PME dynamics of pig's kidney during oxygenated hypothermic pulsatile (HPP) compared to cold static storage (CSS)

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Introduction

With the shortage of brain dead donors for kidney transplantation, marginal donor organs are increasingly considered. Therefore better viability assessment is required. MRI and 31P MRS provide unique physiological insight non-invasively, such as T1 corticomedullary differentiation, perfusion (corticomedullar shunt) and metabolic status [1]. It was shown lately that 31P MRS together with oxygenated pulsatile perfusion (O2+HPP) can be used to measure ATP level, which provide a direct prove of cell viability [2]. In this study, we used this technique to monitor kidney metabolic levels after 8 hours of cold static storage (without perfusion) and we compared the results with a kidney with O2+HPP. We are specifically interested in the recovery of ATP as well as the behavior of PME/Pi ratio after kidney reperfusion.

Material and Methods

Animal preparation and HPP perfusion Kidneys of a young pig were removed "en bloc" and immediately placed in cold storage (4° C). One kidney was maintained in simple static storage (CSS) for 8 hours and the other was perfused (O2+HPP) during the same time period. Both kidneys were then perfused for 13 hours with O2+HPP, while spectra were collected. MRI compatible oxygenated hypothermic pulsatile perfusion (O2+HPP) system was used with a 25 mMolar phosphorus perfusion medium (KPS-1). Oxygen tension of $pO2 \geq 100kPa$ was maintained during HPP.

MR acquisition and analysis MRI/MRS was performed at 3T (Trio, Siemens), with home made 31P interface and surface coil. 1H imaging and shimming were performed with the body coil. T2 sequence (TSE, TR 5000ms, TE 108 ms, 3 mm slices) was used as localizer. 31P MRS consisted of 3D CSI, 16x16x8, resolution 1.56x1.56x2.5 cm^3, TR 1500 ms, weighted k-space, acquisition time 1hour. Standard processing (zero filling, 10 Hz exponential apodization, FFT, acquisition delay (2.5 ms) correction) was performed with SAGE software (General Electric Medical Systems). Individual spectra were corrected for frequency shift and averaged. Metabolites/Pi ratios are reported in %.

Results

31P CSI demonstrates stable ATP level during 13 hours of O2+HPP following 8 hours of O2+HPP (figure 1). PME level decays with a time constant of 0.05 h^{-1}(fig. 1c). Only a slight resonance at -8 ppm is visible (nicotinamide nucleotides, NAD) after CSS for 8 hours (figure 2). ATP level does not significantly increase when O2+HPP is reinitiated for 13 hours (figure 2b). PME decay shows similar time constant of 0.07 h^{-1} (fig. 2c).

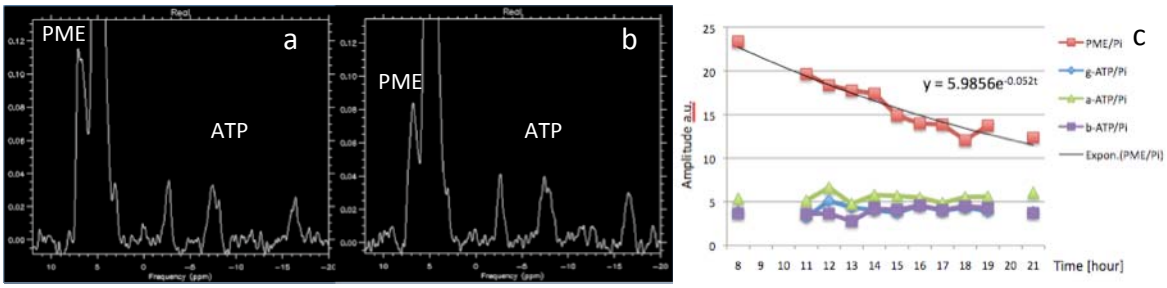

Figure 1: a) Spectra of perfused kidney after 8 hours of O2+HPP. Peak at 7 ppm represents PME. The 3 ATP resonances are visible at -2.3 ppm (gamma), -7.5ppm (alpha) and at -16.1 ppm (beta). b) same kidney after an additional 13 hours of O2+HPP. Similar ATP level is observed, whereas PME is reduced. c) Metabolites/Pi ratio time course showing stable ATP and PME decay. Using a mono-exponential model, a decay constant of 0.05 h^{-1} is found.

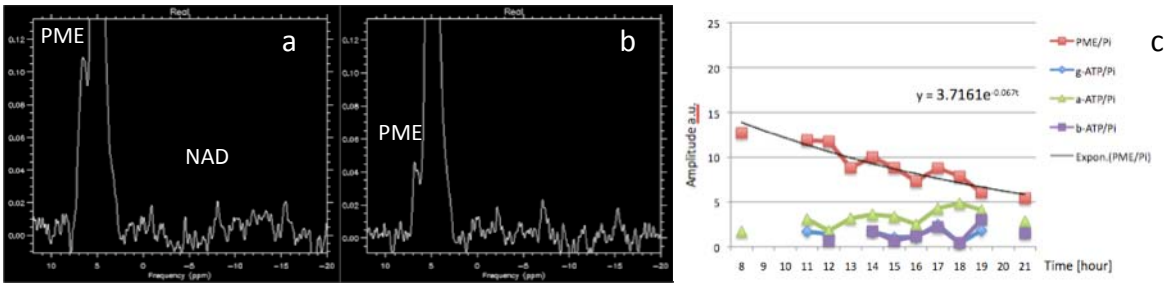

Figure 2: a) Spectra of perfused kidney after 8 hours of CSS. Peak at 7 ppm represents PME. Only a resonance at -8 ppm is visible, which may correspond to nicotinamide nucleotides (NAD). b) same kidney after an additional 13 hours of O2+HPP. ATP did no recover, and PME is reduced. c) Metabolites/Pi ratio time course showing PME decay. Using a mono-exponential model, a decay constant of 0.07 h^{-1} is found.

Discussion and Conclusion

Since Bretan et al. [3], we know that PME/Pi provides a valuable marker for kidney evaluation. It is therefore important to know the dynamics of PME/PI under various storage conditions. In this study, we found a PME decay constant of ~0.05 h^{-1}, which is higher than the value reported in the literature [4]. It is possible that more PME is consumed to synthesize ATP. Although the initial PME level is lower in case of CSS, the time constant is similar, which confirm that long-term PME decay is not influenced by kidney storage condition. ATP level was stable during the whole perfused storage, meaning that kidney perfusion as proposed in this study is able to maintain organs in good bioenergetic state.

References [1] Buchs JB et al, Prog Urol 2009, 19:307-312. [2] Lazeyras F et al., ISMRM 2008, 4543. [3] Bretan PN et al, Am Surg 1993, 59:182-187. [4] Corazza A et al, Trans Proc 2003, 35:3111-3115.