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Gadoxetate Disodium enhanced spectral dual-energy CT for evaluation of cholangiocarcinoma: Preliminary data

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HIGHLIGHTS

- Hepatic parenchyma showed an increase in attenuation measurement at the lower viewing energy.
- No significant difference was observed for measurement for single versus double dose of gadolinium.
- Visually the liver parenchyma did not enhance, limiting evaluation of cholangiocarcinoma.

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ABSTRACT

Purpose: Evaluate Gadoxetate Disodium enhanced dual-energy CT for visualization of perihilar cholangiocarcinoma by exploiting the hepatobiliary uptake of Gadoxetate Disodium and viewing images at the k-edge of gadolinium on the spectrum of simulated monoenergetic energies available with Dual Energy CT.

Material and methods: In this prospective, IRB-approved study in patients with suspected cholangiocarcinoma, subjects who underwent a clinically indicated Gadoxetate Disodium liver MRI were immediately scanned without further IV contrast administration using rapid kVp-switching dual energy CT (rsDECT). Initial Gadoxetate Disodium dose was the FDA approved clinical dose, 0.025 mmol/kg; after additional IRB/FDA approval, 10 subjects were scanned with 0.05 mmol/kg. Both 50 keV and 70 keV simulated monoenergetic images as well as gadolinium(-water) material density images were viewed qualitatively and measured quantitatively for gadolinium uptake in the hepatic parenchyma and any focal lesions identified.

Results: Of 18 subjects (mean age 55 years, 10M, 8F, weight 84 kg), eight were scanned with 0.025 mmol/kg (Group 1) and 10 with 0.05 mmol/kg Gadoxetate Disodium (Group 2). Five patients had cholangiocarcinoma (all in Group 1). On synthetic monoenergetic images using standard and double Gadoxetate Disodium dose, the liver parenchyma did not appear enhanced qualitatively. Comparison of mean hepatic parenchymal HU at 50 and 70 keV showed a measurable increase in attenuation at the lower viewing energy, which corresponded to the k-edge of gadolinium. No statistically significant difference was observed on quantitative gadolinium measurement of hepatic parenchyma for single versus double Gadoxetate Disodium dose using rsDECT gadolinium material density images. Of the five cholangiocarcinomas, the tumor to nontumoral hepatic tissue HU differences were 51.1 (32.2) (mean and std dev) and 49.0(26.5) at 50 and 70 keV, respectively.

Conclusion: In this small pilot population, evaluation of potential hilar/perihilar cholangiocarcinoma using dual energy CT at both the single FDA-approved dose and double dose of gadolinium demonstrated observed differences in attenuation between the hepatic parenchyma and lesions. However, small sample size and heterogeneity of lesions warrants further investigation.

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1. Introduction

Cholangiocarcinoma is a neoplasm originating in the intra or extra-hepatic biliary epithelium. Despite a multimodality approach in the diagnosis and staging of cholangiocarcinoma, determining the extent of disease remains a challenge and the disease is often underestimated [1,4]. Conventional MDCT in conjunction with iodinated IV contrast is currently used to image patients with cholangiocarcinoma, and provides the advantage of a rapid exam of high resolution. Images are obtained during arterial and portal venous phase, as well as delayed phase scanning at 15 min. Cholangiocarcinomas typically show a higher attenuation compared to the surrounding hepatic parenchyma in the delayed phase, a finding that is attributed to abundant fibrous stroma [2].

MRI of the liver using extracellular gadolinium-based agents faces some of the same challenges as CT; however, MRI techniques benefit from inherent tissue contrast, which work to its advantage in evaluating tumors. More recently, the introduction of hepatobiliary agents such as Gadoxetate Disodium – Eovist™ (Bayer Healthcare NJ, USA) increases the contrast between tumoral tissue and normal surrounding hepatic parenchyma, improving visualization of hepatic lesions including cholangiocarcinomas [3]. The hepatobiliary phase is usually reached within 20 min after initiation of contrast injection in patients with normal hepatocyte function and last for at least 60 min [4]. In the hepatobiliary phase, tumors appear dark against brightly enhanced liver parenchyma, and in the case of cholangiocarcinomas might be better depicted this way rather than relying on delayed uptake in fibrotic tissues [4]. However, not all patients can undergo an MRI scan. In addition, patients might not be able to comply with breath holding requirements or tolerate the relatively longer scan times required for MRI compared to MDCT. With hepatobiliary phase imaging, an MRI scan typically lasts at least 30–45 min. To this end, an ideal imaging test for detection and staging of cholangiocarcinoma would be rapid and provide excellent hepatobiliary contrast enhancement.

Gadoxetate Disodium in combination with dual energy CT has the potential to fill this role well [5,6]. Gadolinium, as a chelated molecule, has been used as an MRI relaxation contrast agent for many years. Because of its electronic structure, it is also an effective x-ray contrast agent due to relatively high attenuation and advantageous k-edge in the diagnostic x-ray energy range: 50.2 keV compared to 33.17 keV for Iodine (Figs. 1–2). We hypothesized that utilizing dual energy simulated monoenergetic images corresponding to the k-edge of gadolinium while employing a gadolinium-based hepatobiliary agent such as Gadoxetate Disodium would help better visualize hilar cholangiocarcinomas. The purpose of our project was to perform a qualitative and quantitative evaluation of Gadoxetate Disodium enhanced rapid kVp-switching dual energy CT (rsDECT) in visualizing perihilar cholangiocarcinomas.

2. Materials and methods

This prospective, HIPAA compliant study was approved by our IRB. All patients with suspected cholangiocarcinoma who were referred to the liver transplant clinic of our tertiary care medical center and who had a gadoxetate MRI ordered for clinical evaluation were eligible Patients who had hepatobiliary surgery within the last 2 years, were less than 19 years of age, or were pregnant, were excluded from the study. We did not exclude patients who had percutaneous transhepatic drains in place. After full written informed consent was obtained, subjects underwent a clinically indicated Gadoxetate enhanced MRI scan of the liver per standard of care followed immediately by a research rsDECT scan of the upper abdomen, without additional IV contrast, within 1 h of the

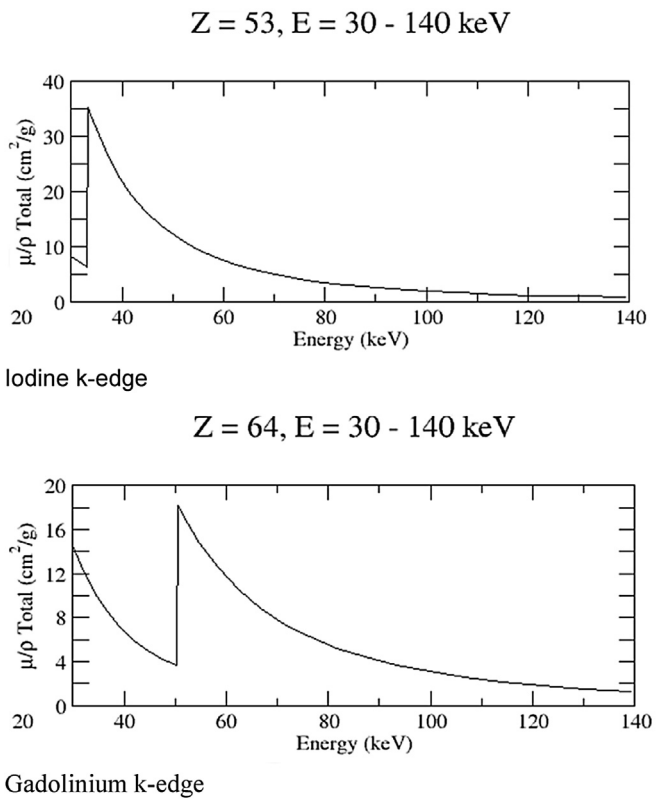

Fig. 1. The k-edge of iodine is 33.17 keV and that of gadolinium 50.2 keV. The relative high attenuation and advantageous k-edge of gadolinium in the diagnostic x-ray energy range makes gadolinium also an effective x-ray contrast agent.

Gadoxetate administration. To expedite the process, subjects were transported in a wheelchair from the MRI scanner to the dual energy scanner located on a different floor in the same outpatient multidisciplinary clinic building. Demographics, time from injection to rsDECT acquisition, total bilirubin, serum Aspartate Amino Transferase (AST), serum Alanine Amino Transferase (ALT), serum creatinine and dose linear product (DLP) were recorded from the electronic medical record (Table 1).

MRI scan of the liver was performed on a Phillips 1.5T Achieva™ scanner (Philips Medical Systems, Best, The Netherlands). The Gadoxetate Disodium enhanced MRI scan protocol included 10–20 min delayed hepatobiliary images in addition to the other standard sequences End point of the hepatobiliary phase was visualization of excreted contrast in the bile ducts. The rsDECT was performed on a GE HD750™(GE Healthcare, Milwaukee, WI USA). After localization, a single acquisition through the liver was obtained in dual energy mode without administering any additional intravenous contrast agent (Table 2). Five mm thick simulated monoenergetic axial images were generated at 50 and 70 keV and gadolinium(-water) basis pair images were also generated at the same slice thickness. Initially, subjects were given the FDA-approved Gadoxetate dose of 0.025 mmol/kg. After the first 8 subjects were accrued, it was apparent that the standard clinical dose was suboptimal for visualization on rsDECT. After obtaining additional regulatory approvals including an Investigative New Drug (IND) letter from the FDA, as well as new approval from our institution's IRB, all subsequent subjects were scanned with 0.05 mmol/kg Gadoxetate Disodium. Both groups were injected with Gadoxetate Disodium at a rate of 1 ml/s [7].

Qualitative evaluation: The IV Gadoxetate Disodium enhanced rsDECT images were reviewed in consensus by two radiologists

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