has been shown to be elevated in amyotrophic lateral sclerosis (ALS), with suggested associations between T2m and progression. Here we analysed multi-echo MRI data to investigate lower-limb T2m longitudinally, correlating T2m and effective fat fraction (ffa) changes with functional assessment and myometry.

Methods: Participants comprised people with ALS and healthy controls. Participants were assessed using the ALS Functional Rating Scale–Revised (ALSFRS-R). Lower limb myometry was obtained (microFET®2 handheld dynamometer) for isometric assessment of knee and ankle extension and flexion. Patients were examined at baseline, 6 and 12 months; controls at baseline and 12 months. MRI was performed at 3T (Siemens Skyra) with a multi-echo CPMG sequence. A multi-component slice-profile-compensated extended phase graph (sEPG) model for CPMG sequence signals was implemented, with the fat signal modelled as two empirically calibrated sEPG components with fixed parameters, and the remaining unknown parameters (B1 field factor, T2m, fat fraction (ffa), global amplitude and Rician noise SD) determined by maximum likelihood estimation.

Results: Mean thigh and calf T2m and ffa were significantly elevated in ALS patients, in varied patterns. A tendency to negative correlation was seen between ALSFRS-R and both T2m and ffa (significant at the calf level at baseline and 6 months.) Correlations were stronger for T2m than ffa (p values: 0.002, 0.002 vs. 0.046, 0.047; R values -0.68, -0.58 vs. -0.47, -0.50, for baseline and 6 months respectively). Correlations with myometry results were significant predominantly for T2m at the calf level. Myometry changes between baseline and 6 months were significant for all muscle compartments. Concomitant T2m
changes were significant in the calf and left anterior thigh; ffa changes were significant in the left limb. Four muscle compartments showed significant correlation between longitudinal T2m change and myometry changes.

Conclusion: Baseline differences of T2m between patients and controls and associations between T2m and both ALFRRS-R and myometry support the validity of T2m as a disease biomarker. This approach using routinely available CPMG pulse sequences provides T2m and ffa estimates from a single acquisition which provide complementary indices of neuromuscular pathology.

P.17: Natural history quantitative MRI in upper limb muscles of dysferlinopathy patients

Author/s: Harmen Reyngoudt, Ericky Caldas de Almeida Araujo, Ian Wilson, Pierre-Yves Baudin, Benjamin Marty, Carla Bolana-Diaz, Jordi Diaz Manera, Laura Rufibach, Heather Hilsden, Giorgia Querin, Elena Pegoraro, Jerry R. Mendell, Tanya Stojkovic, Volker Straub, Pierre G. Carlier, Andrew M. Blamire

Abstract

Background: Dysferlinopathy is a hereditary neuromuscular disorder caused by mutations in the dysferlin gene and is characterized by a variable disease progression rate. The upper limb muscles are affected in the later stages of the disease, and muscle fat replacement of arm and forearm muscles follows thigh and leg involvement. A previous natural history study in the lower limbs has demonstrated a persistent inflammation and muscle replacement by fat, assessed via water T2 and fat-fraction (FF) mapping, respectively.

Aim: Adding to the lower limb MRI natural history study, a longitudinal quantitative MRI study in upper limbs was set up in four clinical centers (UK, France, Italy, USA), investigating both muscle replacement by fat and muscle inflammation.

Methods: The MRI data presented here were acquired in two of the four sites, both at 3 tesla, at baseline, 6-months, and/or 12-months. The MRI acquisitions included FF and water T2 mapping at the level of the upper arm (deltoid, triceps and biceps brachialis) and forearm (extensor, flexor). Student's t-tests were performed ($P < 0.05$).

Results: Patients in this cohort (17 female, 10 male, 89% ambulant, 70% LGMD R2 diagnosis) were 46.1±12.1 years old and had symptoms for 14.9±7.7 years. At baseline, the lowest FF values were found in forearm muscles (23.5±14.6% in flexor, 24.1±16.1% in extensor). FF values in upper arm muscles were 30.1±18.6%, 31.1±21.4% and 35.1±24.1% in deltoid, biceps brachialis and triceps muscles, respectively. Per 6 months, FF increased, on average, by 2 to 3% in forearm muscles and 2 to 5% in upper arm muscles ($P > 0.05$). Biceps brachialis and extensor muscles showed normal water T2 values (< 37.0 ms), whereas elevated water T2 values were found in flexor and triceps muscles (≥ 38.7 ms) across the three visits ($P < 0.05$).

Conclusion: The upper arm muscles were more involved than forearm muscles. An inter-patient heterogeneity of disease progression was observed, resulting in non-significant results for changes in FF in this cohort. The persistent inflammation in some muscles (reflected by elevated water T2 values) was observed across the entire study.

P.18: Effect of sirolimus on quantitative MRI and 31P MRS biomarkers in patients with inclusion body myositis

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Abstract

Background: Inclusion body myositis (IBM) is the most frequent type of myositis in patients older than 50 years. The pathophysiology and the muscle response to treatment in IBM is not well understood. Two categories of histopathological features are characteristic of this disease suggesting inflammatory (myositis) and degenerative (inclusion body) mechanisms. The disease is slowly progressive and leads to severe muscle disability.

Aim: Here, we report the longitudinal analysis of the quantitative MRI data including muscle fat fraction (FF) and contractile cross-sectional area (cCSA), reflecting disease progression, and water T2, reflecting active muscle damage (such as inflammation, necrosis), and 31P MRS indices, reflecting changes in muscle energy and membrane phospholipid metabolism, in the placebo-controlled phase 2b trial of sirolimus in IBM patients.

Methods: In the RAPAMI study (NCT02481453), quantitative MRI and 31P MRS data were obtained at 3 tesla in thigh and leg muscles of 45 patients (sirolimus vs. placebo) at baseline and year-1. Values for FF, cCSA and water T2 values were assessed in leg and thigh muscles and 31P MRS indices (including Pi,tot/PCr and PCr/ γATP) were evaluated in quadriceps or triceps surae. Student's t-tests analyses were performed ($P < 0.05$). Standardized response means (SRM) were calculated to assess the sensitivity to change for the different MRI biomarkers.

Results: No significant differences were found at baseline between both patient groups for FF, cCSA, water T2 and 31P MRS indices in all muscles, muscle groups and global segments ($P > 0.05$). FF increase and cCSA decrease was more prominent in the placebo group and was significant for FF in vastus lateralis, hamstring and global thigh ($P < 0.05$). SRM values for FF were > 0.8 for all thigh muscles in the placebo but not in the sirolimus group. In thigh, water T2 was elevated, especially in quadriceps muscles at baseline and year-1 ($P < 0.05$). At year-1, Pi,tot/PCr was significantly higher ($P < 0.01$) and PCr/ ATP significantly lower ($P < 0.01$) in the placebo group but not in the sirolimus group.

Conclusion: This quantitative study has demonstrated that small yet significant changes can be measured between treated and non-treated IBM patients.

P.19: Diffusion tensor parameters predict quadriceps strength in younger and older adults

Author/s: Yael Vainberg, Jessica Asay, Andrew Schmidt, Julie Muccini, Garry Gold, Feliks Kogan, Valentina Mazzoli

Abstract

Background: Sarcopenia causes reduced muscle strength and is associated with an increased risk of mortality and disability in elderly people. However, strength declines more rapidly than muscle mass, suggesting that not only "muscle quantity" but also "muscle quality" declines with age. Due to its great sensitivity to microstructure, Diffusion Tensor Imaging (DTI) is an ideal tool to investigate the mechanism of muscle strength loss.
Aim: We aim to investigate whether DTI parameters can improve the prediction of muscle strength compared to muscle volume alone.

Methods: 24 healthy adults aged 30-80 (12F) were enrolled. Both thighs were scanned using a whole-body 3 Tesla MRI scanner. Dixon scans were used for anatomical reference, while Radial Diffusivity (RD) and Fractional Anisotropy (FA) were calculated from DTI scans. An isokinetic dynamometer was used to measure eccentric (v=-60deg/s) (ECC60) and concentric (v=120deg/s) (CONC120) quadriceps strength during knee flexion/extension. A multiple linear regression model was used to investigate the effect of age, volume, and DTI parameters on muscle strength. Variables with $p < 0.05$ values were considered significant.

Results: Volume was the strongest predictor of both CONC120 ($p < 0.001$, R2=0.507) and ECC60 ($p < 0.001$, R2=0.389). When normalized for volume, age was associated with a decrease in CONC120 (p=0.025, R2=0.085), however, ECC60 was preserved (p=0.622, R2=0.016). Age had no significant correlation with either FA (p=0.210, R2=0.013) or RD (p=0.233, R2=0.010). When controlling for volume, FA showed a significant negative correlation with CONC120 (p=0.006, R2=0.576), while RD had a significant positive correlation with CONC120 (p=0.001, R2=0.612) and ECC60 (p=0.007, R2=0.469) Conclusion: Type II muscle fibers can generate more strength per unit area and are more prone to atrophy in older adults compared to Type I fibers. The correlation between DTI parameters and muscle strength, independent of volume, could reflect these microstructural changes (1). While histological validation will be needed to identify the biological underpinning of these diffusion parameters, our results clearly highlight that DTI can non- invasively provide information on age-related changes in muscle quality and strength, independently of muscle volume. DTI could help create effective interventions to maintain and restore mobility in older adults.

P.20: Multi-modal magnetic resonance imaging protocols in the multi-site Brain Involvement in Dystrophinopathies (BIND) study

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Abstract

Background: As dystrophin is expressed in the brain, its deficiency underlies brain comorbidities observed in patients with Becker and Duchenne muscular dystrophies (BMD and DMD). Structural and functional differences in the brain have been observed between patients and controls.

Aims: The international BIND (Brain Involvement iN Dystrophinopathies) consortium aims to improve our understanding of brain involvement in BMD and DMD. This abstract briefly summarizes the multi-modal magnetic resonance imaging (MRI) protocols in the BIND study.

Methods: The target is to scan 60 BMD patients, 60 DMD patients, and 120 healthy age- and sex- matched controls. Five sites acquire MRI data: University College London, London, United Kingdom; Leiden University Medical Center, Leiden, the Netherlands; Newcastle University, Newcastle upon Tyne, United Kingdom; Region Hovedstaden, Copenhagen, Denmark; Catholic University of the Sacred Heart, Rome, Italy. The scans in Copenhagen and London are performed on a Siemens Magnetom Prisma 3T (software version VE11E) with a 20-channel head coil. The scans in Leiden and Newcastle are performed on a Philips 3T Achieva (software version 5.7.1) with a 32- and 8-channel head coil, respectively. The scans in Rome are performed on a General Electric SIGNA Premiere 3T (software version 28.1) with a 48-channel head coil.

The protocol designs were informed by the relevant literature while constrained by hardware and scan time. The MRI protocol includes the following: T1-weighted anatomical scan, diffusion-weighted scan (two-shell in London and Copenhagen; single-shell in Leiden, Newcastle, and Rome) for quantifying microstructural properties of brain tissue, blood- oxygenation-level-dependent resting-state and visual checkerboard task for studying functional connectivity, and arterial spin labelling for quantifying cerebral blood flow.

The data is stored in anonymized DICOM files on an XNAT instance. After the dissemination of the results, the data will be shared with the research community and Duchenne Data Foundation under the FAIR data principles following the Brain Imaging Data Structure.

Conclusion: We summarized the ambitious imaging protocol employed in the BIND study to improve the characterization of brain involvement in BMD and DMD. The results of the ongoing study will be disseminated to the community in 2024.

P.21: Probing diffusion of water and metabolites to assess white matter microstructure in Duchenne muscular dystrophy

Author/s: Rosanne Govaarts, Nathalie Doorenweerd, Chloé F. Najac, Emma M. Broek, Maud E. Tamsma, Kieren G. Hollingsworth, Erik H. Niks, Itamar Ronen, Volker Straub, Hermien E. Kan

Abstract

Background: Duchenne muscular dystrophy (DMD) is a progressive X-linked neuromuscular disorder caused by the absence of functional dystrophin protein, which besides muscle is also expressed in the brain. Altered white matter microstructure has been shown with diffusion tensor imaging (DTI). However, DTI measures the diffusion properties of water, a ubiquitous molecule, making it difficult to unravel the underlying pathology. Complementary, diffusion- weighted spectroscopy (DWS) measures diffusion properties of cell-specific intracellular metabolites.

Aims: This study combined DWS and DTI to disentangle intra- and extracellular contributions to white matter differences seen in patients with DMD.

Methods: Scans were obtained at 3 Tesla (Philips Achieva) using an 8-channel head coil. 3DT1-weighted scans were obtained for anatomical reference. DTI scans were obtained to determine the diffusion of water. DWS data were acquired with and without water suppression using a cardiac triggered PRESS sequence to determine diffusion and concentration of metabolites. A volume of interest (VOI; 30x20x15 mm) was positioned in the left parietal white matter. DWS spectra were analysed using an in-house Matlab routine. Apparent diffusion coefficients were calculated for total N-acetyl aspartate (tNAA), choline compounds (tCho), and total creatine (tCr). The ratios of tNAA/tCr and tCho/tCr were calculated from the fitted non-diffusion weighted spectrum. DTI scans were co-registered with T1 and DWS using ExploreDTI to obtain mean diffusivity (MD), radial diffusivity (RD), and axial diffusivity (AD) of water within the VOI.

Results: DWS and DTI data from 18 DMD patients (mean age 15.5 ± sd 4.6 years) and 10 age- matched healthy controls (HCs; mean age 16.3 ± sd 3.3 years) were included. No differences in metabolite diffusion (tNAA, tCho and tCr) and metabolite levels (tNAA/tCr and tCho/tCr ratios) were found between DMD patients and HCs. Water diffusion (MD, RD and AD) within the VOI was significantly higher in DMD patients compared to HCs.

Conclusion: The mean ADC of all three metabolites and their ratios were comparable between DMD patients and HCs. In the same VOI, DMD patients did show increased water diffusivity. This suggests that altered WM microstructure is likely due to extracellular, rather than intracellular, changes.

P.22: Introduction of a graphical interface for fully automated muscle segmentation of the thigh and calf muscles

Author/s: Marlena Rohm, Marius Markmann, Robert Rehmann, Johannes Forsting, Martijn Froeling, Lara Schlaffke

Abstract

Introduction: Segmentation of MRI images is a time-consuming task and often a bottleneck in the quantitative analysis of MRI imaging. To address this challenge, we have developed a user- friendly graphical interface that enables users to automate the segmentation process without the need for in-depth algorithmic knowledge.

Methods: We have created a python-based graphical user interface that incorporates convolutional neural networks (CNNs) based on established literature, such as Resnet and Unet. The tool has been extensively tested using a diverse dataset comprising both healthy control subjects and various patient groups, including LGMD and Pompe disease. It is available in precompiled form for Windows users and also provided as open-source code on GitHub.

Results: The tool comprises two main functions: training and predicting. To train the models, users need labeled images, which are automatically processed and trained using their preferred model and loss function. For prediction, a trained model is utilized to generate segmentations for new data. Initially designed for automatic segmentation of upper and lower leg muscles, the tool includes pre-trained networks for both human and mice legs.

Discussion: The flexibility of HuMITools allows users to employ an iterative approach by training models on their own data from various biological structures. Even with a small set of manually segmented images, the tool enables users to train convolutional neural networks and leverage the implicit knowledge within these manual segmentations. After prediction using the trained models, refinement of segmentations can be performed using tools like 3D Slicer. The improved segmentations can then be used to further refine the model by training it with a larger dataset.

In conclusion, our graphical interface provides a user-friendly solution to the time- consuming task of MR-image segmentation of leg muscles. By automating the process and integrating CNNs, HuMITools empowers users with limited algorithmic expertise to achieve accurate and efficient segmentations. Its versatility allows adaptation to different biological structures, facilitating the exploration and analysis of MRI data in various research and clinical applications.

P.23: Emerging methodologies and dynamic imaging in healthcare systems: a case study on developing countries with focus on ghana

Author/s: Yvonne Owusu Boafo

Abstract

Background: Medical imaging technologies have emerged as indispensable tools in the diagnosis, monitoring, and treatment of various medical conditions. While developed countries have leveraged state-of-the-art imaging technologies for improved healthcare delivery, developing countries like Ghana face numerous challenges including infrastructural limitations, lack of skilled personnel, and financial constraints. As a result, there is a significant gap in the availability and quality of healthcare imaging services between urban and rural settings.

Aims: The study aims to investigate the impact of emerging methodologies and dynamic imaging technologies on healthcare systems in developing countries, focusing on Ghana. Specific objectives include evaluating the adaptability, cost-effectiveness, and improvements in patient care resulting from the integration of these technologies.

Methods: A mixed-method research approach was employed combining both qualitative and quantitative data. Interviews with healthcare providers, administrators, and policy-makers were conducted to assess the current state and challenges of healthcare imaging in Ghana. Additionally, a comparative analysis of traditional vs. emerging imaging technologies, such as mobile ultrasound and cloud-based PACS (Picture Archiving and Communication Systems), was performed using data from three hospitals in different regions. Cost-benefit analyses were conducted to evaluate the economic impact.

Results: Initial findings suggest that emerging imaging technologies can substantially improve healthcare outcomes in developing countries. In particular, portable imaging devices like handheld ultrasounds were found to be highly effective in remote rural areas lacking infrastructure. The implementation of cloud-based PACS allowed for better image storage and sharing, improving the speed and efficiency of diagnosis. Cost-benefit analysis showed a return on investment within two years, making these technologies economically viable options for resource-strained settings.

Conclusion: Emerging methodologies and dynamic imaging technologies hold great promise for improving healthcare systems in developing countries like Ghana. Not only do these technologies bridge the gap between urban and rural healthcare, but they also offer a costeffective solution for improving patient care. Policy initiatives supporting the integration of such technologies could substantially impact healthcare outcomes in developing nations. Therefore, strategic implementation and investment in these technologies should be a priority for healthcare stakeholders and policymakers.

Keywords: Emerging Imaging Technologies, Healthcare Systems, Developing Countries, Ghana, Costeffectiveness

P.24: Clinical evidence for Diffusion Tensor Imaging as biomarker in neuromuscular diseases: A systematic review

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Abstract

Background: Diffusion-Tensor-Imaging- (DTI) derived parameters are currently emerging as potential imaging biomarkers of neuromuscular diseases (NMD) thanks to their potential to give insight into the tissue microstructure, and thus detect muscle fiber disruption.

Aims: As multiple clinical studies exist, we aim to quantitatively analyze the collective evidence to highlight the most promising DTI-derived parameters on the basis of their discriminating power between patients and healthy controls.

Methods: A Pubmed search was performed with a broad query including the keywords "musc*" and "diffusion". The abstracts returned by the query were initially automatically screened by a Large Language Model (LLM, gpt-3.5-turbo) to identify the ones involving neuromuscular diseases. Finally, the screened articles were manually selected to identify those performing DTI in the muscle (and not in the central nervous system) and on human subjects. For each article, the following information was collected:

- Pathology investigated
- Number of subjects
- DTI Sequence parameters
- Endpoints measured (e.g. fractional anisotropy, mean diffusivity)
- Average and standard deviations of the control and patient populations
- p-value (when available)

If possible, for each paper, the effect size (Cohen's d) between patients and controls was calculated for each endpoint.

Results: The pubmed query returned 385 results, reduced to 79 after LLM screening. Of these, 27 were manually selected. The studies involved between 20 and 65 subjects and covered 13 different pathologies. The most frequently reported endpoints were fractional anisotropy (FA) and mean diffusivity (MD), followed by the apparent diffusion coefficient and the tensor eigenvalues. Estimated mean effect sizes for all NMDs were -0.30 ± 0.90 for FA and 0.22 ± 1.07 for MD. As a qualitative trend, FA tended to decrease in most NMD, but increase in Duchenne (DMD). MD followed an opposite pattern, with the two indicators generally showing negative correlation.

Conclusion: The clinical evidence supporting DTI as a quantitative biomarker for NMD, while promising, is currently scattered, and it is difficult to draw a definitive conclusion. Estimate mean effect sizes present large variance and are probably pathology-dependent. Larger studies, focused on a particular pathology of interest, are necessary to demonstrate the clinical effectiveness of DTI

P.25: Analysing diffusion and area volumes in brains of dystrophin deficient mouse models of Duchenne muscular dystrophy

Author/s: M.A.T. Verhaeg, E. Suidgeest, L. van der Weerd, O. Dzyubachyk, L. Kerkelä, A. Aartsma-Rus, M. van Putten

Abstract

Duchenne muscular dystrophy (DMD) is a recessive, X-linked neuromuscular disorder. Next to severe muscle wasting, patients present with cognitive impairments and alterations in brain structure due to the lack of dystrophin in the brain. A correlation has been found between the number of dystrophin isoforms lacking and the severity of brain structure abnormalities in DMD patients. However studies on the direct influence of lack of specific dystrophin isoforms, especially the shorter isoforms Dp71 and Dp40, has been limited mostly due to the low numbers of patients available. Therefore the current study used different DMD mouse models lacking either one, multiple or all dystrophin isoforms to investigate the effects on brain structure.

Hereto, the brain of sixteen C57BL/6J (WT), *mdx*^{5cv} (lacking Dp427), *mdx52* (lacking Dp427+Dp140) and *DMD-null* (lacking all dystrophin isoforms) males were scanned at an age of 16 weeks. Animals were scanned in a 7T Bruker Pharmascan. Scans included T2 and diffusion tensor imaging (DTI) to evaluate brain morphology and diffusion parameters. A reference brain atlas was used to analyse volumes of the whole brain and 23 regions, as described in Boehm-Sturm et al 2017. No differences were found in the volume of the total brain or any of the 23 brain regions of the mouse models. For the DTI scans, 7 regions of interest were selected for analysis; cortex, hippocampus, amygdala, caudate putamen, cerebellum, nucleus accumbens and thalamus. Analysis of the DTI scans to assess fractional anisotropy and mean, axial and radial diffusion is ongoing.

In this study no differences were observed between groups, suggesting that the shorter dystrophin isoforms have no effect on total brain volume or area volumes. Further analysis will determine how the different dystrophin isoforms influence diffusion patterns.

P.26: Prospective Longitudinal Cohort Study of Quantitative Muscle MRI in a Healthy Control Population

Author/s: Johannes Forsting , Robert Rehmann, Marlena Rohm, Hadi Kocabas, Alice De Lorenzo, Anne-Katrin Güttsches, Matthias Vorgerd, Martijn Froeling, and Lara Schlaffke

Abstract

Background: Quantitative muscle MRI (qMRI) is a valuable methodology employed for assessing muscular injuries and neuromuscular disorders. Notably, the utilization of muscle diffusion tensor imaging (mDTI) gives insights into muscle micro- and macrostructural characteristics. However, the longitudinal reproducibility and robustness or these measurements remain relatively unexplored.

Purpose: To assess long-term reproducibility and robustness of qMRI parameters, especially mDTI metrics, in healthy controls.

Study type: Prospective longitudinal cohort study.

Subjects: Twelve volunteers (7 females, 44.1 ± 12.1 years, BMI 23.3 ± 2.0) underwent 5 leg muscle MRI sessions spaced every 6 months ± 8 weeks spanning a total of 1.5 years.

Sequences: A multi-echo gradient-echo Dixon-based sequence, a multi-echo spin-echo (MESE) T2-mapping sequence, and a spin-echo EPI diffusion-weighted sequence were acquired at a Philips 3T Achieva MR System using a 16CH Torso Coil.

Assessment: Fifteen leg muscles were segmented in both lower extremities. qMRI parameters including fat fraction (FF) and water T2 relaxation time were extracted. Diffusion metrics were evaluated using volume-based tractography (VBT) to obtain fractional anisotropy (FA), mean diffusivity (MD), axial diffusivity ($_1$), and radial diffusivity (RD).

Statistical Tests: Coefficients of variance (wsCV), and intraclass correlation coefficients (ICC) were calculated to assess reproducibility of qMRI parameters. A repeated-measures ANOVA was used to assess differences between different timepoints. All tests were applied for all muscles and then for each muscle separately.

Results: wsCV showed good reproducibility (≤10%) for all qMRI parameters in all muscles. ICC revealed good agreement between timepoints [FF = 0.980, T2 = 0.941, FA = 0.952, MD = 0.948). While ANOVA revealed significant differences, muscle-wise post-hoc analysis showed no significant differences between different time points.

Data conclusion: In this study, we showed that qMRI parameters in healthy volunteers are stable over an eighteen-month period, thereby defining a benchmark for the expected range of variation over time.

P.27: Ultrasound and magnetic resonance imaging for assessing muscle contractile performance in FSHD – An exploratory study protocol

Author/s: O. van Iersel, J. Doorduin, D. Cameron, N. van Alfen

Abstract

Background: Magnetic resonance imaging (MRI) and muscle ultrasound have contributed to an enhanced understanding of the pathophysiology of Facioscapulohumeral Muscular Dystrophy (FSHD). Previously, our group demonstrated the potential presence of an intermediate factor between muscle fiber loss and clinical weakness in FSHD. The influence of disrupted muscle architecture in FSHD on muscle contractile efficiency is a likely candidate for this factor, and remains relatively unexplored.

Aim: In this study, we aim to assess the use of ultrasound-defined contractile performance, in comparison with current measures including structural MRI, for monitoring disease progression in FSHD.

Methods: In a two-stage prospective cohort study, we will first conduct a pilot study in healthy adults (n=15) and adult patients with FSHD (n=10) to assess the feasibility and repeatability of ultrasound-defined contractile performance in upper and lower extremity muscles. We will use two ultrasound techniques: speckle-tracking for dynamic assessment and ultrafast shear wave elastography imaging for static assessment, alongside conventional measures.

During the second stage of the study, a group of healthy participants (n=10) and patients (n=50) will undergo both ultrasound and MRI to compare ultrasound-defined contractile performance with clinical measures, as well as MRI outcome measures collected using the Dixon water-fat-separation imaging, diffusion-tensor MRI, and T2 mapping. We will use an automated segmentation framework to obtain individual muscle volumes from MRI data, permitting accurate quantification of the pathological process.

All measurements obtained during the second stage will be repeated in patients with FSHD (n=50) after a one-year interval to assess any longitudinal changes.

Results: Our project will explore a possible intermediate biomarker of muscle dysfunction in FSHD, that may complement current structural and functional (imaging) parameters. We expect some of our imaging biomarkers will be able to predict clinical change after one year, with a relevant correlation between outcome measures at subsequent visits.

Discussion/Conclusion: This study is an essential step to gain more insight into the loss of muscle function and contractile efficiency in FSHD, and find a responsive biomarker to help provide a comprehensive picture of muscle function for use in follow-up and clinical trials in FSHD.

P.28: Diagnostic performance of regression based reference values versus mixture method clustering for quantitative muscle ultrasound

Author/s: JLM van Doorn, RH Reijntjes, J Wijntjes, J Doorduin, MR Tannemaat, N van Alfen

Abstract

Background: Quantitative muscle ultrasound (QMUS) is a useful and validated screening tool for the diagnostic workup of neuromuscular disorders (NMD). Despite its clinical relevance, the need for deriving normative values for each ultrasound system impedes its widespread use. Normative values are currently collected by scanning a reference group of healthy individuals and using regression based techniques (RBT) to predict abnormality. This is costly and time-consuming, and the reference groups are not always comparable to patients in clinical practice. Mixed method clustering (MMC) offers a potential solution by deriving reference values from data collected from regular clinical referrals.

Aim: To compare the diagnostic performance of RBT and MMC in assessing clinical QMUS scans.

Methods: Echogenicity of all muscles studied were collected during routine diagnostic QMUS examinations at our centre between December 2017 and March 2023. Z-scores were derived using RBT and MMC. All patients were classified as having a motor neuron disease, radiculopathy, neuropathy, myopathy, or no NMD. Diagnostic performance was calculated using a previously established z-score cut-off decision rule, using the currently used cut-offs and scenarios favouring either sensitivity or specificity. Diagnostic performance between RBT and MMC was compared.

Results: Data of 22.229 muscles from 1.456 examinations was collected. Diagnostic performance did not differ between the RBT and the MMC method (sensitivity 64% vs 64%, p=0.414, specificity 82% vs 81%, p=0.083). Similarly, when favouring specificity, diagnostic performance did not differ (sensitivity 43% vs 42%, p=0.722, specificity 87% vs 88%, p=0.394). However, when favouring sensitivity, sensitivity was lower using RBT compared to MMC (94% vs 97%, p<0.001), while specificity was higher (13% vs 7%, p<0.001).

Conclusion: Based on the currently used decision rules, diagnostic performance was similar between RBT and MMC. MMC can be used instead of RBT to obtain clinical cut-off values, obviating the need to spend resources on collecting normative values. This can help accelerate the widespread use of QMUS and as MMC is based on a centres' clinical population, the reference values will reflect this specific clinical population more accurately. However, before MMC can be used, QMUS scans can only be qualitatively assessed until sufficient scans are obtained.

P.29: Automatic segmentation of lumbar paraspinal muscles

Author/s: Eduard Snezhko, Marek Dostál, Matej Straka, Peter Krkoška, Pierre Carlier

Abstract

Background: For decades, muscle manual segmentation has been the main obstacle to a widespread use of quantitative NMR imaging in clinical neuromyology. This bottleneck is progressively overcome with the introduction of artificial intelligence (AI) based automatic software.

Aims: To develop an automatic solution for lumbar paraspinal muscles segmentation of Dixon images

Subjects and methods: Sixteen 3D volumes were used to train the convolutional neuronal network (CNN), each referring to an out-of-phase Dixon acquisition. The image parameters were: 336 x 336 x 47 voxels, voxel size is 1.19 x 1.19 x 5 mm. This dataset was divided into 12 cases for the training/validation set and 4 cases for the test set. For each case, a mask containing ROIs of 6 classes (6 paravertebral muscles) was provided. For CNN training, left and right ROIs of the same muscle group were considered as one class, so 3 muscle groups were considered for segmentation - erector spinae, multifidus, and psoas.

Methodology: For CNN training we utilised the DeepLab3+ model architecture. The accepted loss function was chosen as a sum of sigmoid cross entropy (taken with weight 0.5) and a sigmoid dice coefficient (both with given “logits” input). The optimizer during training is NAdam, and the Learning Rate is initialised as 10^{-3} with reduction by 0.2 each time if the validation metrics does not improve after 2 successive epochs. In addition, 5-fold cross-validation was utilised during training. Before each of 5 cross-validations, the CNN was initialised with weights from the model trained on the Pascal VOC dataset. When tested to calculate the muscle mask, the results of the 5 obtained models were averaged.

Results: For the real test, 29 3D volumes were used, each referring to an out-of-phase Dixon acquisition that was not used in CNN training. The corresponding boxplots of the calculated DICE coefficients are depicted below.

Conclusion: These very preliminary results obtained with a small data set indicate that CNN segmentation of this important anatomical region will work similarly as in the lower limb and will provide a substantial help in the quantitative assessment of the axial musculature.

P.30: Apparent intra- and extra-myocellular lipid content indicator using spiral spectroscopic imaging at 3T: a validation study

Author/s: Antoine Naëgel, Magalie Viallon, Jabrane Karkouri, Thomas Troalen, Pierre Croisille, Hélène Ratiney

Abstract

Introduction: This work presents a fast and simple method based on spiral-MRSI for mapping the IMCL and EMCL1,2 apparent content, which is a challenging task3,4 and it compares this indicator to classical quantification results in muscles of interest.

Methods: A spiral-MRSI sequence was developed on a 3T-MRI (MAGNETOM PRISMA, Siemens Healthineers). Main parameters: TR/TE=2s/2ms, voxel-size=3.1x3.1x25mm, temporal resolution/points=500ms/1024, spatial/temporal interleaving=22/5, TAcq=3min48s. Dual resonance 1H/31P coil (Rapid GMBH) positioned under the right calf of 16 volunteers. A diffusion-weighted and T1-vibe-Dixon sequences were subsequently acquired to derive the fibres'orientation and Fat Fraction (FF) images. The analysis of the spectra was centered on the peaks of IMCL/EMCL (1.3ppm/1.5ppm). Automatic phasing and frequency shifting of spectra was performed by FID modulus5. The evolution of the cumulative sum of the amplitudes of a fixed area (1.1-1.7ppm) was used to analyze the apparent content indicator (ACI) of IMCL/EMCL for each voxel (Fig1). The new proposed ACI was compared to the IMCL/(EMCL+IMCL) ratio quantified using LCModel fitting method on ROI selected in soleus medial (SM), and gastrocnemius medial (GM) muscles (Fig2).

Results: The average FF obtained by the 3 methods were resumed in Fig3 and were coherent with the literature6. The ACI and its quantitative equivalent were both significantly different between the GM and SM muscles. There was a significant positive correlation between the ACI and its quantitative equivalent (Fig4).

Discussion: The MRS measurement of IMCL is influenced by the quantity in the tissue and the orientation of the fibers. Despite a less advantageous fiber orientation, the observation of IMCL was feasible in the SM due to its high level in this muscle. The quantification of IMCL/EMCL on MRSI data is fastidious due to phase and frequency shifts and results in time-consuming data processing. The rapid analysis provided by the ACI can be used to rapidly generate maps of the intra/extra lipid distribution.

Conclusion: This exploration technique shows promise for fast and straightforward IMCL compared to EMCL mapping. It correlates with standard quantification. Future work should assess reproducibility before clinical transfer for longitudinal studies.

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P.31: Alteration of skeletal muscle energy metabolism assessed by 31P MRS in clinical routine: a study on COVID19 and MS patients

Author/s: Antoine Naëgel, Hélène Ratiney, Jabrane Karkouri, Djahid Kennouche, Nicolas Royer, Jill M. Slade, Jérôme Morel, Pierre Croisille, Magalie Viallon

Abstract

Introduction: Implementing a standardized 31P-MRS dynamic acquisition protocol to evaluate skeletal muscle energy metabolism and monitor muscle fatigability1,2, while being compatible with various longitudinal clinical studies on diversified patient cohorts, requires a high level of technicality and expertise. The aim is to provide decision support to the operator in order to assist in data processing and obtain reliable results based on objective criteria. An advanced data quality control (QC) approach of a dynamic 31P-MRS protocol3 is first presented. then, we conducted an impact study demonstrating the added value of the QC approach to explore clinical results derived from two patient populations with significant fatigue4: COVID19 and multiple sclerosis (MS).

Methods: Dynamic 31P-MRS was performed on a 3T clinical MRI, in 19 COVID19 patients, 38 MS patients, and 40 matched healthy controls. Long and short TR acquisitions were also made at rest for T1 correction. The advanced data quality control pipeline was applied to the selected patient cohorts to investigate its impact on clinical outcomes(Fig1). We first used power and sample size analysis to estimate objectively the impact of adding QC. Then, comparisons between patients and healthy control groups with validated QC were performed using unpaired T-tests or Mann-Whitney tests ($p<0.05$).

Results: The application of the QC resulted in increased statistical power, changed the mean values of several outcome measures, and reduced variability (Fig2). A significant difference was found between the T1PCr and T1Pi of MS patients and healthy controls. We observed significant differences between the two patient populations and healthy controls for resting and post-exercise. The dynamic indicators τPCr, τPi, ViPCr and Vmax were reduced for COVID19 and MS patients compared to controls (Table1).

Discussion & Conclusion: Our results show that QCS in dynamic 31P-MRS studies results in smaller data variability and therefore impacts study sample size and power. The outcomes include an increased metabolite T1, which directly affect the T1 correction factor applied to the amplitudes of the metabolite, and a prolonged τPCr indicating reduced muscle oxidative capacity for patients with MS and COVID19.

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