

## Gender-dependent effects of dietary-induced changes of the muscle in an animal model for sarcopenic obesity

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### 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. In a previous study with male Sprague Dawley rats we were able to demonstrate an aggravating effect of a fat-enriched diet on muscle loss (i.e. the concept of sarcopenic obesity) (ISMRM 2011, #1159) which was already full-blown at the age of 16 months. The aim of this study was to compare those results in male rats with a female group of the same age to evaluate gender-dependent effects.

### METHODS:

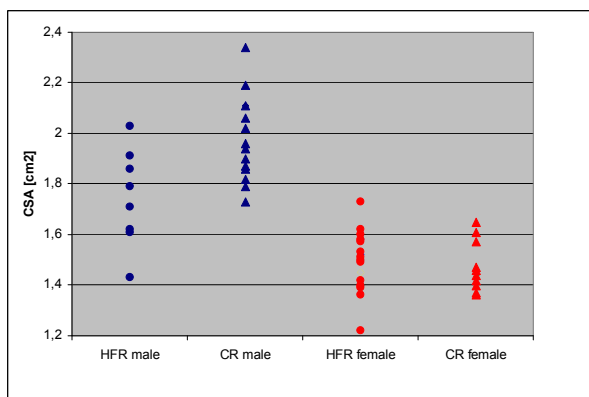
To induce an obese phenotype, 6-month-old Sprague-Dawley rats were fed with a lard-enriched diet containing 43 energy % fat while control animals received a control diet (male rats: 25 energy % fat; female rats: 10 energy % fat). At the age of 16 months, 20 female high fat fed rats (HFR) and 12 female control rats (CR) were examined; the results were compared to a group of 8 male HFR and 14 male CR.

In all animals, MRI of both hindlimbs was acquired on a clinical 1.5 T scanner (Magnetom Avanto, Siemens) using an 8-channel knee coil. T2-mapping was performed applying a multi-echo SE sequence (TE: 14-169 ms; voxel size: 0.4 x 0.4 x 2.0 mm<sup>3</sup>) with a slice orientation perpendicular to the M. quadriceps. T2 relaxation times were measured in a region of interest covering the maximum cross sectional area (CSA) of the M. quadriceps; the maximum CSA was also assessed. Furthermore, SVS 1H MRS (TE: 30 ms; voxel size: 12 x 6 x 7 mm<sup>3</sup>) was acquired and total lipid (Lip<sub>rel</sub>) was evaluated taking into account all lipid signals (Lip: 0.9-1.6 ppm, 1.9-2.6 ppm) relative to the water-signal (W), which was acquired in a separate measurement with the same voxel position (Lip<sub>rel</sub> = 100 (Lip/Lip+W)). 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, was done for male and female rats using the exact two-sided Mann-Whitney test; P-values below 0.05 were regarded statistically significant.

### RESULTS:

Large inter-individual differences were found for the CSA of the M. quadriceps with the muscles being generally larger for male compared to female rats (Fig. 1). Both effects can be explained by differences concerning weight and size of the animals. For male rats, however, CSA was significantly lower in HFR than in CR, T2 relaxation time was significantly prolonged, and the lipid signals were higher in HFR than in CR (without statistical significance). In contrast to those significant diet-related changes in male rats, there were similar trends in female rats of the same age, but no statistically significant differences were seen between animals receiving high fat or control diet (Table 1).

While CSA is a direct parameter for sarcopenia, the remaining parameters yield additional information about dietary-induced changes of the muscle: Longer T2 relaxation times in HFR compared to CR can be – at least partially – understood by an increased fat content of the muscle which could be confirmed spectroscopically by increased total lipids (Lip<sub>rel</sub>).



	HFR male	CR male	HFR female	CR female
CSA [cm <sup>2</sup> ]	*1.71 ± 0.20	*1.98 ± 0.17	1.49 ± 0.13	1.45 ± 0.11
T2 [ms]	*33.2 ± 1.1	*32.2 ± 0.7	31.9 ± 1.1	31.4 ± 0.6
Lip <sub>rel</sub>	1.45 ± 0.30	1.24 ± 0.39	1.03 ± 0.53	0.99 ± 0.34

Table 1: MRI and MRS results in male and female HFR and CR at the age of 16 months: Means and standard deviations for each group.

\*: significant differences (P<0.05) between HFR and CR of male or female rats.

Discrepancies concerning the absolute numbers of T2 relaxation times and lipid content are due to differences in the acquisition protocol of T2 mapping and MRS (TR, number of acquisitions).

Fig. 1: Maximum cross sectional area (CSA) of the M. quadriceps in male and female high fat fed diet (HFR) and control rats (CR).

### CONCLUSION:

Male and female rats at the age of 16 month showed loss of muscle mass and increased fat content within the muscle caused by fat-enriched diet. While this dietary-induced effect was only seen as a subtle trend in female rats, it was much more pronounced in male rats. We therefore conclude, that there are indeed relevant gender-dependent differences in our animal model for sarcopenia which have to be taken into account in further research. Further longitudinal studies will show if significant dietary-induced changes occur later in female than in male rats.

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