

# Contrast ultrasound scan versus contrast enhanced computed tomography in detection of liver metastases: preliminary results

J Kew, RP Davies, D Gluis and T Andrews

## Introduction

Pulse inversion harmonic imaging (PIHI) in combination with contrast-enhanced ultrasound (CUS) has improved detection of lesions particularly in the liver.<sup>1-4</sup> Levovist (Schering AG, Berlin) is an ultrasound contrast agent consisting of microbubbles of air covered by a thin layer of palmitic acid in a galactose solution.<sup>1</sup>

## Purpose of the study

A prospective study was performed to confirm the reported clinical efficacy of CUS versus contrast enhanced computed tomography (CECT) scan in detecting focal lesions including carcinoma secondaries of the liver. Preliminary results are reported here. To the best of our knowledge, there are few, if any, reports in the literature comparing multi-slice CT and CUS.

## Methods and materials

Ethics approval was obtained for the study. Forty-one adult patients undergoing clinically indicated CECT scan for known or suspected liver metastases were recruited. Patient exclusion criteria included galactosemia (Levovist contains galactose) and severe cardiac failure (NYHA stage IV). Five patients were excluded from the study due to poor visualisation caused by severe dyspnoea.

## CT scanning

Ten patients were scanned in a Siemens Somatom Plus 4 spiral scanner (Siemens AG, Forchheim, Germany). Routine dual phase arterial and venous CECT scans were performed through the liver. Intravenous contrast (Ultravist 370, Schering AG, Berlin) at a dose of 1 ml/kg to a maximum dose of 125 ml at an injection rate of 2.5 ml/sec was administered. Scanning parameters used were 300 mA at 0.5 sec and 120 kV with 8 mm collimation scans at a pitch of 1.5

reconstructed in contiguous slices. A scanning delay time of 35 seconds for the arterial phase and 70 seconds for the venous phase was used. The remainder of the patients were scanned using 4 slice scanner (Toshiba Aquilion, Japan) with the following parameters – 350 mA at 0.5 sec/rotation, 135 kV, 3 mm collimation, 5.5:1 pitch reconstructed at 2 mm intervals. 80 ml of intravenous iodinated contrast (Ultravist 370, Schering AG, Berlin) was injected. Images were acquired commencing at 30 seconds post injection for arterial and 70 seconds for venous phase imaging.

## Ultrasound

Pre- and post-contrast (Levovist, Schering AG, Berlin) scans of the entire liver were obtained in the transverse and sagittal planes using a curved array transducer (3.5–7 MHz) (ATL, Bothwell, Washington, USA). Images were recorded on video for later analysis.

Two separate boluses of Levovist (30 ml 300 mg/ml at 2 ml per second intravenous injection) were administered using a Medrad injector (Imaxeon, per Schering AG, Berlin) followed by a 10 ml saline flush.<sup>5,6</sup> Scanning was performed 2 minutes after each dose. Ultrasound settings used included contrast specific imaging (CSI) mode 1, low/ medium frame rate, low line density, compression and map at 150 dB/C4, with the focal zone set at 1/3 and 2/3 from the top of the sector and power mechanical index (MI) = 1.

The patient was asked to suspend respiration. The probe was placed in a 'Freeze' mode prior to scanning to avoid premature rupture of the contrast microbubbles. The liver volume was interrogated in a single sweep in orthogonal planes. Commencing on the left and sweeping to the right improved image acquisition in the sagittal plane. Probe placement in 'Freeze' mode in the xiphisternum allowed more reliable anatomical orientation close to the left margin of the liver immediately scanning commenced. The sweep to the right could then be judged on the real-time appearances. In the transverse plane, separate sweeps of left and right lobes were required as the field of view was insufficient to encompass both lobes simultaneously.

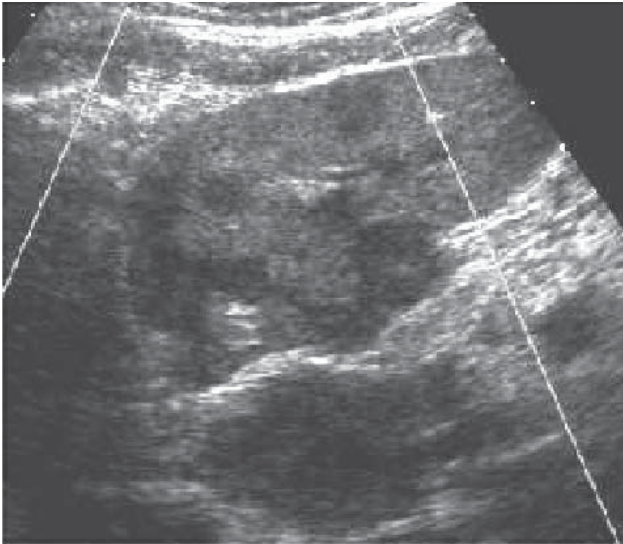
This sequence of three sweeps was first performed using the focal zone in the superficial third of the liver. A second sequence of three sweeps was then performed with the focal zone set to the deep third of the liver. The superficial contrast microbubbles were largely exhausted during the second sweep using the deeper focal zone.

A second series of acquisitions was performed after the

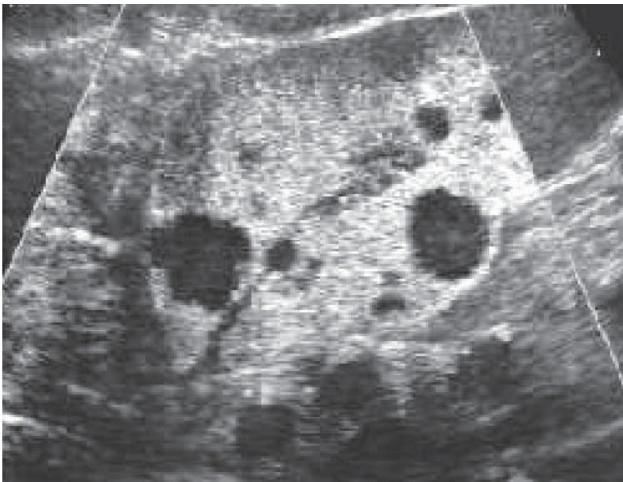
J Kew – Radiologist  
RP Davies – Radiologist  
D Gluis – Sonographer  
T Andrews – Sonographer

North Western Adelaide Health Service  
28 Woodville Road  
Woodville  
Adelaide  
South Australia 5011

**Figure 1** Para-sagittal section of the left lobe of the liver before administration of ultrasound contrast agent (Levovist). Multiple low echogenicity areas are seen in the liver parenchyma. The largest lesion in segment 2 close to the diaphragm on the left of the image is not well defined



**Figure 2** Para-sagittal section of the left lobe of the liver following administration of intravenous contrast agent. The lesion in segment 2 adjacent to the diaphragm is now clearly defined and hypoechoic compared to the brightly enhancing normal liver parenchyma



second injection of contrast. The deeper focal zone was selected first for this series. There was a tendency for the superficial regions of the liver to show less enhancement if the focal zone was first set to scan the deeper regions.

Video recording of this image acquisition sequence was essential to adequately review the findings. CECT and CUS scans were assessed separately and interpreted in a blinded fashion by two radiologists (JK, RPD).

## Results

Thirty-six patients are included in this analysis. There were 19 males and 17 females with an age range 29–88 years. By CUS, there were no lesions in 19 cases (53%), and lesions in 17. Fewer than 5 lesions were found in 7 patients (19%) and greater than 5 lesions in 10 patients (28%). Contrast enhanced ultrasound detected more lesions than CECT in one case (5.3%), equal number of lesions in 12 patients (63.2%) and fewer lesions in 4 (21.5%). In 2 cases, CUS

missed a single lesion seen on CECT (10%). In no case did CUS identify a lesion where none was found on CECT. There were 3 cases of poor visualisation of sub-diaphragmatic and deep areas. Lesion conspicuity increased with contrast in all CUS cases.

## Discussion

From the literature, detection by contrast enhanced ultrasound (CUS) of more lesions than CECT varies between 12 to 22%, equal number of lesions (74% to 67%) and fewer lesions in 14% to 11%.<sup>2,7</sup> Comparing pre-contrast ultrasound to CUS, our data concurs with the reported increased lesion conspicuity after contrast.<sup>8,9</sup> Dalla Palma et al found that accuracy was lower in both deep liver areas and in anterior superficial regions.<sup>2</sup> Demonstration of superficial regions in this study appeared adequate. This may reflect the technique used whereby the superficial regions were first interrogated using the shallower focal zone setting. This reinforces the requirement for familiarity with the technique and the importance of a comprehensive scanning protocol. Manipulation of the focal zone as described may improve conspicuity of both deep and superficial lesions.

Whilst CUS in this series was slightly less sensitive in detecting single lesions than CECT compared to other reports in the literature, the difference was modest in this small series. Detection by the dual phase multi-slice CT technique may also be improved, compared with literature reports based on older single slice technology.

In a limited health care economy it is important to know the cost of diagnostic radiological procedures in order to best-use available resources. A second part of the study to be reported will evaluate the cost effectiveness of CUS as an alternative to CECT. Potential benefits of CUS include high patient tolerance, ability to perform 'bedside' scans outside the imaging department, the reduced radiation exposure to the patient and availability for use in patients with known contrast sensitivity or contra-indications including renal impairment. In areas where CT availability is restricted compared with US, CUS may have a more prominent role. Further study of these aspects is required.

## Acknowledgements

Schering AG, Australia for Levovist, Imaxeon–Medrad for use of the injector, ATL, Acuson (Siemens) for technical support and NWAHS US and CT radiographers for technical skills.

## References

- 1 Blomley MJ, Albrecht T, Cosgrove DO, Eckersley RJ, Butler-Barnes J, Jayaram V, Patel N, Heckemann RA, Bauer A, Schlieff R. Stimulated acoustic emission to image a late liver and spleen-specific phase of Levovist in normal volunteers and patients with and without liver disease. *Ultrasound Med Biol.* 1999 Nov; 25 (9): 1341–1352.
- 2 Dalla Palma L, Bertolotto M, Quaia E, Locatelli M. Detection of liver metastases with pulse inversion harmonic imaging: preliminary results. *Eur Radiol.* 1999; 9 Suppl 3: S382–387.
- 3 Calliada F, Campani R, Boticelli O, Bozzini A, Sommaruga MG. Ultrasound contrast agents. Basic principles. *Eur J Radiol.* 1998; 27: S171–S178.
- 4 Harvey CJ, Blomley MJ, Eckersley RJ, Heckemann RA, Butler-Barnes J, Cosgrove DO. Pulse-inversion mode imaging of liver specific microbubbles: improved detection of subcentimetre metastases. *Lancet.* 2000 Mar 4; 355 (9206): 807–808.
- 5 Campani R, Calliada F, Bottinelli O, Bozzini A, Sommaruga MG, Draghi F, Anguissola R. Contrast enhancing agents in ultrasonography: clinical applications. *Eur J Radiol.* 1998 May; 27 Suppl 2: S161–170.
- 6 Uggowitzner M, Kugler C, Groll R, Mischinger HJ, Stacher R,

Fickert P, Weiglein A. Sonographic evaluation of focal nodular hyperplasias (FNH) of the liver with a transpulmonary galactose-based contrast agent (Levovist). *Br J Radiol.* 1998 Oct; 71 (850): 1026–1032.

7 Quaia E, Bertolotto M, Forgacs B, Rimondini A, Locatelli M, Mucelli RP. Detection of liver metastases by pulse inversion harmonic imaging during Levovist late phase: comparison with conventional ultrasound and helical CT in 160 patients. *Eur Radiol.* 2003; 13 (3): 475–483.

8 Yucel C, Ozdemir H, Gurel S, Ozer S, Arac M. Detection and differential diagnosis of hepatic masses using pulse inversion harmonic imaging during the liver-specific late phase of contrast enhancement with Levovist. *J Clin Ultrasound.* 2002; 30 (4): 203–212.

9 Albrecht T, Blomley MJ, Burns PN, Wilson S, Harvey CJ, Leen E, Claudon M, Calliada F, Correas JM, LaFortune M, Campani R, Hoffmann CW, Cosgrove DO, LeFevre F. Improved detection of hepatic metastases with pulse-inversion US during the Liver-specific phase of SHU 508A: Multicenter Study. *Radiology.* 2003; 227 (2): 361–370.