11 Characterization of Focal Liver Lesions

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11.1 Introduction

Focal liver lesions may be identified incidentally, e.g., during an abdominal ultrasound (US) scan performed for clinical reasons unrelated to the liver lesion or during staging or follow-up procedures for a primary neoplasm or liver cirrhosis. Focal liver lesions may be characterized by baseline gray-scale US and color Doppler US when a typical pattern is identified, as in the case of homogeneously hypoechoic hemangiomas (Vilgrain et al. 2000) or focal nodular hyperplasia with a spoke-wheel shaped central vascular pattern on color Doppler US (Wang et al. 1997). Even though color Doppler US may improve diagnostic confidence in the characterization of focal liver lesions (Taylor et al. 1987; Hosten et al. 1999a; Tanaka et al. 1990; Nino-Murcia et al. 1992; Numata et al. 1993; Reinhold et al. 1995; Lee et al. 1996; Gonzalez-Anon et al. 1999), it does have important limitations since benign and malignant lesions may show a similar appearance on both gray-scale and color Doppler US.

It has been shown that the visibility of peripheral and intratumoral vessels may be improved on color and power Doppler US after the injection of microbubble-based contrast agents (Hosten et al. 1999b; Kim et al. 1999; Lee et al. 2002; Leen et al. 2002). Nevertheless, color signal saturation, motion and blooming artifacts, insensitivity to the flow of capillary vessels and limited sensitivity to the signal produced by microbubble-based agents represent important limitations of color Doppler US.

Microbubble-based contrast agents (Gramiak and Shah 1968) and dedicated US contrast-specific modes were introduced to overcome the limitations of baseline gray-scale and color Doppler US. Air-, perfluorocarbon- or sulfur hexafluoride-filled microbubbles may be employed to characterize focal liver lesions, though the technique of scanning differs according to the employed agent.

Leovist (SH U 508A, Schering, Berlin, Germany) is an air-filled microbubble contrast agent covered by
a shell of galactose and palmitic acid. Since Levovist presents a low acoustic nonlinear response and low production of harmonic frequencies when insonated at a low acoustic transmit power, insonation with high acoustic power is necessary to produce microbubble destruction with emission of a wideband frequency signal detectable by dedicated contrast-specific techniques. Destructive imaging requires intermittent scanning and a limited number of sweeps to minimize bubble rupture and, consequently, does not allow prolonged evaluation of liver contrast enhancement. In comparison with baseline US, the injection of Levovist has been shown to allow the identification of tumoral vessels, to differentiate benign and malignant focal liver lesions according to the enhancement pattern (Bertolotto et al. 2000; Burns et al. 2000; Blomley et al. 2001; Numata et al. 2001; Dill-Macky et al. 2002; von Herbay et al. 2002; Kim EA et al. 2003; Migaleddu et al. 2002; Wen et al. 2004), and to improve the characterization of focal liver lesions in terms of both overall accuracy and diagnostic confidence (Tanaka et al. 2001; Isozaki et al. 2003; von Herbay et al. 2002; Bryant et al. 2004). The late liver-specific phase of Levovist (Blomley et al. 1998, 1999; Quaia et al. 2002b), beginning from 3 to 5 min after injection, has been demonstrated to be the most important dynamic phase for the characterization of focal liver lesions (Blomley et al. 2001; Bryant et al. 2004). During the late phase, benign liver lesions present similar microbubble uptake to the adjacent liver, while malignant liver lesions present lower microbubble uptake (Bertolotto et al. 2000; Burns et al. 2000; Blomley et al. 2001; Bryant et al. 2004).

New generation perfluorocarbon- or sulfur hexafluoride-filled microbubbles covered by a phospholipid shell, such as SonoVue (BR1, Bracco, Milan, Italy), Definity (MRX 115, Bristol-Myers Squibb, North Billerica, MA, NY, USA), and Sonazoid (NC100100, Nycomed Amersham, Oslo, Norway), present a nonlinear response with production of harmonic and subharmonic frequencies (Schneider et al. 1995; Morel et al. 2000; Correas et al. 2000, 2001; Cosgrove et al. 2002) at low acoustic power insonation, allowing the employment of nondestructive imaging and the real-time evaluation of contrast enhancement in focal liver lesions (Albrecht et al. 2003; Brannigan et al. 2004; Nicolau et al. 2003a; Hohmann et al. 2003; Quaia et al. 2004). Preliminary experimental and clinical investigations proved the safety and efficacy of SonoVue in vascular and parenchymal diagnostic applications (Quaia et al. 2003, 2004).

Besides commercial microbubble-based contrast agents, direct intra-arterial CO₂ injection into the proper hepatic artery after selective hepatic arteriography and superior mesenteric arteriography has been proposed for the assessment of vascularity in hepatic tumors and particularly in hepatocellular carcinoma (Chen et al. 2002; Kudo et al. 1992).

11.2 Scanning Technique for Focal Hepatic Lesions

11.2.1 Preliminary Baseline Scan

Before microbubble injection, sonologists must perform a complete and accurate assessment of the liver parenchyma and of each identified focal liver lesion. The baseline scan includes the assessment of lesion appearance on gray-scale and color Doppler US, with the employment of tissue harmonic imaging and compound imaging (Claudon et al. 2002) and of state-of-the-art US equipment provided by wideband frequency transducers. Although tissue harmonic imaging was originally developed for microbubble-based contrast agents (Burns et al. 1996; Ward et al. 1997), it also allows a clear enhancement of the image quality in native tissues. This is achieved by improvement of contrast resolution, particularly in patients who are difficult to image with conventional techniques, by reduction of the artifacts that degrade conventional sonograms, and by improvement in the differentiation between solid and liquid components. Compound imaging may combine multiple coronal images obtained from different spatial orientations, i.e., spatial compound imaging (Jespersen et al. 1998), or may involve the acquisition of images of the same object at different frequencies, combining them into a single image, i.e., frequency compound imaging (Gatenby et al. 1989). The result is the generation of a single image with better delineated margins and curved surfaces, fewer image artifacts, speckles (echoes from subresonation scatterers), and noise, and improved image contrast.

Baseline color Doppler US is performed by using slow-flow settings (pulse repetition frequency 800–1,500 Hz, wall filter of 50 Hz, high levels of color versus echo priority, and color persistence). Color gain is varied dynamically during the examination to enhance color signals and avoid excessive noise, with the size of the color box being adjusted...