Contrast-enhanced ultrasound (CEUS) of focal liver lesions. A useful, rapid and accessible tool.

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Authors: S. Santamaria Jareño¹, J. Carrero Álvaro², M. Barxias Martín³, M. Nogueras⁴, L. Serra Bellver³, J. H. Camacho⁵; ¹Alcorcon (Madrid)/ES, ²Alcorcón (MADRID)/ES, ³Madrid/ES, ⁴Madrid, Sp/ ES, ⁵Alcorcón, MA/ES
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Learning objectives

To know the advantages, indications and technique employed during contrast-enhanced ultrasound, and the different enhancement patterns of focal liver lesions.

Background

The extensive use of ultrasound has contributed to an increase in the detection of focal liver lesions (FLL) in both healthy subjects and in cirrhotic or oncologic patients. The characterization of these lesions is essential for the final diagnosis and to decide upon therapeutic strategy.

Contrast-enhanced ultrasound (CEUS) opens a new window in the diagnosis of these lesions and offers significant advantages over CT and MRI. It is a rapid and accessible technique that does not use ionizing radiation and provides real-time information. Furthermore, Ultrasound Contrast Agents are not nephrotoxic and are very safe with a low incidence of side effects. CEUS allows a continuous assessment of the lesions' vascularity and enhancement with a higher temporal resolution, not limited to the pre-defined time points, as in CT and MRI. Furthermore, contrast injection can be repeated if necessary, due to the excellent patient tolerance.

In recent published studies, such as German and French multicenter study, CEUS was conclusive in approximately 85%-90% of the FLL, and was able to differentiate between benign or malignant lesions in approximately 90%-95% of the cases, with similar performance to CT and MRI. So, CEUS can be the first line investigation (thus avoiding other expensive examinations) in such cases. For non conclusive CEUS evaluations further imaging or morphological evaluation are needed for the final diagnosis.

ULTRASOUND CONTRASTE AGENTS

The ultrasound contrast agents (UCAs) are characterized by a microbubble structure consisting of gas bubbles stabilized by a shell. UCAs act as blood pool agents and provide accurate information about the vascularity of the FLL. There are different types of contrasts, the one used in liver is Sonovue® (sulfur hexafluoride with a phospholipied shell). This second generation agent works using low mechanical index (LMI) ultrasound. Under low mechanical index imaging, the microbubbles have a much higher non-linear behavior than the native tissue, resulting in detectable echoes and the pulse-inversion imaging does not cause disruption of the microbubbles, thus allowing a continuous assessment of the vessels as the contrast agent traverses the imaging field.
KINETICS OF US CONTRAST AGENTS IN LIVER: Due to the dual blood supply of liver tissue by the hepatic artery and the portal vein, three overlapping vascular phases can be defined and visualized using contrast enhanced ultrasound: the **arterial phase** that gives information on the degree and pattern of vascularity, and the **portal** and **late phases**, that give more information about the lesion's behavior. According to the enhancement pattern, the lesion can be classified following EFSUMB (European Federation of Societies in Ultrasound in Medicine and Biology) Guidelines concerning the use of CEUS, thus obtaining a confident diagnosis.

<table>
<thead>
<tr>
<th>Phase</th>
<th>Start</th>
<th>End</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arterial</td>
<td>10-20 seconds</td>
<td>25-35 seconds</td>
</tr>
<tr>
<td>Portal venous</td>
<td>30-45 seconds</td>
<td>120 seconds</td>
</tr>
<tr>
<td>Late</td>
<td>&gt;120 seconds</td>
<td>Bubble disappearance (approx. 240-360s)</td>
</tr>
</tbody>
</table>

**Vascular Phases in Contrast Enhanced Ultrasound of the Liver. EFSUMB 2008.**

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**Indications of CEUS**

| Characterization of FLL | Incidental findings on routine use
|-------------------------|-----------------------------------
|                         | Lesions or suspected lesion in chronic hepatitis or liver cirrhosis
|                         | Lesions or suspected lesion in patients with a history of malignancy
|                         | Patients with inconclusive MRI/CT or cytology/histology results
|                         | Characterization of portal vein thrombosis

| Detection of FLL | All liver ultrasound scans to “rule out” liver metastases or abscess, unless conventional ultrasound shows clear evidence.
|                 | In selected cases, when clinically relevant for treatment planning, to assess the number and location of liver metastases as a complement to CECT and/or CEMRI.
|                 | Surveillance of oncology patients where CEUS has previously been useful.
|                 | Suspected cholangiocarcinoma where other imaging is inconclusive.
|                 | Suspected liver trauma in some situations.

| Monitoring of Local Ablative Treatment | As a complement to CECT and/or CEMRI for pretreatment staging and assessment of target lesion vascularity.
|                                         | Facilitation of needle positioning in cases of incomplete or poor lesion delineation on unenhanced US.
|                                         | Evaluation of immediate treatment effect after ablation and guidance for immediate re-treatment of residual unablated tumor.
|                                         | Assessment of tumor recurrence, when follow-up CECT or CEMRI are contraindicated or not conclusive. CEUS may be used in the follow-up protocols.
Fig. 1: INDICATIONS FOR THE USE OF CEUS. Guidelines of EFSUMB 2008.

References: S. Santamaria Jareño; Alcorcon (Madrid), SPAIN

CONTRAINDICATIONS

- Severe cardiopulmonary disease.
- Ultrasound contrast agents have not been used in patients under the age of 18 years, pregnant or breastfeeding women.

LIMITATIONS

- The same as conventional ultrasonography.
- Very small and deep-sited lesions.
- Since CEUS has limited penetration (cirrhotic or steatosis livers).
- Liver segments with difficult accessibility (subdiaphragmatic lesions).
- Multiple lesions (limitations for the characterization).

Imaging findings OR Procedure details

TECHNIQUE

1. Before ultrasound contrast is injected, a complete ultrasound in B-mode must be performed, including Doppler techniques.
2. After the lesion is identified, the transducer is kept in stable position in order to visualize the mass along the whole exploration.
3. The mechanical index ought to be changed to a low index to prevent a fast destruction of microbubbles, thereby allowing a complete multiphase imaging. The principal vascular structures and other anatomic references like the diaphragm must remain visualized.
4. Some sonographers have a double screen with one of them under a low index state and the other one in B-mode, which facilitates the visualization under both mode conditions at the same time.
5. The contrast is usually administered in bolus through a peripheral vein (20 Gauge) followed by 10ml saline flush. It is recommended that the exploration be performed continuously in the first 90 s to evaluate correctly the arterial and portal phase, but can be explored discontinuously in the late phase.
6. It is recommended to record the exploration.

CHARACTERIZATION OF FOCAL LIVER LESION WITH CEUS
**BENIGN LIVER LESIONS**

*Sustained enhancement in the portal-late phase characterizes most benign solid liver lesions*

**Simple cyst:** It is anechoic with posterior acoustic enhancement in conventional sonography and hypoenhanced in all phases with contrast. Fig. 2 on page 12 Fig. 3 on page 13

**Hemangioma:** It is the most common benign liver tumor. This lesion consists of multiple vessels supported by fibrous interstitium. Ultrasonography shows a hyperechogenic lesion. CEUS shows that hemangiomas present peripheral nodular enhancement with centripetal filling during the portal phase and remaining isoenhanced in the late phase. Fig. 5 on page 14 Fig. 6 on page 15 Fig. 7 on page 16 Fig. 8 on page 17 Fig. 9 on page 18

![Hemangioma in CEUS. Typical peripheral-nodular enhancement in arterial phase.](image)

**Fig. 4:** Hemangioma in CEUS. Typical peripheral-nodular enhancement in arterial phase.
**Focal nodular hyperplasia:** It is a pseudotumor, which is considered a hyperplastic proliferation of normal liver cells in response to a preexisting arterial malformation. Large lesions commonly have a central scar made up from fibrous stroma with a supply artery and hyperplastic bile ducts. CEUS demonstrates that the lesion typically presents a central enhancement in the arterial phase, with a centrifugal filling through radial vascular branches (wheel sign). In the portal phase, the lesion usually remains enhanced with a non-enhancing central scar and becomes iso-enhanced in the late phase. Fig. 10 on page 19  Fig. 11 on page 23  Fig. 13 on page 20  Fig. 14 on page 21  Fig. 15 on page 22

![Image](image.jpg)

**Fig. 12:** Focal Nodular Hyperplasia in CEUS. Hyper-enhancing in the arterial phase with a spoke-wheel pattern.

**References:** S. Santamaria Jareño; Alcorcon (Madrid), SPAIN

**Adenoma:** It is a rare benign liver tumor, predominantly diagnosed in younger women with a prolonged history of oral contraceptives use. It is also described in use of anabolic androgens and type-1 glycogenosis. It is histologically made up of normal or atypical
hepatocytes with none or few bile ducts and Kupffer cells. During CEUS, adenomas show a fast centripetal hyper-enhancement during arterial phase, but in the majority of cases, the enhancement is irregular in the presence of necrosis or hemorrhages. In portal phase, the adenoma begins to wash out contrast becoming iso or hypo-enhanced with the liver parenchyma. The management is surgical due to its high bleeding risk and potential malignant degeneration (5%).

**Regenerative nodule:** Regenerative nodules often appear in cirrhotic livers or after a massive hepatic necrosis. These nodules are iso-enhanced during the three phases of contrast sonography. Progression to HCC is possible. Fig. 16 on page 28  Fig. 17 on page 29

**Focal fat accumulation:** It is present in 10% of patients with liver esteatosis. These fat accumulations are usually located next to the gallbladder, portal veins or the falciform ligament. It is iso-enhanced during the arterial, portal and late phases. Fig. 18 on page 48  Fig. 20 on page 24  Fig. 21 on page 25  Fig. 22 on page 26  Fig. 23 on page 27
Fig. 19: Focal fat accumulation in CEUS is iso-enhancing in the arterial phase. The perfusion of this lesion is not different from that of the surrounding liver parenchyma.  

References: S. Santamaria Jareño; Alcorcon (Madrid), SPAIN

Abscess: Abscesses usually show peripheral rim-like hyper-enhancement without central enhancement in arterial phase. It is hyper or iso-enhanced rim during portal phase, and hypo-enhancing rim in late phase. Septations can be identified traversing the lesion. Fig. 24 on page 30 Fig. 25 on page 31

MALIGN LIVER LESIONS

Hypo-enhancement of solid lesions (darker than the surrounding liver) in the late phase characterizes malignancies.

HCC: It is the most frequent primary tumor of the liver. About 80% of HCCs appear in cirrhotic population. A liver mass in a cirrhotic patient should be considered a HCC until proven otherwise. Two thirds of HCC are hyperechoic in conventional ultrasonography and the other third of HCC are heterogeneous, showing hyper and hypoechoic areas. Small lesions tend to be hypoechoic. Contrast-ultrasonography shows that HCC are enhanced in arterial phase, often with feeding vessels around and inside the tumor. It has a characteristic rapid wash-out in portal phase and frequently remains hypo-enhanced in late phase. Fig. 26 on page 32 Fig. 27 on page 33 Fig. 28 on page 34 Fig. 29 on page 35 Fig. 30 on page 36

Cholangiocarcinoma: It is a tumor of the bile duct. This tumor should be considered in patients with primary sclerosing cholangitis, choledochocoele, intrahepatic lithiasis, parasitic disease, Caroli’s disease, and in patients exposed to thorotrast for radiographic procedures. Cholangiocarcinomas show different enhancement patterns depending on size of the lesion and different pathological components of the tumor. In arterial phase, this tumor may show irregular peripheral rim-like hyper-enhancement, heterogeneous hyper-enhancement, homogeneous hyper-enhancement or heterogeneous hypo-enhancement. In portal phase, it presents complete wash out staying hypo-enhanced. Fig. 32 on page 37 Fig. 33 on page 38 Fig. 34 on page 39 Fig. 35 on page 40
Fig. 31: Cholangiocarcinoma in CEUS. Hyper-enhancing in arterial phase.

References: S. Santamaria Jareño; Alcorcon (Madrid), SPAIN

Metastasis: Metastasis is the most common malignant hepatic tumor. Colorectal cancer most commonly metastasizes to liver. Hypervascular metastases are associated to carcinoid tumors, melanomas, sarcomas, thyroid tumors and hypernephromas. They are completely enhanced in arterial phase with fast wash out and hypo-enhanced in portal and late phases. Fig. 36 on page 41 Fig. 37 on page 42 Fig. 38 on page 43 Fig. 39 on page 44. Hypovascular metastases remain un-enhanced during the three phases. Fig. 40 on page 45 Fig. 41 on page 46 Fig. 42 on page 47 Fig. 44

DIAGNOSTIC ALGORITHM OF FOCAL LIVER LESIONS

Based on published scientific literature and in our experience we propose the following diagnostic algorithm for the management of Focal Liver Lesions.
Fig. 43: Diagnostic Algorithm of Focal Liver Lesions.

References: S. Santamaria Jareño; Alcorcon (Madrid), SPAIN

Images for this section:
### Indications of CEUS

| Characterization of FLL | *Incidental findings on routine use*  
|                         | *Lesions or suspected lesion in chronic hepatitis or liver cirrhosis*  
|                         | *Lesions or suspected lesion in patients with a history of malignancy*  
|                         | *Patients with inconclusive MRI/CT or cytology/histology results*  
|                         | *Characterization of portal vein thrombosis*  
| Detection of FLL        | *All liver ultrasound scans to “rule out” liver metastases or abscess, unless conventional ultrasound shows clear evidence.*  
|                         | *In selected cases, when clinically relevant for treatment planning, to assess the number and location of liver metastases as a complement to CECT and/or CEMRI.*  
|                         | *Surveillance of oncology patients where CEUS has previously been useful.*  
|                         | *Suspected cholangiocarcinoma where other imaging is inconclusive.*  
|                         | *Suspected liver trauma in some situations.*  
| Monitoring of Local Ablative Treatment | *As a complement to CECT and/or CEMRI for pretreatment staging and assessment of target lesion vascularity.*  
|                         | *Facilitation of needle positioning in cases of incomplete or poor lesion delineation on unenhanced US.*  
|                         | *Evaluation of immediate treatment effect after ablation and guidance for immediate retreatment of residual unablated tumor.*  
|                         | *Assessment of tumor recurrence, when follow-up CECT or CEMRI are contraindicated or not conclusive. CEUS may be used in the follow-up protocols.*  

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Conclusion

Contrast-enhanced ultrasound is an emerging technique that offers important advantages over CT and MRI, without a significantly decrease in its sensitivity and specificity, in the study of focal liver lesions. So, CEUS should be considered as the first diagnostic procedure to be performed.

Personal Information


References


