Magic Angle Spinning MRS for Identifying Biomarkers of Perfusion Preservation of Human Hearts After 12 Hour Storage

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Introduction

Heart transplantation is limited by the short ischemic tolerance of preserved myocardium that limits optimal organ allocation and utilization of extended donor organs. Perfusion preservation is a promising strategy for extending the ischemic tolerance of myocardium and permit for the recovery of marginal donor hearts.[1] Reliable preimplantation assessment of graft function after long term preservation or of suboptimal organs is essential to assure a successful patient outcome. We have applied ^{1}H magnetic resonance spectroscopy (MRS) to characterize canine and human heart metabolism of myocardial extracts during perfusion preservation and static storage.[2,3] These experiments demonstrated that important metabolic differences could be determined between these preservation techniques. Because of the limited clinical application of extract data, we subsequently applied ^{1}H magic angle spinning MRS (MAS) to canine left ventricular biopsies and created a mathematical model that was able to identify the preservation strategy.[4] In the current study, we applied ^{1}H MAS MRS to human hearts that were stored for long intervals either by conventional static storage or perfusion preservation. We hypothesized that spectral data could be used the construct a similar model to predict the preservation strategy of human hearts.

Methods

Human hearts unsuitable for transplantation (n=13) were obtained from potential donors throughout our local organ procurement organization. Seven hearts were flushed with University of Wisconsin Machine Perfusion Solution, connected to a perfusion device (Lifecradle®, Organ Transport Systems, Inc) and perfused at 10 mL/100g/min at 5°C for 12 hours with the same solution. Six hearts underwent conventional hypothermic, static storage in the same organ preservation solution at 0-4°C for 12 hours. Temperature, flow, and pressure were recorded in perfused hearts. After 12 hours of perfusion, Hearts were removed and weighed. ^{1}H MAS was carried out on small left ventricular cylindrical biopsies (approx 10mg) with a gHx nanoprobe on the same Varian 14.1T Vnmrs spectrometer. Tissue was placed in a 50 µl volume rotor with 5 µl of D_2O as a lock solvent. Spectra were acquired with the "presat" pulse sequence using a 1s delay, a 3.2s water presaturation pulse, and a 1.8s acquisition time for a T_r of 6s. The data were imported into the statistical computing environment and evaluated with a peak-picking, partial least squares (PLS) algorithm to identify biomarkers that were indicative of the storage method.

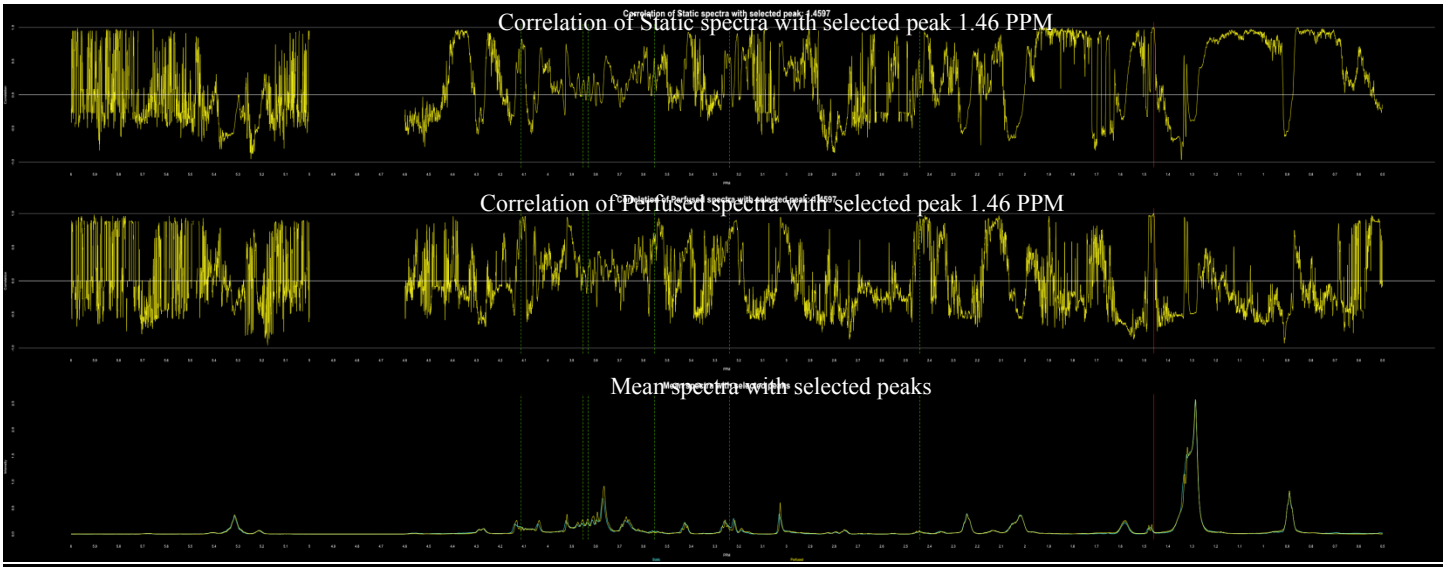

Figure 1 – Peak Assignments of the Resonances Identified by the PLS Algorithm. The alanine resonance is identified in red.

Results

Total analysis time for each sample was less than ten minutes. The peak-picking PLS algorithm identified 7 different resonances at 1.46 PPM (alanine), 2.44 PPM (carnitine), 3.23 PPM (choline), 3.55 PPM (unassigned), 3.83PPM (unassigned), 3.85 PPM (unassigned), 4.11 PPM (lactate) that were sufficient to categorize the spectra as either static storage or perfusion preservation with 100% efficiency. **See Figure 1**. Identified resonances from the human heart model in the current study differed from the previous canine data were five resonances (triglyceride methyl protons, protons alpha to triglyceride double bond, creatinine, glycerol protons, and an unassigned resonance) were required to predict the preservation strategy.

Conclusions

^{1}H MAS MRS allows for rapid evaluation of minute tissue samples to identify metabolic differences that arise from varying cardiac preservation methods. Biomarkers identified in the current study appear useful for predicting successful donor organ perfusion preservation prior to implantation and may provide clinicians with important metabolic data of donor organ prior to implantation. Additional experiments will be required to determine if the model from this study predicts satisfactory reperfusion cardiac function after implantation.

References

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