MRI and MRS in the assessment of dietary-induced and age-related changes of the muscle in an animal model for sarcopenic obesity

C. Fellner[1], C. Hechtl[2], M. Vorbuchner[3], R. Büttner[2], C. Stroszczynski[1], O. W. Hamer[1], and C. Bollheimer[2]
[1]Institute of Radiology, University Medical Center Regensburg, Regensburg, Germany, [2]Department of Internal Medicine I, University Medical Center Regensburg, Regensburg, Germany, [3]Siemens Healthcare, Erlangen, Germany

INTRODUCTION:

Sarcopenia denotes an exceeding decline of muscle mass with aging. Sarcopenia is – both from a medical and economical point of view – an important geriatric issue as it leads to immobility, higher rates of falls, fractures and finally care dependency. The role of concomitant obesity in the development of sarcopenia is not clear yet: Both aggravating ("sarcopenic obesity") and ameliorating effects ("obesity paradox") are currently discussed in literature. Therefore, a rat model has been established to evaluate the influence of obesity in the development of sarcopenia. The aim of this pilot study was to assess the potential role of in vivo MRI and MRS to demonstrate dietary-induced and age-related changes of muscle tissue.

METHODS:

To induce an obese phenotype, 6-month-old male Sprague-Dawley rats were fed with a lard-enriched diet containing 42 energy % fat while control animals received a control diet with 25 energy % of fat. 7 high fat fed rats (HFR) and 14 control rats (CR) were examined at the age of 16 and 21 months. MRI of both hindlimbs was performed at a clinical 1.5 T scanner (Magnetom Avanto, Siemens) using an 8-channel knee coil. T2-mapping and T2*-mapping was performed applying a multi-echo SE sequence (TR: 2000 ms, TE: 14-169 ms; voxel size: 0.4 x 0.4 x 2.0 mm^3) and a multi-echo GRE-sequence (TR: 600 ms, TE: 4.8-33.4 ms; voxel size: 0.6 x 0.6 x 2.0 mm^3). The slice orientation was chosen perpendicular to the M. quadriceps of both hindlimbs. T2 and T2* relaxation times were assessed in user-defined ROIs of color-coded maps within both muscles avoiding areas of bulk fat or visible fatty infiltrations ($T2_{lean\ muscle}$, $T2^*_{lean\ muscle}$). In addition to $T2_{lean\ muscle}$, T2 was measured over the whole maximum cross sectional area (CSA) of the M. quadriceps ($T2_{CSA}$) including fatty infiltrations; the maximum CSA was also assessed. Furthermore, SVS 1H MRS (TR: 1500 ms, TE: 30 ms; voxel size: 12 x 6 x 7 mm^3) was acquired of both hindlimbs and total lipid (Lip_{rel}) was evaluated taking into account all lipid signals (0.9-1.6 ppm, 1.9-2.6 ppm) relative to the water-signal, which was acquired in a separate measurement of the same voxel within the M. quadriceps.
All parameters were assessed for both hindlimbs and means were calculated for further evaluation. Statistical analysis for comparison of both diet groups, HFR and CR, and for age-related effects (16 versus 21 months) was done using the exact two-sided Mann-Whitney test; P-values below 0.05 were regarded statistically significant.

RESULTS:

The CSA of the M. quadriceps was lower in HFR than in CR at both time-points; at the age of 16 months, this difference was even statistically significant (see Tab. 1). The percentage decrease of muscle CSA between the 16th and the 21th month was very similar in both groups, no additional dietary-induced effect was detected with increasing age. While CSA is a direct parameter for sarcopenia the remaining parameters gave additional information about age- and dietary-induced changes of the muscle:
Longer T2 relaxation times were found in HFR compared to CR while the relaxation times were still increasing with age in boths groups (Tab. 1). One possible explanation for T2 prolongation is increased fat content of the muscle which could be confirmed spectroscopically by increased total lipids (Lip_{rel}). However, one might speculate that additional effects like increased extracellular water content may also play a relevant role. $T2_{CSA}$ was always longer than $T2_{lean\ muscle}$ reflecting increased fat contribution if visible fatty infiltrations within the muscle are included. Only minor dietary and age-related changes of $T2^*_{lean\ muscle}$ can be interpreted as the result of two opposed effects, prolongation of T2 by increased fat content and shortening of T2* by increased iron content.

	HFR 16 months	CR 16 months	HFR 21 months	CR 21 months	age-related changes HFR	age-related changes CR
CSA [cm^2]	*1.72 ± 0.20	1.94 ± 0.17	1.48 ± 0.23	1.67 ± 0.18	-14.54 ± 9.98 %	-14.11 ± 0.83 %
$T2_{lean\ muscle}$ [ms]	*32.76 ± 0.95	31.71 ± 0.55	33.97 ± 1.35	33.10 ± 0.92	3.82 ± 6.14 %	4.40 ± 3.03 %
$T2_{CSA}$ [ms]	*33.38 ± 1.22	32.20 ± 0.72	34.03 ± 1.53	33.44 ± 1.47	2.03 ± 5.48 %	3.91 ± 5.20 %
$T2^*_{lean\ muscle}$ [ms]	24.24 ± 0.61	23.71 ± 0.64	24.68 ± 0.75	24.27 ± 0.99	1.87 ± 4.05 %	2.38 ± 3.66 %
Lip_{rel}	1.48 ± 0.31	1.25 ± 0.39	1.63 ± 0.53	1.62 ± 0.73	10.16 ± 25.55 %	31.89 ± 46.02 %

Tab. 1: MRI and MRS results in HFR and CR at the age of 16 and 21 months: Means and standard deviations for each group, age-induced changes relative to the results with 16 months. *: significant differences (P<0.05) between HFR and CR.

CONCLUSION:

In this newly established animal model for sarcopenia, MRI and MRS appears to be valuable tools to describe dietary-induced and age-related muscle changes. For this animal study a clinical 1.5 T scanner was employed in a translational approach with a view to clinical applicability in humans in future. Besides the morphometric quantification of the CSA as a direct parameter for muscle loss and sarcopenia, T2 and T2* relaxation times as well as the relative lipid content provided additional information in terms of changes in muscle quality. From a physiological point of view, this is the first study which demonstrates an aggravating effect of a fat enriched diet on muscle loss (i.e. the concept of sarcopenic obesity) in a standardized experimental setting. Notably in our animal model the diet-induced effects on muscle mass were full-blown already at the age of 16 months, suggesting that these detrimental effects are evident – and have therefore to be encountered – very early.

Acknowledgement: This work is supported by "Robert-Bosch-Stiftung", grant number: 32.5.1141.0030.0.