In vivo [1]H MRS of human Gallbladder Bile using an Optimized 16-Channel Phased Array at 3T

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INTRODUCTION: Identification and quantification of metabolites in bile related to disease pathophysiology is one of the emerging applications of MR spectroscopy. Simultaneous quantification of major biliary lipids (glycine-conjugated bile acids (GCBAs), taurine-conjugated bile acids (TCBAs), total bile acids (TBAs) and choline-containing phospholipids) is the most recent success in our lab using *in vitro* [1]H MRS [1]. Considering the diagnostic value of these metabolites in detecting hepatopancreatobiliary disorders, there is a great interest in performing such analysis *in vivo* [1 - 3]. The study performed by Prescot et al. using a 1.5T MRI scanner was the first attempt to obtain [1]H MR spectra of human gallbladder (GB) bile *in vivo*. Unfortunately, because of the low quality of the spectra, the detection and quantification of individual bile components was impossible except for phospholipids [2]. A more recent study performed by Kunnecke et al. on the bile composition in cynomolgus monkeys was successful in obtaining a high quality spectrum by increasing the magnetic field strength to 4.7T and using a home-built surface coil in transmit/receive mode along with respiratory gated sequences [3]. Our preliminary results on pigs using a 3T clinical scanner and a home-built receive array coil was the first to show the possibility of obtaining high quality spectra in clinical settings [4]. Application of a similar method on human subjects has resulted in comparable spectra with a possibility of quantifying disease-related metabolites. It is also worthwhile to note that some of the important metabolites involved in cancer detection, such as lactate, generally overlap with lipid signals and could not be discriminated by the regular PRESS sequence. Spectral editing MRS sequences are useful for these purposes, but they can only detect one metabolite in each measurement. In such cases, 2-D MRS techniques such as L-COSY will be advantageous [5].

MATERIALS AND METHODS: 1-D MRS experiments were performed on 7 healthy volunteers using a Siemens 3T Magnetom Trio clinical scanner and our home-made receive array coil. We performed single voxel spectroscopy using the Siemens PRESS sequence on GB bile. The voxel size was optimized to 12×12×12 mm^3. The respiration motion artifacts were decreased using respiratory gated sequences. Spatial saturation bands were placed outside the gallbladder to reduce interference due to fat from the liver and water suppression was also performed. The acquisition parameters used in the PRESS sequence were: TE = 30 ms, TR = 2000 ms, bandwidth = 2000 Hz and NS = 256. The PRESS sequence was edited to L-COSY as described by Thomas et al. [5] and the following parameters were used for L-COSY experiments: NS =12, time increment (Δt_1)= 0.8 ms, measurements = 50. The 2007 FELIX software (FELIX NMR Inc., San Diego, California) was used for the analysis of both 1-D and 2-D spectra.

RESULTS & DISCUSSION: In our previous study, we tested the feasibility of obtaining a high quality 1-D spectrum using our home-built receive array coil in pigs [4]. In this study, we are extending the application of a similar method to humans and also supplementing our data with 2-D MRS; the first such data on gallbladder bile in-vivo. Figure 1 shows the *in vivo* [1]H MR spectrum of human GB bile (middle: 1-D, right: 2-D L-COSY). In the 1-D spectrum, we can detect signals from lipids, phosphatidylcholine and even glycine- and taurine-conjugated bile acids. These signals are altered in various cholestatic and neoplastic disorders as shown in *in vitro* studies [1, 6]. Quantification of total bile acids, choline-PLs, and glycine-conjugated bile acids using their methyl (CH_3), trimethylammonium ($-N^+(CH_3)_3$), and methylene (CH_2) signals resonating at 0.65 and 3.22, and 3.73 ppm respectively will be useful in clinical settings for the early detection of cholestatic and neoplastic hepatopancreatobiliary disorders. In the 2-D L-COSY spectrum, cross peaks from phosphatidylcholine-glyceryl signals (5.34ppm/4.2 ppm; 4.4 ppm/4.3 ppm) have been detected which were overlapping with the lipid signal in the 1-D spectrum. The detection of these signals can play a role in the diagnosis of cholestatic diseases [6]. Moreover, the cross peaks from glycine/taurine conjugated bile acids (8.0 ppm/3.7 ppm) are also clearly visible.

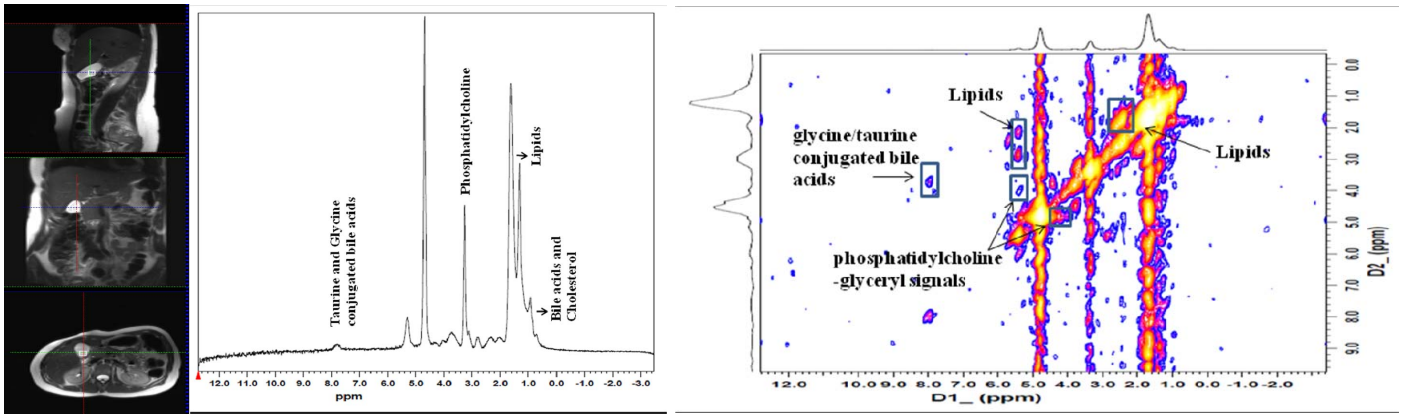

Figure 1. ***In vivo*** **[1]H MRS acquired from human gallbladder bile using home-built 16-channel receive array coil (left voxel position, middle 1-D, and right 2-D L-COSY)**

CONCLUSION: Obtaining a high quality spectrum is the first step in the early and non-invasive detection of various cholestatic and neoplastic hepatopancreatobiliary disorders. Quantification of different bile metabolites such as choline-PLs, and bile acids linked to cell metabolism and pathophysiologic processes of biliary system will be helpful in introducing the technique into the clinic. 2-D MRS could also be helpful in the detection of overlapping signals, specifically those of phosphatidylcholine-glyceryl and lactate signals, thus augmenting 1-D MRS.

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