Contrast enhanced ultrasound and real time elastography in the evaluation of liver metastases

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Learning objectives

To present a comprehensive pictorial review focusing the role of CEUS in liver metastasis diagnosis and detections. To illustrate the imaging appearances of liver metastasis in RT-E.
Background

1. Contrast enhanced ultrasound (CEUS)

B mode sonography represents a useful screening technique for the detection of focal liver masses, but a specific diagnosis can rarely be established based only on the gray scale characteristics. Recently, the introduction of contrast agents has opened new prospects in the characterization of focal liver lesions. Newer microbubbles based on high molecular weight gasses such as sulphur hexafluoride, (used in Sonovue) can persist for much longer in the blood. Contrast-enhanced ultrasound (CEUS) has improved to the point at which it equals the sensitivity and specificity of contrast computer tomography (CT) and magnetic resonance imaging (MRI) [1, 2].

Contrast agents for ultrasound

Four ultrasound contrast agents are currently approved and marketed within European Countries: Levovist, Optison, SonoVue and Luminity. SonoVue (Bracco, Milan) is a second-generation contrast agent that contains a hydrophobic gas (sulphur hexafluoride), an extremely stable and inert molecule [3]. The usual way of administering SonoVue is an intravenous bolus injection followed by a flush with 5 ml sodium chloride 0,9 % [4]. The recommended dose for a single injection is 2,4 mL, but the optimal dose for a particular clinical situation depends on the individual patient and on the scanner technology. During a single examination, a second injection on the recommended dose can be made when deemed necessary by the physician [4]. The contrast agents should not be administered to patients with known hypersensitivity to the components, patients with severe cardiac or pulmonary disease or during pregnancy and lactation. Because of their inert constituents, ultrasound contrast agents are very safe and do not have nephrotoxic effects [4]. The overall reporting rate of serious adverse effects was 0.0086%, lower than or similar to that reported for radiologic and magnetic resonance contrast agents [5].

Clinical application in liver diseases

CEUS applied to the diagnosis of liver diseases has many advantages. Thus, contrast-enhanced digital technologies allow the differentiation of signals produced by the contrast agent in the liver from the time of microbubble arrival in the hepatic artery, portal vein and liver parenchyma, until their disappearance. All vascular phases can be examined and focal liver lesions can be characterized according to the temporal and spatial pattern of contrast perfusion. The method is easy to perform, in real-time, with a very low incidence of severe allergic reactions.

Due to the dual blood supply of the liver provided by the hepatic artery (25-30%) and portal vein (70-75%), three vascular phases can be visualized in CEUS. Arterial phase starts when hepatic artery shows enhancement (10-20 seconds post-injection into a
Peripheral vein) and lasts for approximately 10-15 seconds. Portal venous phase begins when portal vein shows enhancement and lasts for approximately 2 minutes after contrast agent injection. Delayed phase corresponds to the washout period up to approximately 4-6 minutes postinjection of SonoVue. The arterial phase provides information on the degree and pattern of vascularity, while the portal and late phase can provide important information in the differentiation of the benign or malign liver lesion [4].

2. Real time elastography

Real time sonoelastography (RTE) is a new imaging method used for the appreciation of the physical characteristics of the tissues. The method differentiates between the hardness of the diseased tissue and of the surrounding one. Malignant tumors are harder compared to benign ones and about 100 times harder than the surrounding tissue. Because of their reduced elasticity, malignant tumors can change their shape less than the benign ones and the latter less than the surrounding tissue. By means of the ability to appreciate the elasticity of the tissues, the real time sonoelastography can make the difference between benign and malignant tumors. It has already been proved that measuring elasticity is useful in the differential diagnosis of some tumoral lesions, especially breast, prostate, lymph, and pancreatic lesions. However, the role of RTE in differentiating liver lesions is approached in few studies only.
Findings and procedure details

The techniques were performed by Hitachi HI VISION Preirus ultrasound system with two convex probes (EUP-C532 for RT-E and EUP-C715 for CEUS). RT-E included the qualitative analysis of the tumors in a qualitative classification system (ETLT-elasticity type of liver tumors) and evaluation of strain ratio (SR) and strain histogram (SH) for quantitative analysis.

For **CEUS** we administrated 2.4 ml Sonovue in bolus followed by a flush of normal saline 0.9 %. All the three vascular phases were being recorded. Metastases were hypo- or hypervascular in the arterial phase [Figure 1, 3]. Some of them presented a peripheral rim enhancement [Figure 3]. All metastases had washout of the contrast and became hypo-enhanced in the portal and late phase [Figure 2, 4]. Metastases of carcinomas are the most common malignant infiltration of the liver. In addition, the liver is the parenchymatous organ in which metastases are encountered most often. The introduction of CEUS in clinical practice has markedly improved the detection rate of liver metastases versus conventional ultrasound, especially for small size or isoechoic lesions, and also for metastases in difficult anatomical areas (e.g. in the superficial subdiaphragmatic areas and around the ligamentum teres). Some studies have shown that the accuracy in the detection of liver metastases is comparable to CT [6, 7]. It has also been demonstrated that CEUS can detect metastases not visible on CT [6, 8, 9], but can also miss lesions shown on CT. Current recommendations for the use of CEUS in liver imaging include the exclusion of liver metastases in oncology patients, even if the baseline scans do not show any abnormality [4]

In **RTE**, one new classification system developed by Kato K et al, named elasticity type of liver tumour (ETLT), is based on the distribution and degree of strain within the lesion. The authors classified elasticity images into the following four types:

- type A, the entire lesion had even strain (the lesion was homogeneously green);
- type B, the lesion had strain in most areas with some areas of no strain (the lesion had a mosaic pattern with green area dominant);
- type C, the lesion had no strain in most areas with some areas of strain (the lesion had a mosaic pattern with blue area dominant);
- type D, the lesion had no strain [the lesion was homogeneously blue (including a small area of green component)].

In RTE, liver metastases were recognized as 'harder tumours'. We found predominantly blue images (type C or D) of metastasis in RTE [Figure 5, 6, 7].
Fig. 1: The hypervascular metastases in a case of neuroendocrine pancreatic tumor (arterial phase).

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Fig. 2: In the late phase the liver metastasis shows wash out.

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Fig. 3: Liver metastasis with peripheral rim enhancement in the arterial phase.

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Fig. 4: The same lesion became hypo-enhanced in the portal and late phase.

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Fig. 5: RTE in colorectal cancer liver metastasis show lesions with no strain (the lesion was homogeneously blue)- type D elasticity

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Fig. 6: RTE in breast cancer liver metastasis shows one lesion with type D elasticity (ETLT classification system).

Fig. 7: A mosaic pattern with dominant blue areas (type C elasticity) in a case of neuroendocrine pancreatic tumor liver metastasis

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Conclusion

The introduction of CEUS and RT-E in clinical practice has markedly improved the characterization and detection rate of liver metastases versus conventional ultrasound.
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References


