

Myocardial Fibro-fatty Infiltration in Duchenne Muscular Dystrophy Canine Model Detected using Multi-echo Dixon Method of Water and Fat Separation Imaging

P. Kellman¹, D. Hernando², S. Shah³, R. F. Hoyt, Jr.¹, R. M. Kotin¹, B. W. Keene⁴, J. N. Kornegay⁵, A. H. Aletras¹, and A. E. Arai¹

¹National Institutes of Health, Bethesda, MD, United States, ²University of Illinois, Urbana, IL, United States, ³Siemens Medical Solutions, Chicago, IL, United States, ⁴College of Veterinary Medicine, North Carolina State University, NC, United States, ⁵School of Medicine, University of North Carolina, Chapel Hill, NC, United States

Introduction

Progressive cardiomyopathy leading to congestive heart failure is a common form of death in Duchenne Muscular Dystrophy (DMD). The use of late enhancement in cardiac magnetic resonance (CMR) imaging for assessing fibrosis in DMD and correlating with LV function has recently been reported [1,2]. Fatty replacement in fibrotic tissue associated with cardiomyopathy in cases of DMD is readily observed in histology [3]. The purpose of this study was to apply CMR imaging in-vivo to detect and characterize fibro-fatty infiltration in the myocardium. The significance and progression of fatty replacement in DMD is currently unknown, although inducibility of arrhythmias has been reported to correlate with fatty infiltration [4]. Multi-echo Dixon methods for fat and water separation [5-7] provide a sensitive means of detecting small concentrations of fat with improved contrast. In the present study, fat and water separation has been implemented both pre-contrast as well as applied to late enhancement using a multi-echo PSIR-GRE sequence. Initial studies were performed using a canine model.

Methods

CMR imaging was performed on 3 dogs with DMD obtained from the University of North Carolina golden retriever muscular dystrophy (GRMD) colony. Two of the dogs (golden retrievers) were known to have dilated cardiomyopathy, based on ECG and ultrasound. The 3rd dog (Corgi) had normal cardiac function. The ages of the dogs were approximately 5 ½, 9, & 9 years and weighed 13.8, 21, & 10.6 kg (smaller than usual due to muscle wasting). All animal experiments were approved by the Animal Care and Use Committee of the NHLBI. Dogs were anesthetized per guidelines and euthanized at the completion of the study, in order to obtain samples for histologic examination.

The imaging protocol consisted of a retrogated cardiac cine true-FISP sequence for assessment of LV function, a multi-echo GRE sequence for pre-contrast fat-water separation imaging, and late enhancement imaging using segmented PSIR turbo-FLASH with multi-echo readout for fibro-fatty infiltration [7]. Late enhancement imaging began approximately 7 minutes following administration of contrast (0.3 mmol/kg Gd-DTPA) (Magnevist, Bayer Healthcare). Typical parameters for imaging with the Siemens Magnetom Avanto 1.5T MRI scanner were: bandwidth=977 Hz/pixel, echo-train length=4, TE = 1.64, 4.17, 6.7, and 9.23 ms, TR=11.1 ms, flip angle=20-25°, image matrix=256x125, views-per-segment=15. Prospective ECG triggering used single R-R interval for precontrast and 4 R-R intervals for late enhancement. The spatial resolution was 1.1x1.6 mm² (6 mm slice thickness) across FOV of 280x192 mm². Image reconstruction used the VARPRO method [6] to robustly estimate the fieldmap in the presence of field inhomogeneity.

Results

Fibro-fatty infiltration was observed in 2 of the 3 dogs corresponding to the dogs with dilated cardiomyopathy. The LVEF for these 2 dogs was 22 and 26%. The 3rd dog had LVEF = 53%. Fibro-fatty infiltration was observed circumferentially in the LV, emanating from the epicardial surface in both animals with abnormally low ejection fraction. Images for a single short axis slice with fibro-fatty infiltration are shown in Fig. 1-3. Fatty infiltration is evident in both pre-contrast (Fig 2) and in late enhancement images (Fig 3). The fibrotic tissue observed in the late enhancement water image (Fig 3, left) coincides with the region of fatty infiltration (right) but has greater transmural extent.

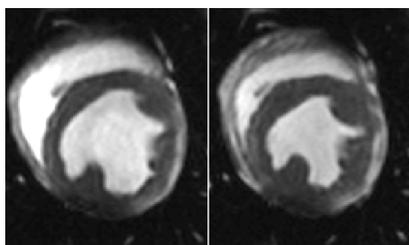


Fig. 1. Cine images for DMD dog with dilated cardiomyopathy showing diastolic (left) and systolic (right) phases.

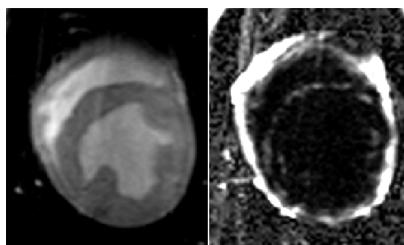


Fig. 2. Intramyocardial fat clearly evident in pre-contrast fat separated image (right).

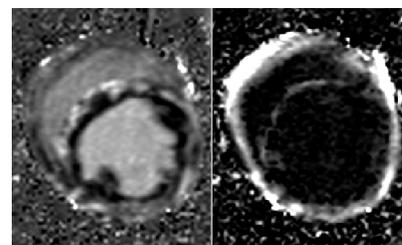


Fig. 3. Fibro-fatty infiltration clearly evident in PSIR late enhancement water (left) and fat (right) separated images.

Discussion

Cardiac images acquired with the multi-echo Dixon method were able to detect intramyocardial fat both pre and post contrast, as well as myocardial fibrosis post-contrast. The proposed approach can be used to characterize intramyocardial fat with positive contrast and greater sensitivity than conventional fat suppression [7]. A benefit of using late enhancement with fat-water separation is the ability to display contrast enhanced myocardial fibrosis in the water image and fatty infiltration in the fat image, both acquired simultaneously, and therefore, spatially registered. With this approach it may be possible to determine the progression of fibro-fatty infiltration and at what stage fatty replacement occurs relative to fibrosis. The presence of intramyocardial fat may form a substrate for arrhythmias [4]. Multi-echo Dixon methods may prove valuable in a wide range of cardiac conditions characterized by intramyocardial fat such as ARVD, fibrosis, and other cardiomyopathies.

References

[1] Puchalski, et al. *Int J Cardiovasc Imaging*. 2008 [Epub ahead of print]. [2] Silva, et al., *JACC*. 2007; 49:1874-1879. [3] Frankel KA, et al., *Hum Pathol* 1976; 7:375-386. [4] Vignaux O, et al., *Radiology*. 2002 Jul;224(1):231-5. [5] Reeder SB, et al., *J Magn Reson Imaging*. 2005 Jul;22(1):44-52. [6] Hernando D, et al., *Magn Reson Med*. 2008 Mar;59(3):571-80. [7] Kellman P, et al., *MRM* 2008 (in press).