

Solutions in **CONTRAST IMAGING**



The Role of CEUS as the Initial Imaging Technique in the Characterization of Incidental Hepatic Lesions

Paul S. Sidhu

Department of Radiology, King's College Hospital, London, United Kingdom

INTRODUCTION

The first line investigation for the majority of patients with symptoms attributable to the upper abdomen is an ultrasound examination. An ultrasound examination is readily accessible, safe, non-invasive and informative for the referring clinician.¹ The expectations of the results of the examination are often negative, in that the ultrasound examination is a test of exclusion in many cases. Vague abdominal pain, the most common reason for referral, may on occasion demonstrate gallstones; abnormal liver function tests may reveal a fatty liver.

Not infrequently an unexpected finding of a focal liver lesion is encountered. This poses a dilemma for the examining sonographer; typical characteristics on the B-mode examination may indicate a benign abnormality but there will always be uncertainty and follow-up ultrasound or further imaging is advocated.

A classic haemangioma may be a straight-forward diagnosis on B-mode ultrasound but often atypical lesions are encountered, requiring further imaging which in many cases is Computed Tomography (CT) or Magnetic Resonance (MR) imaging.²⁻⁴ These investigations are expensive, not readily available but more importantly raise levels of anxiety in the patients as they wait for confirmation of the nature of the incidental lesion demonstrated on the ultrasound examination.⁵ This is particularly pertinent with regards to patient anxiety as the majority of lesions found incidentally on an ultrasound examination will be benign.⁶

Ultrasound has always suffered for the lack of a suitable contrast agent, with sensitivity and specificity of evaluation of focal liver lesions documented as inferior to that of a CT or MR imaging. Unenhanced ultrasound has always been compared with enhanced CT in the evaluation of these lesions, disadvantageous to ultrasound.

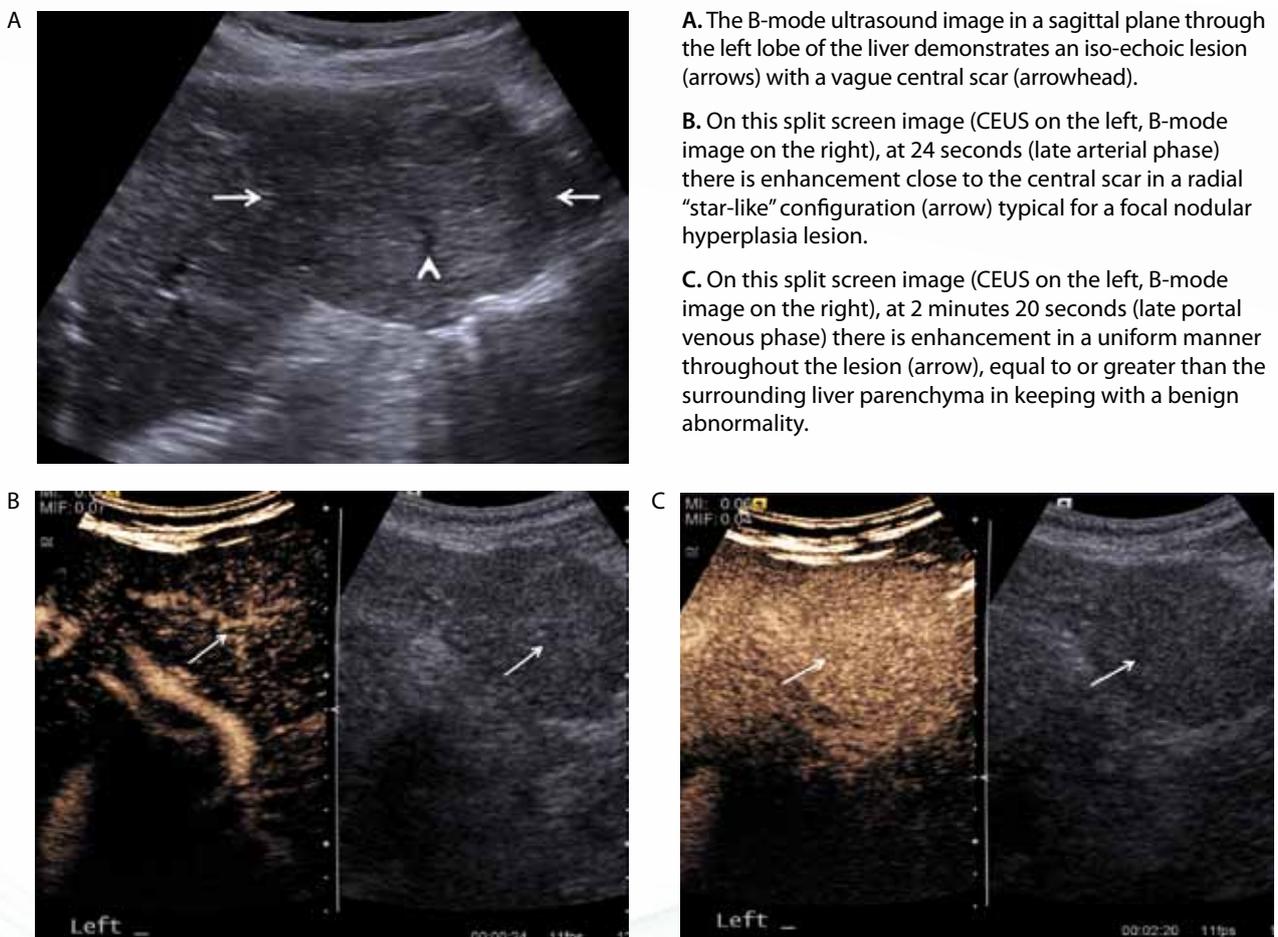
With the advent of ultrasound contrast agents and the development of techniques that allow optimal imaging of the microbubbles, contrast-enhanced ultrasound (CEUS) can now be comparative to contrast-enhanced CT imaging.⁷⁻⁹ This is also achieved without the adverse effects of radiation, and with contrast agents that are inherently safe.¹⁰

The recent well documented difficulties associated with MR contrast agents limit their use in patients with renal impairment,¹¹ precluding contrast-enhanced MR imaging for the characterisation of focal liver lesions. Therefore it would seem at this period, CEUS should be ideally placed to characterise any incidentally discovered focal liver lesion with accuracy and to allow correct imaging and clinical pathways to be instituted for the appropriate management.¹² To this effect two cases will be illustrated and the implications of the use of CEUS in both the cases will be highlighted with respect to the influence on the medical management of the patients.

CASE 1

A 51 year old lady presented with a one month history of vague abdominal pain after return from a holiday. There was no significant clinical history except for a long period on the oral contraceptive pill, stopped five years previously. The general practitioner (GP) performed liver function tests with the liver enzymes slightly elevated. The GP suspected gallstones and referred the patient for further evaluation with an ultrasound examination. The ultrasound examination failed to demonstrate any gallbladder abnormality but did demonstrate a focal abnormality of the left lobe of the liver measuring 58 x 50 mm, of uniform reflectivity and almost iso-echoic to the surrounding normal liver. A possible central scar was observed within the lesion, and the colour Doppler ultrasound examination was unhelpful (Fig. 1A). A CEUS examination was then performed, as the differential diagnosis was essentially between a focal nodular hyperplasia and a hepatic adenoma, with a focal malignant lesion less likely. Using SonoVue® (Bracco Imaging Spa, Milan, Italy) 2.4 mLs as the contrast agent and imaging with CPS™ mode (Siemens, Mountain View, CA, USA) the examination demonstrated an early central “star” pattern (Fig. 1B) with persistent enhancement of the lesion into the late portal venous phase consistent with the appearances seen with a focal nodular hyperplasia, a benign lesion (Fig. 1C). A hepatic adenoma normally demonstrates a rapid uniform appearance with CEUS and also retains contrast in the late portal venous phase.¹³ The appearances clearly indicated to the observer that this was not a malignant abnormality, the correct medical management pathway was instituted, and the patient reassured immediately as the benign nature of the incidentally discovered abnormality.

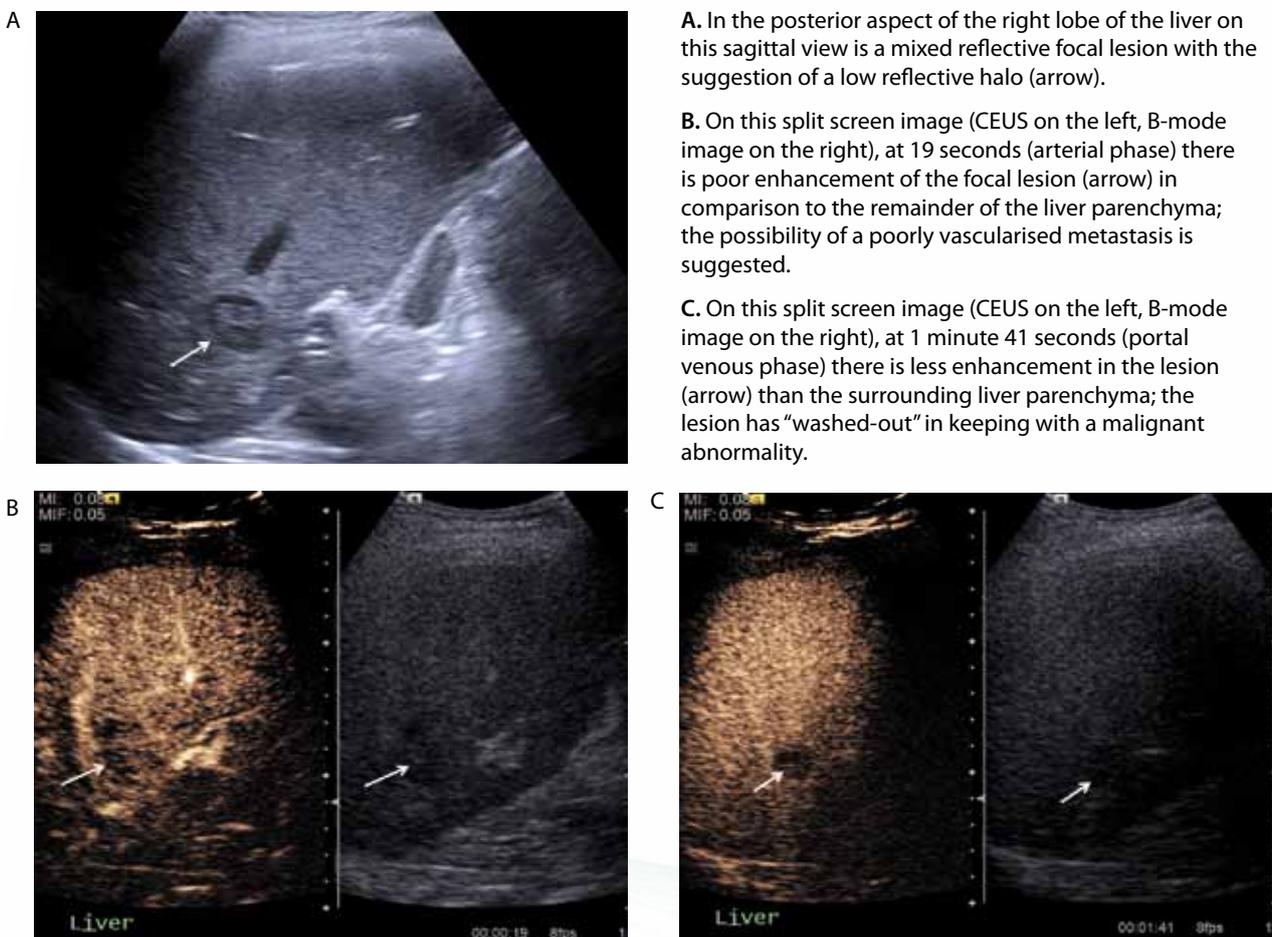
Figure 1



CASE 2

A 65 year old recently retired man sought advice from his general practitioner as to the cause for his recent weight loss associated with nausea and loss of appetite. The patient had previously been fit and well, with no smoking history or occupational history of note. Based on the results of liver function tests, with mild elevation of the liver enzymes, an ultrasound examination of the upper abdomen was requested. The ultrasound examination demonstrated a focal low reflective lesion in the central aspect of the right lobe of the liver measuring 20 x 16 mm, without evidence of vascularity on the colour Doppler ultrasound (Fig. 2A). The nature of the focal lesion was suspicious of malignancy on the B-mode ultrasound although the possibility an atypical haemangioma in a fatty liver was raised. A CEUS examination was performed using SonoVue® (Bracco Imaging Spa, Milan, Italy) 2.4 mLs as the contrast agent and imaging with CPS™ mode (Siemens, Mountain View, CA, USA). The early arterial phase demonstrated poor enhancement (Fig. 2B) with clear evidence of lesion washout on the late portal venous phase (Fig. 2C), an appearance characteristic of a malignant abnormality, most likely a metastasis. A haemangioma demonstrates poor central enhancement initially, but with gradual globular or nodular peripheral enhancement with in-filling of the lesion into the late portal venous phase. The GP was informed of the findings, arrangements were made for an immediate medical review, and a left sided pleural effusion was found on the chest X-ray. An underlying mesothelioma was diagnosed on subsequent CT imaging and the appropriate medical management instituted. The patient was able to appreciate the severity of the condition immediately, allowing rapid management of the situation.

Figure 2



DISCUSSION

The two cases above, with different incidental focal liver lesions, illustrate the utility of CEUS in immediately defining the nature of the abnormality and instigating the appropriate medical management.

The time taken to add the CEUS examination to the B-mode ultrasound examination is minimal, and in effect constitutes the placing of a venous cannula, drawing up and administering the contrast solution and performing a further 5 minute ultrasound examination; probably under 10 minutes in total.¹⁴

The additional cost is that of the contrast agent; again minimal in the context of the imaging and medical pathways that need to be negotiated in order to establish the nature of the focal lesion seen on the B-mode examination.^{5,15} The hidden cost is that of the anxiety and uncertainty of the patient who waits for the correct diagnosis to be established; this is immeasurable.

The majority of the incidentally discovered focal liver lesions will be benign in nature. This is illustrated in a recent study analysing the investigation of 174 lesions with CEUS; 168 (96.5%) were benign with accurate blinded reader assessment allowing the authors to suggest that any follow-up imaging was not necessary in this cohort of non-cancer patients.¹²

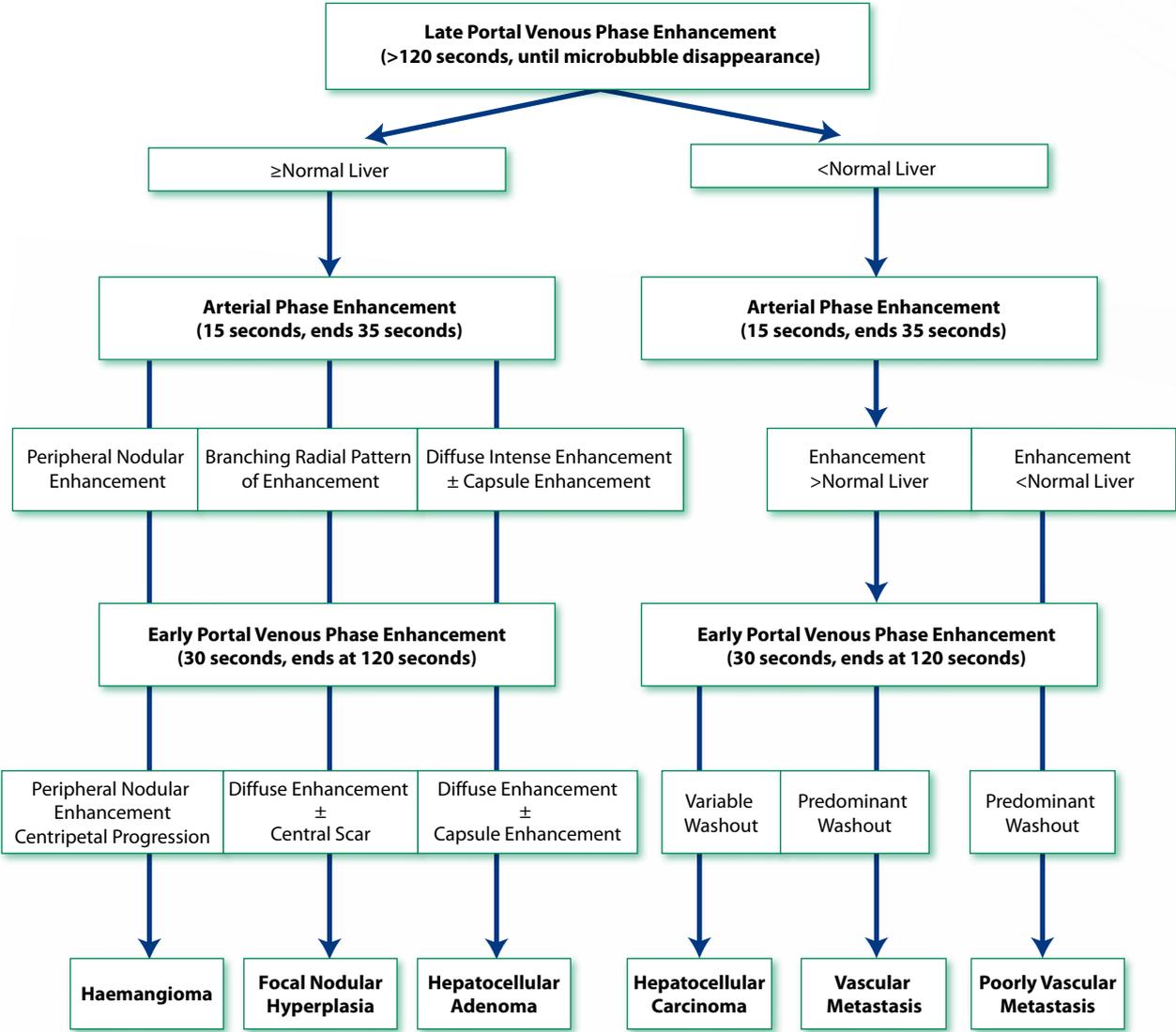
A further study analysing the findings of using CEUS in a cohort of 127 patients with an incidental lesion (which included patients with an underlying known cancer), identified all benign lesions as benign, and identified one malignant lesion as benign.¹⁶

The overall accuracy of CEUS in characterizing the nature of a focal liver lesion is not in doubt with numerous studies testifying to the robustness of the technique in comparison to CT and MR imaging.¹⁷ Often large studies are performed in hospital settings with the lesions already identified and entered into clinical trials to test the utility of CEUS. However in the context of using CEUS in daily routine ultrasound practice this has yet to be fully realised by the imaging community. When there is a focal lesion identified on the B-mode examination, the tendency is to normally follow-up with a B-mode ultrasound if the operator is confident that this is a haemangioma, the only benign focal liver lesion with unmistakable characteristic ultrasound features. If there is any doubt as to the nature of the focal abnormality, a referral pathway is instituted; commonly physician review as an out-patient. This is followed by further imaging, usually a CT examination, and then review in the out-patients again. If the CT is equivocal, as is not infrequent, an MR examination may be considered. Multiple imaging, out-patient visits and the progression of time will intensify patient anxiety. Financial consequences will inevitably occur, often forgotten is the personal financial implications for the patient, particularly if self-employed.

There is much to justify the routine use of CEUS in evaluation of the incidental focal liver lesion and it should become routine in all ultrasound departments. The nature of the incidental lesion is such that in nearly all cases it will be benign. There should be no difficulty in ascertain the characteristics of the lesion on CEUS as the patterns of enhancement are well established (Table 1).

A clear diagnosis will allow appropriate management, return to the GP or forward referral into the hospital system. The cost savings are potentially high, the patient reassurance immeasurable.

Table 1. Flow chart for the assessment of focal liver lesions with CEUS.



REFERENCES

1. Derchi L, Claudon M. Ultrasound: a strategic issue for radiology? *Eur Radiol* 2009;19:1-6
2. Wilson SR, Burns PN. An algorithm for the diagnosis of focal liver masses using microbubble contrast enhanced pulse inversion sonography. *AJR Am J Roentgenol* 2006;186:1401-12
3. Quaia E, Bartolotta TV, Midiri M, et al. Analysis of different contrast enhancement patterns after microbubble-based contrast agent injection in liver haemangiomas with atypical appearance on baseline scan. *Abdom Imaging* 2006;31:59-64
4. Xu HX, Xie XY, Lu MD, et al. Unusual Benign Focal Liver Lesions: Findings on Real-time Contrast-Enhanced Sonography. *J Ultrasound Med* 2008;27:243-54
5. Giesel FL, Delorme S, Kayczor HU, Krix M. Contrast-enhanced ultrasound for the characterization of incidental liver lesions - an economical evaluation in comparison with multi-phase computed tomography. *Ultraschall Med* 2009;30:259-68
6. Karhunen PJ. Benign hepatic tumours and tumour like conditions in men. *J Clin Pathol* 1986;39:183-8
7. Burns PN, Wilson SR. Focal liver masses: enhancement patterns on contrast-enhanced images - concordance of US scans with CT scans and MR images. *Radiology* 2007;242:162-74
8. Quaia E. The real capabilities of contrast-enhanced ultrasound in the characterization of solid focal liver lesions. *Eur Radiol* 2011;21:457-62
9. Quaia E, Calliada F, Bertolotto M, et al. Characterization of Focal Liver Lesions with Contrast-specific US Modes and a Sulfur Hexafluoride-filled Microbubble Contrast Agent: Diagnostic Performance and Confidence. *Radiology* 2004;232:420-30
10. Piscaglia F, Bolondi L. The safety of SonoVue in abdominal applications: retrospective analysis of 23188 investigations. *Ultrasound in Med Biol* 2006;32:1369-75
11. Ledneva E, Karie S, Launay-Vacher V, et al. Renal safety of gadolinium-based contrast media in patients with chronic renal insufficiency. *Radiology* 2009;250:618-28
12. Bartolotta TV, Taibbi A, Midiri M, et al. Indeterminate focal liver lesions incidentally discovered at gray-scale US: role of contrast-enhanced sonography. *Invest Radiol* 2011;46:106-15
13. Claudon M, Cosgrove D, Albrecht T, et al. Guidelines and Good Clinical Practice Recommendations for Contrast Enhanced Ultrasound (CEUS) - Update 2008. *Ultraschall Med* 2008;29:28-44
14. Sidhu PS. Microbubbles are here to be burst! *Radiology Now* 2003;20:2-3
15. Faccioli N, D'Onofrio M, Comai A, Cugini C. Contrast-enhanced ultrasonography in the characterization of benign focal liver lesions: activity-based cost analysis. *Radiol Med* 2007;112:810-20
16. Beaton C, Cochlin DL, Kumar N. Contrast enhanced ultrasound should be the initial radiological investigation to characterise focal liver lesions. *Eur J Surg Oncol* 2010;36:43-6
17. Strobel D, Seitz K, Blank A, et al. Contrast-enhanced ultrasound for the characterization of focal liver lesions - diagnostic accuracy in clinical practice (DEGUM multicenter trial). *Ultraschall Med* 2008;225:499-505



© 2011 Sintesi InfoMedica Srl - Via Ripamonti, 89 - 20141 Milano
Tel. +39 02 56665.1 - Fax +39 02 97374301 - e-mail: info@sintesiinfomedica.it - www.sintesiinfomedica.it

Executive Editor: Daniele Rizzi - Marketing: Marika Calò
Reg. Milan Court n. 128 - March 3, 2003

Product liability: The publisher cannot guarantee the accuracy of any information about dosage and application contained in this publication. In every individual case the user must check such information by consulting the relevant literature. This publication is funded by an educational grant from Bracco. Bracco, however, exercises no editorial comment, review, or any other type of control over the contents of this publication. For any product or type of product, whether a drug or device, referenced in this publication, physicians should carefully review the product's package insert, instructions for use, or user's manual prior to patient administration to ensure proper utilisation of the product.

All rights reserved. No part of this publication may be translated into other languages, reproduced, stored in a retrieval system, or transmitted, in any form or by any means, electronic, mechanical, photocopying, recording or otherwise, without the prior permission in writing of Sintesi InfoMedica Srl.

Printed by Arti Grafiche Turati - Via Laboratori Autobianchi, 1 - 20033 Desio (MB), Italy - November 2011