How to Perform CEUS

CEUS uses microbubble contrast agents. Microbubbles are gasfilled microspheres that are strictly intravascular because their size of several micrometers does not permit them to pass through the vascular endothelium into the interstitial space. There is no renal excretion of microbubbles as the gas within the microbubbles diffuses through the thin shell and the agents have a half-life of only a few minutes in blood. Microbubbles are not shown to have nephrotoxicity; their gas is eliminated with respiration even in patients with chronic obstructive pulmonary disease and the microbubble shell, which is often composed of phospholipids, is metabolized rapidly within the lipid pool of the human body. Therefore microbubbles can be safely used in patients with renal failure for whom the use of CT/MRI contrast agents is contraindicated. Among the CEUS contrast agents currently available for liver imaging, Definity/Luminity (perflutren lipid microspheres, Lantheus Medical Imaging, Billerica, MA, USA) and Sonovue/Lumason (sulfur hexafluoride microbubbles, Bracco Imaging, Milan, Italy) are the most commonly used in western nations. Sonazoid (perfluorobutane, Daiichi-Sankyo, GE Tokyo, Japan), which is actively used in Japan, South Korea, and Norway, enables additional liver evaluation in the Kupffer phase, as Sonazoid microbubbles are internalized by Kupffer cells.

Before CEUS, a thorough conventional ultrasound examination of the entire liver must be performed. The baseline study includes the assessment of the lesions on B-mode imaging and by means of color Doppler ultrasound. In CEUS, 2.4 mL (a much lower dose than with CT and MRI) of microbubble contrast agent is rapidly injected via an antecubital vein followed by a 5-mL saline flush. A sufficiently large needle (20-gauge minimum diameter) should be used to avoid causing bubble rupture. Because microbubbles resist compression better than expansion, when they are insonated at a low mechanical index (lower than 0.3) the expansion and contraction phases are no longer equal and the returning signal shows nonlinear characteristics resulting in the generation of multiple harmonics from bubble-filled vessels. At higher energy levels of insonation, disruption of the bubbles occurs, producing strong but transient harmonic signal. Contrast-specific software integrated in ultrasound scanners cancels the linear ultra-sound signal from tissues and uses the nonlinear responses from microbubbles.

Different dynamic phases of contrast enhancement may be identified in the liver study after the injection of a microbubble-based contrast agent. The arterial phase starts within 10–20 seconds and lasts for 35–40 seconds after the injection. The portal phase is characterized by the arrival of contrast agent through the portal system; it lasts for 2 minutes after the injection, and the overall liver echogenicity becomes more intense. Because microbubbles are purely intravascular, unlike the CT and MR contrast media that present an interstitial phase, there is no interstitial or equilibrium phase, and for the remaining observation time (late phase) they are progressively cleared. Video frames of the entire liver have to be

recorded in all three contrast phases because it is not possible to simultaneously examine multiple lesions in the arterial and portal phases. The late phase of CEUS is useful for detection of malignant (metastases) focal liver lesions. The late phase of CEUS enables better ultrasound hepatic staging in oncologic patients.