In Vivo Localized 1D and 2D MRS of Rat Kidney using a Clinical 3T MRI/MRS Scanner

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Introduction: In obesity, diabetes, and the metabolic syndrome, the balance among lipid uptake, synthesis, and utilization in nonadipose tissues may become disrupted, leading to intracellular lipid accumulation, cellular dysfunction, and injury. Renal lipotoxicity and its role in pathogenesis of renal disease are not fully understood (1) and there is a great interest in developing novel in vivo approaches for investigation of metabolism in kidney. In obesity and the metabolic syndrome, renal lipotoxicity can result from excess delivery of circulating FFA and triglycerides to the kidney (2). Kidney is a challenging organ for investigation by MRI/MRS due to motion and also it overlaps with other body parts. Previous studies have shown accumulation of fat in skeletal muscle, heart, liver but little has been known about fat accumulation in kidney. In this study we have implemented advanced MRS approaches to investigate the rat kidney.

Methods: Experiments were conducted with institutional Animal Care and Use Committee approval on 6 Sprague-Dawley rats (250-350 grams) and 3 adult rats (600-650 grams). The left kidney was immobilized using a plastic cup with a lateral cutout for the renal artery. The cup is attached to a Plexiglas holder (Fig.1). A 12cm T/R coil was employed for all the MRI and MRS experiments (Fig. 1). The rectal temperature was maintained by heating pads/blankets and monitored during the entire experiments. Localized PRESS and L-COSY spectra were acquired using a whole body MRI scanner (GE Signa HD) scanner over a volume of 1.5 cm^3 with TR/TE of 2s/30ms, and 2048 complex points from the left kidney. The PRESS spectra were averaged over 32 scans and the LCOSY spectra were acquired with TR=2s, TE_{min}= 30ms, 16 averages and 40 t_1 increments with a total acquisition time of 21 mts.

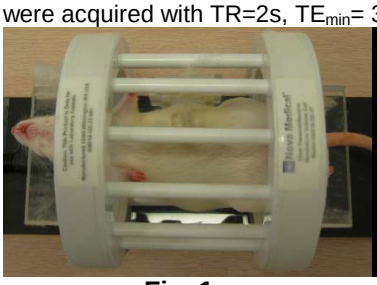

Fig. 1

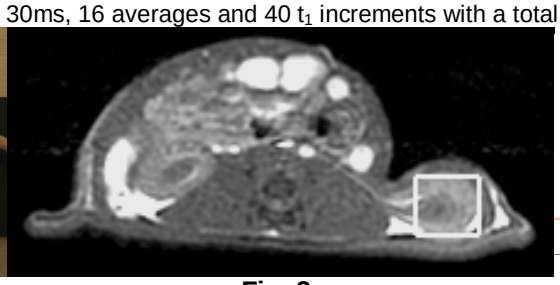

Fig. 2

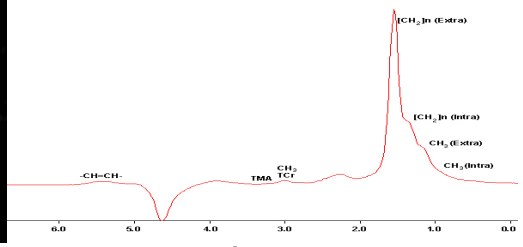

Fig. 3

Results: Figure 1 shows the positioning of the rat inside the RF coil. Fig. 2 shows a 2mm thick slice spin-echo axial image employed for MRS localization. This image clearly shows the clamped left kidney on which all the MRS experiments were performed. Fig. 3 shows the one-dimensional PRESS spectra acquired from the left kidney. By analogy with other tissues (e.g. muscle) (3) we have identified "intracellular signals". The CH_3 and $[CH_2]n$, -CH=CH- resonances were identified from intra- and extracellular lipids along with total creatine (TCr), Trimethyl containing compounds (TMA). Figure 4 shows the localized correlated (L-COSY) spectrum from the identical volume. The spectra display diagonal and cross peaks generated from saturated and unsaturated groups of intra and extracellular lipid pools and other metabolites. In addition to the methyl and n-methylene groups of intra- and extracellular lipids the L-COSY spectrum also shows the cross peaks labeled C1, C2, C3, C4, C5, and C6. Cross peaks C1 and C3 arise from spin-spin coupling between olefinic (-CH=CH-) and allylic methylene protons CH2CH=CH of intra and extra- cellular lipids respectively. Cross peaks C2 and C4 arise from the indirect spin-spin coupling between olefinic (-CH=CH-) and allylic methylene protons $CH_2CH=CH$ of intra- and extracellular lipids. Note that the cross peaks C5 and C6 due to intra and extracellular lipids are not resolved due to the lower spectral resolution along the F1 dimension. Both 1D and 2D MRS spectra confirms the presence of two types of lipids.

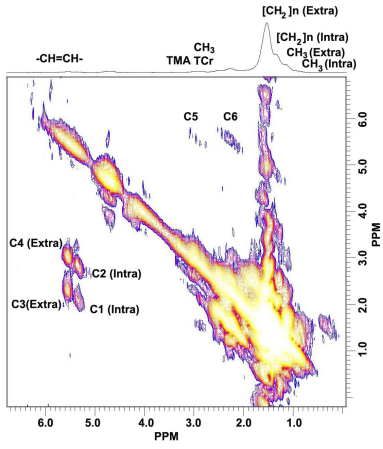

Fig. 4

Discussion: Investigation of the kidney by in vivo MRI/MRS approaches has been hampered by respiratory and cardiac motion. The non-invasive assessment of biochemistry in the kidney should be helpful in understanding physiological responses as well as disease induced adaptation in this complex organ. There is a growing evidence that abnormalities in lipid metabolism contribute to renal disease progression. From our preliminary study both 1D and 2D MRS indicate two sets of lipid signals. We have tentatively assigned them as intra- and extracellular lipids. The intracellular signals may not come from renal cells, they may be from adipose cells or from accumulation of lipids through foam-cell formation (4). Even though earlier electron microscopy studies have shown the presence of intracellular lipids in rodent kidney this is the first in vivo demonstration of detecting these lipid pools.

Conclusion: We have demonstrated the feasibility of detecting intra- and extracellular lipids in rat kidney by one- and two-dimensional MRS techniques. Our preliminary results suggest that MRS can be employed to evaluate lipid toxicity in renal disorders.

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