Optimization of Ectopic Lipids Determination in Kidneys by MRS and Preliminary Results in Obese Diabetic Patients.

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Introduction

There is increasing evidence that accumulation of renal ectopic lipids leads to kidney dysfunction [1-4]. Renal ectopic lipids have been associated with type-2 diabetes, obesity-related glomerulopathy, and with organ function [5,6]. It has also been suggested that renal dysfunction in turn leads to ectopic lipid redistribution [3,4]. A very recent review in Lancet describes the association between ectopic lipid accumulation in the kidney and renal diseases [5].

Changes of ectopic lipids in various diseases have been described in almost all organs in the body, including the liver, heart, muscle, and the kidney. In all these organs, among other methods MRS has been used for estimation of lipids, except for the kidney. Only very recently single voxel spectroscopy (SVS) has been used in healthy volunteers to determine non-invasively the ectopic lipid content [7]. A very low triglyceride content of less than 0.5% was determined. However, to our knowledge no study has been performed in humans to assess renal ectopic lipids non-invasively in diabetic patients or in any other disease.

The lack of MRS studies in kidneys is related to different obstacles rendering renal MRS challenging, including respiratory motion, susceptibility differences, and tissue heterogeneity. For determination of ectopic lipids within the kidney, especially spurious signals from surrounding visceral fat and also from fat in renal sinus need to be entirely excluded, which again is challenging in a moving organ.

The purpose of this study was therefore 1) to optimize the MRS protocol for estimating ectopic renal lipids, 2) to determine in a pilot study the ectopic lipid content in obese patients with type 2 diabetes with the optimized protocol.

Subjects and Methods

Five obese patients with type 2 diabetes (age = 48±6y, weight = 113±18.3kg, BMI = 35±6.5kg/m^2) were investigated on a 3T MR-scanner (Verio, Siemens, Erlangen, Germany). Prior to that, the protocol was optimized in measurements of 10 healthy volunteers.

A single voxel PRESS sequence with PACE respiratory triggering was used (TR = 2000ms, TE = 35ms). Saturation bands were placed around the excited volume to minimize contamination from surrounding fat (Fig. 1). Shimming was performed using GRE-SHIM as well as manual shimming in breathhold if the linewidth indicated a poor shim. The protocol included a quick single voxel scan for a linewidth check. Measurements were performed without water suppression. 16 measurements with 4 acquisitions each were acquired for each subject in order to allow a) for phase-cycling, and b) for detection of individual measurements with poor quality for exclusion from analysis.

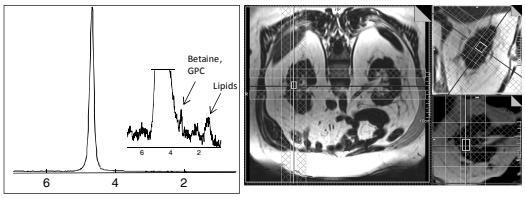

Fig. 1: Single voxel kidney spectrum from an obese diabetic patient demonstrating low visible lipid

First fat/water images were acquired using Dixon type sequences for placing the MRS voxel carefully in virtually fat free regions and secondly to determine the fat content in addition from the MR images, not presented here.

The spectra of the 16 measurements for each subject were investigated for outliers (due to movement), summed, and analyzed using jMRUI fitting the water and lipid peaks.

Results

The applied protocol with controlled shimming, careful voxel positioning on fat images, PACE triggering, and application of saturation bands yielded spectra in volunteers with very low lipid content, suggesting effective suppression and exclusion of bulk lipids from surrounding tissue. An example of a single voxel scan in a slim volunteer using the optimized protocol is shown in Fig. 2. Even the zoomed-in spectrum shows only a peak at ~3.2ppm (Betaine or GPC) and no visible lipid.

The spectra from diabetic patients also yielded relatively low lipid contents (see Fig. 1 for an example), with lipid contents between 0.4% and 1.5% (mean: 0.8±0.4%).

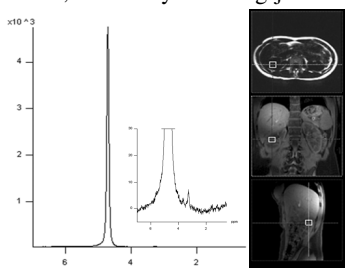

Fig. 2: Single voxel spectrum from a kidney in a volunteer.

Discussion

The preliminary SVS results in obese patients with type 2 diabetes yielded ectopic lipid contributions of only 0.8±0.4%, which is twice as high as was obtained in Ref [7] for healthy controls, but much lower than in diabetic mice with lipid contents of about 10% [8]. However, this comparison does not take into account measurement parameters like echo times, which can impact the results, though cannot explain the difference to 10%. Additional measurements of obese patients with type 2 diabetes are needed to confirm our initial findings.

These initial results with low lipids demonstrate that a very precise measurement is required for detecting ectopic renal lipids. The results also show that because of the low lipid content, I) Dixon measurements need to account for Rician noise to avoid bias towards too high values; II) MRS measurements may be considered to be applied in addition with water suppression, to avoid artefacts due to the very intense H_2O signal compared to the very low lipid content reported here.

Conclusion

Reliable fat estimations in renal tissue were obtained using a protocol optimized for ectopic lipid determination. Low ectopic lipid content was obtained in few obese diabetic patients, a finding which requires confirmation.

References

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