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Guidelines for the Use of Contrast Agents in Ultrasound

January 2004

Ultrasound contrast agents (UCA), in conjunction with contrast specific imaging techniques, are increasingly accepted in clinical use for diagnostic imaging and post-interventional workup in several organs. Presently, there is no guidance document providing a description of essential technical requirements, proposed investigator qualifications, suggested investigational procedures and steps, guidance on image interpretation, recommended and established clinical indications and safety considerations.

The need for these guidelines was highlighted following the EFSUMB Board of Directors (Delegates) meeting at the EUROSON Congress at Copenhagen in March, 2003. During their development these guidelines were presented at the EFSUMB special consensus meeting for the use of contrast agents in ultrasound in Rotterdam in January 2004.

These guidelines are based on comprehensive literature surveys including results from prospective clinical trials. On issues where no significant study data were available, evidence was obtained from expert committee reports or was based on the actual consensus of experts in the field of US and contrast enhanced Ultrasound (CEUS) during the consensus conference.

These guidelines are intended to create standard protocols for the use and administration of UCA and improve the management of patients. The first version, dated January 2004, will be focused on the evaluation of known or suspected focal liver lesions (FLL).

These guidelines are intended to give general advice for the use of UCA. Individual cases must be managed on the basis of all clinical data available for that specific case. The guidelines will be subject to change to reflect future advances in scientific knowledge and the rapidly evolving field of US technology.

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Note

With the advice and educational grant provided by the following companies: Amersham, Bristol-Myers Squibb Medical Imaging; Bracco; Esaote; GE Ultrasound; Hitachi; Philips; Schering; Siemens; Toshiba.

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Ultraschall in Med 2004; 25: 249–256 © Georg Thieme Verlag KG Stuttgart · New York
DOI 10.1055/s-2004-813245
ISSN 0172-4614

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Appendix 1, 2 available under www.efsumb.org

1 General Considerations

1.1 Introduction

The development of ultrasound contrast agents (UCA), which perform as blood pool tracers, have overcome the limitations of conventional B-Mode and colour or power Doppler US and enable the display of parenchymal microvasculature. Dependent on contrast agent and US-mode, the dynamic lesion enhancement pattern is visualized during intermittent or continuous insonation. Enhancement patterns are described during subsequent vascular phases (e. g. arterial, portal-venous and late phase for liver lesions), similar to contrast enhanced computer tomography (CECT) and/or contrast enhanced magnetic resonance imaging (CEMRI). Contrast enhanced ultrasound (CEUS) and CECT or CEMRI are not fully superimposable, as UCA remain in the intravascular space, whereas the majority of currently approved contrast agents for CT and MRI are rapidly cleared from the blood pool into the extracellular space.

An inherent advantage of CEUS is the possibility to assess the contrast enhancement patterns in real time, without the necessity to predefine scan-timepoints or to perform bolus-tracking and furthermore the possibility to perform repeated examinations due to the excellent patient toleration of UCA.

1.2 Commercially Available Ultrasound Contrast Agents (UCA) in Europe

Three transpulmonary UCA are currently approved and marketed within European Countries:

- 1.2.1 Levovist® (air with a galactose/palmitic acid surfactant)(Schering, introduced in 1996). Main indications include heart, abdomen including vesico-ureteric reflux and transcranial.
- 1.2.2 Optison® (octafluoropropane (perflutren) with an albumin shell) (Amersham, introduced in 1998). Sole indication is cardiac.
- 1.2.3 SonoVue® (sulfur hexafluoride with a phospholipid shell)(Bracco, introduced in 2001). Main indications are cardiac, macrovascular, liver and breast lesions.

Respective composition, packaging, storage, contraindications and indications of these three agents are detailed in Appendix 1.

There are other UCA approved outside Europe or under investigation.

1.3 Imaging Techniques using Ultrasound Contrast Agents

1.3.1 Background [1 – 6]

The UCA which are currently used in diagnostic US are characterized by a microbubble structure consisting of gas bubbles stabilized by a shell. UCA act as blood pool agents. They strongly increase the US backscatter and therefore are useful in the enhancement of blood echogenicity for the assessment of blood flow in the vasculature. Levovist contains air whereas SonoVue (sulfur hexafluoride) and Optison (perflutren) contain low solubility gases improving microbubble stability.

The assessment of microbubbles usually requires contrast specific imaging modes.

Contrast specific US modes are generally based on the cancellation and/or separation of linear US signals from tissue and utilization of the nonlinear response from microbubbles [7 – 10].

Non-linear response from microbubbles is based on two different mechanisms:

- non-linear response from microbubble oscillations at low acoustic pressure, chosen to minimize disruption of the microbubbles.
- high energy broadband non-linear response arising from microbubble disruption.

Non-linear harmonic US signals may arise also in tissues themselves due to a distortion of the sound wave during its propagation through the tissue. The extent of the harmonic response coming from the tissue is dependent on the MI settings (= mechanical index, which is correlated to the acoustic pressure).

US imaging with air filled microbubble (e. g. Levovist®) leads to microbubble disruption as the resistance to acoustic pressure for these UCA is low. Therefore intermittent imaging with low frame rates to allow refill of the microbubbles into the microvasculature is necessary. Alternatively it is possible to use fast sweep techniques with offline review of the digital stored cine loops.

Low solubility gas UCA (e. g. SonoVue®, Optison®) are characterized by the combination of an improved stability with favorable resonance behavior at low acoustic pressure. This allows minimally disruptive contrast specific imaging at low MI and enables effective investigations over several minutes with the visualization of the dynamic enhancement pattern in real time.

Low MI techniques furthermore lead to effective tissue signal suppression, as the non-linear response from the tissue is minimal when low acoustic pressures are used [9 – 11].

In summary low MI imaging with SonoVue® and Optison® allows real time CEUS while Levovist® requires higher MI intermittent CEUS.

1.3.2 Equipment and Technical Requirements

Although microbubbles are occasionally used to enhance conventional Doppler studies almost all current applications require contrast specific imaging modes.

See systems specification in Appendix 2.

1.4 Investigator Training

The EFSUMB minimal training requirements for the practice of medical ultrasound in Europe define three levels of minimal training requirements. It is likely that most UCA examinations would be performed by level 2 or 3 investigators.

It is recommended that investigators wishing to undertake UCA examinations should gain experience by observing contrast studies being performed in a department with expertise in this area. They should also ensure that their equipment is optimised for contrast examination by discussion with their equipment manufacturers. It is also important that in their own department there are adequate numbers of examinations being performed and different types of pathological processes being observed to acquire and maintain their skills.

Practitioners need to be competent in the administration of contrast agents, familiar with any contra-indications and be able to deal with any possible adverse effect, within the medical and legal framework of their country.

1.5 Safety Considerations

In general, UCA are extremely safe with a low incidence of side effects. They are not nephrotoxic or cardiotoxic and the incidence of hypersensitivity or allergic events appears much lower than current X-ray or MR contrast agents. It is not necessary to perform laboratory tests of renal function before administering them. UCA are not licensed in pregnancy and breastfeeding is a contra-indication in some countries.

There is a theoretical possibility that the interaction of diagnostic ultrasound and UCA could produce bioeffects. Data from small animal models suggest that microvascular rupture could occur when gas bodies are insonated. This might be a potential safety issue in special situations where such vascular damage would be clinically important such as ocular US and brain without an intact skull. In addition, premature ventricular contractions have been described when high MI end systolic triggering is used in echocardiography.

The MI provides a useful, albeit rough, on-screen indicator of the potential for non-thermal effects. The potential for non-thermal bioeffects exists in all modes, including conventional 2D imaging and 3D methods.

Users should balance the potential clinical benefit from the use of UCA against the theoretical possibility of associated adverse bioeffects in humans.

Some general recommendations would be:

- 1.5.1 Caution should be considered for the use of UCA in tissues where damage to microvasculature could have serious

clinical implications, such as in the brain without an intact skull, the eye, and the neonate.

- 1.5.2 Investigators should be aware of the possibility of inducing premature ventricular contractions in contrast enhanced echocardiography, when using high MI and end-systolic triggering, and take appropriate precautions.
- 1.5.3 As in all diagnostic ultrasound procedures, the operator should be mindful of the desirability of keeping the displayed thermal index (TI) low by prudent setting of the controls, and of avoiding unduly long exposure times.
- 1.5.4 The use of contrast agents should be avoided 24 hrs prior to extra-corporeal shock wave therapy.

Focal liver lesions (FLL)

In most imaging centers US is the initial examination requested for patients with known or suspected focal liver disease in the sense of either defining the FLL (by their US characteristics, number, size, position) or for ruling out the presence of FLL (as far as possible). Additionally, US imaging frequently reveals hepatic lesions as an incidental finding in patients undergoing an ultrasound examination for screening purposes or for the investigation of a nonhepatic disease.

Once a lesion has been detected, the foremost question is always the differentiation between a benign and malignant lesion. However, since detection and characterization of FLL using unenhanced US is limited to the visualization of grey-scale morphology and macrovascular flow, sensitivity and specificity values of unenhanced ultrasound appear generally inferior to those of dynamic helical (multidetector) CT and MRI, which can exploit contrast enhancement effects for better delineation and characterization of FLL.

Based on characteristic enhancement patterns throughout the vascular phases, CEUS of the liver permits clear improvements in the characterization and detection of FLL when compared to unenhanced US, with close diagnostic agreement with other well established radiological imaging methods such as CECT or CEMRI [12, 13].

The following recommendations on the application of ultrasound contrast agents for detection and characterization of focal liver lesions and their use in the monitoring of treatment effects following local ablative treatment represent a consensus document issued by the European Federation of Societies for Ultrasound in Medicine and Biology (EFSUMB) with the contribution of experienced experts (see the list above).

2 Characterization of Focal Liver Lesions

2.1 Background

Due to the dual blood supply of liver tissue by the hepatic artery (25–30%) and the portal vein (70–75%), three vascular phases can be defined and visualized using contrast enhanced sonography. Tissue enhancement resulting exclusively from the hepatic artery supply usually starts from 10–20 seconds postinjection into a peripheral vein and lasts for approximately 10–15 seconds. This is followed by the portal venous phase which usually

lasts until 2 minutes after UCA injection. The late phase lasts until the clearance of the US contrast agent from the hepatic parenchyma, up to approximately 4–6 minutes post injection for SonoVue® and 15 to 20 minutes for Levovist®. This late phase differs from the equilibrium phase of extracellular CT and MRI agents. The origin of this late phase is the subject of ongoing scientific discussion; suggested mechanisms include sinusoid pooling and RES/Kupffer cells uptake [14].

The arterial phase provides information on the degree and pattern of vascularity. The portal and late phase provide information about the wash out of UCA from the lesion compared to normal liver tissue. In the case of haemangiomas a progressive filling can be observed during these phases. Portal and late phase enhancement can provide important information regarding the character of the lesion: most malignant lesions are hypo-enhancing while the majority of solid benign lesions are iso- or hyper-enhancing [15–26].

2.2 Investigational Procedure

2.2.1 Low Mechanical Index (MI) Techniques

Low MI contrast specific techniques allow dynamic imaging with subsequent evaluation of the three different vascular phases using a low solubility gas UCA.

The steps recommended in the investigational procedure are as follows:

- 2.2.1.1 Baseline investigation in B-Mode, potentially including colour and Doppler techniques
- 2.2.1.2 After identification of the target lesion(s) the transducer is kept in a stable position while the imaging mode is changed to low MI contrast specific imaging.
- 2.2.1.3 Adjust the MI setting to provide sufficient tissue cancellation with maintenance of adequate depth penetration. Major vascular structures and some anatomical landmarks like the diaphragm should remain barely visible.
Note: In some recent contrast specific US modes a simultaneous display of tissue and contrast signals has been implemented.
- 2.2.1.4 UCA is administered as a bolus injection followed by a 5–10 ml saline flush. The needle diameter should not be smaller than 20 Gauge to avoid loss of bubbles due to mechanical impact during injection. A stop clock should be started at time of UCA injection.

2.2.1.5 Continuous scanning for 60–90 seconds is recommended to continuously assess the arterial and portal-venous phase. For assessment of the late phase scanning may be used intermittently until the disappearance of the UCA from the liver microvasculature has been observed.

2.2.1.6 Because of the dynamic nature of real time CEUS, it is recommended to document the investigation on video or digital media.

2.2.2 High Mechanical Index (MI) Techniques

High MI techniques in which microbubbles are deliberately destroyed are probably more useful for FLL detection (see 3.2.2) but can be used for characterization. When required intermittent scanning of the lesion is performed during all 3 phases.

2.3 Image Interpretation and Evaluation (Enhancement Pattern of FLL)

2.3.1 Benign Lesions

Benign solid lesions are characterized by persistence of contrast enhancement during the portal-venous and late phase and can be further characterized by enhancement patterns during the arterial phase, (e. g. enhancement of the whole lesion (focal nodular hyperplasia (FNH), adenoma) or initial peripheral globular-nodular enhancement [haemangioma]).

The typical enhancement patterns are summarized in Table 2a for the following lesions: haemangioma, FNH, focal fatty sparing, focal fatty change, regenerative nodule, cyst, adenoma, abscess).

2.3.2 Malignant Lesions

Malignant lesions are characterized by wash out of microbubbles during the portal and late phase. This is particularly true for liver metastases, while HCC can show some late phase enhancement, or may be isoenhancing.

The arterial phase is important for demonstrating hypervascularization of HCC and hypervascular metastases.

The enhancement patterns for the characterization of malignant lesions (HCC, hypovascular mets, hypervascular mets, cholangio carcinoma) are summarized in Table 2b.

2.4 Recommended Use and Indications

Characterization of lesions such as haemangioma, focal nodular hyperplasia, metastasis and HCCs can be obtained at a high level of probability by CEUS in association with clinical and laboratory data, baseline and Doppler US, if typical enhancement patterns are present. Focal liver lesions with atypical enhancement patterns or technically suboptimal studies require further investigation.

Low solubility gas UCA are superior for the use of FLL characterization due to the possibility of dynamic imaging in real time using low MI contrast specific techniques.

Recommended Indications

CEUS is indicated in all patients with uncertain liver lesions, particularly including the following clinical situations:

Table 1 Vascular Phases in Contrast Enhanced Ultrasound of the Liver. The individual global hemodynamic situation in a given patient will influence the time of onset of the three vascular phase times

Phase	Visualization Post-injection Time (seconds)	
	Start	End
Arterial	10–20	25–35
portal-venous	30–45	120
Late	> 120	Bubble disappearance (approx. 240–360)

- 2.4.1 Incidental findings on routine US
- 2.4.2 Lesions or suspected lesion in chronic hepatitis or liver cirrhosis
- 2.4.3 Lesions or suspected lesion in patient with a known history of malignancy.
- 2.4.4 Patient with inconclusive MRI/CT or cytology/histology results.

Limitations

- 2.4.5 UCA for characterization is subject to the same limitations as other types of ultrasound, and sensitivity is markedly reduced in attenuating livers and deep lesions. As a general rule, if the baseline ultrasound is very suboptimal, CEUS may be disappointing.

Table 2a Enhancement (E) patterns of benign focal liver lesions

<i>Tumor Entity</i>	<i>Arterial Phase</i>	<i>PV Phase</i>	<i>Delayed Phase</i>
Haemangioma			
Typical Features	peripheral-nodular E, no central E Rim E	partial/complete centripetal filling	complete E.
Additional Features	small lesion: complete, rapid centripetalE		non-enhancing central areas (partial thrombosis, fibrosis)
FNH			
Typical Features	hyper-enhancing, complete, early	hyper-enhancing	iso-,hyper-enhancing
Additional Features	spoke wheel arteries, centrifugal filling feeding artery	hypo-enhancing central scar	hypo-enhancing central scar
Focal fatty sparing			
Typical Features	iso-enhancing	iso-enhancing	iso-enhancing
Focal fatty change			
Typical Features	iso-enhancing	iso-enhancing	iso-enhancing
Regenerative nodule			
Typical Features	iso-enhancing	iso-enhancing	iso-enhancing
Additional Features	hypo- or hyper-enhancing		
Cyst			
Typical Features	non-enhancing	non-enhancing	non-enhancing
Adenoma			
Typical Features	hyper-enhancing, complete	iso-enhancing	iso-enhancing
Additional Features	non-enhancing areas (haemorrhage)	hyper-enhancing non-enhancing areas (haemorrhage)	non-enhancing areas (haemorrhage)
Abscess			
Typical Features	rim E, no central E	hyper-/iso-enhancing rim, no central E	hypo-enhancing rim, no central E
Additional Features	enhanced septa hyper-enhanced liver segment	hypo-enhancing rim enhanced septa	

Table 2b Enhancement (E) patterns of malignant focal liver lesions

<i>Tumor Entity</i>	<i>Arterial Phase</i>	<i>PV Phase</i>	<i>Delayed Phase</i>
HCC			
Typical Features	hyper-enhancing, complete non-enhancing areas (necrosis)	iso-, hypo-enhancing non-enhancing areas (necrosis)	hypo-enhancing
Additional Features	„chaotic“ vessels enhancing tumor thrombus in PV + HCC/ portal vein		
Hypovascular Mets			
Typical Features	rim E	hypo-enhancing	hypo-, non enhancing
Additional Features	complete E non-enhancing areas (necrosis)	non-enhancing areas (necrosis)	
Hypervascular Mets			
Typical Features	hyper-enhancing, complete	hypo-enhancing	hypo-, non enhancing
Additional Features	„chaotic“ vessels		
Cholangio carcinoma			
Typical Features	rim E	hypo-, non enhancing	hypo-, non enhancing
Additional Features	non-enhancing		

- 2.4.6 UCA for characterization of small lesions may be difficult; also for larger lesions that do not behave in a diagnostically typical fashion.

3 Detection of Focal Liver Lesion

3.1 Background

Conventional US is the most frequently used imaging procedure for the primary diagnosis of abdominal organs and the liver, but is less accurate in detection and staging of liver lesions than contrast-enhanced spiral CT and MRI. The main reasons for this are problems in the detection of small sized and/or isoechoic lesions, especially for deep lesions or in difficult anatomical areas (e.g. in the subdiaphragmatic areas).

Clinical studies evaluating CEUS have shown the accuracy to detect liver metastases is improved and may be raised to be comparable to spiral CT. Some studies have suggested CEUS can detect lesions not visible on CT [13, 27–29]. Most published data, however, relates to intermittent imaging with the late liver-specific phase of Levovist®. Published data using the much simpler method of low MI real time scanning using SonoVue® is still scanty [30]. However current data from single center and multicentre clinical trials are highly encouraging.

3.2 Investigational Procedures

3.2.1 Low Mechanical Index (MI) Techniques

Recommended investigational procedure:

- 3.2.1.1 Baseline investigation in B-Mode, potentially including Doppler techniques
- 3.2.1.2 Change to low MI contrast specific imaging mode
- 3.2.1.3 Using low MI contrast specific imaging modes which lack simultaneous tissue displays it is crucial to provide sufficient tissue cancellation with maintenance of adequate depth penetration. Adequate cancellation of tissue signals is characterized by disappearance of the B-Mode parenchymal liver structures. Major vascular structures and some anatomical landmarks like the diaphragm remain barely visible.
- 3.2.1.4 UCA is administered as quick bolus followed by a 5–10 ml saline flush. A stop clock should be started at time of UCA injection
- 3.2.1.5 A single bolus is usually adequate, and the examination is usually complete within 5 minutes.
- 3.2.1.6 The complete examination of the liver using various sweeps is possible within a timeframe of approximately 4–6 min (using all vascular phases).
- 3.2.1.7 Image Documentation: Essential clips for each vascular phase should be stored digitally on the system hard drive, as DICOM clips and/or MOD according to the technical capacities of the respective systems.
- 3.2.1.8 Scan in sweeps to cover the whole liver.
- 3.2.1.9 For hypovascular metastasis detection, the benefit of scanning before 90 s is debatable and some experts would avoid scanning before this time.

3.2.2 High Mechanical Index (MI) Techniques

Recommended investigational procedure:

- 3.2.2.1 Baseline investigation in B-Mode, potentially including Doppler techniques
- 3.2.2.2 Change to the respective contrast specific high MI mode and do not scan after this time
- 3.2.2.3 UCA is administered as bolus followed by a 5–10 ml saline flush. A stop clock should be started at time of UCA injection
- 3.2.2.4 US examination is restarted in the late phase after a delay of approximately 2–5 min.
- 3.2.2.5 A series of fast sweeps are performed (at least one separate sweep through the complete right and left liver lobe), to enable adequate coverage of the whole liver parenchyma. The sweeps are reviewed offline from the recorded cine loops
- 3.2.2.6 Image Documentation: Essential clips for each sweep should be stored digitally on the system hard drive, as DICOM clips and/or MOD according to the technical capacities of the respective systems.

3.3 Image Interpretation

3.3.1 Metastases

Please see the description in table 2B. In the portal-venous and the late phase, metastases usually show as hypoechoic defects and these phases are the most useful time to detect them. In comparison, most benign lesions show uptake at this time and are therefore not likely to be confused with metastases.

The appearance of metastases in the arterial phase is variable. Hypovascular metastases show in CEUS as hypoechoic lesions with or without an additional rim enhancement, while hypervascular metastases show as brightly enhancing hyperechoic and homogeneous lesions. Hypervascular metastases occur most often from primary tumors of neuroendocrine origin or from renal or breast cancer.

A common pitfall is that small cysts are sometimes detected on late phase scanning. These can usually be distinguished from metastases as they characteristically show increased through transmission.

3.3.2 HCC

Detection of HCCs, especially in the cirrhotic liver, is problematic. They may be detected as areas of increased enhancement in the arterial phase, but the short duration of the arterial phase can make full surveillance of the whole liver problematic. The late phase appearances are variable as previously described but in a proportion of patients HCCs are well shown as relative defects at this time.

3.3.3 Abscess

Abscesses often show enhancement on the arterial phase, usually peripheral, but then washout to appear as relative defects on late phase scanning.

3.3.4 Trauma

Traumatic liver lacerations and haematoma are well shown in all phases as non-enhancing defects. The same method is of value in other solid organs such as the spleen and kidney.

3.4 Recommended Use and Indications

Based on published literature [12, 13, 20, 27, 28, 31], there is evidence that CEUS improves detection of metastases. Some studies have suggested that the accuracy in the detection of intrahepatic metastatic disease is comparable to CECT [13] provided scanning conditions are adequate to perform a complete investigation of all liver segments.

Recommended Indications

- 3.4.1 All liver ultrasound scans to rule out liver metastases or abscess, unless conventional ultrasound shows clear evidence of these lesions.
- 3.4.2 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.
- 3.4.3 Surveillance of oncology patients where CEUS has previously been useful.
- 3.4.4 Suspected cholangiocarcinoma where other imaging is inconclusive or not scheduled
- 3.4.5 Suspected liver trauma in some situations including
CT not available or contra-indicated
Patient requires resuscitation before CT
CT is inconclusive or associated with artifacts
Monitoring of known traumatic lesions
Minor blunt trauma especially in children

Limitations

- CEUS for detection is subject to the same limitations as other types of ultrasound, and sensitivity is markedly reduced in attenuating livers and deep lesions. As a general rule, if the baseline ultrasound is very suboptimal, CEUS may be disappointing.

4 Monitoring of Local Ablative Treatment

4.1 Background

Percutaneous ablation therapies play a key role in the management of patients with liver malignancies, both HCC and metastases [32–36].

Diagnostic imaging in patients undergoing local ablative treatment includes US, CECT and/or CEMRI during pretreatment diagnostic work-up and at distinct time points within the follow-up of the patient (usually within the first week post treatment and after 1, 3, 6 etc. months).

Unenhanced US, even when combined with color/power Doppler, does not provide any reliable information about the outcome of ablation treatments. In fact, the assessment of vascularization and tissue perfusion is crucial to differentiate, necrosis from residual viable tumor. Biphasic helical CT or dynamic gadolinium-enhanced MRI can predict the extent of the coagulation area to within 2–3 mm.

When US is used as the imaging modality for guiding ablations, the addition of UCA can provide important information in each of the following procedural steps [37, 38]:

- 4.1.1 pre-treatment assessment of lesion vascularity in order to compare pre- and post-ablation patterns at the end of ablation and for better delineation of lesions poorly visualized on baseline US scans
- 4.1.2 guidance of the ablation needle/probe into lesions not visualized or not well delineated with unenhanced US
- 4.1.3 immediate assessment of the therapeutic result to detect residual viable tumour areas
- 4.1.4 post-ablation follow-up to assess treatment response

4.2 Investigational Procedures

4.2.1 Pre-treatment Contrast-Enhanced Ultrasound

- 4.2.1.1 For procedure, refer to 2.2
- 4.2.1.2 Images and/or movie clips are to be video- or digitally stored for comparison with immediate post-ablation studies.

4.2.2 Positioning of probe/needle (only when the lesion is not visible on unenhanced US)

- 4.2.2.1 For procedure, refer to 2.2
- 4.2.2.2 Probe/needle is inserted during the vascular phase in which the target is optimally depicted.

4.2.3 Periprocedural Assessment of Treatment Response (for thermal ablation)

- 4.2.3.1 Unenhanced US is used to monitor the reduction of the hyperechoic “cloud” due to gas formation caused by ablation. This usually requires 5–15 minutes
- 4.2.3.2 for procedure, refer to 2.2
- 4.2.3.3 Images and/or movie clips are to be digitally stored for comparison with previously stored pre-ablation images
- 4.2.3.4 If additional probe/needle insertions are performed, repeated administrations of UCA can be given.

4.2.4 Follow-up Investigation to Assess Tumor Recurrence

- 4.2.4.1 See procedure described at 2.2.

4.3 Image Interpretation – Definition of Complete Treatment Response

The most important imaging finding that suggests complete ablation is the disappearance of any previously visualized intraleSIONAL enhancement on contrast-enhanced images. Residual viable tumour tissue is suspected when a portion of the original lesion maintains hypervascularity in the arterial phase or clearly enhances in the portal phase.

In hypoenhancing lesions (e. g. most liver metastases), completeness of treatment can be assessed by the comparison of pre-treatment lesion size and location with the size and location of the post-treatment coagulation necrotic area. This also determines whether if a sufficient perilesional “safety” margin has been achieved.

In the early (e. g., within the first 30 days) post-ablative evaluation using CEUS, a thin and uniform enhancing rim of hypervascularity can be visible along the periphery of the necrotic area, similar to corresponding findings observed on CECT. Misinterpretation of this perilesional hyperemic halo as residual viable tumour can be avoided by comparing post-ablation images with pre-ablation scans.

4.4 Recommended Use and Indications

- 4.4.1 Complementary to CECT and/or CEMRI for pretreatment staging and assessment of target lesion vascularity. Pretreatment optimized CECT and/or CEMRI are recommended.
- 4.4.2 Facilitation of needle positioning in cases of incomplete or insufficient lesion delineation on unenhanced US.
- 4.4.3 Evaluation of immediate treatment effect after ablation.
- 4.4.4 Assessment of tumour recurrence in follow-up in cases when CECT or CEMRI are contraindicated or not conclusive. Although CECT and/or CEMRI are considered as the standard techniques for the assessment of treatment outcome, CEUS may be used in the follow-up protocols.

Appendix 1 and 2 available under www.efsumb.org

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