Proper settings of technical parameters in contrast enhanced ultrasound examinations to avoid pitfalls and artifacts - tips and tricks

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Learning objectives

The poster aims to:

- Describe the settings of technical parameters during contrast enhanced ultrasound (CEUS) examinations.
- Help avoiding the most common pitfalls.
- Highlight the optimal methods and conditions.

Background

The growing spectrum of indications, spreading of contrast harmonic imaging capable ultrasound machines, lack of nephrotoxicity, and the bedside availability justifies the increasing role that CEUS is taking in the day to day clinical practice.

The principle of contrast harmonic imaging is based on the differentiation of non-linear signals that are generated by assymetrically oscillating microbubbles, and between those linear signals that are generated from the surrounding tissues. As it is a dynamic examination, the result depends not only on the ultrasound contrast agent (UCA) administration, but the examination technique and the continuously adapted settings as well.

The potential source of errors encountered by examiners, are the following:

1. inappropriate UCA administration,
2. wrong examination technique,
3. inaccurate configurations and settings.

The purely intravascular contrast agent we use is SonoVue™, consisting of sulphur hexafluoride (SF₆) coated by phosolipid shell.

This presentation intends to focus on critical points which could be common sources of errors encountered mostly during characterisation of focal liver lesions, since this is the most widespread indication of CEUS.

Imaging findings OR Procedure details
**Contrast administration:**

**Cannula set:**

By optimising the mode of contrast administration, early microbubble destruction can be avoided.

Superficial veins of the limbs are used to gain venous access. The diameter of the cannula used should be at least 20 G, avoiding the bubble destruction during bolus-injection, which can damage the phospholipid shell of the microbubbles leading to their early destruction in the narrow lumen of the cannula.

A three-way stopcock is attached to the venous cannula, that allows optimal administration of the UCA through the attached syringe and the saline solution in another syringe attached for washing in the UCA. The contrast agent should be injected directionally (Fig. 1) to insure the laminar flow.

**Dosage:**

A single injection of 2.4 or 4.8 ml UCA is sufficient for characterising liver lesions. Even less contrast agent (1-2 ml) can be sufficient according to our experience, and the latest guidelines.

The required dose depends on multiple factors as:

- sensitivity of different ultrasound machines,
- circulation of the investigated organ,
- location of the lesion,
- physique of the patient.

**Settings:**

**Frame rate:**

The parameter with which we can alter the temporal resolution is the frame rate. Choosing the desired frame rate there are two factors that we have to count with.

- Low frame rate sampling makes judging the flow direction difficult especially in fast filling lesions (FNH, adenoma).
- Higher frame rate increases the degree of microbubble destruction, limiting the assessment of the venous phase due to the reduction of contrast difference between the examined lesion and the surrounding parenchyma.
Changing the technique - by periodically suspending the examination - can be a solution for this problem as well.

Gain:

In contrast harmonic imaging (CHI), the amplification of tissue signals is considered as noise from the point of view of image reconstruction, since it has to be separated from signals originating from the microbubbles. It is obvious therefore that increasing the gain makes separating linear and non-linear tissue signals more difficult, by deteriorating the signal-to-noise ratio.

CHI requires low gain. In the grayscale image of the splitscreen, the lesion is just barely depictable generally, which is usually sufficient for keeping the lesion in the field of view. In certain cases the gain can be lowered when large acoustic impedance induces signal amplification (diaphragm, septae, gall-bladder, walls of portal vessels, etc.).

There are several options for increasing the signal intensity of the lesions during CEUS examination instead of changing the gain level:

- increasing the amount of injected UCA
- altering the transducer position (superficial lesions)
- increasing the mechanical index/ultrasound output

**Mechanical index (MI)/ Ultrasond output:**

MI is a value derived from the acoustic pressure and the frequency. Increasing the acoustic pressure or decreasing the frequency raises the mechanical index.

The second-generation of UCA are destroyed significantly faster exposed to high MI sound waves reducing the microbubble lifetime and deteriorating the contrast resolution. The MI is set at a predetermined value by the manufacturer - usually less than 0.2- but it can be adjusted at the beginning of each examination. It is advisable to start with the factory default settings.

MI is an important dynamic parameter comparable to the gain in conventional B-mode ultrasonography. The MI value must always be adapted to each individual case. With lower MI values the contrast resolution is also lower but the microbubble lifetime is longer.

Highly increasing the MI results in increasing the reflection from the superficial layers of the liver, decreasing our ability to judge deeper areas.

Lesions with slower blood flow (hemangiomas, focal nephritis) are more prone to microbubble destruction, than surrounding parenchyma, so precaution has to be made by keeping the MI low in such cases.

Focus:
By positioning the focus deeper than the area of interest we avoid early microbubble destruction. Areas located at the level of focal point or beyond are difficult to evaluate (Fig. 2). Our aim is to avoid focusing on the examined area, but to have a focus point located as deeply as possible.

**Timer:**

In order to be able to characterise the enhancement dynamics of the lesions we continuously need to record the elapsed time.

Reviewing the CEUS examination is frequently essential. Each pixel on the saved image, or video can be considered as a recorded intensity value from a certain point in the given moment on a time-intensity-curve, therefore for accurate assessment of contrast enhancement dynamics time display is indispensable.

In clinical practice we start the timer right after the injection of the contrast bolus.

**Split-screen:**

Split-screen mode helps us keeping the target lesion in the field of view until the first microbubbles arrive. Single screen mode can be used searching for intrahepatic metastasis not depictable on B-mode imaging in sinusoidal phase. In the latter case when a new lesion is discovered turning back to split screen mode is advised to rule out the presence of a previously not discovered small liver cyst.

Split-screen mode is also needed in case significant differences in the acoustic impedance of tissue structures generating artefacts in contrast-harmonic imaging before the injection of UCA to rule out false positive enhancement.

**Examination technique:**

**Breathing:**

Holding the breath during CEUS examinations is rarely helpful by causing a negative thoracic pressure with Valsalva manoeuvre which delays the contrast arrival time. As soon as the patients are not able to hold their breath anymore, the lesion often moves away from our field of view, making it difficult to evaluate in the early arterial phase. Contrary to conventional ultrasonography it is worth examining the patient with normal breathing, finding a transducer position from where the area of interest can be kept in sight (frequently this means examining the liver from an intercostal space).
Continuous examination:

In arterial phase the continuous monitoring of the organ or lesion to be characterised is mandatory to evaluate its enhancement pattern even if it raises microbubble destruction rate. After elapsing of the arterial phase (30-40 seconds after the appearance of first microbubbles) the area of interest should be only examined from time to time for short intervals to avoid early microbubble destruction. This way late venous phase can be assessed fairly well if needed (HCC, late enhancing hemangiomas).

Pressure of the transducer:

Desired UCA concentration will not be reached in the superficial tissues when the mechanical pressure of the transducer due to compression leads to decreased blood flow in the superficial areas underneath (Fig. 3). This pitfall can be avoided by decreasing the pressure on the transducer during the examination. Avoiding this pitfall can be achieved by intercostal examination of the liver.

Deep lesions:

The depth of the lesion has primary importance. It is generally true that the deeper the lesion is, the more difficult it is to examine it. The reason for this is the poor spatial resolution, and the poor contrast resolution. This issue can be handled by decreasing frequency, and not by raising the acoustic pressure (which would raise the MI while keeping the frequency constant).

Raising the UCA dose does not necessarily improve the resolution, because the increased microbubble concentration in the superficial layers will limit the assessibility of the deeply located areas because of higher reflection.

Early arterial phase:

The early arterial phase is limited to the first few seconds after the arrival of the first microbubbles to the area of interest. Missing it poses real differential diagnostic problems.

The fast filling hemangiomas and some metastases commonly start their enhancement in this phase. If the early enhancement of hypervascularised metastasis are missed then their differentiation from small hemangiomas and cysts with thick fluid content can be very difficult.

Recording this phase for further evaluation and starting the timer in time is mandatory.

Late venous/sinusoidal phase:
Performing CEUS examination we frequently encounter hemangiomas with late enhancement. In such hemangiomas the peripheral nodular enhancement might be delayed as well. To avoid microbubble loss in such cases continuous scanning is not advised. In these hemangiomas the microbubbles are more prone to destruction due to the slow circulation (Fig. 4-5). This might miss-lead us by mimicking hypovascular metastases. With a technically well performed exam we are able to eliminate such false positive results. One of the greatest challenges of CEUS is the characterisation of hepatocellular carcinoma in cirrhotic liver. In these patients late enhancement can be a diagnostic clue.

Images for this section:

Fig. 1: Cannula set used during CEUS examinations consisting of three-way stopcock and a directionally attached syringe of the ultrasound contrast agent.
**Fig. 2:** Splenic infarction with a non-enhancing, sharply marginated area in the lower pole. Green arrowheads indicate the position of the focus. The lowest possible focus position on the right improves the contrast resolution.
Fig. 3: Decreased signal intensity in the superficial area of the liver according to the higher compression with the transducer
Fig. 4: Late filling hemangioma in the late venous/sinusoidal phase
**Fig. 5:** The same late filling hemangioma shows progressive "wash in" even in the late venous/sinusoidal phase compared to previous image. Avoiding continuous scanning after the arterial phase helps us to preserve the microbubbles.
Conclusion

Appropriate administration of ultrasound contrast agents together with being able to adapt our examination technique to the given circumstances by using settings that are tailored for each individual case is essential to avoid the common sources of errors encountered during CEUS.

Understanding the pathomorphology and contrast enhancement dynamics of the different pathologies is necessary as it is the case with other modalities. By knowing the limitations and the potential pitfalls CEUS becomes a rapid, safe, cost-effective and reliable way of complementing other imaging modalities.

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