Optimization and Characterization of Two-Dimensional Correlated Spectroscopy of Transplanted Kidney

Alexander Peter Lin[1], Sai Merugumala[1], Saadallah Ramadan[2], Huijun Liao[1], Paolo Fiorina[3], Anil Chandraker[4], and Carolyn Mountford[1,2]

[1]Radiology, Center for Clinical Spectroscopy, Brigham and Women's Hospital, Boston, MA, United States, [2]Centre for MR in Health, University of Newcastle, Callaghan, New South Wales, Australia, [3]Transplant Research Center, Children's Hospital Boston, Boston, MA, United States, [4]Renal Division, Brigham and Women's Hospital, Boston, MA, United States

Introduction: Over 17,000 kidney transplants occur each year in the United States alone[1]. With the rise of diabetes and high blood pressure, the two leading causes of end-stage kidney disease, it is likely that more transplants will be required. Despite improvements in immunosuppression and surgical techniques, chronic allograft dysfunction is one of the major problems in transplanted patients. Early intervention has been shown to be effective in reversing the dysfunction however, it is unclear if there are earlier biomarkers that precede creatinine increases and are non-invasive. Magnetic resonance spectroscopy (MRS) may be able to provide such a marker. Previous studies have shown that changes in MRS metabolites often precede morphological or symptomatic changes in the brain, breast, and other organs[2]. Only two studies[3-4] have used MRS to characterize kidney metabolites and those that did were limited to conventional 1D MRS where resonances can be difficult to disambiguate. Two-dimensional correlated spectroscopy (2D COSY) utilizes a two-dimensional Fourier transformation that produces a 2D spectrum whereby j-coupling between protons in molecules results in cross-peaks that allow for unambiguous identification of different metabolites that may not be visible on 1D MRS[5-6].

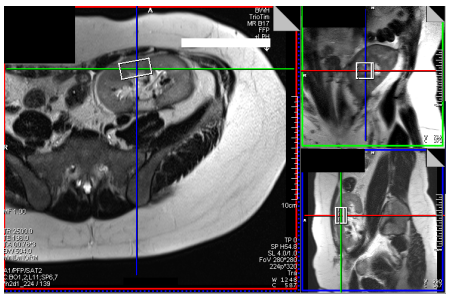

Figure 1. *MRS voxel location in the transplanted kidney shown on three plane T2w MRI*

Objective: The goal of this study was to optimize the data acquisition of 1D and 2D MRS on patients with healthy transplanted kidneys and characterize the metabolites that can be detected with the 2D COSY method.

Methods: Ten subjects with healthy transplanted kidneys (3 females, 7 males, ages 32-63) were recruited for this study. All subjects were consented under local IRB approval and scanned on a 3T clinical MR scanner (Siemens Verio). The optimization protocol used multiple data acquisitions in the same subject to compare the effect of receiver coil choice (3 inch surface coil vs. 4 channel torso phased array), water suppression (with strong suppression, weak suppression, and without water suppression), voxel location (cortex vs. medulla), voxel size (10-24 cm^3), and number of increments for COSY (55 to 96 increments). In each case, localizer imaging sequences using T2w MRI in the three planes were acquired to locate the transplanted kidney. Single voxel MRS was then acquired using the "universal body PRESS" sequence (ubPRESS) that uses an enhanced feature of online frequency correction with TE=135ms, TR=2000ms, 128 averages. 2D COSY was acquired using 55-96 t1 increments with increments size of 0.8 ms in giving an indirect spectral width of 1250 Hz, TR 1.5 s, RF carrier frequency at 2.0 ppm, weak water suppression using WET, spectral width=2000 Hz, 8 averages per increment, and 1024 data points will be acquired. After optimization of the protocol was complete, data acquired from the optimal parameters were then processed and compiled. ubPRESS data was reconstructed on the scanner and evaluated for single-to-noise ratio and presence of artifacts. 2D COSY data was post-processed using Felix 2007 where crosspeak volumes were measured including location (F2, F1 in ppm), amplitude, and volume.

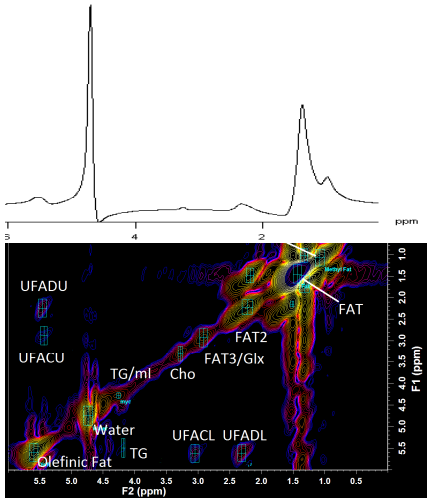

Figure 2. *Representative MRS of Transplanted Kidney. Top: 1D ubPRESS, Bottom: 2D COSY.*

Results and Discussion: The advantage of the surface coil was that it provided better SNR for those kidneys that were transplanted and placed near the surface of the body; however it performed poorly in those cases where there was substantial fat between the coil and the transplanted kidney. The phased array coil provided superior coverage for imaging which avoided re-positioning of the coil and did not offer significantly lower SNR. Strong water suppression often leads to significant artifacts in the spectra, especially out-of-phase lipid artifacts that could dangerously be interpreted as lactate in the 1D MRS. Unsuppressed water did not suffer from that problem but often obscured metabolites, particularly those close to the water peak. The way to overcome this was to acquire spectra with weak water suppression, and a reference spectrum without water suppression, to serve as an internal reference and as a check for artifacts. Voxels located in the medulla resulted in magnitude linewidths that were on the average greater than 40 Hz which were of unacceptable quality. Spectra obtained from the cortex however were much more homogeneous with linewidths on average of 24 Hz. Voxel size was often dictated by the size of the transplanted kidney. As the cortex of the transplanted kidney is often thin in chronic patients, the optimal voxel size was determined to be 1.5 x 3.0 x 3.0 cm^3 to provide sufficient SNR. In COSY, there was not a significant improvement in SNR when using additional increments in the COSY protocol, possibly due to compounded movement artifacts, thus 55 increments were found optimal for a scan time of 11 minutes. The optimized protocol used the torso phased array coil, weak water suppression with a water reference, voxel size of 13.5 cm^3 located in the cortex as shown in Figure 1 for a total exam time of less than 30 minutes. Figure 2 shows a representative COSY spectrum with the identified resonances that are summarized in Table 1. Possible resonances of myo-inositol (mI) and glutamate/glutamine (Glx) may lie under the lipid crosspeaks and remain to be characterized. Lactate crosspeaks were also evaluated but none were present in these healthy kidneys as to be expected.

Peak	F2 (ppm)	F1 (ppm)
Methylene Fat (FAT2)	2.10	2.09
Methylene Fat (FAT)	1.31	1.29
Olefinic Fat Diagonal (UFD)	5.35	5.34
Choline (CHO)	3.28	3.28
Methylene Fat (FAT3)	2.77	2.77
Unsaturated Fatty Acid D, lower (UFADL)	5.30	1.99
Unsaturated Fatty Acid C, lower (UFACL)	5.34	2.78
Triglyceride, G' (TG)	4.20	4.17
Unsaturated Fatty Acid D, upper (UFADU)	2.81	5.36
Unsaturated Fatty Acid C, upper (UFACU)	2.07	5.37

Table 1. Peak name and chemical shift

Conclusion: The results of our study demonstrates that high quality 1D MRS and 2D COSY can be obtained in transplanted kidneys providing multiple metabolite measurements that may have a role in assessing kidney function and health. Future studies to examine chronic kidney failure will determine the efficacy of these metabolites and their subsequent use for treatment monitoring.

References: 1) USRDS 2010 Annual Data Report. United States Renal Data System Web site. www.usrds.org/adr.htm 2) Mountford et al. Chem Rev. 2010; 110(5):3060-86. 3) Shah et al. Magn Reson Med. 1991;20(2):292-8. 4) Dixon and Frahm. MRM 1994; 31:482-487 5) Thomas et al. J Magn Reson Imaging. 2001;14(2):181-6. 6) Ramadan et al. J Magn Reson. 2010;204(1):91-8.