Hypoenhancing liver lesion on both portovenous and delayed phase gadobutrol and gadofosveset-enhanced MRI as a sign of malignancy in the diagnosis of colorectal liver metastases (CRLM)

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TARGET AUDIENCE
The target audience members are abdominal MRI radiologists.

PURPOSE
Colorectal cancer is the third leading cause of cancer deaths in North America (1). Most deaths are related to metastatic disease (2). Approximately 50% of patients with colorectal cancer will develop colorectal liver metastases (CRLM) (3). Surgery is currently the standard of care for treating CRLM due to improved morbidity and mortality (3). Not all lesions are metastatic and accurate per lesion diagnosis is crucial for surgical planning. Classically, CRLM appear hypoenhancing (contrast-to-noise ratio, CNR < 0) on portovenous and delayed phases with dynamic contrast MRI using extracellular contrast agents (eg. gadobutrol) (4). These CRLM tend to be easy to diagnose because benign lesions rarely demonstrate this sign. However, some CRLM will not follow this enhancement pattern and can be difficult to distinguish from benign lesions. This may be due to leakage of contrast into the lesion via the interstitium (5). We hypothesize that imaging of CRLM with intravascular MRI contrast agents such as gadofosveset will demonstrate less leakage of contrast and be more likely to appear hypoenhancing (CNR<0) on both portovenous and delayed phase imaging. The goal of this study is to determine the prevalence of CRLM lesions that demonstrate this sign and its diagnostic accuracy with gadobutrol- and gadofosveset-enhanced MRI in this population.

METHODS
This is an REB-, Health Canada-approved, prospective study. Any patients with known colorectal cancer referred for a clinical gadobutrol-enhanced liver MRI at our institution were eligible for our study. Exclusion criteria included contraindications to MRI or MR contrast agents and inability to obtain acceptable quality imaging. Patients received a gadofosveset-enhanced MRI in addition to the standard clinical gadobutrol-enhanced MRI. The CNR for all solid liver lesions were measured at the portovenous and 10 minute delayed phases for both gadobutrol and gadofosveset. We determined the prevalence of CRLM that demonstrated hypoenhancement on both portovenous and delayed phase with gadobutrol vs. gadofosveset. We also determined the sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV). Sensitivities and specificities were compared using the McNemar Chi Square Test (6).

RESULTS
We had a total of 14 patients with 116 lesions (97 malignant, 19 benign). For gadofosveset-enhanced MRI, 90% of CRLM lesions were hypoenhancing on portovenous and delayed phases compared to 65% for gadobutrol-enhanced MRI, an increase of 25%. The sensitivities, specificities, PPV's, and NPV's of this sign were 90%, 79%, 96%, and 60% respectively with gadofosveset and 65%, 89%, 97%, and 33% respectively with gadobutrol. The sensitivities were statistically different (p<0.0001), but the specificities were not (p=0.625).

Tables: 2x2 Tables for Gadobutrol and Gadofosveset

Gadobutrol	Test Positive	Test Negative
Malignant	63	34
Benign	2	17

Gadofosveset	Test Positive	Test Negative
Malignant	87	10
Benign	4	15

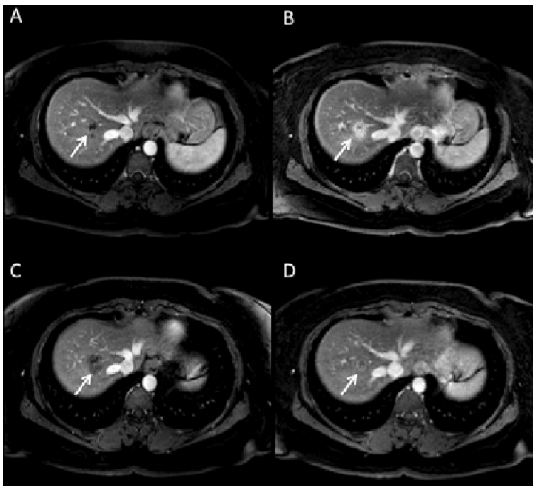

Figure: Axial T1-weighted images of the liver. An example of a CRLM that is hypoenhancing on portovenous phase (A) and hyperenhancing on delayed phase (B) with gadobutrol, but hypoenhancing on both portovenous (C) and delayed phase (D) with gadofosveset

DISCUSSION
Hypoenhancement on both portovenous and delayed phase is a helpful sign in diagnosing CRLM with high PPV for both gadobutrol- and gadofosveset-enhanced liver MRI. More CRLM lesions demonstrated this sign with gadofosveset (25% increase) compared to gadobutrol, resulting in a statistically increase in sensitivity from 65% to 90%. There is currently limited literature on the use of gadofosveset-enhanced MRI for liver imaging. Other than a small pilot study, no studies have been published to date on the use of intravascular agents in MR liver imaging (7).

CONCLUSION
There were 25% more CRLM lesions that demonstrated hypoenhancement on both portovenous and delayed phase gadofosveset- compared to gadobutrol-enhanced MRI, resulting in improved sensitivity (65% to 90%, p<0.0001). Gadofosveset-enhanced MRI may be helpful in diagnosing CRLM in this setting.

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