

¹H MR Spectroscopy of Human Bile for Rapid and Non-invasive Diagnosis of Pancreatic Cancer

T. Bezabeh¹, O. B. Ijare¹, N. Albiin², B. Lindberg², U. Arnelo³, and I. C. Smith¹

¹MR Research & Development, NRC Institute for Biodiagnostics, Winnipeg, MB, Canada, ²Radiology, Karolinska Institutet, Stockholm, Sweden, ³Surgery, Karolinska Institutet, Stockholm, Sweden

INTRODUCTION: Pancreatic cancer, one of the major causes of cancer deaths worldwide, is difficult to diagnose in its early stage and has a dismal prognosis. More than 90% of patients with pancreatic cancer die within 12 months of diagnosis. Thus, rapid diagnostic methods are desirable for the detection of pancreatic cancer. Diagnostic imaging methods such as computed tomography (CT), ultrasound (US), magnetic resonance imaging (MRI), and positron emission tomography (PET) can detect tumors after the disease has progressed to a certain extent. Analysis of biofluids is useful in identifying the tumor markers in the early stages of the disease. CA 19-9 is a mainstay tumor marker for pancreatic cancer, but has a sensitivity of only 70% and specificity of 87%. Identification of new tumor markers is essential for the rapid detection of this malignancy. Pancreatic cancer is strongly associated with diabetes mellitus, but there is a debate over whether diabetes is a cause or consequence of pancreatic cancer. Recent studies have suggested that pancreatic cancer causes diabetes mellitus by releasing soluble mediators which interfere with both beta-cell function and liver and muscle glucose metabolism [1]. Recent onset of diabetes has been observed in patients with pancreatic cancer after a few months of the tumor diagnosis. Glucose is virtually absent in human bile at normal and hyperglycemic concentrations of glucose in plasma [2]. We propose that the presence of glucose in bile is an indication of pancreatic cancer, and the detection of glucose in bile by ¹H MRS may lead to a rapid and non-invasive diagnosis of pancreatic cancer, including its differentiation from pancreatitis (acute/chronic inflammation of the pancreas).

MATERIALS AND METHODS: Bile samples were collected from subjects with normal bile ducts (n=5), pancreatitis (n=2), pancreatic cancer (n=3) and stone in the bile duct (n=5) during ERCP examination, after securing optimal catheter position in the common bile duct (contrast agent iohexol; Omnipaque® 240 mg I/ml). Both single pulse and Carr-Purcell-Meiboom-Gill (CPMG) spin-echo pulse sequence 1D ¹H MR spectra were obtained for the bile samples on a 360 MHz spectrometer (Bruker Instruments) with presaturation of the water resonance. The CPMG spin-echo pulse sequence allowed spectral editing by the attenuation of signals arising from components with short T₂ relaxation times.

RESULTS & DISCUSSION: We have analysed human bile samples from patients suffering from various hepatopancreaticobiliary diseases using 1D ¹H MRS. We have found that glucose was not detected in all the normal bile samples, observed in a negligible amount in pancreatitis patients, and detected in a considerable amount in all the three bile samples from pancreatic cancer patients (Fig. 1). This observation clearly indicates that the secretion of glucose in bile might be an early indication of pancreatic cancer and may serve as a tumor marker for the diagnosis of this malignancy. Furthermore, it is possible to differentiate between pancreatitis and pancreatic cancer by observing the ¹H MR spectra of human bile samples. Bile is a complex secretion of hepatocytes which is iso-osmotic with respect to plasma but contains a diversity of solutes whose biliary concentrations are either greater than or similar to or less than their respective concentrations in plasma. Glucose is an example of such a solute that is found in human bile in concentrations less than that in plasma. It is virtually absent in human bile. The reason for the absence of glucose in bile is unknown, but it is believed that glucose is being removed from the bile by active transport at some site along the biliary tree [2]. There is evidence that shows pancreatic cancer causes glucose metabolic alteration and impairs the process of glycolysis [1]. This may be the reason for the increased levels of glucose in bile in pancreatic cancer patients. In addition, pancreatic cancer is believed to be one possible cause of diabetes mellitus and very high concentrations of glucose in serum may enhance the levels of glucose in bile. Glucose can be conveniently detected in bile by ¹H MRS, and by measuring the relative concentration of glucose, the present method can be used to differentiate between pancreatitis and pancreatic cancer which may lead to a rapid and non-invasive diagnosis of pancreatic cancer.

CONCLUSION: Secretion of glucose in human bile is an indication of pancreatic cancer and may serve as a tumor marker for the early detection of pancreatic cancer. Glucose in bile can be conveniently analyzed by ¹H MRS and may be used for the rapid and non-invasive diagnosis of pancreatic cancer. The findings, although very promising, are preliminary and need to be proven with a larger patient cohort.

REFERENCES

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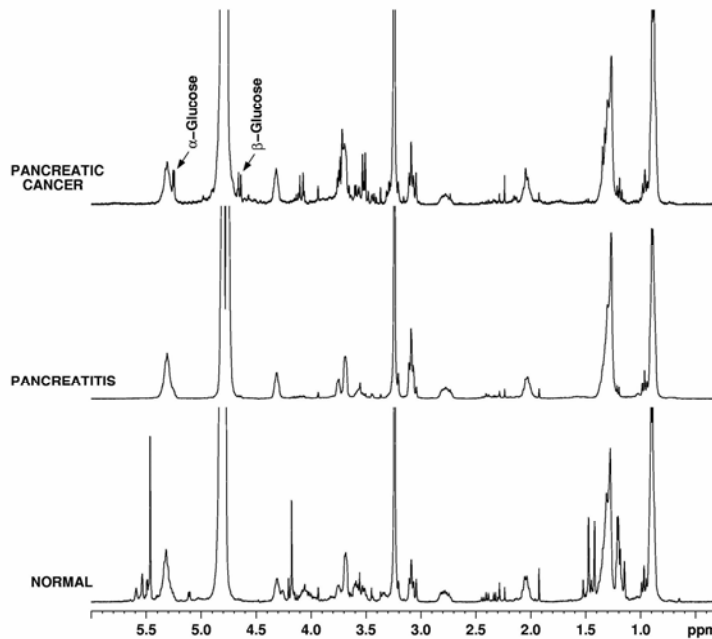


Figure 1: ¹H MR spectra of bile from normal, pancreatitis and pancreatic cancer patients obtained by CPMG spin-echo pulse sequence