PRELIMINARY MR DTI STUDY OF AGE-RELATED REGENERATION PROCESS OF SKELETAL MUSCLE WITH ISCHEMIA INJURY

Ke Jiang[1], Xiaotian Wang[1,2], Hulong Lei[1], Wei Yang[1], and Yin Wu[1]

[1]*Paul C. Lauterbur Research Center for Biomedical Imaging, Shenzhen Key Laboratory for MRI, Shenzhen Institutes of Advanced Technology, Chinese Academy of Sciences, Shenzhen, Guangdong, China,* [2]*Sino-Dutch Biomedical and Information Engineering School, Northeastern University, Shenyang, Liaoning, China*

Introduction Skeletal muscle is vulnerable to ischemia injury after direct trauma or indirect causes, such as neuromuscular disease and diabetes [1]. Diffusion tensor imaging (DTI) is as a powerful tool to nondestructively investigate biological tissue structures, and has been demonstrated to be a specific and sensitive indicator in evaluation of acute muscle injury [2]. So far, most DTI studies of probing microstructural alteration of ischemic muscle were performed on adult species [3]. As biological components and physiological structures of muscle vary with age [4], its evolution course in response to ischemia may be different with age. Therefore, the existing results obtained from adults may not directly apply on other age populations. In this work, age-related regeneration process of ischemic muscle was explored for the first time to provide supplemental information for muscle repair evolution.

Method The IRB approved study was conducted on a 3T Siemens MR scanner. Ten young (~4 weeks) and old (~11 months) SD rats were induced ischemia in hind limbs with permanent ligation of abdominal aorta. Hind limbs were scanned with a multi-slice readout-segmented EPI DTI sequence [5] before, 2 hrs, and 2, 9, 21 days after surgery. The imaging parameters were: TR/TE = 5000/55ms, matrix size = 128×128, image resolution = 1×1×2mm^3 with 0.2mm slice gap, b = 500s/mm^2, diffusion directions = 6, number of shots = 7, NEX = 4. A MATLAB program was developed to measure fractional anisotropy (FA), mean diffusivity (MD), axial ($\lambda_{//}$) and radial ($\lambda_{\perp}$) diffusivities of gastrocnemius with bones and large vessels excluded. For each time point, 6 rats were scanned and 1 was sacrificed after imaging for H & E histological analysis in each group. One-way ANOVA with post hoc Bonferroni's multiple comparison analysis was performed with p<0.05 regarded as significance.

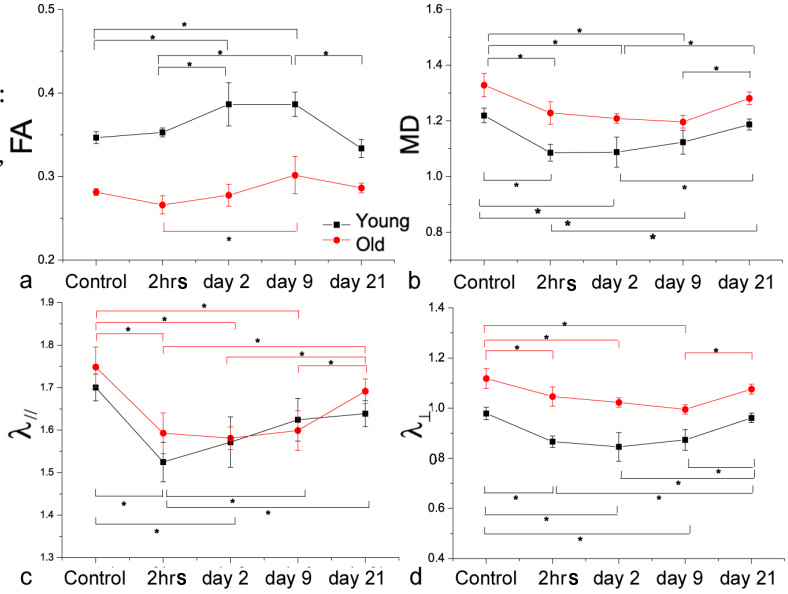

Fig 1 Alterations of DTI indices of gastrocnemius. *p<0.05

Results Sequential alterations of the DTI indices were shown in Fig. 1. For young group, FA was observed to significantly increase at day 2 and last till day 9 after surgery, and then was renormalized at day 21. Mean and directional diffusivities substantially decreased 2 hrs after ischemia induction, and gradually increase afterwards with recovery at day 21. For old group, significant change of FA only occurred at day 9 with the value increased by 13.4% compared to that of 2hr. Mean and directional diffusivities substantially reduced 2hrs after surgery and continuously dropped till day 9. Then the values were almost renormalized at day 21. Fig. 2 displays the histological observations of representative gastrocnemius structures with 400 magnifications. At typical time points following ischemia surgery (e.g., 2hrs for young and day 9 for old groups), myocyte swollen with shrinkage of extracellular space appeared, and more anisotropic fiber structure was exhibited with increase of myocyte packing density. The muscle microstructures at day 21 presented to be similar with those of controls.

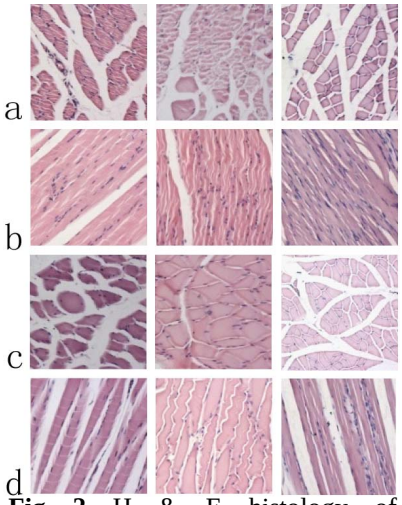

Fig 2 H & E histology of gastrocnemius in young (a, b) and old (c, d) groups with cross- (a, c) and longitudinal- (b, d) sections at three typical time points (left column - control; middle column - young group at 2hrs and old group at day 9; right column - day 21).

Discussion and conclusion In this study, age-related alteration courses of DTI indices of ischemic muscle were investigated in young and old rats. Generally, FA increased after ischemia injury, probably due to increase of myocyte packing density or augmentation of intracellular space arising from edema or inflammation. Concurrently, shrinkage of extracellular space resulted in decrease of mean and directional diffusivities. The DTI indices were observed to be renormalized at day 21 owing to the capability of muscle regeneration [1]. However, change of FA in young group (day 2) preceded that in old group (day 9). In addition, recovery of mean and directional diffusivities in the young group occurred earlier (2 hrs) than that of the old group (day 9). The observed sensitive response and rapid recovery in young rats may be associated with the strong ability of myogenic proliferation for new myofiber formation during growth stage. In summary, the current study confirmed the age-associated discrepancy of muscle regeneration process after ischemia injury, which may provide supplemental information for understanding of muscle repair evolution.

References [1] Charge et al, Physiological reviews 2004; [2] McMillan et al, ISMRM 2011; [3] Heemskerk et al, Radiology 2007; [4] Khalil et al, EJR 2010; [5] Porter et al, MRM 2009.

Acknowledgments NSFC 30900387, GIRTF-LCHT, BRPSZ JC201005270311A