MRI Appearance of Focal Liver Lesions with Gadofosveset Trisodium

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**Objectives**

Focal liver lesions (FLL’s) are common and can be challenging to diagnose. Accurate diagnosis is often crucial to patient management, particularly those with possible malignancy. With new advances in treatments for malignancy, early and accurate diagnosis of focal liver lesions may affect outcomes including the possibility of curative treatment.

The diagnosis of FLL’s has significantly improved with new advances in imaging techniques over the recent years. These include contrast-enhanced ultrasound, PET/CT, improved MRI resolution, and hepatobiliary-specific MRI contrast agents. However, there are still limitations in diagnosis, particularly in smaller lesions. For example, in one meta-analysis comparing various imaging methods for colorectal metastases, the sensitivity of MRI for lesions less than 1mm is 0.60 and even lower for CT at 0.47 (1).

Gadofosveset trisodium (Gdfos; Ablavar) binds to albumin and has a long intravascular half-life. It acts as a blood pool contrast agent. Its original intended use is for MR angiography. From contrast-enhanced ultrasound (CE-US) literature, we know that blood-pool contrast agents can be very helpful in characterizing focal liver lesions as benign or malignant based on late phase enhancement pattern (hyper- or iso-vascular with benign lesions and washout with malignant lesions). However, CE-US has a number of limitations. It can be time consuming and only one lesion can be imaged at a time. It is operator dependent. The detection rate is lower than cross-sectional imaging (2). The use of a blood-pool MRI contrast agent would combine the benefits of CE-US with the advantages of cross-sectional imaging.

Our group has performed a small proof-of-concept pilot study on a group of 12 patients with 22 focal liver lesions including hemangiomas, metastases, cysts, FNH, and adenomas. In this small sample, the benign lesions showed retention of contrast whereas the metastases showed washout of contrast on delayed phase imaging with Gdfos. The enhancement pattern and appearance of the FLLs were otherwise the same as with extracellular contrast agents (3). However, despite this encouraging initial data, a larger sample and a larger variety of FLLs (including different types of metastases and primary liver cancer) is needed in order better characterize the MR appearance of FLLs with Gdfos.
**Hypothesis**

Malignant lesions will show washout of contrast on delayed phase imaging with Gdfos, whereas benign lesions will not.

**Approach**

This will be a prospective study with a qualitative and a quantitative component. The patient population will be those with a known focal liver lesion as seen on a previous MRI with gadobutrol (EcGd; Gadovist) performed as part of standard of care. Inclusion criteria are: age > 18 years old and glomerular filtration rate (GFR) > 30mL/min within 60 days of scan. Exclusion criteria are: any standard contraindication to MRI, GFR < 30mL/min within 60 days of scan, allergy to MR contrast agent, or pregnancy.

We have chosen 50 participants for our sample size. In our pilot data, we were able to show statistical significance with metastases with 12 patients. However, the pilot data was limited in the type of lesions we were able to characterize. Our goal would be to characterize the enhancement pattern of a broader range of patients including metastases from different primaries (eg. colorectal cancer, breast cancer, mucinous metastases, neuroendocrine tumours, and renal cell carcinoma), primary liver cancer (hepatocellular carcinoma and cholangiocarcinoma) as well as a broad range of benign lesions.

The study participants will receive a dynamic Gdfos-enhanced study with acquisitions in the precontrast phase, arterial phase, portal-venous phase, 5-minute delay, and 10-minute delay (Gdfos dose: 0.1mL/kg up to 10mL). This will be done within 1 month of the original MRI.

The Gdfos-enhanced MRI will be compared to the original gadobutrol-enhanced MRI as well as to the “truth standard” as defined as by pathology or follow-up imaging.

Quantitative analysis will be done to describe the enhancement pattern with Gdfos. Mean ROIs of each lesion and their standard deviations will be obtained. The average background value will be subtracted from each reading. We will use this to obtain enhancement curves for each type of lesion.

The liver lesions will also be sub-grouped into “benign” and “malignant” categories to compare Gdfos and EcGd. The relative enhancement pattern for at each of the phases will be compared using a linear mixed effects model accounting for repeated measures.
Research Plan

Sept 2013 – Aug 2014: Recruit patients for MRI and scan patients
Sept 2014 – Dec 2014: Analyze data
Jan 2015 – beyond: Prepare manuscript for publication

Ethics Approval

Our group had received institutional ethics approval for the original pilot study. A revision to this approval for the proposed larger study will be submitted in the near future.

Role of the Applicant

I am an Abdominal Radiologist at Sunnybrook Health Sciences Centre and an Associate Professor at the University of Toronto, Affiliated Scientist at the Sunnybrook Research Institute and Associate Member of the Institute of Medical Science at the University of Toronto. I will be the Principal Investigator for this project and will oversee the project from research design to data collection/analysis and manuscript preparation.

References

(1) Niekel MC, Bipat S, and Stoker J. Diagnostic imaging of colorectal liver metastases with CT, MR imaging, FDG-PET, and/or FDG PET/CT: a meta-analysis of prospective studies including patients who have not previously undergone treatment. Radiology 2010; 257(3): 674-684.