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Solutions in CONTRAST IMAGING

Economic and practical impact of CEUS on contrast imaging

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INTRODUCTION

Like iodized X-ray contrast media (CM) in computed tomography (CT) and gadolinium-containing contrast agents in magnetic resonance imaging (MRI), second generation ultrasound contrast agents provide imaging of physiological and pathological tissue perfusion using ad hoc ultrasound imaging protocols.

In 2001, a microbubble suspension (hexafluoride gas in a phospholipid shell, SonoVue®, Bracco Imaging, Milan, Italy) was approved by the European drug authorities as the only second generation contrast agent labelled for non-cardiac examinations (macrovasculature and microvasculature in liver and breast). Since then numerous scientific studies have evaluated the protocols and results of contrast-enhanced ultrasound (CEUS) in a still growing number of applications.[1,2]

A small number of casualties in chronological relation to SonoVue®-enhanced echocardiography during acute myocardial infarction raised some initial scepticism about the possible side-effects of the product. However, after acute coronary syndrome had been accepted as a contraindication for CEUS beyond clinical trials, and with growing CEUS experience, the positive risk/benefit ratio of SonoVue® has been demonstrated in more than 2.5 million patients.

The risks for the patient from i.v. administration of SonoVue® appear far smaller than those associated with MRI CM and CT/X-ray CM.

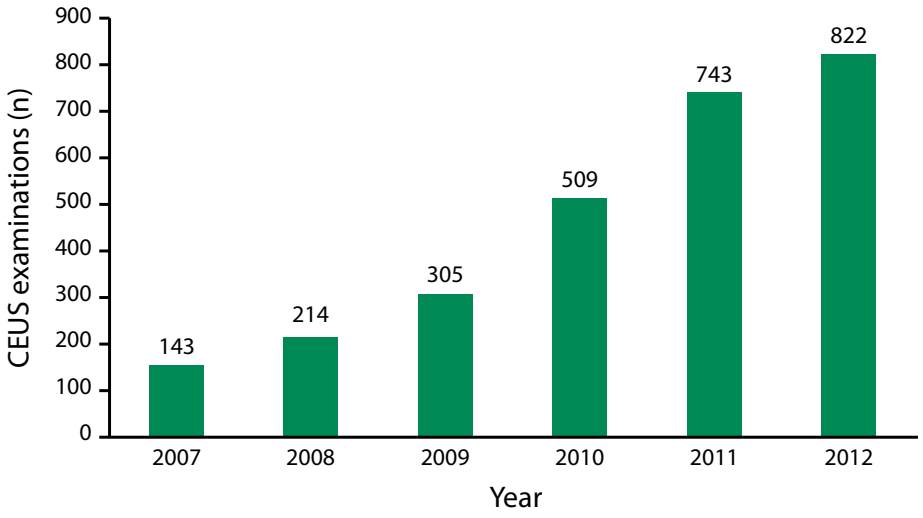
As a matter of principle, SonoVue® does not harm kidney function because it is not excreted through the kidneys. In addition, SonoVue® does not contain iodine, so it cannot interfere with thyroid function as do CT/X-ray CM. Last but not least, the biochemical properties of hexafluoride gas and phospholipid molecules, and the low volume of substance needed (1.2 ml SonoVue® as standard dosage for liver imaging in most modern ultrasound systems) compared to the hundred-fold volume in CT or MRI contrast imaging suggest that in the long run even allergic effects could be expected less frequently in CEUS than in contrast-enhanced CT (CECT) - not to mention the radiation exposure of CT and the medical and psychological limitations of MRI tunnel imaging.
In contrast with the above-mentioned patient-friendly aspects, CEUS:

- is restricted by the known technical limitations of ultrasound imaging (gas superposition, operator dependency, etc.);
- requires new and extended education and training of examiners;
- makes the formerly handy and quick method of ultrasound imaging significantly more complex, time-consuming and cumbersome, disturbing the former standard workflow in an ultrasound laboratory;
- is more expensive than conventional ultrasound.

IMPLEMENTATION OF CEUS IN THE DAILY ROUTINE OF AN IMAGING CENTRE - OUR EXPERIENCE

Our central interdisciplinary ultrasound department in the imaging centre of a maximum care hospital in Germany introduced CEUS according to expanding study evidence, reported especially in the series of EFSUMB guidelines on CEUS.[1-4] Figure 1 shows the development of CEUS activities in our department since 2007.

Figure 1. Annual number of CEUS examinations in the centralized interdisciplinary ultrasound section (CIS, Brüderkrankenhaus Trier, Germany).



The slope seems to flatten, perhaps to a saturation level of 900. However, by the end of August 2013 we had performed 665 CEUS examinations compared with 505 in 2012. The difference (+160; 31%) implies an expectation of further growth.

Purpose of the study

To establish whether the added efforts and costs of CEUS are worthwhile for the hospital in terms of costs and patient management.

Materials and methods

Most CEUS examinations were performed with a Philips IU22 system while a small number of emergency or bedside cases were investigated with Philips CX50 machines. CECT examinations were performed with a Philips Brilliance 64, and CEMRI examinations with a Philips Intera 1.5 Tesla (since mid year 2010 Philips Ingenia 3T).

The CIS department is part of the Imaging Centre of our hospital.[5-7] All examinations of all imaging modalities are recorded by the shared radiology information system (RIS, Gapit®, i-Soft, Mannheim, Germany) and all images, including ultrasound pictures and video loops, are recorded in the PACS (Sectra®).

We analyzed data on the overall application of CEUS in our hospital. For the imaging of focal liver lesions, the main indication for CEUS today (see Table 1), we also compared the numbers of CECT and CEMRI examinations and calculated the costs on the basis of full-cost pricing as provided by Schuler et al.[8,9]

Table 1. Breakdown of CEUS examinations (n=743) by different specialties (CIS, Brüderkrankenhaus Trier, 2011).

Liver	381	Parathyroid	9	Abdominal cavity	2
Kidney	115	Retroperitoneum	8	Abdominal wall	2
Drainage	99	Soft tissue	7	Urinary bladder	1
Aorta post EVAR	37	Lung	5	Testicles	1
Spleen	27	Adrenal	5	Thyroid	1
Pancreas	20	US-guided cholangiogram	5	Vena cava	1
Arteries*	16	Bowel	4		
Bile tract (i.v.)	12	Thorax	4		

EVAR: Endovascular aortic repair.
** 11 carotid + 5 peripheral*

Results

Implementation of CEUS in daily practice

CEUS requires a number of special preconditions that do not exist as a matter of course in a conventional ultrasound unit.10 The need is for CEUS-capable US-machines (high end), special training of doctors (in our experience, two years minimum), special education of support staff, and specific changes in work routine.

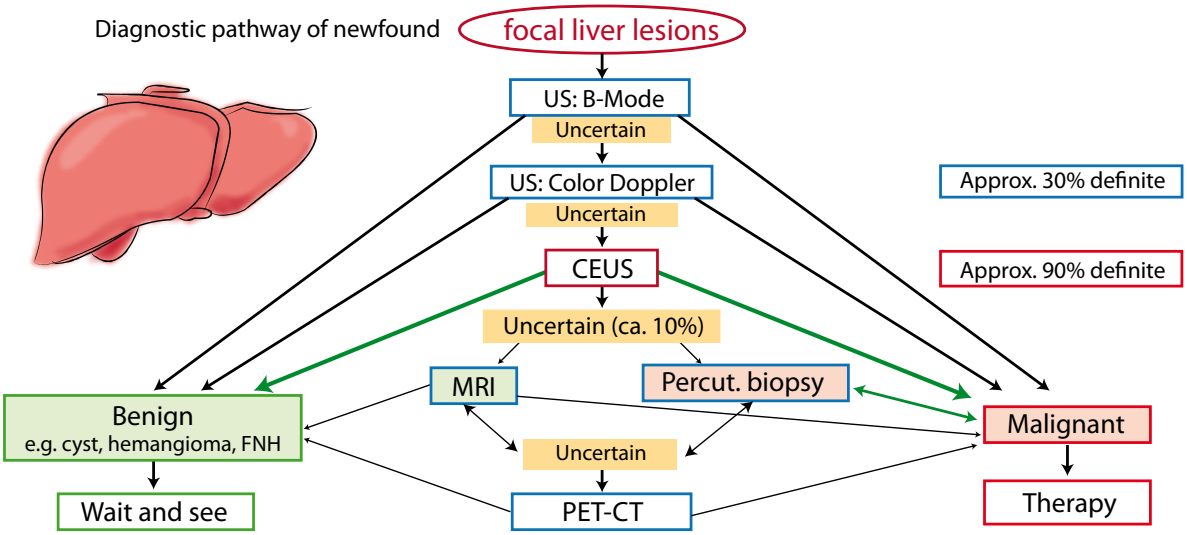
Due to the growing numbers of CEUS (Figure 1) and interventional procedures, our centre changed to work with "in-room assistance" on a regular basis.

We even had to enlarge examination rooms to accommodate the greater workload and new standard ultrasound working teams (typically comprising at least two people – a doctor and support staff).

Consequences of CEUS in imaging of focal liver lesions

In the years up to 2009, CEUS of focal liver lesions had become a routine procedure in our department, with reliable results compared to CECT or CEMRI studies of the same cases. Considering the patients' hospitalization period, radiation load and comfort, we started to try and spare double and even triple examinations of CEUS, CECT and CEMRI in cases in which the first modality was technically adequate and led to a consistent and plausible result. For this purpose, radiologists, CEUS doctors, oncologists and surgeons of our hospital negotiated and finally agreed on an "imaging pathway" on the basis of published study results,[11] as described in Figure 2.

Figure 2. Imaging pathway for focal liver lesions (Brüderkrankenhaus Trier, 2010).[11]



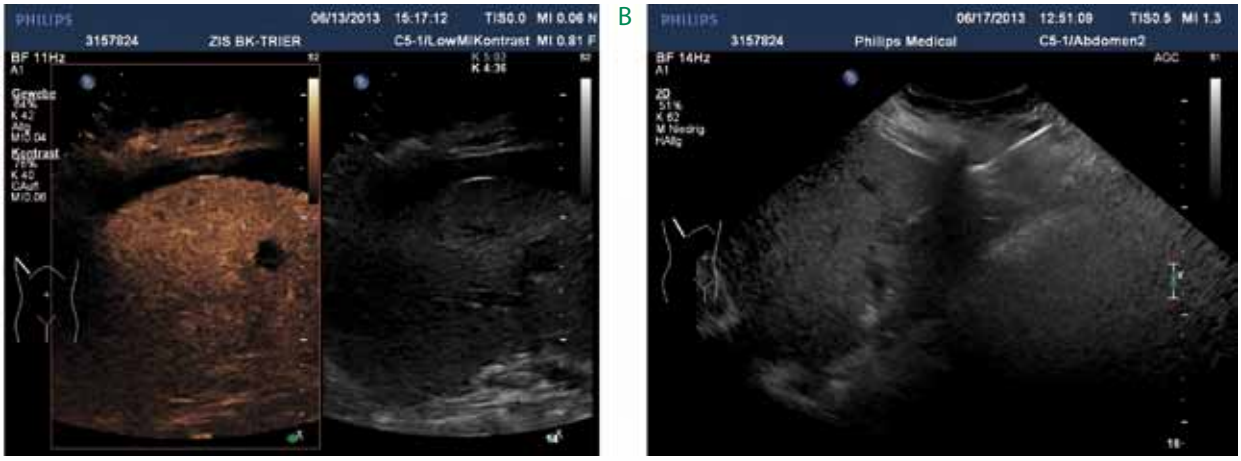
Improvement of patient management with CEUS

Numerous publications state that CEUS can compete with CT and MRI in terms of diagnostic accuracy, not only for focal liver lesions, but also in a still growing number of non-hepatic applications.[1-4,12-14] In addition, CEUS is advantageous as it does not suffer the same drawbacks as CT or MRI with regard to contrast administration: there is no exposure to iodine and no renal excretion and hence no risk of renal failure; likewise, there is no exposure to ionizing radiation.

Moreover, the patient's subjective view is important. The option to include contrast information in the ultrasound examination, which is often the first imaging procedure ("one stop shopping"), spares waiting time for the patient for the second imaging procedure spent in an anxious state of concern.
Finally, healthcare systems are currently in a fundamental situation of scant economic resources and hence in many countries hospitals are now in a competitive situation. Both these aspects push the care provider to efficiency. Time-effective optimization of patient paths through a conventional set of procedures per case is one major issue. Another is innovation that spares part of the conventional set of procedures needed per case. Such an innovation is provided by the introduction of CEUS. Conventional ultrasound was used as a low level imaging procedure to somehow influence the further application of high level imaging and other costly and time-consuming procedures. One main objective of the costly imaging coming beyond ultrasound was the addition of information on tissue vascularization by contrast enhancement.
Nowadays this vascularization information can be provided by CEUS as a matter of principle and in many cases be achieved in the primary imaging procedure of ultrasound. That makes the whole case process more streamlined and faster – and brings an economic advantage to a hospital in competition by sparing hospitalization time and the costly high level imaging it entails.
Figures 3-6 show CEUS images of cases with malignant and benign focal liver lesions, a kidney tumour and a surprising finding in the pelvic region.

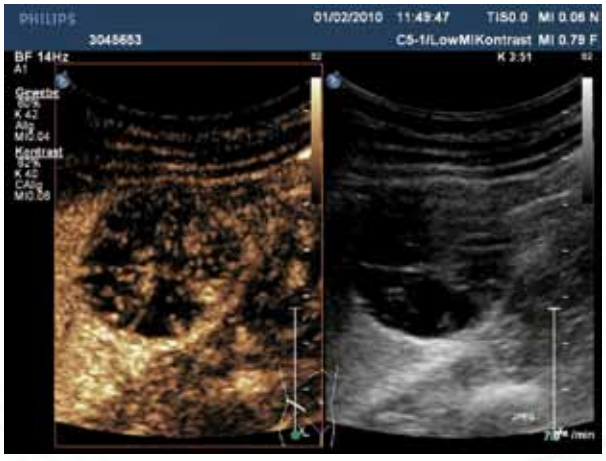
Figure 3

A B



Female patient, 88 yo. May 31, 2013: Emergency unit for worsening of general condition and oedema: erysipelas left lower leg, pneumonia, urinary infection, renal insufficiency, anaemia. June 6, 2013: US abdomen (poor examining conditions): 1 focal liver lesion, 23 mm, ascites. June 13, 2013: CEUS liver: 2 focal liver lesions (FLL) suspicious for metastases (contrast washout in late phase, see fig. 3A). June 17, 2013: US-guided biopsy of FLL (see fig. 3B) after aspiration of ascites: poorly differentiated adenocarcinoma, unknown primary, tumour cells also in ascites. June 27, 2013: exitus after steady worsening. Conclusion: no CT and no MRI were performed. All the evidence necessary for the decisions to be made to manage this case could be established by ultrasound, including US-guided biopsy.

Figure 4

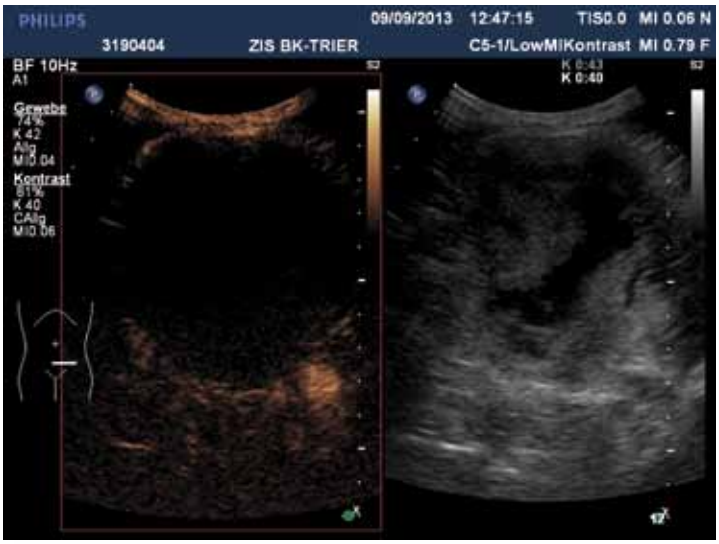


Female patient, 29 yo. Feb. 01, 2010: referral for Bosniak 2F cyst rt. kidney (ext. CT). Fundamental B-mode US: cyst with broad septae. CEUS: septae with pronounced perfusion, strong suspicion of renal cell carcinoma (RCC, see figure). Feb. 10, 2010: right side partial renal resection. Histopathology: cystic RCC (pT1b, pNx). Follow-up: no recurrence. Conclusion: in a young female patient no internal/ second CT was necessary to verify the indication for surgery for malignant kidney cyst.

Figure 5

Female patient, 46 yo. Oct. 3, 2011: resuscitation after fulminant lung embolism. Thrombolytic therapy, stabilization, secondary worsening and consumptive coagulopathy for haemorrhage of left liver lobe. Oct. 4, 2011: CEUS (bedside with compact machine, see figure): microbubbles invading a non-enhanced haematoma demonstrating active bleeding left LL. Consecutive CT angiography: bleeding stagnant. Recovery, Oct. 24, 2011: discharge for rehab with phenprocoumon. Conclusion: in a life-threatening haemorrhage at the ICU, patient transport to CT only after bedside CEUS proof of active bleeding.

Figure 6



Male patient, 83 yo. Sept. 09, 2013: fast growing (8 cm), clinically evident tumour left iliac region, suspected metastasis of malignant melanoma left toe V (2009). US-guided biopsy requested. Fundamental US: lesion left iliac region with suggestive features for haematoma. CEUS instead of biopsy: No CM uptake (see figure). Fine-needle biopsy: old blood.
Final diagnosis: diffuse plasmacytoma of spine and pelvic bones, haematoma left iliac region in anticoagulant therapy. Conclusion: avoidance of a misleading histopathologic exam by revealing a suspected tumour to be an avascular haematoma instead.

Cost-effectiveness of CEUS

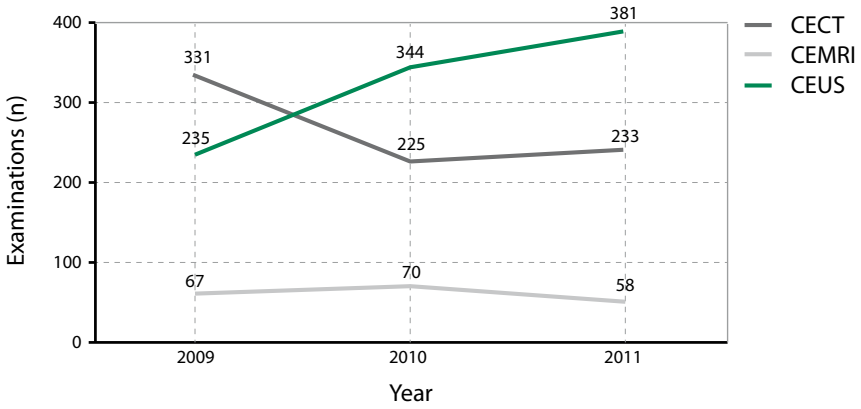
But isn´t CEUS expensive? Recently, Schuler et al. contributed greatly to discussions over the costs of diagnostic imaging.[8,9] According to their realistic models based on full-cost pricing in Germany in 2010, a CT examination of the liver with 3 contrast phases costs €198.09 with a 16-detector machine or €227.97 with a 64-detector machine. Likewise, a CEMRI examination of the liver at 1.5 Tesla costs €238.83. In contrast, a CEUS examination of the liver costs €141.74 with a level 3 machine or €121.73 with a level 2 machine.[9]

After we had introduced the above-mentioned algorithm in imaging of focal liver lesions (Figure 2), we wanted to find out whether we would really succeed in changing daily routines in this field. For this reason we analyzed the numbers of contrast-enhanced (multiphase) examinations of the liver from 2009 to 2011 on the shared database of the radiology information system (RIS) that consistently records the data of all procedures in our centre. Figure 7 shows the examination numbers of 3-phase contrast imaging of the liver in our hospital.

The data suggest that after setting up the algorithm CEUS has taken about a third of the previous upper abdomen CECT workload. This hypothesis is supported by the almost exact equivalence of the CECT decrease and the CEUS increase. This effect remained stable in the second year.

If we apply Schuler's prices for the liver imaging modalities, we find that the above CECT+CEUS set of examinations in 2011 in Figure 7 was €5,538 cheaper than that in 2009, assuming Schuler's presumption of one vial of SonoVue® per case.

Figure 7. Contrast-enhanced (multiphase) examinations of the liver (ZfRNSN, Brüderkrankenhaus Trier).



In an early phase of CEUS implementation we noticed one amazing effect. Despite a growing number of CEUS examinations, the consumption of contrast agent decreased. In 2008 we performed 214 CEUS examinations and consumed 184 vials of SonoVue®. In 2009 we performed 305 CEUS examinations (+91), and consumed only 150 (-34) vials of SonoVue®.
One precondition for the decreased consumption of contrast agent is that modern ultrasound machines need less than 1 vial of SonoVue® per examination. However, possible savings in terms of contrast agent can only be realized if the remaining SonoVue® is used before its expiry date, instead of disposing of it. For efficient utilization of contrast agent a sufficient frequency of CEUS examinations is necessary, e.g. 4 x CEUS exams per day means using 4 x 1.2 ml SonoVue® portions for 4 examinations from one vial.[10]

Considering that since 2009 we have an average consumption of less than 2.4 ml SonoVue® per CEUS case, the savings induced by the CEUS-based imaging pathway only for focal liver lesions add up to more than €8,000 per year.

In our experience this effect applies analogously to the smaller fields of CEUS imaging in which hospitalization time, patient discomfort and money can be saved in a comparable dimension when CM-based vascularization information can be achieved during the ultrasound exam (which is normally the first-line imaging procedure) instead of performing a second "big machine" exam at a later point.

CONCLUSIONS

- Unlike CECT and CEMRI, CEUS is capable of answering many questions relating to tissue perfusion, etc.
- CEUS is cheaper than CECT and CEMRI.
- The main risks of contrast agents like renal failure and iodine exposure can be avoided by CEUS.
- Substitution of CECT or CEMRI by CEUS in a "one stop shopping" procedure with standard ultrasound normally results in a saving of hospitalization time.
- Regarding contrast-enhanced liver diagnostics, in the setting of an imaging centre a shift from CECT to CEUS with SonoVue® could be established, saving a mid-size hospital an amount in the region of more than €8,000 per year.
- The same saving effects through CEUS are most likely to appear also in the other indications for contrast-enhanced slice imaging.

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