

# P-31 MRS for Detection of Myocardial Microvascular Disease in Latino Type-I Diabetes Mellitus Patients

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## Introduction

Patients with Type-1 diabetes mellitus (DM) are known to have microvascular disease involving retina and kidney [1]. Such patients have a remarkable increase in the incidence of coronary artery disease. However, the presence and impact of diabetic microvascular disease on the myocardium is not well documented. Traditional stress electrocardiography, stress echocardiography and radionuclide perfusion imaging have been disappointing for detecting microvascular dysfunction. It was reported cardiac P-31 MRS allows for the determination of cardiac muscle ischemia by depletion of the phosphocreatine(PCr) during stress in patients with coronary stenosis [2]. We have previously reported abnormal drop of PCr/ATP during stress in women with chest pain but normal coronary arteries that we believe is evidence of microvascular dysfunction [3,4]. The present study is aimed at determining if there are metabolic changes in the myocardium in diabetics that could suggest microvascular dysfunction. We used P-31 MR spectroscopy during rest and stress to induce changes in high energy phosphates (HEP) that would suggest myocardial ischemia with Type-1 DM patients.

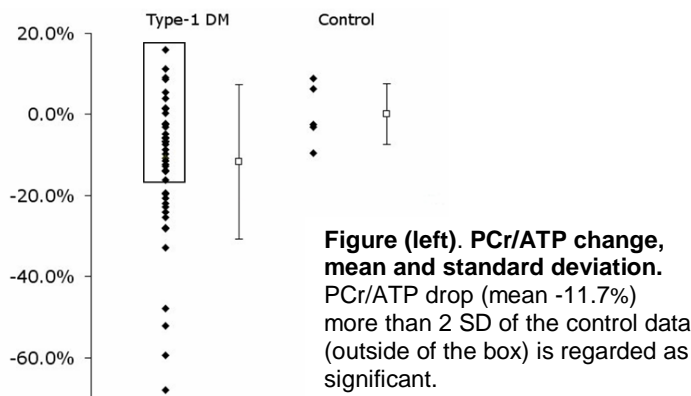
## Methods

**Patients:** Latino patients with Type-1 DM of greater than 10 years in duration were selected from a large registry of more than 2,000 Type-1 DM patients at USC. They are younger with a lower incidence of large vessel coronary artery disease compared to patients with Type-2 DM. Patients with signs or symptoms of epicardial coronary artery disease (CAD) or of overt renal disease were excluded. A comprehensive history, physical examination was reviewed for all subjects. All study subjects underwent metabolic panel, urinalysis and fundoscopic examination. Among 64 patients enrolled in the study, 46 successfully underwent stress 31P MR spectroscopy. All were Latino, mean age was 29±7 years, duration of diabetes was 16±4 years, body mass index was 29.7±6.1, hemoglobin A1C was 9.6±2.2, total cholesterol was 183±40 gm/dl, and triglyceride was 123±10.6 gm/dl. Microalbuminuria and diabetic retinopathy was present in 12.5%, and in 31% of the patients, respectively.

**MRI & 31P MRS:** MR examinations were done at 3T (Signa, GE, Milwaukee). Both ejection fraction and HEP were evaluated using cMRI and P-31 MRS during rest and stress. During stress phase, mild level exercise was applied using home-built digital handgrip stressor with McMaster Cu-Be strain gauge in which the stress was measured in pressure [Kg-g/m<sup>2</sup>]. **Coil:** Either a laterally elongated quadrature surface coil (transceiver mode), or single-turn linear coil was used as previously reported [5]. The circular linear coil (10cm in dia.) was primarily used as it showed higher signal-to-noise ratio for deeper slices (>6 cm), yet limited the contamination signal from the liver. The coil was placed as the homogeneous B1 field was overlaid on the anterior left ventricle and septum [5]. The Beekley MR-spots (Bristol, CT) were placed on the surface coil to correctly place the coil during scout imaging. **MR/MRS:** The cine MR imaging with 2D FIESTA sequence was done for function study during rest and stress. After B<sub>0</sub> shimming with PRESS voxel, P-31 signal was obtained from the 20 mm-thick double-oblique DRESS [6] slice which mainly covers anterior left ventricle and septum (3 R-R TR, 128 avg, 5kHz). Three sets of P-31 spectra were obtained: rest, stress and recovery. During the stress acquisition, the subject was asked to press the handgrip by 30% of maximum voluntary contraction. **Analysis:** HEP level was evaluated by processing P-31 spectra in the time domain using AMARES (MRUI 3.0 package, European Union). T1 and blood correction was done, accordingly.

## Results and Discussion

Thirteen of 46 subjects (28%) showed a significant drop (> 2 SD [3,4]) in PCr/ATP (mean drop: -11.7% ± 0.19) during handgrip stress whereas healthy normal controls show no significant drop (0.2% ± 0.08). No significant change in ejection fraction during stress was observed. Retinopathy was present in 43% of the diabetics and none of the controls. Albuminuria was present in 30% of diabetics and none of the controls. In Type-1 DM with albuminuria, there was a substantial decrease (>20%) in myocardial PCr/ATP, 33% in women but no such significant change in men. This stress-induced reduction in PCr/ATP is suggestive of microvascular abnormality in myocardium. This abnormal response probably occurs earlier than retinal or renal involvement. Our findings may indicate that in a subgroup of Type-1 DM patients, stress 31P MRS can identify abnormal cardiac metabolism that is likely microvascular in origin. A non-invasive 31P cardiac MRS that identifies metabolic abnormality may facilitate the prediction of cardiomyopathy in Type-1 DM patients.



**Figure (left).** PCr/ATP change, mean and standard deviation. PCr/ATP drop (mean -11.7%) more than 2 SD of the control data (outside of the box) is regarded as significant.

## References

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