

## Invited Editorials

assessment would have significant resource and financial implications, given the relative limited capacity of these modalities compared to ultrasound in most societies. Neither modality is without risk. CT involves significant radiation doses and both CT and MRI require the administration of intravenous contrast for optimum examination which can be associated with significant side effects.<sup>7</sup>

Despite its limitations, ultrasound will remain the primary imaging modality for HCC for the foreseeable future. It is therefore crucial to maximise the performance of ultrasound as a screening tool by ensuring it is performed and reported by adequately trained operators; they need to be experienced in hepatobiliary imaging in order to obtain high-quality diagnostic examinations and to minimise the referral rate for CT/MRI imaging surveillance, and the ensuing financial and resource implications associated with this.

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## Editorial: ultrasound surveillance of hepatocellular carcinoma in the 21st century – authors' reply

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The letter from Dr Patel<sup>1</sup> raises some interesting points that are worthy of further discussion.

Surveillance ultrasound has the potential for high sensitivity and specificity as demonstrated in prospective cohort studies,<sup>2</sup> although recent data have demonstrated a substantial gap between its efficacy and its effectiveness when implemented in clinical practice, including low sensitivity for early tumour detection<sup>3</sup> and suboptimal specificity leading to screening-related harms.<sup>4</sup> Our

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study adds to this literature suggesting subgroups of patients, including obese individuals, patients with non-alcoholic steatohepatitis (NASH), and those with Child Pugh B or C cirrhosis, may be particularly prone to suboptimal ultrasound quality and the potential for surveillance failure in detecting early stage hepatocellular carcinoma.<sup>5</sup>

Dr Patel highlights that ultrasounds in our study were interpreted retrospectively based on stored hard copy images, resulting in an overestimation of the proportion of inadequate exams. Although we agree real-time performance of the exam by the interpreting radiologist may improve exam quality, this is unfortunately not standard practice in many parts of the world, including the USA. Instead, technologists typically perform ultrasounds using a set protocol, recording representative still images to document exam completeness, which are subsequently interpreted by radiologists at a later time. It is possible operator experience, specific technologist training, and real-time exam interpretation could overcome some of ultrasound's operator dependency and improve its performance for early HCC detection; however, these interventions are unlikely to overcome all of ultrasound's potential limitations, and some exams will still likely be compromised by poor

visualisation in obese patients and those with nodular, heterogeneous hepatic parenchyma.<sup>5</sup>

Although alternative surveillance strategies may be needed long term as HCC epidemiology shifts from hepatitis C to NASH-related cirrhosis, we agree with Dr Patel that using multi-phasic CT and MRI in all patients with cirrhosis is likely not feasible given issues of cost, potential harms, and radiologic capacity. Furthermore, the performance of CT and MRI for surveillance in patients prone to ultrasound failure, such as those with obesity, is unknown. Discovery of highly sensitive and specific serum biomarkers is an important effort in improving HCC surveillance performance, as some biomarker panels have shown potentially high sensitivity for early HCC detection.<sup>6</sup> However, we are still likely years away from sufficient validation for their routine use in clinical practice. In the interim, ultrasound, with or without alpha fetoprotein, continues to be our primary HCC surveillance modality and efforts to maximise ultrasound effectiveness are critical.

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## Editorial: volatile organic compounds in irritable bowel syndrome – technology for an accurate and reliable point-of-care test?

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Symptom-based diagnostic criteria are the current preferred method for diagnosing irritable bowel syndrome (IBS). However, these have been shown to perform only modestly in several studies.<sup>1–3</sup> As a result, interest in the use of biomarkers to facilitate an accurate diagnosis of IBS has increased although, in a recent meta-analysis, they performed no better than symptom-based diagnostic criteria, or were not available outside of a research setting.<sup>4</sup>

Aggio *et al.*<sup>5</sup> have conducted a study that uses a prototype device based on gas chromatography to separate volatile organic compounds (products from digestion and fermentation by the intestinal microbiota), from faecal gas, in order to identify patterns that could be used

to differentiate between IBS, inflammatory bowel disease and health. Patients were recruited prospectively between October 2010 and October 2011, and faecal samples were obtained from 28 patients with IBS, as defined by the Rome II criteria [26 patients with diarrhoea-predominant IBS (IBS-D)], 33 patients with active inflammatory bowel disease, 50 patients with inactive inflammatory bowel disease and 41 healthy controls. A simple clinical activity index score  $\geq 3$  or a Harvey Bradshaw index  $\geq 4$  were used to define active ulcerative colitis and active Crohn's disease respectively.

Faecal samples were stored at  $-20\text{ }^{\circ}\text{C}$ , and samples were analysed by gas chromatography, which works by characterising the volatile organic compounds contained in the faecal samples. Patterns in the volatile compounds were then detected for each of the individual medical disorders. This prototype device had a runtime of only 40 min, therefore potentially providing a means for a point-of-care test. The device was able to distinguish between IBS and active inflammatory bowel disease with a maximum sensitivity and specificity of 93% and 90%, respectively; between IBS and inactive inflammatory bowel disease with a maximum sensitivity and specificity of 89% and 80%, respectively; between IBS and all inflammatory bowel disease patients with a maximum