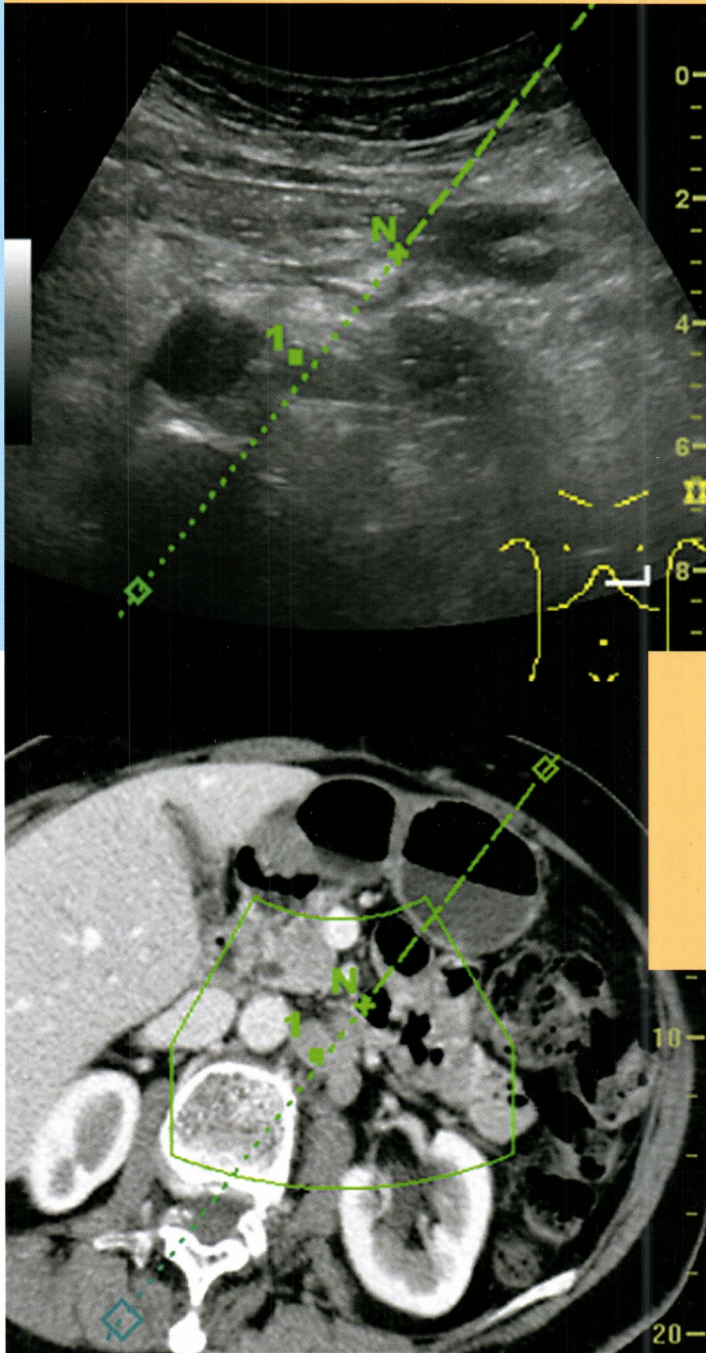




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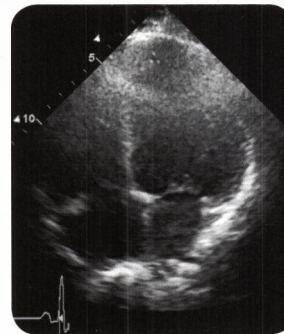
OPTISON™ 0,19 mg/ml Injektionsdispersion
Wirkstoff: Perflutrenhaltige Mikrosphären aus hitzebehandeltem Albumin vom Menschen. **Zusammensetzung:** OPTISON™ besteht aus perflutrenhaltigen Mikrosphären aus hitzebehandeltem Albumin vom Menschen, die in einer 1%igen Albuminlösung vom Menschen suspendiert sind. Konzentration: 5–8 x 10⁹/ml perflutrenhaltige Mikrosphären mit einem mittleren Durchmesser von 2,5–4,5 µm. Die durchschnittliche Menge an Perflutren beträgt 0,19 mg pro ml OPTISON™. Sonstige Bestandteile: Humanalbumin, Natriumchlorid, N(2)-Acetyl-DL-tryptophan, Octansäure, Natriumhydroxid (pH-Einstellung), Wasser für Injektionszwecke. 1 ml enthält 0,15 mmol (3,45 mg) Natrium. **Anwendungsgebiete:** Dieses Arzneimittel ist ein Diagnostikum. OPTISON™ ist ein lungengängiges Ultraschallkontrastmittel für die Echokardiographie zur Anwendung bei Patienten mit Verdacht auf bzw. mit nachgewiesenen Herzerkrankungen. OPTISON™ kontrastiert die Herzkammern und verstärkt das Echosignal der linksventrikulären Endokardgrenze, wodurch die Sichtbarkeit der Wandbewegungen verbessert wird. OPTISON™ soll ausschließlich bei Patienten angewendet werden, bei denen die Untersuchung ohne Kontrastverstärkung zu keinem ausreichenden Ergebnis geführt hat. **Art und Dauer der Anwendung:** OPTISON™ ist ausschließlich von Ärzten anzuwenden, die über Erfahrungen auf dem Gebiet der Bildgebung mittels diagnostischem Ultraschall verfügen. Das Arzneimittel ist für die Darstellung der linken Herzkammer nach intravenöser Injektion bestimmt. Da ein optimaler Kontrast sofort nach der Verabreichung von OPTISON™ erreicht wird, muss die Ultraschalluntersuchung während der Injektion erfolgen. **Gegenanzeigen:** Überempfindlichkeit gegen den Wirkstoff oder einen der sonstigen Bestandteile. OPTISON™ darf nicht angewendet werden bei Patienten mit pulmonalem Hochdruck mit einem systolischen Druck in den Lungenarterien von über 90 mm Hg. **Warnhinweise und Vorsichtsmaßnahmen für die Anwendung:** Fälle von Überempfindlichkeit wurden berichtet. Daher ist Vorsicht geboten. Die Vorgehensweise für das Auftreten einer schwerwiegenden Reaktion ist im Voraus zu planen, damit erforderliche Arzneimittel und Ausrüstung für eine sofortige Behandlung bereitstehen. Die Erfahrungen bei der Anwendung von OPTISON™ bei Patienten mit schwerwiegenden Erkrankungen sind begrenzt. Es gibt wenige klinische Erfahrungen mit der Anwendung von OPTISON™ bei Patienten mit bestimmten schweren Herz-, Lungen-, Nieren- und Lebererkrankungen. Dazu gehören Atemnotsyndrom der Erwachsenen (ARDS), künstliche Beatmung mit positiv-endexpiratorischem Druck, schwere Herzinsuffizienz (NYHA IV), Endokarditis, akuter Myokardinfarkt mit fortschreitender oder instabiler Angina, Patienten mit Herzklappenprothesen, akute

Stadien systemischer Entzündungen oder Sepsis, bekanntes hyperkoagulables System und/oder rezidivierende Thromboembolie sowie terminale Leber- oder Niereninsuffizienz. OPTISON™ soll bei diesen Patientengruppen nur nach sorgfältiger Abwägung angewendet werden, wobei die Patienten während und nach der Anwendung engmaschig zu überwachen sind. Eine andere Form der Verabreichung als unter Art und Dauer der Anwendung beschrieben (z. B. intrakoronare Injektion) wird nicht empfohlen. Zu den Standardmaßnahmen zur Verhinderung von Infektionen, die durch die Anwendung von Arzneimitteln verursacht werden können, die unter Verwendung von menschlichem Blut oder Plasma hergestellt werden, zählen die sorgfältige Auswahl der Blutspender, die Untersuchung einzelner Blutspenden und von Mischplasmen auf bestimmte Infektionsmarker sowie wirksame Maßnahmen während der Herstellung zur Inaktivierung und/oder Entfernung von Viren. Trotz dieser Vorkehrungen kann bei der Anwendung von Arzneimitteln, die unter Verwendung von menschlichem Blut oder Plasma hergestellt werden, die Möglichkeit einer Übertragung von infektiösem Material nicht völlig ausgeschlossen werden. Dies gilt auch für bisher unbekannte oder neue Viren oder sonstige Arten von Infektionen. Es gibt keine Berichte über die Übertragung von Viren durch Albumin, das gemäß den Vorgaben des Europäischen Arzneibuchs mittels herkömmlicher Verfahren hergestellt wurde. Es wird empfohlen, bei jeder Anwendung von OPTISON™ bei einem Patienten Namen und Chargennummer zu notieren, um eine Verbindung zwischen dem Patienten und der jeweiligen Charge des Arzneimittels zu haben. Kontrastverstärkte Ultraschalluntersuchungen mit OPTISON™ sind unter EKG-Überwachung durchzuführen. Die Anwendung von Ultraschall-Kontrastmitteln zeigte in Studien am Tier biologische Nebenwirkungen (z. B. endotheliale Zellschäden, Kapillarruptur) durch Wechselwirkung mit dem Ultraschall. Obwohl diese biologischen Nebenwirkungen beim Menschen nicht beobachtet wurden, werden ein niedriger mechanischer Index und enddiastolisches Triggern empfohlen. Die Wirksamkeit und Unbedenklichkeit bei Patienten unter 18 Jahren ist nicht untersucht worden. **Schwangerschaft und Stillzeit:** Die Unbedenklichkeit von OPTISON™ bei der Anwendung während der Schwangerschaft beim Menschen wurde nicht untersucht. Bei trächtigen Kaninchen, denen während der Organogenese täglich Dosen von 2,5 ml/kg (etwa das 15-fache der maximal empfohlenen klinischen Dosis) verabreicht wurden, ist eine mütterliche und embryo-fetale Toxizität beobachtet worden, die eine erhöhte Häufigkeit von leichten bis schweren Ventrikel-erweiterungen im Hirn der sich entwickelnden Kaninchen-embryos beinhaltet. Die klinische Relevanz dieser Beobachtung ist nicht bekannt. OPTISON™ soll während der

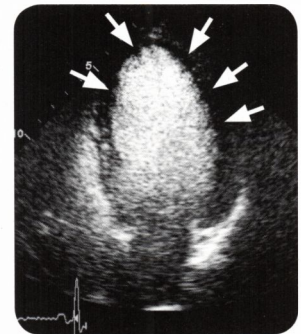
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Schwangerschaft nicht angewendet werden, sofern nicht der Nutzen das Risiko übersteigt und die Anwendung vom Arzt als notwendig erachtet wird. Es ist nicht bekannt, ob OPTISON™ in die Muttermilch übertritt. Daher ist bei der Anwendung während der Stillzeit Vorsicht geboten. **Nebenwirkungen:** Unerwünschte Reaktionen auf OPTISON™ sind selten und in der Regel nicht schwerwiegend. Im Zusammenhang mit der Gabe von Humanalbumin ist über vorübergehende Geschmacksstörungen, Übelkeit, Gesichtsröte, Hautausschlag, Kopfschmerzen, Erbrechen, Schüttelfrost und Fieber berichtet worden. Das Auftreten von anaphylaktischen Reaktionen wurde mit der Verabreichung von humanalbuminhaltigen Produkten in Verbindung gebracht. Die Nebenwirkungen, die nach Anwendung von OPTISON™ in klinischen Studien der Phase III am Menschen berichtet wurden, waren leicht bis mittelschwer mit nachfolgender vollständiger Wiederherstellung des Patienten. In klinischen Studien mit OPTISON™ wurden unerwünschte Ereignisse mit folgender Häufigkeit beobachtet (Sehr häufig $\geq 1/10$; häufig $\geq 1/100$ bis $< 1/100$; gelegentlich $\geq 1/1.000$ bis $< 1/100$; selten $\geq 1/10.000$ bis $< 1/1.000$; sehr selten $< 1/10.000$), nicht bekannt (Häufigkeit auf der Grundlage der verfügbaren Daten nicht abschätzbar): **Erkrankungen des Blutes und des Lymphsystems:** Gelegentlich: Eosinophilie. **Erkrankungen des Nervensystems:** Häufig: Dysgeusie (Geschmacksstörungen), Kopfschmerzen. Selten: Tinnitus, Schwindel, Parästhesien. **Augenerkrankungen:** Häufigkeit nicht bekannt: Sehstörungen. **Herzerkrankungen:** Selten: Ventrikuläre Tachykardie. **Erkrankungen der Atemwege, des Brustraums und Mediastinums:** Gelegentlich: Dyspnoe. **Gefäßerkrankungen:** Häufig: Gesichtsrötung. **Erkrankungen des Gastrointestinaltrakts:** Häufig: Übelkeit. **Allgemeine Erkrankungen und Beschwerden am Verabreichungsort:** Häufig: Wärmegefühl. Gelegentlich: Brustschmerzen. **Erkrankungen des Immunsystems:** Häufigkeit nicht bekannt: Allergieähnliche Symptome (z. B. anaphylaktoidale Reaktion oder Schock, Gesichtsschwellung, Urtikaria). **Verschreibungspflichtig.** GE Healthcare AS, N-0401 Oslo, Norwegen. Lokaler Vertreter des Zulassungsinhabers: GE Healthcare Buchler GmbH & Co. KG, 38110 Braunschweig. Stand: November 2010.

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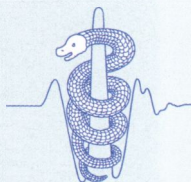
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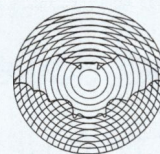
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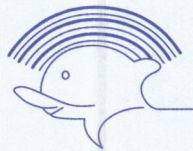
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There is a continuous trend with the journal for articles in English language, currently clearly more than 50%. Also, all of the German-language articles feature detailed summaries in English – organised according to Methods/Results/Conclusion. In addition, all figures are accompanied by legends in English.

All members of EFSUMB receive the present first issue of 2012, which also includes the EFSUMB Newsletter. In addition, 2 pages of EFSUMB news in each issue will enable us to keep in touch with members on a more regular basis. Among others the plans for 2012 foresee the publication of the least 2 sets of important guidelines from EFSUMB, one of which is included in the present issue.

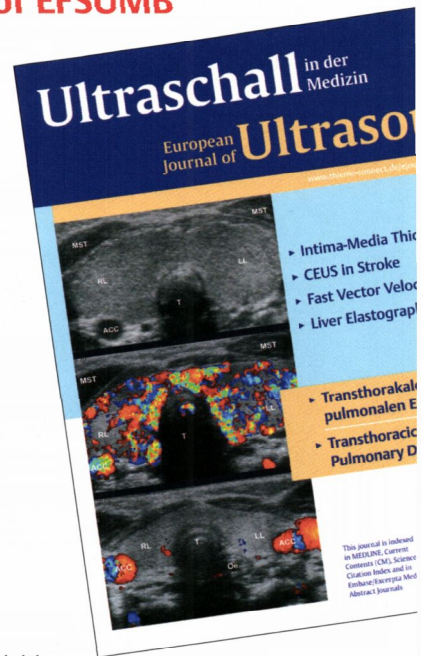
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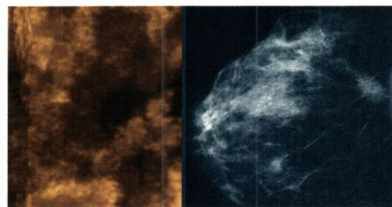
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Stanzbiopsie eines kleinen retroperitonealen Lymphoms gestützt durch Bildfusion und elektromagnetischem Nadel-Tracking

Core Needle Biopsy from a Small Retroperitoneal Lymphoma Guided by Image-Fusion and Electromagnetic Needle Tracking

Einleitung

Die Bildfusion („image fusion“), bei der eine zuvor durchgeführte CT- oder MRT-Untersuchung zusammen mit Echtzeit-Ultraschall-Aufnahmen und elektromagnetischem Nadel-Tracking aufgezeichnet wird, wurde kürzlich in diesen Arbeiten beschrieben (C. Ewertzen et al. Ultraschall in Med 2011; 32: 191–197; A. Hakime et al. Cardiovasc Intervent Radiol 2011: E-Publikation vor Druck). Bei Verwendung dieser Methoden ist es möglich, sehr kleine Läsionen und solche, die in Bereichen liegen, die dem Ultraschall nicht zugänglich sind (z. B. Läsionen hinter Luft), darzustellen. Des Weiteren ist ein perkutaner ultraschallgestützter Eingriff möglich, da die Nadelspitze und die Punktionsstrecke elektronisch sowohl in US- als auch in CT-/MRT-Bildern sichtbar gemacht werden kann.

Die Nadel für das elektromagnetische Nadel-Tracking besteht aus einem dünnen Magnetsensordraht von 0,9 mm, der in eine Trocharnadel eingesetzt ist, die von einer äußeren Kanüle von 16 Gauge (1,6 mm) umhüllt ist, durch die Biopsienadeln von mehr als 16 Gauge eingesetzt werden können (Abb. 1).

Mittels elektromagnetischem Tracking-System kann das Ziel markiert werden. Es wird mit einem Plus (+) gekennzeichnet, wenn es sich in der Scanebene befindet und mit Kästen verschiedener Größen und Farben, wenn sich das Ziel außerhalb der Ebene befindet (Abb. 2).

Das Mantelzell-Lymphom ist ein seltenes Non-Hodgkin-Lymphom, das nur 6% aller Fälle mit Non-Hodgkin-Lymphom ausmacht. Das mittlere Alter bei Diagnosestellung beträgt 63 Jahre und die Erkrankung tritt mit tastbaren Lymphknoten und systemischen Symptomen in Erscheinung. Die 5-Jahres-Überlebensrate beträgt etwa 25% (D.L. Longo et al. Harrison's principles of internal medicine, 18ed. Mc Graw Hill, New York, 2011). Wie bei jeder Lymphomdiagnostik ist die Histologie des Lymphknotens entscheidend, um eine genaue Charakterisierung durchzuführen.

Wir berichten über einen Fall, bei dem Bildfusion und elektromagnetisches Nadel-Tracking angewandt wurden, um ein kleines Lymphom, das in der Nähe der Bauchschlagader lag, zu lokalisieren und eine Biopsie zu entnehmen.

Fallbeschreibung

Eine 75-jährige Frau, die aufgrund eines Mantelzell-Lymphoms vor 7 Jahren bereits erfolgreich mit Chemotherapie behandelt wurde, unterzog sich einer Routine-Nachuntersuchung mittels

Introduction

Image fusion, where a previously obtained CT or MRI examination is co-registered with real-time ultrasound (US) images and electromagnetic needle tracking have been described in recent papers (C. Ewertzen et al. Ultraschall in Med 2011; 32: 191–197; A. Hakime et al. Cardiovasc Intervent Radiol 2011: epub ahead of print). Using these techniques, it is possible to visualize very small lesions and lesions in areas inaccessible to US (i. e. lesions behind air). Furthermore, percutaneous US-guided intervention is possible, because the needle tip and the route of puncture can be visualized electronically on both the US and CT/MRI images.

The needle for electromagnetic needle tracking consists of a small magnetic sensor wire of 0.9 mm inserted into a trochar needle, which is covered by an outer cannula of 16 gauge (1.6 mm) through which biopsy needles of more than 16 gauge may be inserted (Fig. 1).

Using the electromagnetic tracking system a target may be marked. It is marked with a plus (+) when being in the scan plane and displayed with boxes of different sizes and colors when the target is out of plane (Fig. 2).

Mantle cell lymphoma is a rare non-Hodgkin lymphoma comprising only 6% of the non-Hodgkin lymphoma cases. Median age at diagnosis is 63 years and the disease presents with a palpable

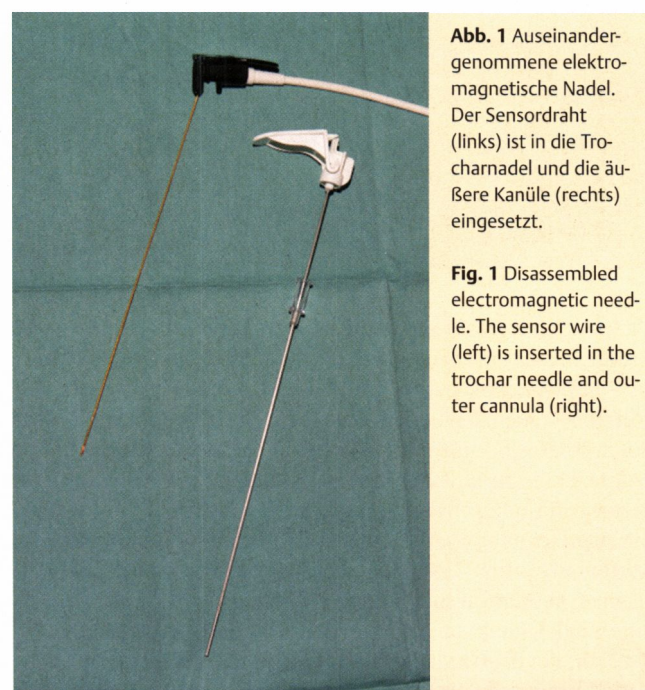


Abb. 1 Auseinandergenommene elektromagnetische Nadel. Der Sensordraht (links) ist in die Trocharnadel und die äußere Kanüle (rechts) eingesetzt.

Fig. 1 Disassembled electromagnetic needle. The sensor wire (left) is inserted in the trochar needle and outer cannula (right).

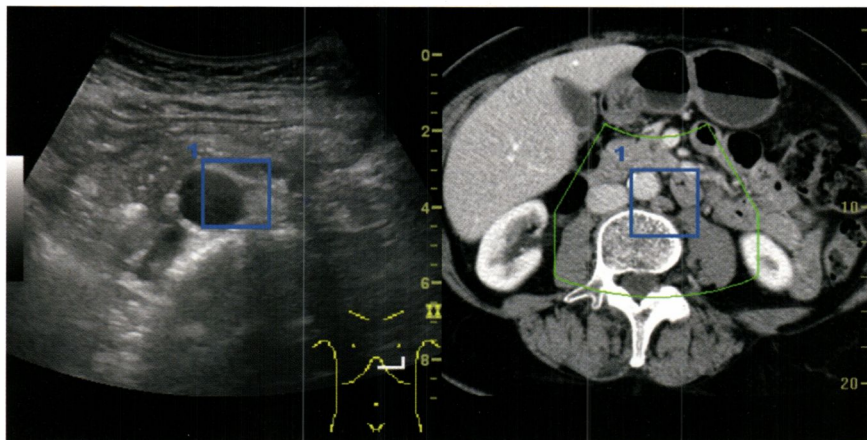


Abb. 2 Gemeinsam aufgenommene Bilder im US (links) und im CT (rechts). Die blauen Kästen zeigen das markierte Ziel (1), das sich außerhalb der Ebene befindet. Der grüne Kasten im CT-Bild stimmt mit dem US-Bild überein. Zu beachten ist, dass die Skalierung der Bilder nicht übereinstimmt.

Fig. 2 Co-registered images of US (left) and CT (right). The blue boxes indicate the marked target (1) being off-plane. The green box on the CT image corresponds to the US image. Please note that the scaling of the images is not identical.

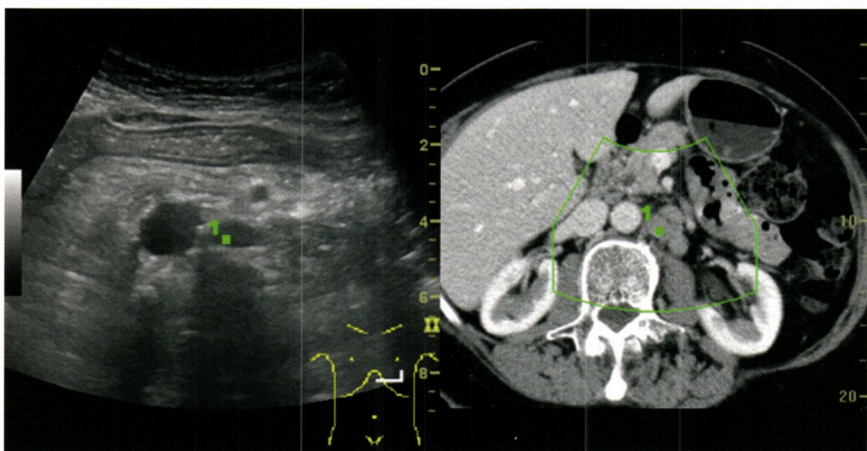


Abb. 3 Das kleine Lymphom ist mit „1“ gekennzeichnet.

Fig 3 The small lymphoma is marked with „1“.

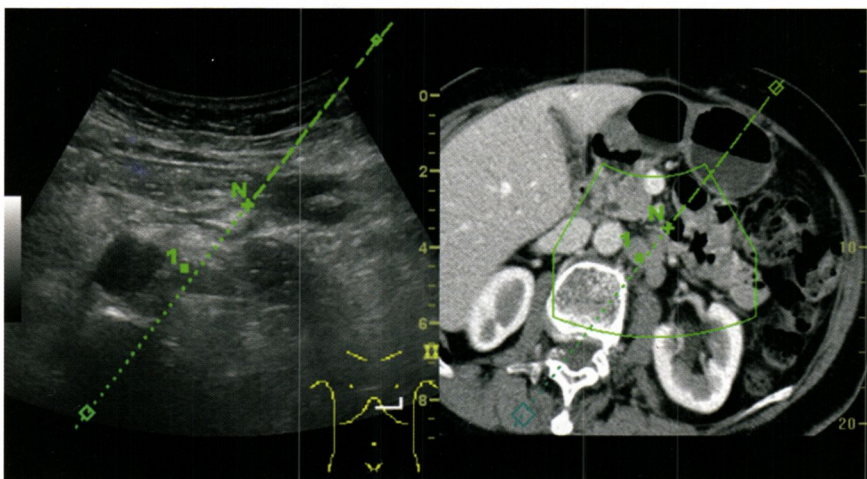


Abb. 4 Der Verlauf der Punktion ist in beiden Bildern elektronisch gekennzeichnet. Die Nadelspitze ist mit „N+“ markiert, wenn sie sich in der Ebene befindet. Die gestrichelte Linie zeigt die bereits zurückgelegte Strecke an. Die gepunktete Linie zeigt den geplanten Punktionsverlauf an. Das Lymphom ist mit „1“ gekennzeichnet.

Fig. 4 The route of puncture is electronically marked on both images. The needle tip is marked with a „N+“ when being in-plane. Dashed line indicates the route already travelled. Dotted line indicates the projected route of puncture. The lymphoma is marked with „1“.

CT. Die CT-Untersuchung zeigte 3 vergrößerte Lymphknoten, der Größte in der Nähe der Bauchaorta maß 14 x 31 mm (Abb. 3). Zur Diagnostik wurde die Patientin zur perkutanen US-gestützten Stanznadelbiopsie überwiesen. Das Verfahren wurde durch Bildfusion mit einer CT, die 17 Tage zuvor durchgeführt wurde, unterstützt. Anfangs war das Lymphom wegen überlagerter Luft im Darm sonografisch nicht sichtbar. Eine gemeinsame Aufzeichnung wurde unter Zuhilfenahme des Nabels, der Aortenbifurkation und von verschiedenen anderen anatomischen Orientierungspunkten durchgeführt und es wurde eine gute Angleichung der Bilder erzielt. Da das kleine Lymphom in der Nähe der Bauchaorta lag, wurde die elektromagnetische Nadelführung mit einer 16-Gauche-Nadel, die einen elektroma-

lymph node and systemic symptoms. The 5-year survival is about 25% (D.L. Longo et al. Harrison's principles of internal medicine, 18ed. Mc Graw Hill, New York, 2011). As for all lymphoma diagnostics, histology from a lymph node is crucial to establish the correct characterization.

We present a case where image fusion and electromagnetic needle tracking have been used to localize and biopsy a small lymphoma lying in proximity to the abdominal aorta.

netischen Sensor enthielt, durchgeführt, um sicherzugehen, dass die Biopsienadel richtig platziert wurde (Abb. 4). Durch diese Nadel wurde eine automatische 18-Gauge-Stanzbiopsienadel durchgeführt und 3 Biopsien konnten gewonnen werden. Es wurden keine Komplikationen beobachtet. Die Histologie ergab ein Mantelzell-Lymphom. Zur Stadieneinteilung wurde eine PET/CT durchgeführt und eine einschlägige Chemotherapie wurde eingeleitet.

Diskussion

Wir bewerteten die Bildfusion und die elektromagnetische Nadelführung bei der Biopsie eines kleinen retroperitonealen Lymphoms. Dieses identifizierten wir erfolgreich und erhielten charakteristische Biopsien davon.

In der Lymphomdiagnostik sind immer histologische Biopsien für die genaue Klassifizierung nötig. Die Behandlung kann nicht eingeleitet werden, bevor die Diagnose gesichert ist, deshalb ist die Biopsie der entscheidende Schritt. Leicht vergrößerte retroperitoneale Lymphknoten sind jedoch in Folge von Luftüberlagerungen oder Fettleibigkeit nicht immer leicht zu erkennen. Darüber hinaus kann die Lokalisation der Lymphknoten in Nähe der großen Gefäße schwierig sein.

Das elektromagnetische Nadel-Tracking der Nadelspitze ermöglicht die fortlaufende Darstellung der Nadelspitze während des gesamten Eingriffs, da die Nadelspitze am Bildschirm grün markiert ist. Es wurde gezeigt, dass die Erfolgsquote dieses Verfahrens der konventionellen bildgestützten Biopsie in einem Phantom gleicht (C. Ewertsen et al. *Ultraschall in Med* 2011; 32: 314–318). Bei der konventionellen bildgestützten Biopsie mit mechanischer Nadelführung kann sich die Registrierung der Echos der Nadelspitze schwierig gestalten, insbesondere in großen Tiefen und in Bereichen mit Luftüberlagerungen.

Die Bildfusion und das elektromagnetische Nadel-Tracking kann etwas zeitaufwendiger sein als die herkömmliche bildgestützte Biopsie, aber der Zeitaufwand wird mit zunehmender Erfahrung mit diesem System geringer. Wir empfehlen jedoch, dass diese Methode nur den schwierigen Fällen vorbehalten sein sollte, insbesondere in anatomischen Bereichen mit begrenztem US-Überblick.

Case Description

A 75-year-old female, who had been successfully treated with chemotherapy for mantle cell lymphoma seven years previously, underwent routine follow-up with CT. The CT examination showed three enlarged lymph nodes, the largest measuring 14 x 31 mm located close to the abdominal aorta (Fig. 3). The patient was referred to percutaneous US guided core needle biopsy for diagnosis. The procedure was guided by image fusion with a CT made 17 days previously. Initially, the lymphoma was invisible to US due to overlying air in the bowel. A co-registration was made using the umbilicus, the aortic bifurcation and several other anatomical landmarks, and a good alignment of the images was obtained. Because the small lymphoma was lying adjacent to the abdominal aorta, electromagnetic needle guidance with a 16-gauge needle containing an electromagnetic sensor was used to ensure that the biopsy needle was placed correctly (Fig. 4). Through this needle, an 18-gauge automatic core biopsy needle was passed and three biopsies were obtained. No complications were observed. Histology revealed mantle cell lymphoma. PET/CT was performed for staging and relevant chemotherapy was initiated.

Discussion

We evaluated image fusion and electromagnetic needle guidance for biopsy of a small retroperitoneal lymphoma. We successfully identified the small lymphoma and obtained representative biopsies from it.

In lymphoma diagnostics, histological biopsies are always needed for the specific classification. Treatment cannot be initiated before the diagnosis is established, thus biopsy is crucial. However, slightly enlarged retroperitoneal lymph nodes are not always easily identified due to overlying air in the bowel or obesity. Furthermore the location of the lymph nodes close to the large vessels may be challenging.

Electromagnetic needle tracking of the needle tip enables continuous visualization of the needle tip during the entire procedure, because the needle tip is electronically marked on screen. The rate of success of the method has been shown to equal conventional image-guided biopsy in a phantom (C. Ewertsen et al. *Ultraschall in Med* 2011; 32: 314–318). For conventional image guided biopsy with mechanical needle guidance the registration of the echoes from the needle tip may be difficult especially in large depths and in areas with overlying air.

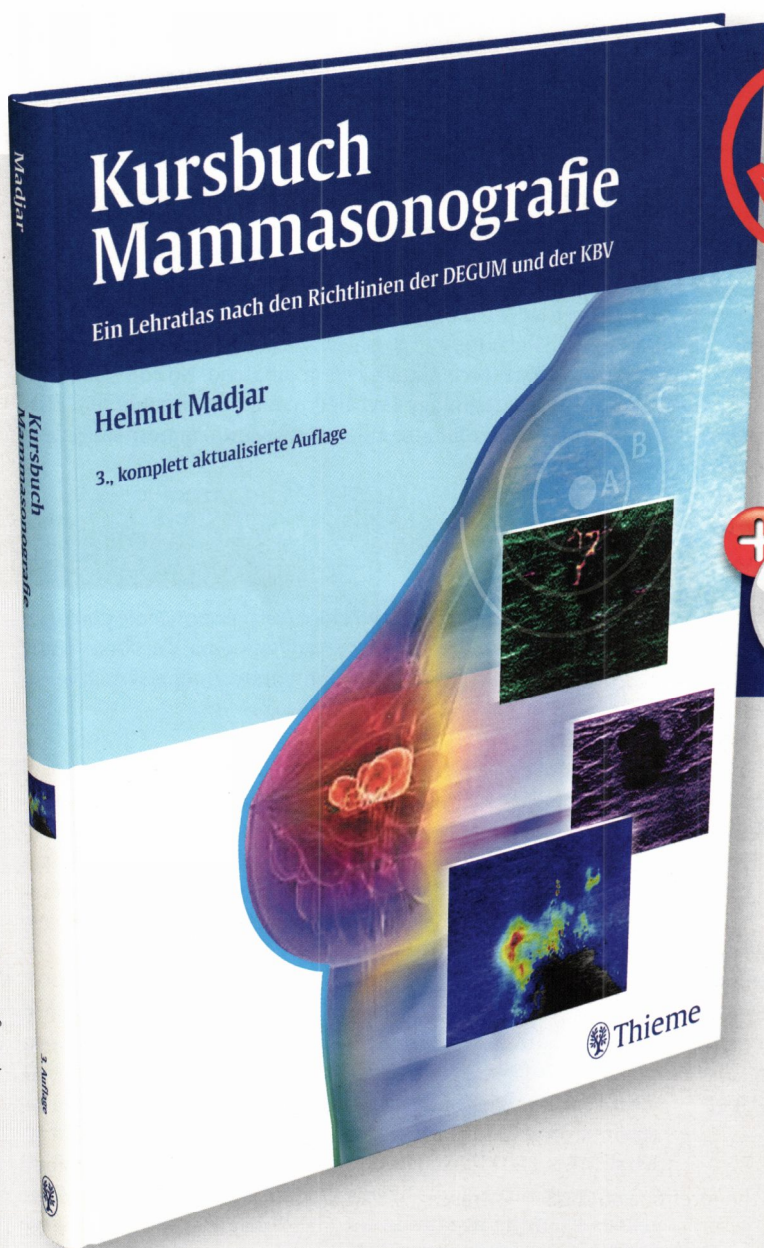
Image fusion and electromagnetic needle tracking may be more time consuming than conventional image guided biopsy, but the time spent decreases with increasing experience with the system. However, we recommend that the method should be reserved for difficult cases especially in anatomical areas with limited US overview.

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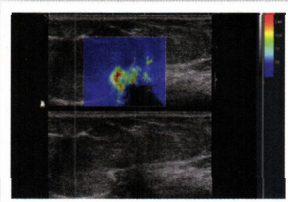
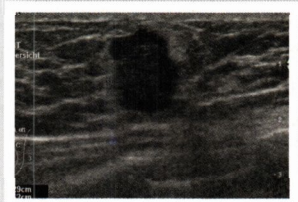
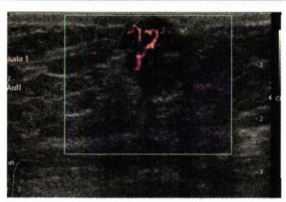
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The EFSUMB Guidelines on the Non-Hepatic Clinical Applications of Contrast Enhanced Ultrasound (CEUS): a New Dawn for the Escalating Use of This Ubiquitous Technique

EFSUMB-Richtlinien für nicht hepatische klinische Anwendungen der kontrastverstärkten Sonografie (CEUS): Anbruch einer neuen Ära mit zunehmender Anwendung dieser universellen Technik



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Bibliografie

DOI <http://dx.doi.org/10.1055/s-0031-1299141>

Ultraschall in Med 2011; 32: 5–7
© Georg Thieme Verlag KG
Stuttgart · New York · ISSN 0172-4614

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The publication this month of the new EFSUMB guidelines on the deployment of contrast-enhanced ultrasound (CEUS) in areas outside the liver marks an important milestone in the acceptance of this technique in the wider ultrasound community [1]. These guidelines are a natural evolution of the previous guidelines published in 2004 [2] and 2008 [3], with recognition of the rapid advancement and innovative use of CEUS outside the traditional use in the liver. The devolvement of the non-liver applications is timely; many researchers and clinicians are developing new areas in which CEUS is useful in improving the diagnostic capabilities of the ultrasound examination to the ultimate benefit of the patient. In this respect we must acknowledge the contribution made by numerous practitioners of ultrasound who continue to innovate, experiment and ultimately establish applications for the use of CEUS. These practitioners come from across the world, with many colleagues in Asia at the forefront of CEUS development. However it has been the European community that has lead on the development of CEUS over the last 15–20 years and it is only fitting that the European Federation for Societies in Medicine and Biology (EFSUMB) should take the lead in producing guidelines. This may change in due course with the interest the liver guidelines [2, 3] have generated and with future collaboration with the World Federation of Societies for Ultrasound in Medicine and Biology (WFUMB). Hopefully in the future colleagues worldwide will be drawn into this exciting phase in the evolution of the use of medical ultrasound.

The new guidelines encompass many new areas and outline the progress attained in previously

Die in diesem Monat veröffentlichten neuen EFSUMB-Richtlinien über den Einsatz der kontrastverstärkten Sonografie (CEUS) in anderen Einsatzgebieten als der Leber stellen einen wichtigen Meilenstein dar, was die Akzeptanz dieser Methode bei der größer werdenden Gemeinschaft der Ultraschall-Anwender anbelangt [1]. Diese Richtlinien sind die natürliche Weiterentwicklung der vorangegangenen 2004 [2] und 2008 [3] veröffentlichten Leitlinien, wobei der schnellen Weiterentwicklung und den innovativen Anwendungen von CEUS neben den traditionellen Leberanwendungen Rechnung getragen wird. Die Übertragung auf die nicht hepatischen Anwendungen ist zeitraubend; viele Forscher und Kliniker entwickeln neue Fachgebiete, in denen sich CEUS bewährt hat, wenn es darum geht, die diagnostischen Möglichkeiten der Sonografie zum größtmöglichen Nutzen für den Patienten zu verbessern. In diesem Zusammenhang müssen wir den Beitrag der zahlreichen Ultraschallanwender würdigen, die beim Einsatz von CEUS fortlaufend Neuerungen eingeführt, Versuche durchgeführt und schließlich die Anwendungen etabliert haben. Diese Ärzte kommen aus der ganzen Welt, darunter viele Kollegen aus Asien an vorderster Front der CEUS-Entwicklung. Es war jedoch die europäische Gemeinschaft, die zur Weiterentwicklung des CEUS in den letzten 15–20 Jahren geführt hatte, daher ist es angebracht, dass die „Europaen Federation for Societies in Medicine and Biology“ (EFSUMB) die führende Rolle bei der Erarbeitung dieser Richtlinien innehat. Dies mag sich in gegebener Zeit ändern, sowohl aufgrund des Interesses, das die Leber-Richtlinien [2, 3] hervorgerufen haben, als auch wegen der zukünftigen Zusammenarbeit mit der „World Fe-

detailed areas of use, all outside the liver. The guidelines are comprehensive and may be used as a "stand-alone" document; coverage of the background, agents, equipment, training, terminology and safety introduce the document, clearly and concisely written in a form understandable even to the novice user of CEUS. The range of organs and disease processes investigated is truly comprehensive and more are likely to follow [4–14]. Perhaps there are now few "frontiers" available for investigation!

However it is important to understand that all these new areas are in effect "off-label" to the use of the contrast agents, and are unlikely ever to become a "licensed" usage. This has been discussed in the guidelines but is worth emphasizing further and deliberating the consequences especially in paediatric applications; physician obligations are particularly pertinent to the further development for "off-label" use of CEUS.

As stated in the guidelines, the manufacturer of the contrast agent is obliged to promote use only in the areas that the product is licensed, designation for new applications require new data on safety and efficacy, which implies further cost and is very unlikely to be pursued by the manufacturer. The application for paediatric license with the products currently available will not be forthcoming and this application will remain "off-label". Furthermore any new developed product will not undergo clinical trials in children. Ultrasound is a highly desirable imaging technique in children; child-friendly, interactive, informative and safe without the burden of radiation exposure. Ultrasound contrast agents have a proven safety record in adults [15], and would offer much to the diagnostic capabilities of ultrasound in children [16].

The legal obligations to using any licensed product "off-label" are clearly defined by many medical regulatory authorities. The guidelines for prescribing medicines for use out-side the terms of their licence is sanctioned by the General Medical Council of the United Kingdom [17] under the following circumstances:

1. Be satisfied that it would better serve the patients' needs.
2. Be satisfied that there is sufficient evidence base and/or experience of using the medicine to demonstrate its safety and efficacy.
3. Take responsibility for prescribing the medicine and for overseeing the patient's care.

Furthermore acknowledgement is given in the regulations that this is most likely to arise in the use of such medicines in children. A point additionally acknowledged by the Royal College of Paediatrics and Child Health of the United Kingdom [18] in a document addressing the prescribing of unlicensed medicines in paediatric practice, and detailing in particular parental consent; "no further steps to prescribe unlicensed medicine is required other than that which is normally taken when prescribing licensed medicines". This implies that there is no special consent procedure required of the parents when using unlicensed medicine, the physician assumes responsibility. The basis for this is the opinion of paediatricians that children should be able to receive "adult" medicines that are safe, effective and appropriate for their condition.

Clearly the use of CEUS "off-label" is of benefit to all our patients, and we should not be constrained by the perceived lack of a licence for use in a particular area. The safety and efficacy in the licensed areas for the use of CEUS is beyond doubt with numerous studies to date. The really important step, to publish "off-label" studies, has been achieved with un-

deration of Societies for Ultrasound in Medicine and Biology" (WFUMB). Hoffentlich werden zukünftig weltweit Kollegen in diese spannende Entwicklungsphase der medizinischen Ultraschallanwendung miteinbezogen.

Die neuen Richtlinien umfassen viele neue Gebiete und skizzieren den Fortschritt, der in den zuvor detaillierten, ausnahmslos nicht hepatischen Einsatzbereichen erreicht wurde. Die Leitlinien sind umfassend und können wie ein „für sich stehendes“ Dokument benutzt werden; in dem in Hintergrund, Materialien, Geräteausstattung, Ausbildung, Terminologie und Sicherheit eingeführt wird; es ist sehr deutlich und präzise in einem, selbst für den Neuling der CEUS-Anwendung, verständlichen Stil geschrieben. Die Bandbreite der untersuchten Organe und Erkrankungen ist umfassend und wird sich wahrscheinlich noch erweitern [4–14]. Vielleicht ergeben sich jetzt einige neue „Grenzgebiete“ für weitere Forschung!

Allerdings sollte man wissen, dass bei all diesen neuen Fachgebieten die „Off-label“-Heilanzwendung von Kontrastmitteln gilt, bei denen es kaum je zu einer „lizenzierter“ Anwendung kommen dürfte. Dies wurde in den Richtlinien diskutiert, aber es ist wichtig, es besonders hervorzuheben und die Folgen hierfür insbesondere bei der Anwendung in Kindern zu bedenken; zu den Pflichten des Arztes gehört insbesondere die entsprechende Weiterentwicklung der „Off-label“-Anwendung des CEUS.

Wie in den Richtlinien ausgeführt, ist der Hersteller eines Kontrastmittels verpflichtet, die Anwendung nur in Gebieten, in denen das Produkt lizenziert ist, zu fördern; die Zulassung für neue Anwendungen erfordert neue Daten zur Sicherheit und Wirksamkeit, was auf weitere Kosten hinausläuft und daher kaum von den Herstellern weiterverfolgt wird. Die lizenzierte pädiatrische Anwendung der derzeit verfügbaren Produkte wird nicht vorankommen und ihr Einsatz wird „off-label“ bleiben. Darüber hinaus wird auch keines der neu entwickelten Produkte eine klinische Studie bei Kindern durchlaufen. Die Sonografie ist bei Kindern das am meisten gewünschte bildgebende Verfahren; kinderfreundlich, interaktiv, informativ und risikofrei ohne Belastung mit radioaktiver Strahlung. Ultraschallkontrastmittel haben einen geprüften Sicherheitsstandard bei Erwachsenen [15] und würden bei Kindern sehr große diagnostische Möglichkeiten in der Sonografie erschließen [16].

Die gesetzlichen Verpflichtungen bei der „Off-label“-Anwendung eines lizenzierten Produkts sind durch viele medizinische Zulassungsbehörden genau definiert. Die Richtlinien für die Verordnung von Arzneimitteln außerhalb ihres lizenzierten Einsatzgebiets ist durch das „General Medical Council“ von Großbritannien [17] unter folgenden Voraussetzungen geduldet:

1. Wenn Sie überzeugt sind, dass das Medikament den Bedürfnissen des Patienten besser gerecht wird.
2. Wenn Sie überzeugt sind, dass es ausreichend evidenzbasiert ist und/oder es Erfahrung für den Einsatz dieses Medikaments gibt, die dessen Sicherheit und Wirksamkeit belegen.
3. Wenn Sie die Verantwortung für die Verordnung dieses Medikaments und die Gewährleistung der Patientenversorgung übernehmen können.

Darüber hinaus ist in den Leitlinien bestätigt worden, dass dies am wahrscheinlichsten bei der Anwendung dieser Medikamente bei Kindern zutrifft. Ein weiterer Aspekt, der vom „Royal College of Paediatrics and Child Health“ in Großbritannien [18] in einer Stellungnahme zur Verschreibung nicht

abashed enthusiasm, by workers across the globe. The publication of these current guidelines by EFSUMB recognises the importance of the application of CEUS in diagnostic ultrasound in many areas and importantly this document sets the standards for non-liver CEUS examinations. The publication of this document will allow all practitioners of ultrasound to move forward with the application of CEUS "off-label". More importantly the aspiration to apply CEUS to the paediatric population will be encouraged to the benefit of this important group of patients.

lizenzierter Arzneien in der klinischen Pädiatrie herausgestellt und im Detail ausgeführt wird, ist das Einverständnis der Eltern; „bei der Verordnung nicht-lizenzierter Medikamente sind keine zusätzlichen zu den normalerweise bei lizenzierten Medikamenten durchzuführenden Schritten, erforderlich“. Das bedeutet, dass bei der Anwendung nicht lizenzierter Medikamente keine spezielle elterliche Einverständniserklärung erforderlich ist, der Arzt übernimmt die Verantwortung. Die Grundlage hierfür ist die ärztliche Auffassung, dass Kinder sichere, wirksame und auf ihre Verfassung passende „Erwachsenen“-Medikamente erhalten sollten.

Eindeutig ist die „Off-label“-CEUS-Anwendung für all unsere Patienten von Nutzen und wir sollten uns nicht vom Fehlen einer Lizenz beschränken lassen, wenn es um die Anwendung in einem bestimmten Bereich geht. Es gibt keine Zweifel an der Sicherheit und Wirksamkeit bei den lizenzierten CEUS-Anwendungsbereichen aufgrund einer Vielzahl von Studien bis zum heutigen Zeitpunkt. Der wirklich entscheidende Schritt – die Veröffentlichung von „Off-label“-Studien – wurde durch Anwender auf dem ganzen Globus mit unerschrockenem Enthusiasmus bewirkt. Die Veröffentlichung der aktuellen Richtlinien der EFSUMB erkennt die Wichtigkeit der CEUS-Anwendung beim diagnostischen Ultraschall in vielen Fachbereichen an und setzt bedeutende Standards für die nicht hepatischen CEUS-Untersuchungen. Die Veröffentlichung dieses Papiers erlaubt es allen Ultraschall-Anwendern, die „Off-label“-Anwendung der CEUS voranzutreiben. Am bedeutendsten ist es, die Bestrebungen zu ermutigen, CEUS bei Kindern anzuwenden, um dieser wichtigen Gruppe von Patienten von Nutzen zu sein.

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Ultraschall bei Pfortaderhochdruck – Teil 2 – und EFSUMB-Empfehlungen zur Durchführung und Dokumentation von Ultraschalluntersuchungen bei Pfortaderhochdruck

Ultrasound in Portal Hypertension – Part 2 – and EFSUMB Recommendations for the Performance and Reporting of Ultrasound Examinations in Portal Hypertension



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VNR 2760512012137990746

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DOI <http://dx.doi.org/10.1055/s-0031-1299145>
 Online-Publikation: 2012
 Ultraschall in Med 2012; 33: 8–32 © Georg Thieme Verlag KG Stuttgart · New York · ISSN 0172-4614

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Lernziele

- ▶ Kenntnisse über die Hauptindikationen und klinischen Informationen die mittels Sonografie auf dem Gebiet des Pfortaderhochdrucks gewonnen wurden, insbesondere in Bezug auf die prognostischen Aussagen und der Beurteilung der Behandlungen des Pfortaderhochdrucks.
- ▶ Kenntnis der von der EFSUMB unterstützten Empfehlungen zur Dokumentation der sonografischen Untersuchungen auf diesem Gebiet.
- ▶ Kenntnis der Parameter, die auf einem klinisch signifikanten Pfortaderhochdruck (KSPH) hinweisen, die jeder US-Befund je nach Qualitätsstufe der Ultraschalleinrichtung (Zentrum der Stufe 1, 2 oder 3) beinhalten sollte.

Einleitung

Die folgenden von der EFSUMB unterstützten Empfehlungen sind als Leitfaden für die Standardisierung und Gewährleistung einer hochqualifizierten und Dokumentation des US bei Patienten mit Verdacht auf bzw. bestätigtem Pfortaderhochdruck vorgesehen. Sie können auf der EFSUMB-Webseite in voller Länge eingesehen werden (<http://www.efsumb-portal.org/ep/>).

Zu beachten ist, dass die technischen Einzelheiten der sonografischen Variablen und die Anwendung bei Patienten mit Verdacht auf bzw. bestätigtem Pfortaderhochdruck bereits ausführlich im ersten Teil dieser Arbeit (publiziert in Ultraschall in der Medizin/European Journal of Ultrasound [1]) behandelt wurden. Der vorliegende Teil 2 der Arbeit bietet zusätzliche US-Bilder, welche die wichtigsten Merkmale der dopplersonografischen Untersuchung zur Diagnose eines Pfortaderhochdrucks aufzeigen und gibt abschließende Empfehlungen zur Anwendung von Ultraschall bei dieser klinischen Situation. Zusätzlich werden frühere sonografische Arbeiten zur por-

talenen Hypertension mit den Empfehlungen der EFSUMB besprochen.

Klinisches Bild, Indikationen und sonografisch wichtige Befunde bei Pfortaderhochdruck

Es gibt 4 klinische Haupteinsatzgebiete der Sonografie bei Pfortaderhochdruck, für die am Ende jedes Kapitels Schlussempfehlungen angeführt sind. Die beiden ersten Indikationsgebiete sind nur kurz zusammengefasst, da über sie bereits in Teil 1 der Publikation berichtet wurde.

1. Patienten mit klinischen und/oder labordiagnostischen Befunden eines PH ohne nachgewiesener chronischer Lebererkrankung (CLD) und Patienten mit sonografischen Zeichen eines möglichen Pfortaderhochdrucks

In dieser Situation sollten die morphologischen Zeichen einer Zirrhose zuerst untersucht werden; jedoch ist bei diesen Patienten die Wahrscheinlichkeit erhöht, dass keine Zirrhose der PH zugrunde liegt. Die häufigsten Ursachen eines nicht zirrhotischen Pfortaderhochdrucks sind eine Pfortaderthrombose oder eine Thrombose der Lebervenen, daher sollte besonders auf deren Durchgängigkeit geachtet werden.

Die Farb- (und Power)- Doppler-Sonografie (CDUS) besitzt eine >90%ige diagnostische Treffsicherheit für Pfortaderthrombose, Pfortaderkavernome und Budd-Chiari-Syndrom (Abb. 1). Kardiale Ursachen und arteriportale Fisteln können ebenso erkannt werden. Seltener Ursachen eines PH (einschließlich dem idiopathischen PH oder der nodulären regenerativen Hyperplasie) sollten bei Patienten mit Anzeichen eines PH und ohne andere augenscheinliche Ursache in Erwägung gezogen werden und mit den angemessenen invasiven Methoden untersucht werden.

** EFSUMB Education and Professional Standards Committee members: Jan Tuma (chairman); Radu Badea, Vito Cantisani, Christoph F. Dietrich, Hilde Berner Hammer, Gebhard Mathis, Dieter Nürnberg, Frantisek Zatura.

Ultrasound in Portal Hypertension – Part 2 – and EFSUMB Recommendations for the Performance and Reporting of Ultrasound Examinations in Portal Hypertension

Ultraschall bei Pfortaderhochdruck – Teil 2 – und EFSUMB- Empfehlungen zur Durchführung und Dokumentation von Ultraschalluntersuchungen bei Pfortaderhochdruck



Learning objectives



- ▶ To recognize the main indications and clinical information derived from US in the field of portal hypertension, particularly regarding prognostic information and assessment of treatments of portal hypertension.
- ▶ To be aware of EFSUMB-endorsed recommendations on how to report US examinations in this field.
- ▶ To be familiar with the parameters related to the presence of clinically significant portal hypertension (CSPH) which should be included in all US reports according to the level of care of the ultrasound unit in which the patient is investigated (primary, secondary or tertiary referral center).

Introduction



The following EFSUMB-endorsed recommendations are intended as a guide for standardizing and ensuring a high-quality examination and reporting of US in patients with suspected/established portal hypertension. They can also be fully read in full on the EFSUMB website (<http://www.efsumb-portal.org/ep/>).

Please note that technical details of US variables and the approach to patients with suspected or confirmed portal hypertension have been presented in detail in part 1 of this article, published in *Ultraschall in der Medizin/European Journal of Ultrasound* [1]. Part 2 of the article provides additional US images further illustrating the most important aspects of US Doppler assessment for diagnosing portal hypertension and provides the final recommendations for the use of US in these settings. Additionally, previously unexamined aspects about the use of US in portal hypertension will be reviewed in the present article.

Clinical scenario, indications and main information derived from US in the field of portal hypertension



There are four main clinical US application scenarios in the field of portal hypertension for which the final recommendations are reported at the end of each section. The first two are only very briefly summarized herein, since they were already reported in Part 1 of the article.

1. Patients with clinical/laboratory findings of PH in the absence of known chronic liver disease (CLD), and patients with sonographic signs of possible portal hypertension

Morphological signs of cirrhosis should initially also be looked for in this setting. However, the chance of encountering non-cirrhotic causes of PH is increased in these patients, and special attention should be paid to the assessment of vascular patency, since portal vein thrombosis and hepatic veins thrombosis are the most frequent causes of non-cirrhotic portal hypertension. Color (and power) Doppler US (CDUS) is > 90% accurate for diagnosing portal vein thrombosis/portal cavernomas and hepatic vein disturbances (Budd-Chiari Syndrome) (● Fig. 1). Cardiac causes and arterioportal fistulae can be also identified. Rarer causes of PH (including idiopathic PH or nodular regenerative hyperplasia) should be suspected in patients with signs of PH and no other apparent cause, and should be investigated with appropriate invasive means.

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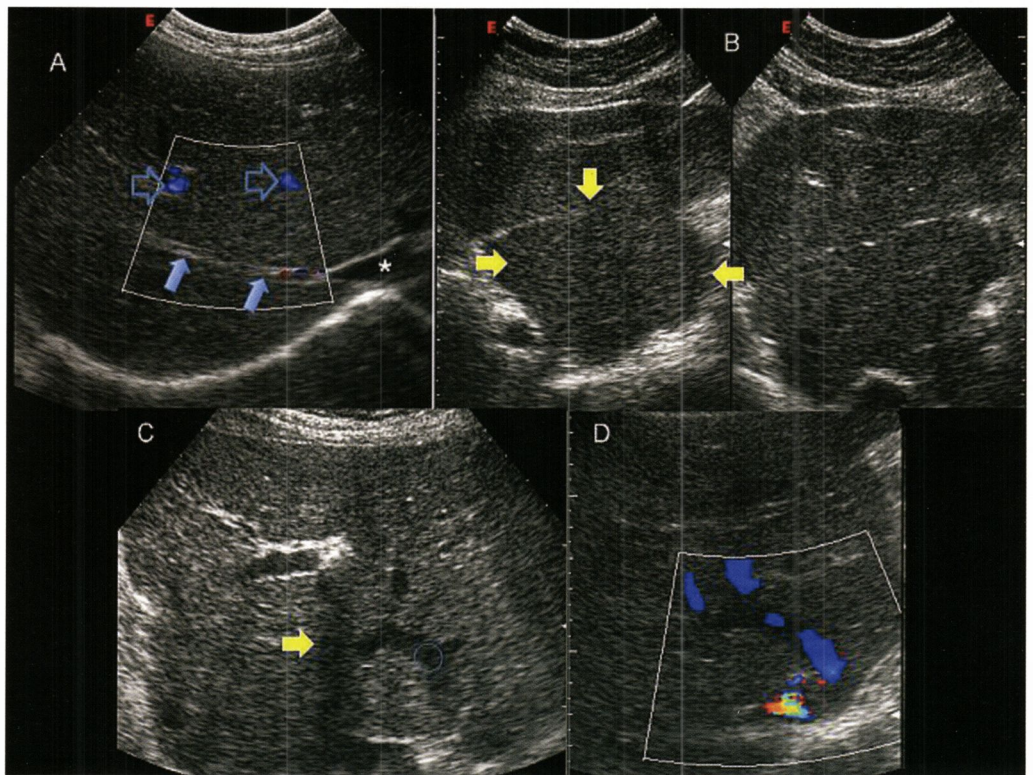


Abb. 1 Farbdoppler-Sonografie eines chronischen Budd-Chiari-Syndroms. Die rechte Lebervene im Subkostalschnitt (Abschnitt A) erscheint durch echoreiches fibröses Gewebe ersetzt (hellblaue Pfeile), ohne jegliches sichtbare Lumen oder irgendwelche Flusssignale in der Doppler-Sonografie. Die Pfortaderäste (leere Pfeile) sind, wie durch die Farbsignale angezeigt, durchgängig, was auch für einen Umkehrfluss in der Pfortader spricht. Die V. cava inferior ist echofrei (Stern), was auf Durchgängigkeit hinweist, obwohl diese nicht in der Farbdarstellung einbezogen ist. Bei einem weiteren Patienten mit Budd-Chiari-Syndrom ist der Lobus caudatus (begrenzt durch gelbe Pfeile, B und C, jeweils in Längs- und Transversalschnitten des Epigastriums) deutlich vergrößert. In Abschnitt C ist eine Erweiterung der Kaudatusvene (die Anschluss an die kurzen Lebervenen hat und den Lobus caudatus drainiert) gut erkennbar (Venen sind durch den offenen Kreis gekennzeichnet). Der Farbdoppler D beweist, dass diese Lebergefäße offen sind.

Fig. 1 Colour Doppler US of chronic Budd-Chiari Syndrome. The right hepatic vein seen through a subcostal scan (panel A) appears replaced by hyperechoic fibrous tissue (light blue arrows), without any visible lumen nor any flow signal detectable at Doppler US. Portal branches (empty arrows) are patent as indicated by presence of colour signals, which also suggest reversal of portal flow direction. The inferior vena cava (asterisk) appears echofree, suggesting patency, despite not included in the colour box. In another patient with Budd-Chiari Syndrome the caudate lobe (delimited by the yellow arrows, panel B and C, respectively in longitudinal and transverse scans at the epigastrium) is markedly enlarged. In panel C a dilatation of the caudal vein (corresponding to short hepatic veins draining the caudate lobe) is clearly evident (veins indicated by the empty circle). Their nature as patent outflow liver vessels is confirmed by colour Doppler (panel D).

Empfehlung

Bei Patienten mit eindeutigen klinischen Befunden eines Pfortaderhochdrucks ist die Duplex-Doppler-Sonografie eine sehr treffsichere Methode zur Klärung der Ätiologie.

Insbesondere kann sowohl eine Pfortaderthrombose als auch eine Lebervenenthrombose mittels Duplex/Doppler-US diagnostiziert oder ausgeschlossen werden.

Wie in **Tab. 1, 2** genau beschrieben, können die zu untersuchenden und dokumentierenden Parameter, je nach Qualifikation der Einrichtung, zu der der Patient zur Erstuntersuchung überwiesen wurde, variieren. Wenn keine Diagnose gestellt werden kann oder der untersuchende Arzt keine ausreichenden Informationen für eine adäquate klinische Betreuung gewinnen kann, sollte der Patient in einer höher spezialisierten Ultraschall-Einrichtung oder mit anderen diagnostischen Techniken untersucht werden.

2. US-Untersuchung des PH bei Patienten mit bekannter kompensierter chronischer Lebererkrankung (CLD)

Es sollte immer nach Leberveränderungen gesucht werden, ob die chronische Lebererkrankung bereits zur Zirrhose fortgeschritten ist; das treffsicherste Einzelmerkmal einer Zirrhose ist die mit einem linearen Schallkopf ($\geq 7 - 10$ MHz) nachgewiesene noduläre Leberoberfläche [2]. Bis zu 70% aller Patienten mit kompensierter Zirrhose haben bereits einen KSPH (definiert als HVDG ≥ 10 mmHg).

Die grundlegenden Befunde für die nicht invasive Diagnose des KSPH wurden bereits im vorausgegangenen Teil beschrieben und sind hier nur kurz aufgelistet und bebildert:

- ▶ portosystemische Kollaterale (**Abb. 2**)
- ▶ Splenomegalie (**Abb. 3**)
- ▶ Erweiterung der Pfortader (**Abb. 4**), Milzvene (**Abb. 5**) und Mesenterialvene



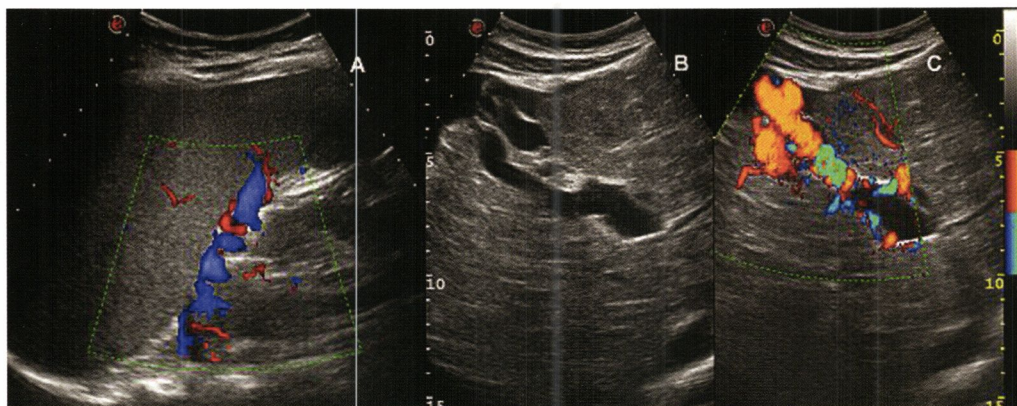


Abb. 2 Portosystemische Kollateralgefäße. In Abschnitt **A** werden Kollateralgefäße gezeigt, die sich zwischen Milz und linker Niere befinden, und die möglicherweise mit den spontanen spleno-renalen Anastomosen entsprechen. Eine paraumbilikale Vene, festgestellt durch einen rechten schrägen Subkostalschnitt wird im herkömmlichen B-Bild **B** und in der Farbdoppler-Sonografie **C** wiedergegeben.

Fig. 2 Porto-systemic collateral vessels. In panel **A** collateral vessels located between the spleen and the left kidney are shown, likely corresponding to spontaneous spleno-renal shunts. A paraumbilical vein, assessed through a right subcostal oblique scan is depicted at conventional grey scale US (panel **B**) and at color Doppler US (panel **C**).

Recommendation

In patients with clear clinical signs of portal hypertension, duplex Doppler US is an accurate method to establish the cause.

Specifically, portal vein thrombosis and hepatic vein thrombosis can be identified or ruled out by duplex Doppler US.

The parameters to be investigated and reported may vary according to the level of expertise of the center to which the patient is referred for first examination, as detailed in [Tables 1, 2](#) (Tab. 2, see online: www.thieme-connect.de/ejournals). If a diagnosis is not reached or the clinician in charge has not obtained enough information for adequate clinical management, the patient is to be assessed by US at a higher level of care or by other diagnostic techniques.

2. US assessment of PH in patients with known compensated chronic liver disease (CLD)

Signs indicating that chronic liver disease has already progressed to the cirrhotic stage should always be sought. The most accurate single sign of cirrhosis is liver surface nodularity examined with a linear transducer [2]. Up to 70% of patients with compensated cirrhosis already have CSPH (defined as HVPG ≥ 10 mmHg).

The fundamental signs for the noninvasive diagnosis of CSPH were already described in part 1 and are only briefly listed and illustrated here:

- ▶ Porto-systemic abdominal collaterals ([Fig. 2](#))
- ▶ Splenomegaly ([Fig. 3](#))
- ▶ Portal vein ([Fig. 4](#)), splenic vein ([Fig. 5](#)) and mesenteric vein dilatation
- ▶ Reduction of the respiratory variations of splenic ([Fig. 5](#)) and mesenteric vein diameters
- ▶ Hepatofugal flow (reversal of flow) in the portal vein system ([Fig. 6](#))

- ▶ Reduction of portal vein blood velocity ([Fig. 7](#))

- ▶ Subclinical ascites (arrow in [Fig. 3](#), right panel)
- Ancillary US parameters of PH are the congestion index of the portal vein [3], flattening of physiological phasicity of the hepatic vein Doppler flow pattern [4,5] ([Fig. 8](#)) and arterial parameters (renal Doppler impedance indexes – [Fig. 9](#), splenic artery Doppler impedance indexes – [Fig. 10](#) and superior mesenteric artery Doppler impedance indexes) [6,7].

Recommendation

All patients with chronic liver diseases should undergo a US Doppler examination at the time of first diagnosis to assess the presence of signs of cirrhosis and portal hypertension, since US signs provide satisfactory sensitivity and a high specificity for the diagnosis of these conditions.

The essential parameters to be described ([Table 2](#)) (Tab. 2, see online: www.thieme-connect.de/ejournals) are: signs of cirrhosis, portal vein patency, diameter and direction of flow, splenic vein and mesenteric vein diameters with respiratory variation and direction of flow, spleen size, presence/absence of porto-systemic abdominal collaterals and presence/absence of ascites.

Most US Doppler signs show high specificity for the diagnosis of clinically significant portal hypertension. Since US Doppler is noninvasive and repeatable, the search for these specific findings according to the level of care reported in [Tables 1, 2](#) (Tab. 2, see online: www.thieme-connect.de/ejournals) is recommended.

US Doppler examination should be repeated in patients with cirrhosis every time a new clinical event occurs, to rule out portal vein thrombosis and hepatocellular carcinoma, which are frequent causes of rapid worsening of portal hypertension and clinical decompensation.



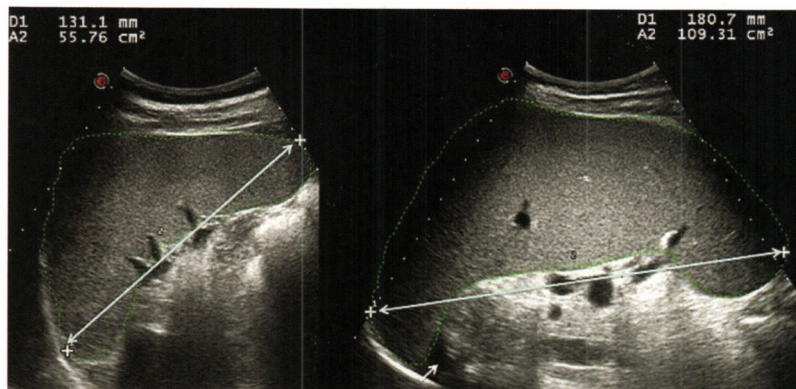


Abb. 3 Ultraschall-Bewertung der Milzgröße (linke Interkostalschnitte). Im ersten Fall (Bild links) eines Patienten mit kompensierter Zirrhose und ohne Ösophagusvarizen ist die Milz gering vergrößert (Durchmesser 130 mm, Querschnittsfläche 56 cm², Normbereiche jeweils: ≤ 12 cm und ≤ 45 cm²); im zweiten Fall (rechts) eines Mannes mit Ösophagusvarizen und dekomensierter Zirrhose ist die Milzvergrößerung sehr ausgeprägt (Durchmesser 180 mm; Fläche 109 cm²); eine geringe Menge Aszites war auch am oberen Milzpol sichtbar (Pfeil).

Fig. 3 Ultrasound assessment of spleen size (left intercostal scans). In the first case (image on the left side), corresponding to a patient with compensated cirrhosis and no esophageal varices, spleen size was mildly increased (diameter 130 mm; cross sectional area 56 cm², normal values respectively ≤ 12 cm and ≤ 45 cm²); in the second case (right panel), corresponding to a man with esophageal varices and decompensated cirrhosis spleen enlargement was more marked (diameter 180 mm; area 109 cm²); a small amount of ascites at the upper pole of the spleen is also visible (arrow).

- Verringerung der respiratorischen Durchmesser-Differenz von Milz- (Abb. 5) und Mesenterialvene
 - hepatofugaler Fluss (Flussumkehr) im Pfortadersystem (Abb. 6)
 - Verringerung der Blutflussgeschwindigkeit in der Pfortader (Abb. 7)
 - subklinischer Aszites (Pfeil in Abb. 3, rechts)
- Zusätzliche US-Parameter sind der Congestion-Index der Pfortader [3]; eine Abflachung des triphasischen Doppler-Flussmusters der Lebervenen [4, 5] (Abb. 8) und Widerstandsindizes (Doppler-Impedanz-Indizes der Niere – Abb. 9, der Milzarterie – Abb. 10 und der A. mesenterica superior) [6, 7].

Empfehlungen

Bei allen Patienten mit chronischen Lebererkrankungen sollte bei Erstdiagnose eine dopplersonografische Untersuchung durchgeführt werden, um das Vorliegen einer Zirrhose und eines Pfortaderhochdrucks zu erkennen, da die US-Befunde bei der Diagnose dieser Erkrankungen eine zufriedenstellende Sensitivität und hohe Spezifität besitzen.

Die unverzichtbaren Befunde, nach denen gesucht werden muss (Tab. 2), sind: Zeichen einer Zirrhose, Durchgängigkeit der Pfortader, deren Durchmesser und Richtung des Blutflusses, Durchmesser der Milz- und Mesenterialvenen mit Darstellung deren respiratorischen Differenzen und Flussrichtung, Milzgröße, Nachweis/Fehlen von portosystemischen abdominalen Kollateralen und Nachweis/Fehlen von Aszites.

Die meisten dopplersonografischen Befunde besitzen eine hohe Spezifität für die Diagnose eines klinisch signifikanten Pfortaderhochdrucks. Da die Doppler-Sonografie nicht invasiv und wiederholbar ist, wird, wie in Tab. 1, 2 (Tab. 2 finden Sie online unter www.thieme-connect.de/ejournals), gezeigt, wird die Erhebung dieser speziellen Befunde in jeder Einrichtung unabhängig von deren Zentrumsstufe empfohlen.

Die dopplersonografische Untersuchung sollte bei Patienten mit Zirrhose jedes Mal bei Auftreten einer neuen klinischen Symptomatik wiederholt werden, um eine Pfortaderthrombose oder ein hepatozelluläres Karzinom auszuschließen, welche die häufigsten Ursachen für eine plötzliche Verschlechterung des Pfortaderhochdrucks und der klinischen Dekompensation sind.

3. Prognostischer Wert der US-Befunde bei Patienten mit Zirrhose und PH Korrelation zwischen US- und Doppler-Parametern und dem HVDG

Wenige Studien untersuchten den Zusammenhang zwischen HVDG und CDUS-Befunden; die Gesamtdaten legen nahe, dass die einzelnen CDUS-Parameter bei Patienten mit Pfortaderhochdruck nicht treffsicher den HVDG vorhersagen können. Taourel und Kollegen fanden eine signifikante inverse Beziehung zwischen Pfortaderflussgeschwindigkeit oder Blutfluss und HVDG ($r = -0,69$ und $r = -0,58$, $p < 0,001$) [7] bei Patienten mit alkoholinduzierter Zirrhose, dieser Zusammenhang war weniger deutlich bei Patienten mit Zirrhosen anderer Ätiologie [8, 9]. Die Widerstands- (RI) und der Pulsatilitäts-Indizes (PI)

$$RI = \frac{\text{syst. max. Geschwindigkeit} - \text{enddiast. Geschwindigkeit}}{\text{syst. max. Geschwindigkeit}}$$

$$PI = \frac{\text{syst. max. Geschwindigkeit} - \text{enddiast. Geschwindigkeit}}{\text{mittlere syst. max. Geschwindigkeit}}$$

der Leberarterie zeigten in 2 Studien eine bessere direkte Übereinstimmung ($r = 0,70$) mit dem HVDG [8, 10].

Andere Parameter, die einen signifikanten, wenn auch geringeren Zusammenhang mit dem HVDG zeigen, sind der Doppler-RI und der PI der Milzarterie [11], der PI der A. mesenterica superior [12] und der RI und PI der Nierenarterie [13]. Die beste Annäherung für die Abschätzung des HPVG durch CDUS ($r = 0,71$) erhielten Bolognesi und Kollegen durch die Kombination des PI der intralialen Milzarterie und der Berechnung des Pfortaderblutflusses mittels Duplex-Doppler-Sonografie [14], aber bisher wurde dieses Modell noch nicht anderweitig extern validiert. Zusammenfassend ist kein Doppler-Parameter verlässlich genug, um den Pfortaderdruck mit ausreichender Genauigkeit für die klinische Anwendung zu bestimmen.



3. Prognostic information provided by US findings in patients with cirrhosis and PH Correlation of US and Doppler parameters to HVPG

Few studies have explored the correlation between the HVPG and CDUS signs. The overall data suggest that individual CDUS parameters cannot accurately predict HVPG in patients with portal hypertension. Taourel and colleagues found a significant inverse correlation between the portal velocity or flow and HVPG ($r = -0.69$ and $r = -0.58, p < 0.001$) [7] in patients with alcoholic cirrhosis. This correlation was weaker in patients with cirrhosis of other etiologies [8, 9]. Hepatic arterial resistance (RI) and pulsatility (PI) indexes

$$RI = \frac{\text{Peak systolic velocity} - \text{End diastolic velocity}}{\text{Peak systolic velocity}}$$

$$PI = \frac{\text{Peak systolic velocity} - \text{Minimum velocity}}{\text{Time averaged maximal velocity}}$$

showed a better direct correlation ($r = 0.70$) with the HVPG in two studies [8, 10].

Other parameters which show a significant, even though weak, correlation with HVPG are splenic artery Doppler RI and PI [11], superior mesenteric artery PI [12] and renal artery RI and PI [13]. The best approximation to HVPG estimation by CDUS ($r = 0.71$) was obtained by Bolognesi and colleagues by combining the PI of the intraparenchymal splenic artery and the portal blood flow duplex Doppler US calculation [14], but this model has not yet been externally validated. Altogether, no Doppler parameter is considered reliable enough to measure portal pressure with sufficient accuracy for use in clinical practice.

Presence of varices and variceal formation, growth and bleeding

Models for the prediction of any varices or of large varices including portal vein diameter or spleen size in combination with blood tests (platelet count and prothrombine time) have been developed in prospective studies in compensated cirrhosis [15–17] initially showing a good discriminative ability. Validation studies in different series showed that none of them is sufficiently accurate for varices prediction, and could not replace screening endoscopy. Regarding the prognostic role of different US findings, porto-systemic collaterals strongly suggest the presence of esophageal varices [18] and endoscopy should be recommended if not already recently performed. Porto-systemic collateral appearance and an increase in number, and spleen enlargement during follow-up have been associated with a higher rate of variceal formation and growth [19, 20]. The congestion index of the portal vein

$$\text{Congestion index} = \frac{\text{cross sectional area}}{\text{PV mean velocity}}$$

$$= \frac{(\text{diameter (in cm)} \times \text{diameter}) \times \pi}{4 \times \text{TAM velocity (in cm/sec)} \times 0.57}$$

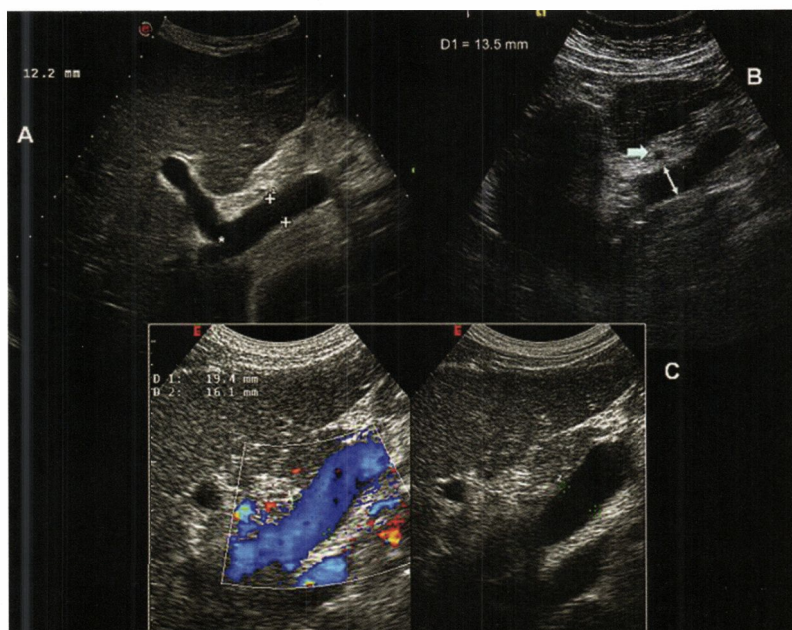


Abb. 4 Der Durchmesser der Pfortader kann in der B-Bild-Sonografie bestimmt werden als Abstand zwischen innerer Vorderwand und innerer Rückwand senkrecht zur Pfortaderlängsachse am Überkreuzungspunkt mit der Leberarterie oder etwas weiter kaudal (aber ≥ 2 cm oberhalb der Pfortaderkonfluenz), wo die Gefäßwände regelmäßig am besten darstellbar sind. Diese Abbildung zeigt die Messung bei einem zirrhotischen Patienten, mit einer diskreten Erweiterung (Durchmesser: 12,2 mm, Abschnitt A, wo die Pfortaderverzweigung flussabwärts deutlich sichtbar ist, durch einen Stern gekennzeichnet); in Abschnitt B wird eine leicht erweiterte Pfortader wiedergegeben (doppelseitiger Pfeil, 13,5 mm, am Überkreuzungspunkt mit der Leberarterie, angezeigt durch einen einseitigen Pfeil). Messungen beim selben Patienten mit und ohne Farbdoppler in Abschnitt C zeigen das Problem einer Überschätzung des Lumendurchmessers bei Verwendung des Farbdopplers (Durchmesser 19,4 mm, linker Rahmen in Abschnitt C) im Vergleich zur Graustufen-B-Bild-Sonografie (16,1 mm).

Fig. 4 Portal vein diameter can be measured during B-mode US examination as the distance from inner anterior wall to inner posterior wall, perpendicular to the long portal axis, at the crossing point with the hepatic artery or slightly downstream (but ≥ 2 cm upstream from portal bifurcation) wherever the vessel walls are best visualized. This Figure shows measurement in cirrhotic patients, with mild dilation (diameter: 12 mm, panel A, where the downstream portal bifurcation is clearly visible, indicated by the asterisk); in panel B a slightly enlarged portal vein is depicted (double sided arrow, 13.5 mm, at the crossing point with the hepatic artery, indicated by single sided arrow). Measurements taken in the same patient with and without colour Doppler in panel C highlight the risk of overestimation of the lumen diameter when using colour Doppler (diameter 19.5 mm, left frame of panel C) in comparison to grey-scale B-mode US (16 mm).

was an independent predictor of first variceal bleeding in the 6 months following the inclusion in a prospective study in patients with varices [21] (but not on a longer term basis), while hepatofugal portal vein flow was associated with a reduction of bleeding risk in a small series [22]. Additionally, some authors suggested that patent paraumbilical vein and spleno-renal circulation might reduce the risk of variceal bleeding, but this has not been confirmed by larger series.

First clinical decompensation

Spleen enlargement (> 1 cm in bipolar diameter/year) during periodic follow-up was associated with a higher probability of developing any first clinical decompensation of cirrhosis in one study [20]. Similarly, in patients with compensated cirrhosis, the US detection of porto-systemic collate-



Tab. 1 Zusammenfassung der zu untersuchenden und zu dokumentierenden Parameter bei Durchführung einer dopplersonografischen Untersuchung bei Patienten mit Verdacht auf bzw. diagnostiziertem Pfortaderhochdruck und damit korrespondierende klinische Befunde.

Untersuchungsparameter	mit US und Doppler-US korrespondierende klinische Befunde
Qualität der sonografischen Untersuchung: Stufe 1 – Zeichen einer Zirrhose (Leberkontur, Sonomorphologie und Echotextur der Leber) – fokale Leberläsionen – Durchgängigkeit und Durchmesser der Lebervenen – Durchgängigkeit, Durchmesser und Flussrichtung der Pfortader und der intrahepatischen Hauptäste – Vorliegen von portosystemischen Kollateralen – Milzgröße (Durchmesser/Fläche) – Vorliegen eines Aszites	1) Umkehrfluss in der Pfortader, Pfortaderthrombose und portosystemische Kollateralen sind jeweils individuelle pathognomonische Zeichen eines klinisch signifikanten Pfortaderhochdrucks (KSPH), unabhängig vom Vorliegen einer Zirrhose. 2) Splenomegalie, Aszites und Pfortaderdilatation zusammen sind ein deutlicher Hinweis auf einen KSPH, jedoch nur bei Patienten mit Zirrhose; beim Fehlen einer Zirrhose und einer Obstruktion der Lebervenen/Pfortader sollte intensiv nach anderen Ursachen gesucht werden. 3) Eine Obstruktion der Lebervenen bei Fehlen von Lebertumoren ist pathognomonisch für ein Budd-Chiari-Syndrom (dessen ätiologische Klärung weitere spezielle Untersuchungen erfordert).
Qualität der sonografischen Untersuchung: Stufe 2 Alle Parameter der Stufe 1 zusätzlich zu: – Verlauf, Durchmesser und Doppler-Spektralanalyse der Lebervenen – Durchgängigkeit und Flussrichtung der segmentalen intrahepatischen Pfortaderäste sowie der Milzvenen und der V. mesenterica superior; Ausbreitung eines Pfortaderthrombus – Pfortaderflussgeschwindigkeit – Bestimmung der respiratorischen Veränderungen der Diameter der Milzvene und der V. mesenterica superior	Wie in Stufe 1 beschrieben, zusätzlich: 1) Abflachung des Dopplerspektrums der Lebervenen kann bei chronischen Lebererkrankungen unabhängig vom Krankheitsstadium auftreten; beim Auftreten bei Zirrhose negativer prognostischer Wert. 2) Dilatierte Lebervenen (und der V. cava inferior) sind Hinweis auf eine posthepatische Ursache des KSPH (z. B. Stauungsleber). 3) Umkehrfluss in der rechten Pfortader oder in den Milzvenen oder der V. mesenterica superior sind ein Hinweis für KSPH; ein lokalisierter intrahepatischer Umkehrfluss kann auf arterioportale Fisteln hinweisen. 4) Der Nachweis einer Pfortaderthrombose (Pfortaderstamm und intrahepatische Äste, Milzvene oder V. mesenterica superior), auch als wandständiger Thrombus, ist pathognomonisch für Pfortaderhochdruck. 5) Ein Absinken der Flussgeschwindigkeit in der Pfortader bei kompensatorischer chronischer Lebererkrankung spricht für die Diagnose einer Zirrhose; ein sehr starker Abfall der Flussgeschwindigkeit in der Pfortader weist auf einen KSPH hin und ist ein negativer Vorhersagefaktor für eine kompensierte Zirrhose. 6) Das Fehlen von respiratorischen Diameteränderungen der Milzvene und V. mesenterica superior ist ein deutlicher Hinweis auf Pfortaderhochdruck.
Stufe 3 (höchste Qualifikation Referenzsonografie) Alle Parameter der Stufe 1 und 2, zusätzlich zu: – Untersuchung der Milz- und Nierenarterien – Charakterisierung der Pfortaderthrombose und der Untersuchung der portalen Biliopathie – genaue Untersuchung der Lebervenen und auf ihre Durchgängigkeit	Alle wie oben beschrieben, zusätzlich: 1) Anstieg der Impedanz-Indizes der Milzarterie ist ein deutlicher Hinweis auf einen KSPH bei Patienten mit Zirrhose 2) Anstieg der Impedanz-Indizes der Nierenarterie ist ein unabhängiger Vorhersagemarker für eine Nierenfunktionsstörung. 3) Unterscheidung zwischen gewöhnlicher und maligner Pfortaderthrombose (CEUS). 4) Gesamtüberblick über die Kreislagsituation bei Patienten mit Budd-Chiari-Syndrom oder Venenverschlusskrankheiten, einschließlich der genauen Untersuchung der Hämodynamik.

Auftreten und Entstehung von Varizen, Wachstum und Blutung

Modelle für die Vorhersage von Varizen bzw. überhaupt von großen Varizen, die den Durchmesser der Pfortader oder die Milzgröße im Zusammenhang mit Blutuntersuchungen (Thrombozytenzahl und Prothrombinzeit) untersuchten, wurden in prospektiven Studien zur kompensierten Zirrhose entwickelt [15–17] und zeigten zunächst eine hohe Trennschärfe. Validierungsstudien bei verschiedenen Testreihen zeigten, dass kein Modell eine ausreichende Genauigkeit für die Vorhersage von Varizen besitzt und das endoskopische Screening ersetzen könnte.

In Bezug auf den prognostischen Wert der unterschiedlichen Ultraschallbefunde weisen die portosystemischen Kollateralen sehr deutlich auf das Vorhandensein von Ösophagusvarizen hin [18] und es wird, falls nicht bereits kurz zuvor durchgeführt, eine Endoskopie empfohlen. Das Auftreten und die zahlenmäßige Zunahme portosystemischer Kollateralen sowie die Vergrößerung der

Milz bei Kontrolluntersuchungen wurden mit einer höheren Rate für Varizenbildung und -wachstum in Verbindung gebracht [19,20]. Der Congestion-Index der Pfortader war

$$\text{Congestion Index} = \frac{\text{Querschnittsfläche PV}}{\text{mittlere PV Flussgeschwindigkeit}}$$

$$= \frac{(\text{Durchmesser (in cm)} \times \text{Durchmesser}) \times \pi}{4 \times \text{TAM Flussgeschwindigkeit} \times 0,57}$$

in einer prospektiven Studie bei Patienten mit Varizen ein unabhängiger prädiktiver Marker für eine erste Varizenblutung innerhalb von 6 Monaten (aber nicht innerhalb eines längeren Zeitraums) nach Studienbeginn [21], während der hepatofugale Pfortaderfluss in einer kleinen Fallserie mit einem verminderten Risiko für Blutungen einherging [22]. Zusätzlich vermuteten einige Autoren, dass eine offene paraumbilikale Vene und ein splenorenal Kreislauf das Risiko für Varizenblutungen verringern könnte, dies wurde jedoch nicht in größeren Studien bestätigt.



Table 1 Summary of parameters which should be explored and reported when performing a Doppler ultrasound examination in patients with suspected/diagnosed portal hypertension, and their clinical correlates.

parameters to be assessed	clinical correlates of US and Doppler US findings
level of US examination: Primary level – signs of cirrhosis (liver profiles, hepatic morphology and echotexture) – focal liver lesions – patency and diameter of hepatic veins – patency, diameter and flow direction of the portal vein and main lobar branches – presence of porto-systemic collaterals – spleen size (diameter/area) – presence of ascites	1) Reversal of portal flow, portal vein thrombosis and porto-systemic collaterals are all individual pathognomonic features of clinically significant portal hypertension (CSPH), regardless of the presence of cirrhosis. 2) Splenomegaly, ascites and portal vein dilation are all highly suggestive of CSPH only in patients with cirrhosis; in the absence of cirrhosis and hepatic/portal vein obstruction, an intensive search for other causes must be performed. 3) Obstruction of hepatic veins in the absence of liver tumors is pathognomonic of Budd-Chiari Syndrome (whose etiologic assessment requires specific investigations).
level of US examination: Secondary level all parameters of primary level, plus: – course, diameter and flow Doppler tracing in hepatic veins – patency and flow direction in segmentary intra-hepatic portal branches and in splenic and superior mesenteric veins; portal vein thrombus extension – portal vein flow velocity – assessment of respiratory variations of caliber in the splenic and superior mesenteric veins.	All the above, plus: 1) Flattening of hepatic vein flow tracing may occur in chronic liver disease regardless of disease stage; when occurring in cirrhosis, it holds a negative prognostic value. 2) Enlargement of the hepatic veins (and inferior vena cava) suggesting a post-hepatic cause of PH (e. g. cardiac liver). 3) Reversal of flow in the right portal vein or in the splenic or superior mesenteric veins suggests CSPH; localized intrahepatic reversal might reveal an arterio-portal fistula 4) Presence of portal thrombosis (portal trunk, splenic vein or superior mesenteric vein, and lobar intrahepatic branches), even if mural, is pathognomonic of portal hypertension. 5) Decrease in portal vein flow velocity contributes to the diagnosis of cirrhosis in compensated chronic liver disease; severe decrease in portal vein flow velocity indicates CSPH and is a negative prognostic factor in compensated cirrhosis. 6) Stiffness (absence of respiratory variations) of splenic or superior mesenteric veins is highly suggestive of portal hypertension.
level of US examination: Tertiary (referral) level all parameters of primary and secondary levels, plus: – splenic and renal artery assessment – characterization of portal vein thrombosis, and assessment of portal biliopathy – thorough assessment of hepatic vein circulation	All the above, plus: 1) Increase in splenic artery impedance indexes is highly suggestive of CSPH in patients with cirrhosis. 2) Increase in renal artery impedance indexes is an independent predictor of renal dysfunction. 3) Distinction between bland and malignant portal vein thrombosis (CEUS). 4) Complete overview of the vascular situation in patients with Budd-Chiari Syndrome or veno-occlusive disease, including thorough assessment of hemodynamics.

als was associated with a higher risk of first clinical decompensation in the mid-term follow-up [23].

Development of portal vein thrombosis

Time-averaged maximum portal vein velocity < 15 cm/sec, corresponding to slow flow, was the only variable independently associated with a high risk for the development of non-malignant (bland) portal vein thrombosis in a recent prospective study in cirrhotic patients [24].

Hepatocellular carcinoma

The presence of porto-systemic collateral circulation was independently associated with an increased incidence of hepatocellular carcinoma in a recent study performed in 129 unselected cirrhotic patients [25]. This is consistent with the observation that the HCC incidence rate is higher in patients with CSPH [26].

Ascites

US is highly sensitive in diagnosing ascites, which is the most common clinical decompensation of cirrhosis, and is extremely prognostically significant [27,28]. The visualization of ascites and of

hepatic hydrothorax is simplified by US, which can diagnose even small quantities of liquid [29]. The use of contrast-enhanced US allows the visualization of peritoneal-pleural communications confirming the diagnosis of hepatic hydrothorax in doubtful cases [30].

Hepato-renal syndrome

Doppler US permits the quantification of arterial renal vasoconstriction occurring in cirrhosis. Vasoconstriction in this setting is a consequence of the activation of renin-angiotensin-aldosterone and catecholamine pathways due to the reduction of effective volemia induced by cirrhotic splanchnic vasodilatation [31]. Platt and colleagues [32] first described that the increase in intrarenal arteriolar RI in patients with cirrhosis was associated with the subsequent onset of hepato-renal syndrome. Increased renal arterial RI is observed in about 40% of patients with ascites [33], and in one study it predicted hepato-renal syndrome with 71% sensitivity and 80% specificity [34]. Interestingly, vasoactive therapies aimed at correcting portal hypertension also decreased renal arterial RIs in some pilot studies, suggesting that this index might be useful in the follow-up of pa-



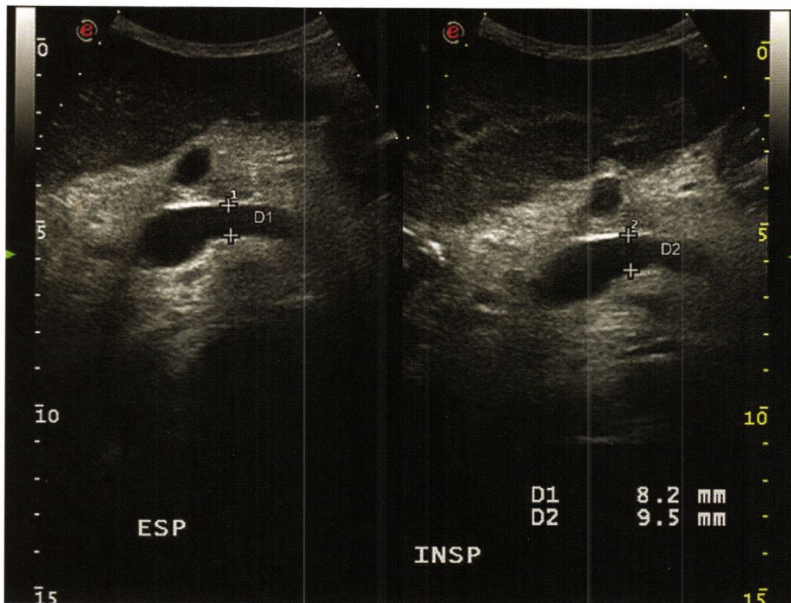


Abb. 5 Der Durchmesser der Milzvene, bestimmt im epigastrischen Querschnitt, sieht weit aus und verändert sich nicht signifikant (Ausmaß der Änderung $<40\%$) zwischen forcierter Einatmung (rechter Rahmen, D2 = 9,5 mm) und Ausatmung (linker Rahmen, D1 = 8,2 mm), passend zu einem erhöhten Binnendruck, einem Diagnosemerkmal für Pfortaderhochdruck. Eine kleine liquide Läsion findet sich im Pankreas.

Fig. 5 The splenic vein diameter, assessed through a transverse epigastric scan, shows a trend to be large and does not significantly change (extent of change $<40\%$) between forced inspiration (right frame, D2 = 9.5 mm) and expiration (left frame, D1 = 8 mm), corresponding to a stiff condition, diagnostic for portal hypertension. A small fluid lesion is present within the pancreas.

Die erste klinische Dekompensation

Eine Vergrößerung der Milz (>1 cm im bipolaren Durchmesser/Jahr) während der regelmäßigen Nachuntersuchung wurde in einer Studie in Zusammenhang mit einer höheren Wahrscheinlichkeit für das Auftreten der ersten klinischen Dekompensation gebracht [20]. In ähnlicher Weise zeigte sich bei Patienten mit kompensierter Zirrhose ein Zusammenhang zwischen dem sonografischen Nachweis von portosystemischen Kollateralen und einem höheren Risiko für die erste klinische Dekompensation während mittelfristiger Kontrolluntersuchungen [23].

Entwicklung einer Pfortaderthrombose

Die gemittelte maximale Flussgeschwindigkeit der Pfortader <15 cm/s, welche einer langsamen Strömungsgeschwindigkeit entspricht, war in einer kürzlich durchgeführten prospektiven Studie bei Patienten mit Zirrhose die einzige unabhängige Variable, die mit dem Entstehen einer nicht malignen (herkömmlichen) Pfortaderthrombose zusammenhängt [24].

Hepatozelluläres Karzinom

Bei vorhandenen portosystemischen Kollateralen zeigte sich in einer kürzlich durchgeführten Studie bei 129 unselektionierten zirrhotischen Patienten ein unabhängiger Zusammenhang mit dem häufigeren Auftreten von hepatozellulären Karzinomen [25]; dies stimmt mit der Beobach-

tung überein, dass die Wahrscheinlichkeit für ein HCC bei Patienten mit KSPH erhöht ist [26].

Aszites

Für die Diagnose eines Aszites, der häufigsten klinischen Dekompensation einer Zirrhose, ist der US hochsensitiv und besitzt eine sehr große prognostische Signifikanz [27, 28]. Die Darstellung des Aszites und des hepatischen Hydrothorax wird durch US vereinfacht, der selbst kleinste Flüssigkeitsansammlungen nachweisen kann [29]. Die Verwendung der kontrastmittelverstärkten Sonografie erlaubt die Darstellung einer peritoneal-pleuralen Kommunikation, die in zweifelhaften Fällen die Diagnose des hepatischen Hydrothorax sichert [30].

Das hepatorenale Syndrom

Die Doppler-Sonografie erlaubt die quantitative Bestimmung der arteriorenalen Gefäßkonstriktion, die bei Zirrhose auftritt. Bei dieser Erkrankung ist die Gefäßkonstriktion die Folge einer Aktivierung der Renin-Angiotensin-Aldosteron- und Katecholamin-Kaskaden, die Folge der Abnahme des effektiven Zirkulationsvolumens sind, welche durch die zirrhotische splanchnische Gefäßerweiterung hervorgerufen wurde [31]. Platt und Kollegen [32] waren die Ersten, welche die Zunahme des intrarenalen arteriellen RI bei Patienten mit Zirrhose einen anschließend beginnenden hepatorenalen Syndrom beschrieben. Ein erhöhter RI der Nierenarterie wird in etwa 40% der Patienten mit Aszites beobachtet [33], und in einer Studie sagte dieser ein hepatorenales Syndrom mit Sensitivität von 71% und einer Spezifität von 80% vorher [34]. Interessanterweise senken in einigen Pilotstudien gefäßaktive Therapien, die darauf zielen, den Pfortaderhochdruck zu korrigieren, auch die Widerstandsindizes der Nierenarterie und lassen vermuten, dass dieser Index für das Follow-up von Patienten mit hepatorenalem Syndrom zur Vorhersage des Ansprechens auf die Therapie nützlich sein könnte [35, 36]. Im Gegensatz dazu erhöht eine diuretische Therapie Dopplerimpedanz der Nierenarterie aufgrund eines prärenal Mechanismus (Abfall des systemischen arteriellen Druckes und unzureichendes arterielles Blutvolumen führen zur kompensatorischen renalen Gefäßverengung: die übermäßige diuretische Therapie bei Zirrhose kann ein hepatorenales Syndrom herbeiführen); deshalb sollte immer die laufende Therapie in die Interpretation der renalen Doppler-Befunde miteinbezogen werden.

Mortalität

Die US-Bestimmungen der Leber- und Milzgröße liefert eine prognostische Aussage bei Patienten mit kompensierter Leberzirrhose. Zoli et al. zeigten, dass eine geringere Lebergröße (bestimmt durch den hepatischen volumetrischen Index) mit einer höheren Sterblichkeit im Follow-up von Patienten mit kompensierter Zirrhose einher-



tients with hepato-renal syndrome to predict the response to therapy [35, 36].

At variance diuretic therapy increases renal arterial Doppler impedance with a pre-renal mechanism (decrease in systemic arterial pressure and in effective arterial blood volume leading to compensatory renal vasoconstriction: excessive diuretic therapy in cirrhosis may induce hepato-renal syndrome). Therefore, the ongoing therapy should be taken into account when interpreting the results of renal Doppler examination.

Mortality

US measurement of liver and spleen size provides prognostic information in patients with compensated cirrhosis. Zoli et al. showed that a smaller liver size (as evaluated by the hepatic volumetric index) is associated with a higher mortality on follow-up in patients with compensated cirrhosis [37, 38]. A spleen bipolar diameter over 14.5 cm [39], mean portal vein velocity <10 cm/sec [40] and loss of pulsatility of hepatic veins [41, 42] have also been found to be independently associated with mortality, even in patients with compensated disease.

It should be noted that in patients with cirrhosis and portal hypertension, the occurrence of clinical episodes of decompensation can be facilitated by rapid increases in portal pressure due to portal vein thrombosis and/or hepatocellular carcinoma. Therefore, anytime new clinical events occur, patients should be re-assessed by Doppler US to screen for these complications.

4. Follow-up of patients receiving treatment for portal hypertension

4a) Medical treatment

Life-long pharmacological treatment with non-selective beta-blockers such as propranolol or nadolol is warranted when high-risk varices are diagnosed (primary prophylaxis) or if the patient experienced an episode of bleeding from varices (elective treatment or secondary prophylaxis) [43]. The aim of the pharmacological therapy is to reduce portal pressure (assessed by HVPG) below 12 mmHg or at least by 20% vs. baseline values, since this reduces the risk of recurrent bleeding [43] and results in a reduction of other portal hypertension-related events and mortality [44]. However, this hemodynamic goal is achieved in less than 50% of the patients receiving beta-blockers, leading to the need for monitoring HVPG response to assess which patients respond satisfactorily to treatment and which patients do not [43], since the latter are candidates for alternative treatments. The clinical question is therefore whether US can provide information able to distinguish responders from non-responders to beta-blockers, thus avoiding invasive measurement of HVPG.

After starting pharmacological prophylaxis of variceal bleeding, Doppler US indicates hemodyna-

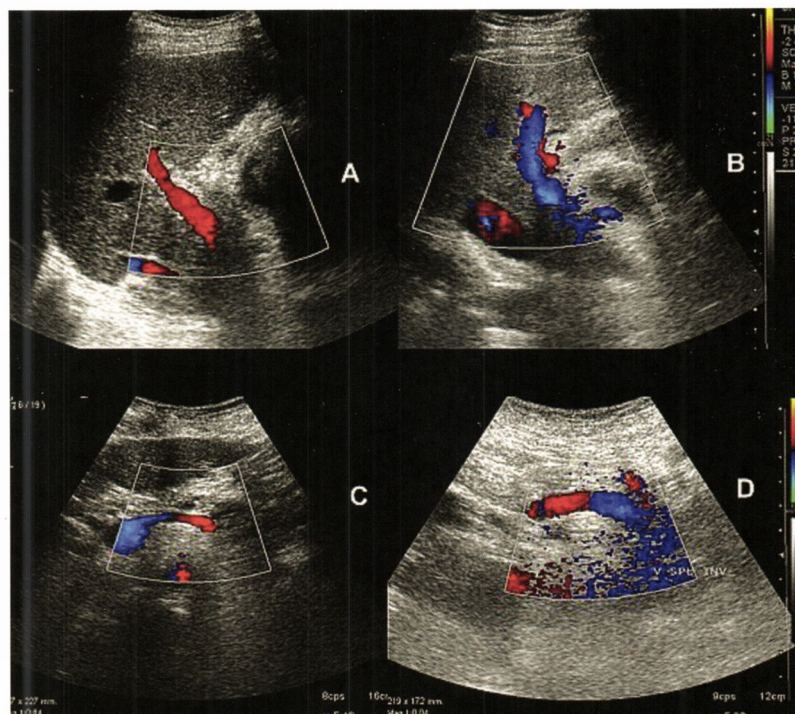


Abb. 6 Eine Flussumkehr in jedem Hauptabschnitt des Pfortadersystems (Pfortader, Milzvene oder Mesenterialvene) ist pathognomonisch für Pfortaderhochdruck. Abschnitt **A** und **B** zeigen die Farbdoppler-Untersuchung (Interkostalschnitte durch die Leber) bei normalem hepatopetalem Pfortaderblutfluss, in roter Farbe sichtbar gemacht **A** und einen Umkehrblutfluss in der Pfortader in blauer Farbe (**B**, die rote Farbe parallel zum rechten Pfortaderast zeigt die rechte Leberarterie). Gleichzeitig kann in epigastrischen Transversalschnitten die Farbdoppler-Untersuchung sowohl einen normalen hepatopetalen Fluss in der Milzvene **C** oder einen hepatofugalen Umkehrfluss **D** nachweisen. Zu beachten sind die unterschiedlichen Farben in den verschiedenen Abschnitten der Milzvene zwischen Abschnitt **C** und **D**.

Fig. 6 Reversal of flow in any main tract of the portal system (portal vein, splenic vein or mesenteric vein) is pathognomonic of portal hypertension. Panel **A** and **B** show a Color-Doppler examination (intercostals scans across the liver) of a normal hepatopetal portal blood flow, visualized in red color (panel **A**), and a reversed portal blood flow visualized in blue (panel **B**, red color parallel to the right portal branch represents the right hepatic artery). Similarly, in epigastric transversal scans color-Doppler examination can demonstrate either normal hepatopetal flow in the splenic vein (panel **C**) or reversed hepatofugal flow (panel **D**). Please note the opposite colors in the different portions of the splenic vein between panels **C** and **D**.

mic changes consisting of the reduction of portal vein blood flow and/or an increase in superior mesenteric artery impedance indexes. **Table 3** summarizes the results of the studies assessing CDUS for the prediction of the hemodynamic response to medical treatment of portal hypertension. As shown, the overall accuracy is inadequate. However, available data suggest that the negative predictive value of some US variables may help detect non-responders.

The majority of studies have been performed after acute administration of propranolol [45, 46] or other portal hypotensive drugs. After an intravenous injection of propranolol, HVPG responders show a greater constriction of the superior mesenteric artery (as indicated by flow velocity decrease and impedance index increase) [46] and a greater portal vein velocity reduction [45]. However, it is important to note that the chronic effects of beta-blockers on Doppler parameters may not be predicted by their acute effect [47, 48]. The re-



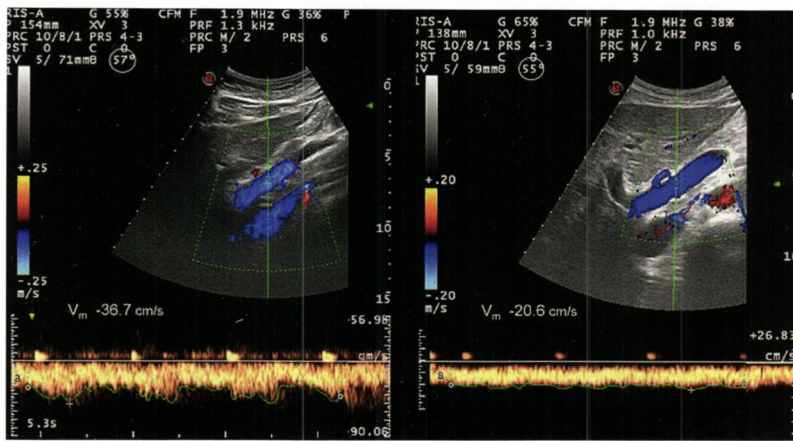


Abb. 7 Die Flussgeschwindigkeit der Pfortader wird in einem subkostalen Schrägschnitt bestimmt, die Portalvene wird dabei entlang ihrer Längsachse über mindestens 3–4 cm eingestellt. Das Doppler-Gate ($\geq 50\%$ des PV-Diameters) liegt in die Mitte des Lumens auf Höhe der kreuzenden Leberarterie. Der Dopplerwinkel sollte $<55^\circ$ sein und keinesfalls 60° überschreiten (hier li. 57° und re. 55° , die angezeigten Doppler-Winkel sind durch Kreise hervorgehoben). Die manuelle Tracing des pw-Spektrums erfolgt über mindestens zwei Herzzyklen, das US-Gerät errechnet die zeitlich gemittelte maximale Flussgeschwindigkeit (cm/s). Der li. Frame zeigt die normale portale Flussgeschwindigkeit bei einem Gesunden (TAM oder $V_m = 36,7$ cm/s) Bei Zirrhose und Pfortaderhochdruck nimmt die Flussgeschwindigkeit in der Pfortader ab, im re. Frame geringe Abnahme der V_m (20,6 cm/s) bei einem Patienten mit kompensierter Zirrhose. Der empfohlene Grenzwert ist geräteabhängig, wird aber gewöhnlich im Bereich von 21 bis 24 cm/s angegeben. Der PV-Diameter wird an derselben Stelle bestimmt (siehe [Abb. 4](#)). Der Congestion Index wird aus PV-Durchmesser und Flussgeschwindigkeit berechnet.

Fig. 7 Portal vein velocity is measured in an oblique-transversal scan in epigastrium/right subcostal region to visualize the vein along its longitudinal axis for at least 3–4 cm. The Doppler sample volume ($\geq 50\%$ of the diameter of PV) is to be set in the middle of the lumen, possibly at the crossing with hepatic artery. The Doppler angle should be set preferably at 55° , and in any case it should be kept $\leq 60^\circ$ (57° in left frame and 55° in right frame, the documented angles are outlined by circles). Manual tracing of Doppler signal is carried out over at least 2 cardiac cycles; time averaged maximum velocity is calculated by the equipment in cm/sec. Left frame shows a normal portal vein velocity in a healthy subject (time averaged maximal velocity TAM or $V_m = 37$ cm/sec); in patients with cirrhosis and portal hypertension portal vein velocity decreases (right frame shows a slight velocity decrease, $V_m 21$ cm/sec in a patient with compensated cirrhosis). The recommended threshold to diagnose a decrease in flow velocity slightly varies according to different equipments, manufacturers and cases series, usually reported in the range between 21–24 cm/sec. PV diameter is measured in the same site ([Fig. 4](#)). Congestion index can be calculated knowing PV diameter and velocity: PV cross sectional area in squared cm divided by portal vein mean velocity in cm/sec.

geht [37, 38]. Ein bipolarer Durchmesser der Milz von über 14,5 cm [39]; eine mittlere Pfortader-Flussgeschwindigkeit von <10 cm/s [40] und der Verlust des Strömungsprofils der Lebervenen [41, 42] werden unabhängig voneinander mit erhöhter Mortalität in Verbindung gebracht, sogar bei Patienten im kompensierter Zirrhose.

Es sollte erwähnt werden, dass bei Patienten mit Zirrhose und Pfortaderhochdruck klinische Episoden einer Dekompensation auf den plötzlichen Anstieg des Pfortaderdrucks Folge einer Portalthrombose oder eines hepatozellulären Karzinoms sein können. Deshalb sollten die Patienten jedes Mal, wenn ein neues klinisches Ereignis auftritt, einer dopplersonografischen Untersuchung unterzogen werden, um nach diesen Komplikationen gezielt zu suchen.

4. Kontrolluntersuchungen bei Patienten unter Therapie wegen Pfortaderhochdruck 4a) Medikamentöse Therapie

Eine lebenslange pharmakologische Behandlung mit nicht selektiven Betablockern wie Propranolol oder Nadolol ist gerechtfertigt, wenn blutungsgefährdete Varizen nachgewiesen werden (Primärprophylaxe) oder wenn der Patient eine Varizenblutung durchgemacht hat (elektive Therapie oder Sekundärprophylaxe) [43]. Das Ziel der pharmakologischen Therapie ist die Senkung des Pfortaderdrucks (bestimmt durch den HVDG) unter 12 mmHg oder zumindest um 20% gegenüber den Ausgangswerten, da dies das Risiko von Rezidivblutungen [43] sowie anderer Ereignisse in Zusammenhang mit Pfortaderhochdruck und die Mortalität verringert [44].

Jedoch wird dieses hämodynamische Ziel bei weniger als 50% aller Patienten, die Betablocker erhalten, erreicht. Dies führt dazu, dass das Ansprechen des HVDG überwacht werden muss, um die Patienten zu identifizieren, die befriedigend auf die Therapie ansprechen, und auch welche nicht ansprechen [43], da letztere für alternative Therapien infrage kommen. Die klinische Frage ist deshalb, ob die Sonografie unter Vermeidung der invasiven Messung des HVDG genügend Informationen bietet, um zwischen Respondern und Non-Respondern der Betablocker-Therapie zu unterscheiden.

Nach Beginn der pharmakologischen Prophylaxe der Varizenblutung zeigt die Doppler-Sonografie die hämodynamischen Veränderungen an, die in der Abnahme des Pfortaderblutflusses und/oder dem Anstieg der Impedanz-Indizes des A. mesenterica superior bestehen. [Tab. 3](#) fasst die Ergebnisse von Studien zusammen, die CDUS anwenden, um das hämodynamische Ansprechen auf die medikamentöse Therapie des Pfortaderhochdrucks vorherzusagen. Wie gezeigt ist die Treffsicherheit insgesamt unzureichend, dennoch lassen die verfügbaren Daten vermuten, dass der negative Vorhersagewert einiger dieser Techniken beim Auffinden von Non-Respondern helfen kann.

Die Mehrzahl der Studien wurde nach akuter Gabe von Propranolol [45, 46] oder anderen Pfortaderblutdrucksenkenden Medikamenten durchgeführt. Nach einer intravenösen Gabe von Propranol zeigen die HVDG-Responder eine stärkere Verengung der A. mesenterica superior (wie durch die Abnahme der Flussgeschwindigkeit und Zunahme der Impedanz-Indizes gezeigt) [46] und eine stärkere Abnahme der Pfortaderflussgeschwindigkeit [45]. Dennoch ist es wichtig zu betonen, dass die chronischen Wirkungen von Betablockern auf die Dopplerparameter nicht durch ihre akute Wirkung vorhergesagt werden können [47, 48]. Die Verringerung der Durchmesser von Milzvene und V. mesenterica superior unter chronischen Betablockern sprach in einer Studie für eine Verringerung des Pfortaderdrucks [49]. In einer weiteren Studie zeigten HVDG-Non-Responder unter chronischer Nadolol-Therapie eine deutlichere Dilatation der



duction in splenic vein and superior mesenteric vein diameter on chronic beta-blockers predicted the reduction in portal pressure in one study [49]. In another study, HVPG non-responders to chronic nadolol treatment showed a greater baseline splanchnic vasodilatation (as indicated by a low PI and RI in the splenic, mesenteric and hepatic artery) than responders [50]. From a practical point of view, it should be noted that the observation of a portal vein velocity similar to pre-treatment values suggests scarce adherence to therapy, and might be reported.

In conclusion, Doppler US is not accurate enough to identify hemodynamic responders to beta-blockers, who do not need additional treatment. Moreover, even if Doppler US is slightly better at identifying hemodynamic non-responders, it is still not sufficiently accurate to directly shift patients to different therapies. In this regard it should be noted that the only therapy alternative to beta-blockers available for non-responders is endoscopic variceal band ligation, which entails a risk of severe adverse events. Therefore, the hemodynamic failure of pharmacological therapy needs to be clearly documented with absolute accuracy, which is not achieved by Doppler US, so that repeated measurements of HVPG are still needed.

4b) Porto-systemic shunt surgery

Ultrasonography is useful for the follow-up of patients having undergone porto-systemic shunt surgery, which is now rarely performed since the advent of the Transjugular Intrahepatic Portosystemic Shunt (TIPS). The possible surgical interventions consist of side-to-side porto- or meso-caval shunts, end-to-side porto-caval shunt and proximal or distal spleno-renal shunts (Warren's shunt). The goal of the latter small diameter „calibrated“ shunt is to sufficiently reduce portal pressure and decompress gastro-esophageal varices selectively, while maintaining hepatopetal flow in the meso-portal venous bed in order to reduce the post-procedural incidence of encephalopathy due to porto-systemic shunting. The preferred techniques in Europe in recent decades are the side-to-side meso-caval shunt and the Warren's shunt.

The patency of the shunt may be directly assessed by US Doppler by observing a direct confluence between the portal or superior mesenteric vein and the inferior vena cava (• Fig. 11), or between the splenic and left renal veins, together with the flow inside it directed from the portal system towards the systemic circulation. • Table 4 summarizes the technical details for the performance of US Doppler examination of surgical shunts.

Direct assessment of flow through the anastomosis was feasible in 55 to 87% of patients in different series. Turbulent, high speed flow (> 30 cm/sec) towards the systemic circulation can be detected within the shunt itself. In some cases this

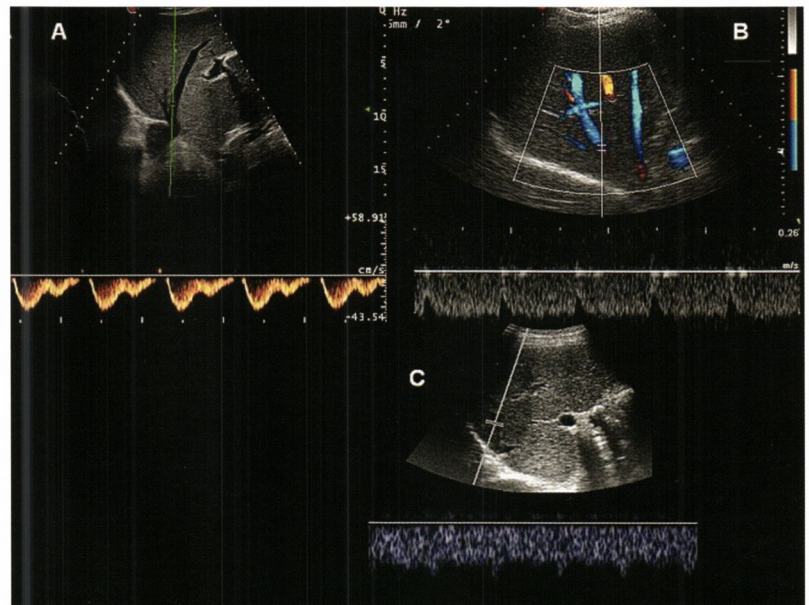


Abb. 8 Doppler-Flussmuster der Lebervenen. Abschnitt **A** zeigt ein normales triphasisches Muster; bei chronischer Lebererkrankung kann eine Reduzierung der Phasizität beobachtet werden. Der Fluss kann biphasisch werden **B** oder sogar monophasisch, mit fast ganz abgeflachtem Spektrum **C**. Solche Muster, insbesondere die monophasischen, haben eine schlechte Prognose, aber sind kein Diagnosemerkmal für Pfortaderhochdruck, da sie auch bei früheren Stadien einer chronischen Lebererkrankung beobachtet werden können.

Fig. 8 Hepatic veins Doppler flow pattern. Panel **A** shows a normal triphasic pattern; reduction of phasicity can be observed in chronic liver disease. The flow can become biphasic (panel **B**) or even monophasic, with a almost completely flattened trace (panel **C**). Such patterns, especially the monophasic one are associated with worse prognosis, but are not diagnostic for portal hypertension, since they can be observed in chronic liver disease also at earlier stages.

flow may show a phasic profile in response to variations in inferior vena cava pressure. Extremely high velocity turbulent flow ($> 100 - 150$ cm/sec) within a narrowed tract may suggest shunt stenosis.

When the shunt cannot be directly visualized, indirect signs of patency (direction of flow in the portal system towards the shunt) can be identified in virtually all patients with a patent shunt. For example, when a side-to-side porto-caval shunt cannot be directly visualized, the presence of hepatofugal flow in the intrahepatic portal branches is a reliable indicator of the patency of the shunt. Similarly, when a distal spleno-renal shunt is not directly seen, a typical flow pattern in the splenic vein showing phasic profile synchronous with caval pulsatility indicates shunt patency.

4c) TIPS

The TIPS procedure consists of the creation of intrahepatic communication between a hepatic vein and the portal vein, which is stabilized by placing a stent, through a transjugular interventional radiological technique (• Fig. 12). US guidance is useful during TIPS placement to avoid puncturing of the portal vein in the extrahepatic space, and to quickly detect possible complications such as hemoperitoneum.



Tab. 3 Wichtige Studien zur Bedeutung der Doppler-Sonografie für die Vorhersage des hämodynamischen Ansprechens auf Medikamente bei Pfortaderhochdruck im Vergleich zur invasiven Bestimmung des hepatischen Venendruckgradienten (HVDG).

Autor und Literaturzitat	Studienmedikament; akut oder chronisch	Patientenzahl	Parameter, die einen Zusammenhang zwischen einer HVDG-Abnahme und der Prognose der Patienten aufzeigen	Grenzwert und positiver und negativer Vorhersagewert (PVW und NVW) für die Vorhersage eines guten hämodynamischen Ansprechens (Senkung des HVDG > 20 %, „Responder“)
Luca A. Hepatology 1995 [64]	Propranolol akut	44	Abnahme des femoralen Arterienblutflusses (FBF)	Abnahme des FBF > 20 %: PVW 57 % NVW 94 %
Albillos A. J Hepatol 1997 [65]	Propranolol akut	80	Abnahme des Blutflusses der Pfortader (PBF)	Abnahme des PBF > 20 %: PVW 81 % NVW 94 %
Iwao T. J Hepatol 1998 [46]	Propranolol akut	26	Abnahme der mittleren Flussgeschwindigkeit (vel) in der A. mes. sup. (AMS) und Femoralarterie (FA) Anstieg des Pulsatilitäts-Index in der AMS	Abnahme der AMS vel > 20 %: (PVW 89 % NVW 93 %) Abnahme der FA vel > 25 %: (PVW 57 %, NVW 83 %) Zunahme des AMS PI > 15 %: PVW 57 % NVW 83 %
Schepke M. Am J Gastroenterol 2000 [45]	Propranolol akut	11	Abnahme der Flussgeschwindigkeit der Pfortader (PVV)	Abnahme der PVV > 20 %: PVW 90 %, NVW nicht berichtet
Zoli M. Radiology 1985 [49]	Atenolol chronisch	10	Abnahme des Durchmessers von V. mesenterica superior und der Milzvene	nicht berichtet; die Abnahme der Durchmesser von V. mesenterica superior und Milzvene korreliert mit der Abnahme des HVDG
Merkel C. J Hepatol 1998 [9]	Nadolol chronisch	19	Abnahme der Flussgeschwindigkeit in der Pfortader und Congestion-Index	Keine Unterschiede zwischen Respondern und Non-Respondern
Merkel C. Aliment Pharmacol Ther 2005 [66]	Nadolol akut und chronisch	24	Abnahme des PBF (keine Übereinstimmung zwischen akutem und chronischem Ansprechen bei 12 Patienten)	nicht berichtet; nach akuter Gabe zeigten Responder eine größere Abnahme des PBF im Vergleich zu Non-Respondern
Berzigotti A. J Hepatol 2006 [50]	Nadolol chronisch	30	ausgeprägtere splanchnische Gefäßerweiterung bei schlechten Respondern. Abnahme des PBF	mittlere Flussgeschwindigkeit in der Leberarterie im Normalzustand < 36 cm/s: PVW 93 % NVW 80 % PI der Milzarterie im Normalzustand < 1,49: PVW 81 % NVW 78 % Abnahme des PBF nur bei Respondern beobachtet
Kim MY. Liver Int 2007 [5]	Propranolol chronisch	19	Zunahme der Phasizität des Doppler-Flussmusters in den Lebervenen (Abnahme des Damping-Index – DI)	nicht berichtet; Veränderungen des DI stimmen mit den Veränderungen des HVDG überein
Choi YJ. J Gastroenter Hepatol 2003 [67]	Terlipressin akut	43	Abnahme des PBF	keine Unterschiede zwischen Respondern und Non-Respondern
Baik SK. Radiology 2006 [68]	Terlipressin akut	21	Zunahme der Phasizität des Doppler-Flussmusters in den Lebervenen (Abnahme des Damping-Index – DI)	nicht berichtet; Zunahme der Phasizität des Blutflusses in den Lebervenen korreliert mit einer Abnahme des HVDG

splanchnischen Gefäße im Vergleich zum Ausgangsbefund (niedrigerer PI und RI in den Milz-, Mesenterial- und Leberarterien) als die Responder [50]. Vom praktischen Standpunkt aus sollte die Messung einer Pfortaderflussgeschwindigkeit, die den Werten vor Therapiebeginn entspricht, kaum dafür sprechen, die Therapie beizubehalten. Darauf sollte hingewiesen werden, auch wenn man dies nicht bewiesen ist.

Schlussendlich ist die Doppler-Sonografie nicht ausreichend genau, um die hämodynamischen Responder auf Betablocker, die keine weiteren Behandlungen benötigen, zu diagnostizieren; darüber hinaus ist die Doppler-Sonografie, obgleich sie etwas besser für die Identifizierung der hämodynamischen Non-Responder geeignet ist, nicht treffsicher genug, um die Patienten direkt den unterschiedlichen Therapien zuzuführen. In diesem Zusammenhang sollte erwähnt werden, dass für Non-Responder die einzig verfügbare alternative Therapie zu Betablockern die endoskopische Gummibandligatur der Varizen darstellt, die jedoch mit starken Nebenwirkungen einhergehen kann. Deshalb muss das hämodynamische Versagen der pharmakologi-

schen Therapie mit größter Sorgfalt dokumentiert werden, sodass weitere Bestimmungen des HVDG benötigt werden, da dies mittels Dopplerdiagnostik nicht möglich ist.

4b) Portosystemische Shunt-Chirurgie

Die Ultrasonografie hat sich im Follow-up bei Patienten mit portosystemischer Shunt-OP, die seit Einführung des transjugulären, intrahepatischen portosystemischen (Stent-)Shunts (TIPS) jetzt selten durchgeführt wird, als nützlich erwiesen. Die möglichen chirurgischen Eingriffe sind die Seit-zu-Seit porto- oder mesokavale Anastomose, die End-zu-Seit portokavale Anastomose und der proximale oder distale splenorenale Shunt (Warren-Shunt). Der Zweck des letztgenannten „kalibrierten“ Shunts mit kleinem Durchmesser ist es, den Pfortaderdruck ausreichend zu senken und die gastroösophagealen Varizen selektiv zu dekomprimieren, während der hepatopetale Fluss im mesoportal Venenbett aufrechterhalten wird, um das Auftreten einer Enzephalopathie durch das portosystemische Shunting nach dem Eingriff zu verringern. Die in Europa bevorzugten Techniken in den letzten Dekaden sind die Seit-



Table 3 Main studies reporting the value of Doppler US in the prediction of the hemodynamic response to drugs for portal hypertension as assessed with invasive measurement of the hepatic venous pressure gradient (HVPG).

author and citation	study drug; acute or chronic	no. of pts	parameters showing a correlation with the reduction of the HVPG or with patient prognosis	cut-off and positive and negative predictive value (PPV and NPV) for the prediction of a good hemodynamic response (reduction of HVPG > 20 %, „responders“)
Luca A. Hepatology 1995 [64]	Propranolol acute	44	Reduction of femoral artery blood flow (FBF)	reduction of FBF > 20 %: PPV 57 % NPV 94 %
Albillos A. J Hepatol 1997 [65]	Propranolol acute	80	Reduction of portal vein blood flow (PBF)	reduction of PBF > 20 %: PPV 81 % NPV 94 %
Iwao T. J Hepatol 1998 [46]	Propranolol acute	26	reduction of mean velocity in the superior mesenteric artery (SMA) and femoral artery (FA) increase in SMA pulsatility index	reduction of SMA vel > 20 %: (PPV 89 % NPV 93 %) reduction FA vel > 25 %: (PPV 57 %, NPV 83 %) increase in SMA PI > 15 %: PPV 57 % NPV 83 %
Schepke M. Am J Gastroenterol 2000 [45]	Propranolol acute	11	reduction of portal vein velocity (PVV)	reduction of PVV > 20 %: PPV 90 % NPV not reported
Zoli M. Radiology 1985 [49]	Atenolol chronic	10	reduction of the diameter of superior mesenteric vein and splenic vein	not reported; the reduction of the diameter of superior mesenteric vein and splenic vein showed a correlation with the HVPG reduction.
Merkel C. J Hepatol 1998 [9]	Nadolol chronic	19	reduction of portal vein velocity and congestion index	no differences between responders and non-responders
Merkel C. Aliment Pharmacol Ther 2005 [66]	Nadolol acute and chronic	24	reduction of PBF (discordance between acute and chronic response in 12 patients)	not reported; after acute administration responders showed a greater reduction of PBF vs. non-responders
Berzigotti A. J Hepatol 2006 [50]	Nadolol chronic	30	greater splanchnic vasodilatation before treatment in poor responders. reduction of PBF	mean velocity in hepatic artery at baseline < 36 cm/sec: PPV 93 % NPV 80 % Splenic artery PI at baseline < 1.49: PPV 81 % NPV 78 % PBF reduction observed only in responders
Kim MY. Liver Int 2007 [5]	Propranolol Chronic	19	Increase in the phasicity of Doppler pattern in the hepatic veins (decrease in the damping index – DI)	not reported; changes of the DI correlated with changes of HVPG
Choi YJ. J Gastroenter Hepatol 2003 [67]	Terlipressin acute	43	reduction of PBF	no differences between responders and non-responders
Baik SK. Radiology 2006 [68]	Terlipressin acute	21	increase in the phasicity of Doppler pattern in the hepatic veins (decrease in the damping index – DI)	not reported; increase in the phasicity of flow in the hepatic veins correlated with the decrease in HVPG

A major problem after TIPS placement is the development of stenosis (also called TIPS dysfunction), occurring frequently over a relatively short period of time if a standard metallic stent is placed. The recent introduction of polytetrafluoroethylene (PTFE)-covered stents reduced the incidence of TIPS dysfunction. However, this still remains a relevant problem [51]. In TIPS stenosis, the portal pressure gradient increases again above 12 mmHg, and eventually causes the reappearance of complications of portal hypertension such as ascites or variceal bleeding [52]. TIPS occlusion (• Fig. 13), mostly occurring in patients with pro-thrombotic conditions, is an irreversible situation unless promptly corrected by placing a smaller stent within the thrombosed one (restenting, which is only occasionally accomplished with success; • Fig. 14). Duplex Doppler is accepted as a reliable technique to assess and monitor whether the stent is still patent or is occluded (complete absence of flow).

A timely diagnosis of stent stenosis (• Fig. 15) allows angiographic correction, and therefore any dysfunction of the shunt should be carefully

sought ideally before the appearance of clinical signs.

Even though the accuracy is not optimal and there is still room for improvement, Doppler is useful for detecting TIPS dysfunction. The following parameters should be evaluated: a) assessment of the flow direction in the intrahepatic portal branches b) measurement of the flow velocity within the portal vein and c) measurement of the flow velocity within the TIPS stent. The latter should be assessed in the portal, medium and hepatic vein part of the stent, with the hepatic vein part being the most common site of stenosis. • Table 4 summarizes the technical details for the performance of US Doppler examination of TIPS.

The intrahepatic portal flow direction is reverted in at least 55 % of patients with well functioning shunts. Therefore, the reacquisition of an antero-grade portal flow direction (• Fig. 13) in a patient in whom a flow reversal had appeared after stent positioning suggests an increase in hepatic resistance due to stent dysfunction.

In a prospective study comparing Doppler parameters and invasive hemodynamic data to predict



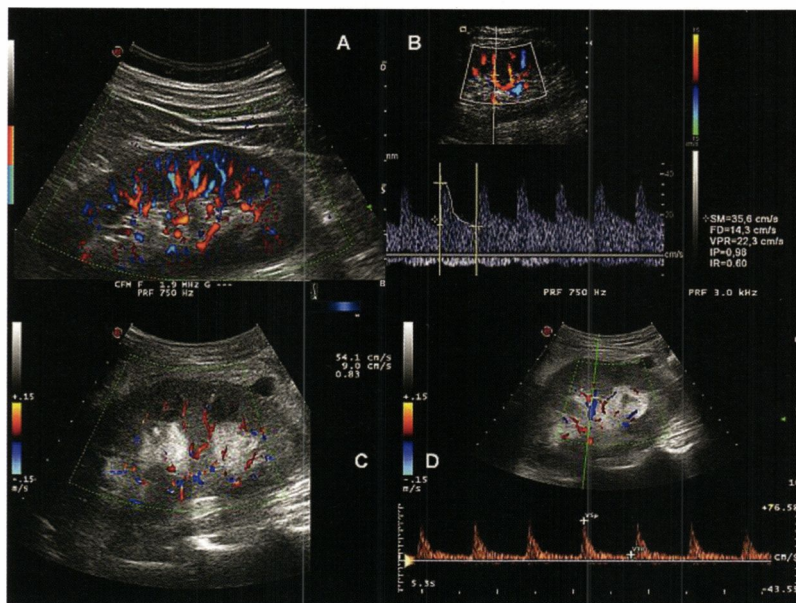


Abb. 9 Impedanzmessung der intrarenalen interlobären Nierenarterien. Aus der pw-Doppleranalyse werden die Flussgeschwindigkeit und die Impedanz-Indizes errechnet. Der Pulsatilitätsindex (PI) benutzt die mittlere Flussgeschwindigkeit und ist weniger abhängig von der Herzfrequenz. **A** und **B** zeigen eine normale Niere mit normal hohem diastolischen Fluss und normalem RI von 0,60 (Normalwert $RI \leq 0,70$, **B**). Bei KSPH insbesondere mit hepatorenalem Syndrom kommt es zu einer ausgeprägten arteriellen Gefäßkonstriktion, mit schwachen arteriellen Signalen im Farbdoppler (**C**) und zu einem deutlich erniedrigten diastolischen Fluss, wie die Spektralanalyse der interlobären Arterie zeigt (RI mit 0,83 deutlich erhöht). Der Anstieg des $RI > 0,70$ ist ein negativer prognostischer Marker für Patienten mit Zirrhose und identifiziert Patienten mit einem HDVG > 16 .

Fig. 9 Duplex Doppler US assessment of intraparenchymal interlobular renal arteries. Analysis of the tracing allows to assess flow velocity and to measure semi-quantitative indices, like the impedance indices described here below. Pulsatility index takes into account the mean velocity of flow and is therefore less dependent on heart rate. Colour Doppler shows a normally perfused kidney in a healthy subject (panel **A**) and Doppler flow tracing show normally high diastolic flow (corresponding to normal impedance indices, $RI = 0.60$, normal values $RI \leq 0.70$, panel **B**). In patients with severe portal hypertension and particularly with hepato-renal syndrome an intense arterial vasoconstriction takes place leading to a poor arterial flow mapping at colour Doppler (panel **C**) and markedly decreased diastolic flow as depicted by Doppler tracing of interlobar artery (renal artery $RI = 0.83$, markedly increased) (panel **D**). Note that the increase in renal artery $RI > 0.70$ is a negative prognostic indicator in patients with cirrhosis and identifies patients with Hepatic Venous Pressure Gradient values > 16 mmHg.

zu-Seit mesokavale Anastomose und der Warren-Shunt.

Die Durchgängigkeit des Shunts kann mittels Farbdoppler-Sonografie durch die direkte Darstellung der Anastomose zwischen Pfortader oder V. mesenterica superior und der V. cava inferior (**Abb. 11**) nachgewiesen werden, ebenso zwischen der Milz- und linker Nierenvene. Zusätzlich zeigt das Dopplerprofil eine Blutströmung vom Pfortadersystem zum systemischen Blutkreislauf. **Tab. 4** fasst die technischen Einzelheiten zur Durchführung der dopplersonografischen Untersuchung von chirurgischen Anastomosen zusammen.

Die Bewertung des Flussmusters in der Anastomose war in 55–87 % der Patienten in verschiedenen Fallserien möglich. Eine turbulente sehr schnelle Blutströmung (> 30 cm/s) zum systemischen Blutkreislauf kann direkt in der Anastomose nachgewiesen werden. In einigen Fällen kann

dieses Flussmuster ein biphasisches Profil als Folge des Druckunterschieds zur V. cava inferior aufweisen. Extrem hohe und turbulente Strömungsgeschwindigkeiten ($> 100 - 150$ cm/s) innerhalb einer engen Anastomose sind verdächtig für eine Stenose.

Wenn die Anastomose nicht direkt dargestellt werden kann, können indirekte Zeichen für die Durchgängigkeit (Flussrichtung im Pfortadersystem auf die Anastomose hin) in beinahe allen Patienten mit offenem Shunt nachgewiesen werden. Wenn z. B. eine Seit-zu-Seit angelegte portokavale Anastomose nicht direkt dargestellt werden kann, kann der Nachweis eines hepatofugalen Flusses in den intrahepatischen Pfortaderästen als verlässlicher Hinweis für die Durchgängigkeit der Anastomose gelten. In gleicher Weise spricht bei einer nicht direkt einsehbaren distalen splenorenalen Anastomose ein typisches mehrphasisches, vena-cava-synchrones Flussmuster in der Milzvene für die Durchgängigkeit der Anastomose.

4c) TIPS

Beim TIPS-Verfahren wird durch eine transjuguläre interventionelle radiologische Technik eine intrahepatische Kommunikation zwischen der Lebervene und der Pfortader gebildet, die durch Einsetzen eines Stents stabilisiert wird (**Abb. 12**). Die Ultraschall-Überwachung ist beim Platzieren des TIPS nützlich, um insbesondere extrahepatische Fehlpunktionen der Pfortader zu vermeiden und um mögliche Komplikationen wie z. B. ein Hämiperitoneum schnell zu erkennen.

Ein Hauptproblem nach der TIPS-Anlage ist die Entwicklung einer Stenose (auch als TIPS-Dysfunktion bezeichnet), die häufig in relativer kurzer Zeit nach dem Einsetzen eines metallischen Standard-Stents auftritt. Die kürzliche Einführung von Tetrafluoroethylen (PTFE)-beschichteten Stents reduzierte die Häufigkeit einer TIPS-Dysfunktion; dennoch bleibt diese weiterhin ein wichtiges Problem [51]. Bei der TIPS-Stenose steigt der Pfortaderdruckgradient wieder über 12 mmHg und verursacht schließlich ein Rezidiv von Komplikationen des Pfortaderhochdrucks wie Aszites oder Varizenblutung [52]. Ein TIPS-Verschluss (**Abb. 13**) tritt meistens bei Patienten mit prothrombotischer Konstellation auf und ist irreversibel, wenn dieser nicht sofort durch das Einbringen eines kleineren Stents in den verschlossenen Stent beseitigt wird. Dieses Re-Stenting ist nur gelegentlich erfolgreich (**Abb. 14**). Die Duplex-Doppler-Sonografie gilt als zuverlässige Untersuchungstechnik, um im Follow-up Durchgängigkeit oder Verschluss der Stents (keine Strömungssignale detektierbar) zu erfassen. Die zeitnahe Diagnose der Stentstenose (**Abb. 15**) erlaubt eine angiografische Korrektur und deshalb sollte jegliche TIPS-Dysfunktion idealerweise noch vor Auftreten von klinischen Symptomen durch eine sorgfältige Untersuchung erfasst werden.



TIPS dysfunction in patients without obvious clinical signs, the decrease in portal vein flow velocity in the portal trunk was the only independent predictive parameter together with the direction of intrahepatic portal flow [53]. In detail, TIPS dysfunction was diagnosed with 90% sensitivity when the time-averaged maximum portal vein velocity was below 39 cm/sec in patients with hepatopetal intrahepatic flow or below 28 cm/sec in patients with hepatofugal intrahepatic flow [53]. In a patent stent the average maximal blood flow velocity is rather high, ranging normally between 70 and 180 cm/sec (● Fig. 14) [54–56]. Therefore, a flow velocity below 50 cm/sec or focal marked flow velocity accelerations within the stent (>200 cm/sec) should raise the suspicion of stent stenosis [54,55]. A decrease in velocity <50 cm/sec tends to signal a downstream or upstream stenosis, while a marked flow velocity acceleration is detectable within the stenosis itself. Thus, the two signs can be detected either alone or in combination and a search should be performed for both.

The specificity and sensitivity of these criteria are reported to be different according to the design of the various studies, but overall the accuracy is still not optimal. However, although US Doppler seems inadequate to exactly quantify the degree of TIPS stenosis, it should be considered a reliable tool for determining patients with a higher probability of TIPS dysfunction needing to be referred to angiography, and is a recommended tool for routine clinical practice for this purpose. Contrast-enhanced US may provide additional information in this setting since it is able to depict the vessel lumen (● Fig. 13) as in carotid arteries [57], helping to depict the shape of the stent lumen in suspicious cases. However, sufficiently large studies with an adequate reference standard are lacking. Porto-systemic collateral vessels persist after TIPS placement (and therefore are not useful to assess TIPS function).

4 d) Mesenterico-left portal (or meso-Rex) bypass

Mesenterico-left portal (or meso-Rex) bypass is a surgical intervention which is currently considered the treatment of choice, when technically feasible, for children with portal hypertension due to extrahepatic obstruction of the portal vein (EHPVO) [58]. A graft is used to anastomose the intrahepatic left portal vein (Rex recessus) with the mesenteric or splenic vein. This resolves portal hypertension, with the added advantage of restoring intrahepatic hepatopetal flow, leading to physiological growth of the liver.

While noninvasive imaging methods (ultrasound Doppler and angio-TC/RM) are not accurate for assessing whether Rex recessus is patent pre-operatively, the patency of the graft can be followed-up by Doppler ultrasound after the bypass [59].

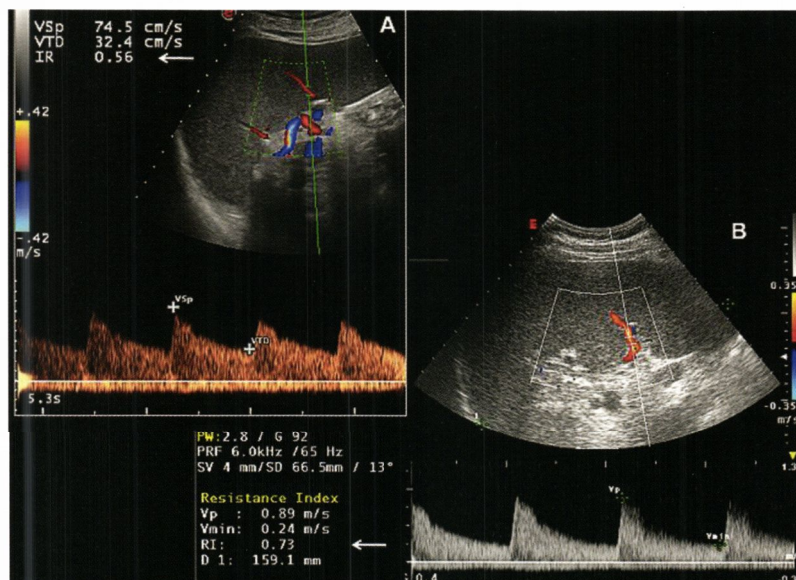


Abb. 10 Intralivale Impedanz-Indizes (RI und PI der Milzarterie). Das Sample volume liegt ca. 1 cm nach Eintritt ins Parenchym in einem intralivalen Hauptast der Milzarterie. **A** zeigt den RI (0,56) eines Gesunden. RI (und PI) nehmen bei Pfortaderhochdruck signifikant zu, z. B. bei einem HVDG von 16 mmHg mit Ösophagusvarizen auf 0,73 (**B**).

Fig. 10 Intraparenchymal Doppler impedance (RI and PI) of the splenic artery. The sample volume is set in a main splenic branch, close (approximately 1 cm) to where it enters the parenchyma. **A** RI (0.56) in a normal subject. RI (and PI) increase significantly in patients with portal hypertension, for example to RI=0.73 (Panel **B**) in a patient with hepatic venous pressure gradient (HVPG) of 16 mmHg and presence of esophageal varices.

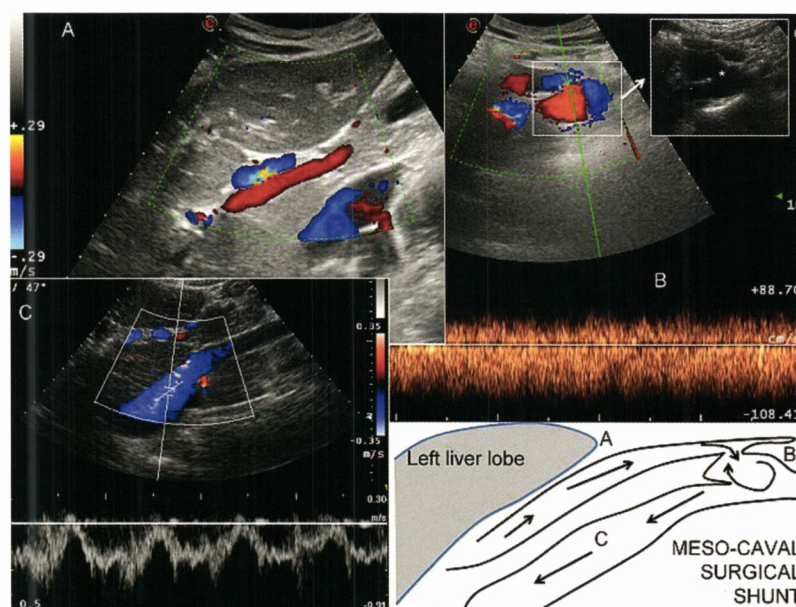


Abb. 11 Offene mesokavale chirurgische Anastomose. Shunt-Anatomie schematisch im rechten Oberbauch-Längsschnitt (rechts unten). Die Pfortader zeigt einen retrograde Fluss (rot kodiert), die weite Leberarterie (blau kodiert, normale Strömungsrichtung, kompensiert den fehlenden Portalfluss (**A**)). Das Blut der Pfortader fließt retrograd durch die mesokavale Anastomose mit turbulenter Strömung im Farb- und im pw-Doppler (**B**). Die Flussgeschwindigkeit in der Anastomose (*) ist mit 60–70 cm/s relativ hoch (**B**). Die V. cava inferior (**C**) ist wegen des Shuntvolumens vermehrt gefüllt, die Strömungsgeschwindigkeit erhöht.

Fig. 11 Patent meso-causal surgical shunt. Scheme of the splanchnic anatomy (low right) is reported as seen in a longitudinal right epigastric scan. Flow direction (shown in red in panel **A**) in the portal vein is reversed; the hepatic artery (shown in blue) is enlarged to compensate for the lack of portal inflow (**A**). The flow in the portal vein runs backward to the meso-causal shunt where turbulences and vortices can be observed in pw-Doppler US (**B**). The flow velocity within the shunt (*) is fairly high (60–70 cm/sec) (**B**). Because of the shunt volume the V. cava inferior (**C**) is enlarged and contains abundant flow.

Tab. 4 Technische Einzelheiten der sonografischen Untersuchung von chirurgischen Anastomosen und des transjugulären intrahepatischen portosystemischen Shunts (TIPS). Zu beachten ist, dass bei den Doppler-Parametern mindestens drei aufeinanderfolgende Messungen durchgeführt werden und der Mittelwert als Endergebnis genommen wird.

Shunt-Typ	Schnittebene	Befunde zur Prüfung der Durchgängigkeit
chirurgische Anastomosen	Transversal- und Längsschnitt am passenden Ort je nach Art der Anastomose (splenorenale Anastomose; portokavale Anastomose; mesokavale Anastomose)	B-Bild und Farbdoppler-Untersuchung wenn möglich; falls wegen Darmgasüberlagerung nicht durchführbar, Bewertung der indirekten Zeichen der Durchgängigkeit: Fehlen von Aszites und Umkehrfluss in der Pfortader (porto- und mesokavale Anastomose) oder in der Milzvene (proximale splenorenale Anastomose) sprechen für Durchgängigkeit. Bei einer distalen splenorenalen Anastomose (Warren-Shunt) deutet die typische kavale Phasizität des Blutflusses der Milzvene- auf Durchgängigkeit hin.
TIPS	Interkostalschnitt, der die Darstellung des TIPS von der Pfortader bis zur Lebervene ermöglicht	– Bestimmung der Durchgängigkeit des TIPS (Nachweis eines Flusses) durch Farbdoppler. – Bestimmung der Flussgeschwindigkeit im TIPS (proximal, mittlerer und distaler Bereich); eine fokale Zunahme der Flussgeschwindigkeit im TIPS deutet auf eine TIPS-Dysfunktion/Stenose hin. – Bewertung der Flussrichtung innerhalb der intrahepatischen Äste der Pfortader; hepato-fugaler (Umkehr-)Fluss steht im Zusammenhang mit einer normalen TIPS-Funktion, während das Wiederauftreten eines hepatopetalen Flusses (wenn dieser zuvor umgekehrt war) bei Folgeuntersuchungen mit einer TIPS- Dysfunktion assoziiert ist. – Messung der Flussgeschwindigkeit in der Pfortader: Eine zunehmende Abnahme bei den Folgekontrollen weist auf eine TIPS-Dysfunktion hin. – Nachweis von Aszites ist ein deutlicher Hinweis auf eine TIPS-Dysfunktion.

Auch wenn die Doppler-Sonografie noch keine optimalen Ergebnisse liefert und Verbesserungsmöglichkeiten bestehen, erweist sich nützlich zur Detektion der TIPS-Dysfunktion. Folgende Parameter sollten untersucht werden: a) Bestimmung der Flussrichtung der intrahepatischen Pfortaderäste, b) Messung der Flussgeschwindigkeiten innerhalb der Pfortader und c) Messung der Flussgeschwindigkeit innerhalb des TIPS-Stents. Dabei sollten die Strömungsgeschwindigkeiten in den portalvenösen, zentralen und hepatisch-venösen Abschnitten des Stents bestimmt werden, wobei am hepatischen Venenabschnitt am häufigsten eine Stenose auftritt. **Tab. 4** zeigt eine Übersicht der technischen Details für die Durchführung einer dopplersonografischen Untersuchung bei TIPS.

- ▶ Die intrahepatische Pfortaderflussrichtung ist in mindestens 55 % der Patienten mit gut funktionierenden Anastomosen retrograd. Deshalb besteht bei Wiederauftreten einer anterograden Flussrichtung in der Pfortader (**Abb. 13**) bei Patienten mit einem Umkehrfluss unmittelbar nach der TIPS-Prozedur der Verdacht auf Zunahme des Leberwiderstands infolge einer Stentdysfunktion.
- ▶ In einer prospektiven Studie, die Doppler-Befunde und invasive hämodynamische Befunde zur Vorhersage der TIPS-Dysfunktion bei Patienten ohne auffällige klinische Symptomatik verglich, waren die Abnahme der Flussgeschwindigkeit in der Pfortader im Pfortaderstamm zusammen mit der Richtung des intrahepatischen Pfortaderflusses die einzigen unabhängigen prädiktiven Parameter [53] für eine TIPS-Dysfunktion. Im Detail wurde die TIPS-Dysfunktion mit einer Sensitivität von 90 % diagnostiziert, wenn bei Patienten mit hepatopetalem intrahepatischem Fluss die über die Zeit gemittelte maximale Pfortaderflussgeschwindigkeit unter 39 cm/s

oder bei Patienten mit hepatofugalem intrahepatischem Fluss unter 28 cm/s lag [53].

- ▶ Bei offenem Stent ist die durchschnittliche maximale Blutflussgeschwindigkeit ziemlich hoch, normalerweise im Bereich von 70 – 180 cm/s (**Abb. 14**) [54 – 56]. Deshalb sind Flussgeschwindigkeiten unter 50 cm/s oder zirkumskripte deutliche Erhöhungen der Flussgeschwindigkeit innerhalb des Stents (> 200 cm/s) verdächtig für eine Stentstenose [54, 55]. Ein Abfall der Geschwindigkeit < 50 cm/s zeigt möglicherweise eine Stentstenose unter- oder oberhalb der Stenosierung an [54, 55], während eine deutliche Beschleunigung der Flussgeschwindigkeit innerhalb der Stenose selbst nachweisbar ist. Diese Befunde können einzeln oder in Kombination auftreten, weshalb nach ihnen gezielt gesucht werden sollte.
- ▶ Die Spezifität und Sensitivität dieser Kriterien werden je nach Design der verschiedenen Studien unterschiedlich angegeben, wobei die diagnostische Treffsicherheit immer noch nicht optimal ist. Obwohl die Doppler-Sonografie nicht geeignet erscheint, das Ausmaß einer TIPS-Stenose exakt zu quantifizieren, ist sie verlässlich geeignet, um Patienten mit erhöhtem Risiko für eine TIPS-Dysfunktion zu erkennen und, wenn nötig, eine Angiografie zu veranlassen, welche in der klinischen Routine die empfohlene Methode für diese Indikation darstellt. Die kontrastmittelverstärkte Sonografie (CEUS) kann zusätzliche Informationen bei dieser Fragestellung liefern, da sie – wie bei den Karotiden [57] – das Gefäßlumen darstellt (**Abb. 13**). Im Verdachtsfall kann CEUS helfen, die Form des Stentlumens darzustellen, wenn gleich derzeit ausreichend große Studien mit einem angemessenen Referenzstandard fehlen.

Table 4 Technical details of US examination of surgical shunts and transjugular intrahepatic porto-systemic shunts (TIPS). Note that for Doppler parameters at least three consistent measurements should be taken, and their mean used as the final result.

type of shunt	scanning section	US findings to demonstrate patency
surgical shunts	transverse and longitudinal scan in the anatomical site according to the type of shunt (spleno-renal shunt; porto-caval shunt; meso-caval shunt)	B-mode and color Doppler examination if possible; if not feasible due to abdominal gas, evaluate indirect signs of patency: absence of ascites and reversal of flow in the portal vein (porto- and meso-cava shunt) or in the splenic vein (proximal spleno-renal shunt) suggest patency. For distal spleno-renal shunt (Warren's shunt) typical caval phasicity in splenic vein flow tends to suggest patency.
TIPS	intercostal scan allowing TIPS visualization from the portal vein up to the hepatic vein	– assess TIPS patency (presence of flow) by color and power Doppler – assess flow velocity within TIPS (proximal, medium and distal part); a focal increase in velocity suggests TIPS dysfunction/stenosis – evaluate the direction of flow within the intrahepatic branches of portal vein; hepatofugal (reversed) flow is associated with normal TIPS function, while the re-appearance of hepatopetal flow (if previously reversed) in the follow-up is associated with TIPS dysfunction – measure portal vein velocity: a progressive reduction in subsequent controls suggests TIPS dysfunction – presence of ascites is highly suggestive of TIPS dysfunction

This can be done immediately after the intervention and in the following months/years.

The graft is identified from the middle of the left lobe where it is anastomosed to the Rex recessus of the left portal vein. The patent graft vessel shows continuous hepatopetal flow from the left portal vein to the right portal vein. Therefore, the direction of flow in the left portal vein is away from the transducer and toward the right portal vein. Acute thrombosis of the graft is the main cause of bypass graft dysfunction, while stenosis is less common. Both can be easily identified by US Doppler (echogenic material in the lumen, with no flow in the first instance and narrowing of a segment of the vessel with turbulent flow in the second instance).

Recommendation

Doppler US does not provide accurate information on the hemodynamic response to beta-blockers, utilized for the prevention of variceal bleeding, in patients with cirrhosis and portal hypertension. Thus, it cannot be utilized to discriminate responders from non-responders to drug treatment. Doppler US is useful and recommended for the non-invasive follow-up of patients with TIPS, porto-systemic surgical shunts and meso-Rex bypass.

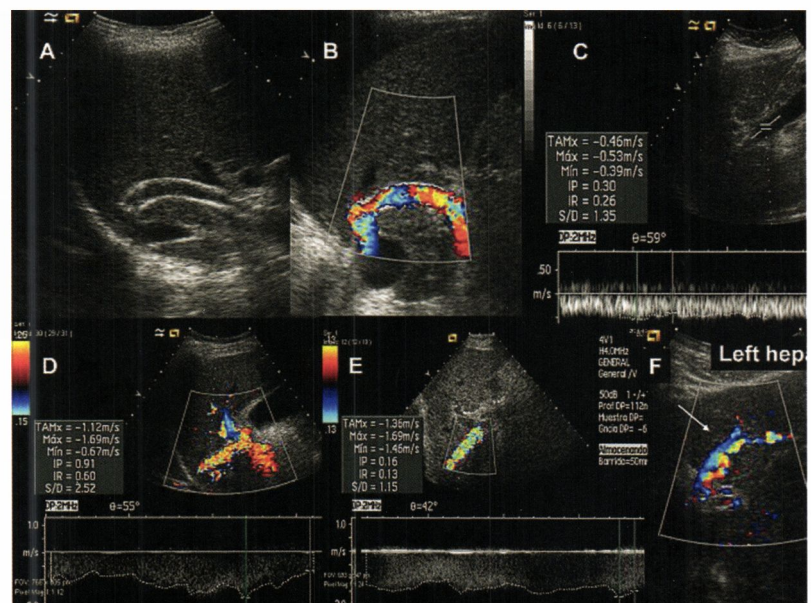


Abb. 12 Dopplersonografische Untersuchung eines transjugulären intrahepatischen portosystemischen Shunts (TIPS). Abschnitt A zeigt den TIPS-Stent im B-Bild. Ein turbulenter Fluss zeigt sich innerhalb des TIPS im Farbdoppler B. Die Befunde für einen regulär offenen TIPS sind: übermäßiger Pfortaderfluss (Flussgeschwindigkeit in der Pfortader TAMx= 46 cm/s, C), moderat hohe Flussgeschwindigkeiten innerhalb des TIPS, zwischen 100 und 150 cm/s in verschiedenen Abschnitten des Stents, D und E) und Umkehr der Blutflussrichtung in den intrahepatischen Ästen der Pfortader F. Das Fehlen eines Aszites spricht ebenfalls für eine normale TIPS-Funktion.

Fig. 12 US-Doppler assessment of transjugular intrahepatic porto-systemic shunt (TIPS). Panel A shows the appearance of TIPS stent in B-mode. Turbulent flow is seen within the TIPS by color-Doppler (panel B). Findings of a regularly patent TIPS are: abundant portal flow (portal vein velocity TAMx= 46 cm/sec, panel C), moderately high flow velocities within the TIPS, between 100 and 150 cm/sec in different parts of the stent, panel D and E) and reversal of blood flow direction in the intrahepatic branches of portal vein (panel F). The absence of ascites is also a sign consistent with normal TIPS function.

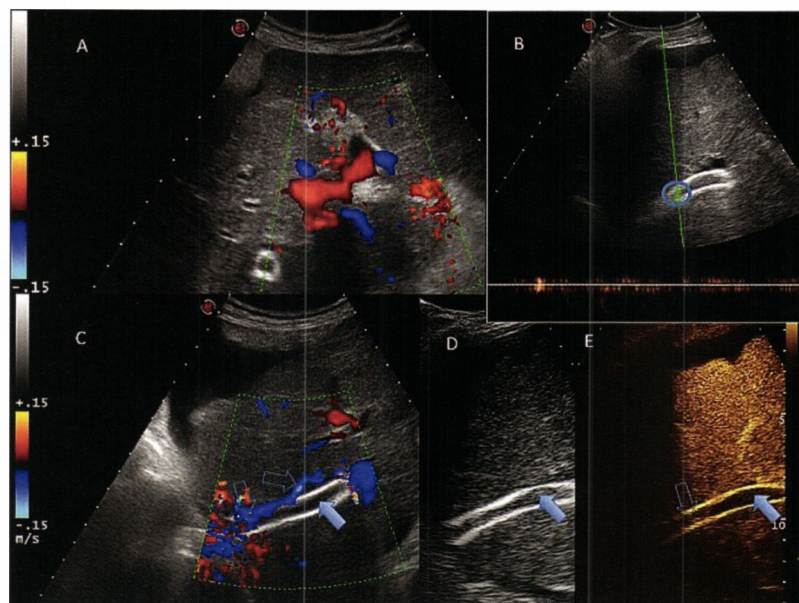


Abb. 13 Verschluss eines TIPS-Stents 3 Tage nach der Implantation. Die Flussrichtung im linken Pfortaderast ist weiterhin hepatopetal **A**. Die Doppler-Spektralanalyse kann keinen Fluss im Mittelteil des TIPS nachweisen, nur ein diskretes artifizielles Störsignal (**B**, der hellblaue Kreis zeigt die Position des Doppler-Gates innerhalb des Stentlumens an). Eine geringe Menge Aszites ist um die Leber herum sichtbar. Das Farbdoppler-Mapping **C** bestätigt das Fehlen eines Flusses im Inneren des zentralen Abschnitts des TIPS (hellblauer gefüllter Pfeil), während das Ende des Stents am Lebervenenaustritt einen geringgradigen Fluss aufrechterhält, der von der punktierten Lebervene herrührt (leere Pfeile). Im konventionellen B-Bild bei kontrastverstärktem Ultraschall zeigt sich echoreiches Material im Inneren des TIPS Lumen **D**, das Fehlen jeglicher Kontrastverstärkung beweist eine komplette Thrombosierung im Mittelteil des TIPS (hellblauer Pfeil, **E**), während eine moderate Perfusion am Stentende auf Durchgängigkeit am Übergang in die Lebervene (leerer Pfeil, **E**) hinweist.

Fig. 13 Obstruction of TIPS stent 3 days after placement. The flow direction in the main left portal branch is maintained hepatopetal (panel **A**). Doppler spectral tracing sampling does not detect any flow within the middle portion of the TIPS, but only noise signal (panel **B**, light blue circle indicates the position of the Doppler sample volume inside the stent lumen). A mild amount of ascites is visible around the liver. Colour Doppler flow mapping (panel **C**) confirms absence of flow inside the middle portion of the TIPS (light blue full arrow), whereas the terminal part of the stent towards the hepatic vein outflow maintains some flow deriving from the punctured hepatic vein (empty arrows). Conventional B-mode US during contrast enhanced ultrasound confirms presence of echoic material inside the TIPS lumen (panel **D**). Absence of any contrast enhancement in the middle portion of the TIPS indicates complete thrombosis (full light blue arrow, panel **E**) whereas lumen enhancement of the terminal portion of the TIPS, at the conjunction with the hepatic vein (empty arrow, panel **E**) indicates persistent patency of this terminal part of the stent.

4 d) Mesenterico-links-portaler (oder Meso-Rex) Bypass

Der Mesenterico-links-portale (oder Meso-Rex) Bypass ist ein chirurgischer Eingriff, der derzeit, wenn technisch durchführbar, bei Kindern mit Pfortaderhochdruck aufgrund eines extrahepatischen Verschlusses der Pfortader (EHPVO) als die

Behandlungsmethode der Wahl angesehen wird [58]. Um die intrahepatische linke Pfortader (Rex recessus) mit der Mesenterial- oder Milzvene zu anastomosieren, wird ein Transplantat verwendet, welches den Pfortaderhochdruck rückgängig macht, mit dem zusätzlichen Vorteil einer Wiederherstellung des intrahepatischen hepatopetalen Flusses, was zu einem physiologischen Leberwachstum führt.

Während die nicht invasiven bildgebenden Verfahren (Doppler-Sonografie und Angio-TC/RM) nicht ausreichend genau sind, um präoperativ zu bewerten, ob der Rex recessus offen ist, kann nach der Bypassoperation die Durchgängigkeit des Transplantats mittels Doppler-Sonografie nachverfolgt werden [59]. Dies ist sowohl sofort nach dem Eingriff möglich als auch in den folgenden Monaten bzw. Jahren.

Das Transplantat wird in der Mitte des linken Lappens identifiziert, wo es an den Rex recessus der linken Pfortader anastomosiert ist. Das offene transplantierte Gefäß zeigt einen beständigen hepatopetalen Fluss von der linken in die rechte Pfortader. Deshalb ist die Flussrichtung in der linken Pfortader weg vom Schallkopf und auf die rechte Pfortader zu. Die akute Thrombose des Transplantats ist die Hauptursache für ein Transplantatversagen, während eine Stenose weniger häufig auftritt. Beides kann sehr leicht mit der Doppler-Sonografie nachgewiesen werden (echogenes Material im Lumen, zunächst ohne Fluss und Verengung eines Gefäßabschnitts mit darauf folgendem turbulentem Fluss).

Empfehlungen

Bei Patienten mit Zirrhose und Pfortaderhochdruck bietet die Doppler-Sonografie keine exakten Informationen über das hämodynamische Ansprechen auf Betablocker, die zur Vermeidung von Varizenblutungen eingesetzt werden. Daher kann sie nicht eingesetzt werden, um zwischen Respondern und Non-Respondern der medikamentösen Therapie zu unterscheiden.

Die Doppler-Sonografie ist sinnvoll und wird daher zur nicht invasiven Nachuntersuchung von Patienten mit TIPS, postsystemischen chirurgischen Anastomosen und Meso-Rex-Bypass empfohlen.



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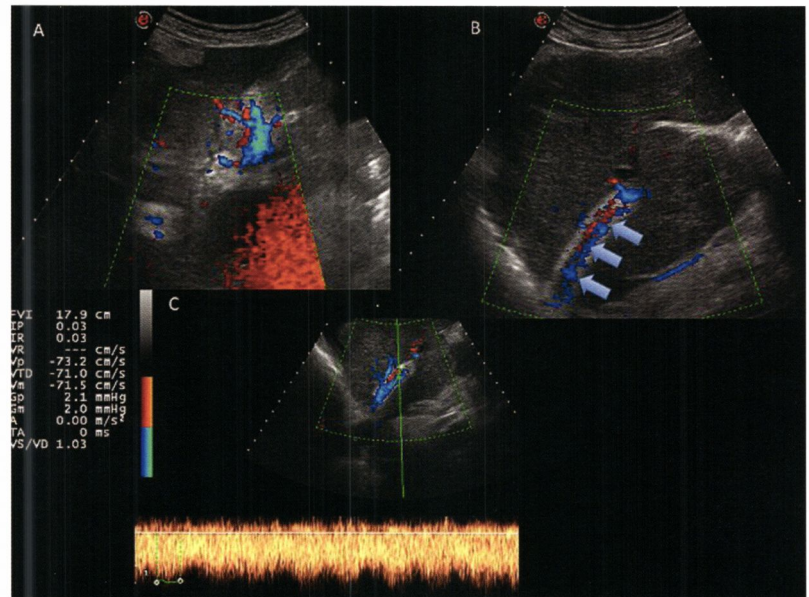


Abb. 14 Erfolgreiches Re-Stenting (ident. Fall [Abb. 13](#)) durch Platzierung eines kleineren Stents 3 Tage nach Verschluss des neu implantierten TIPS. Neu: umgekehrter Fluss im linken intrahepatischen Hauptfortaderast (A). Im Farbdoppler (B) gleichmäßiger, normal gerichteter Fluss innerhalb des gesamten TIPS (Pfeile), im pw-Doppler (C) gleichmäßiger normal-turbulenter Fluss (71 cm/s)

Fig. 14 Successful re-stenting (same case as [Fig. 13](#)) obtained by placement of a smaller stent inside the previous TIPS, early after the obstruction. The flow direction in the main left portal branch has now become reversed (A). Color Doppler (B) (arrows) and pw-Doppler (C), showing high velocity turbulent flow (71 cm/sec) in all tracts of the stent, indicate regular patency.

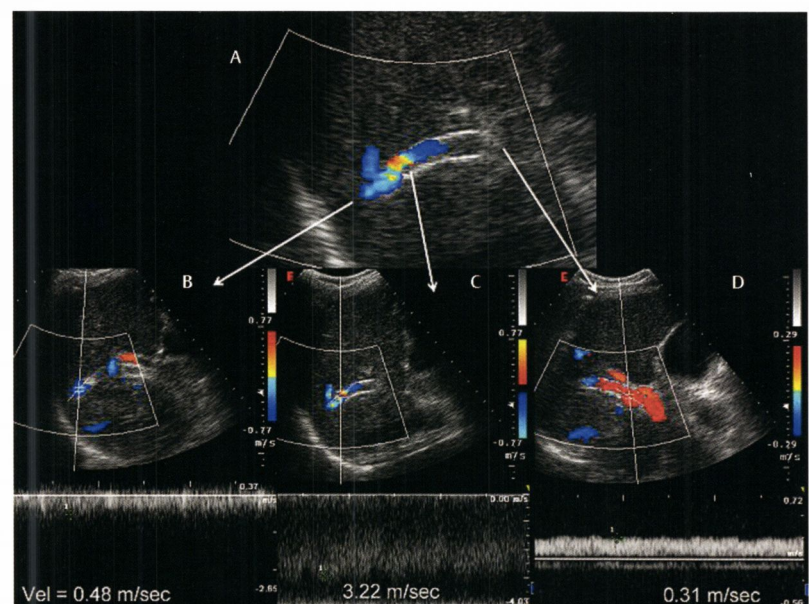


Abb. 15 Stenose (Dysfunktion) des TIPS. Im Interkostalschnitt re. zeigt sich oben im distalen Stent-Drittel ein Aliasing mit einer hohen Flussgeschwindigkeit von 3.2 m/s, (C), während diese stromabwärts (B, maximal 0,48 m/s) und stromaufwärts (D) der Stenose erniedrigt sind.

Fig. 15 Stenosis (dysfunction) of TIPS. The right intercostal scan shows in the middle-distal part of the stent an aliasing with high velocity flow of 3.2 m/sec (C) whereas the flow velocity is reduced downstream (B, max. 0.48 m/sec) and upstream (D) from the stenosis.

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CME-Fragen **Ultraschall bei Pfortaderhochdruck – Teil 2**

- 1** Die Ultraschalluntersuchung ist treffsicher, um die häufigsten Ursachen eines Pfortaderhochdrucks abzuklären. Welche der folgenden Ursachen können nicht durch Ultraschall entdeckt werden sondern benötigen entsprechende invasive diagnostische Verfahren?
- A Leberzirrhose
 - B Pfortaderthrombose
 - C Leberventhrombose
 - D idiopathischer Pfortaderhochdruck
 - E intrahepatische arteriportale Fisteln
- 2** Welches sind die grundlegenden sonografischen Parameter, die bei einem Patienten mit kürzlich diagnostizierter chronischer Lebererkrankung bei dessen Erstvorstellung in einem Zentrum der Stufe 1 erhoben werden sollten?
- A Nachweis oder Fehlen von Zeichen einer Zirrhose und Aszites
 - B Durchgängigkeit der Pfortader, Durchmesser und Flussrichtung und Nachweis / Fehlen von portosystemischen abdominalen Kollateralen
 - C Durchgängigkeit der Lebervenen
 - D Milzgröße
 - E alle zuvor genannten Parameter
- 3** Welche sonografischen Parameter sollten darüber hinaus bei einem Patienten mit diagnostizierter chronischer Lebererkrankung in einem Zentrum der Stufe 2 erhoben werden?
- A Pfortader: Blutflussgeschwindigkeit in der Pfortader, Durchgängigkeit ihrer intrahepatischen Hauptäste und segmentalen Äste und bei Vorliegen einer Thrombose Bestimmung der Ausdehnung des Verschlusses (teilweise oder total; prozentualer Anteil des Lumens, der durch die Thrombose besetzt ist).
 - B Lebervenen: Verlauf, semiquantitative Bestimmung von Durchmesser und Blutflussmuster.
 - C Milzvene und V. mesenterica superior: Durchgängigkeit, Durchmesser und deren respiratorische Modulation sowie Blutflussrichtung.
 - D Aszites: semiquantitative Bestimmung des Menge (minimal, geringgradig, moderat, ausgeprägt).
 - E Alle zuvor genannten Parameter.
- 4** Welche der folgenden dopplersonografischen Befunde sprechen für eine Durchgängigkeit des Shunts bei Patienten, bei denen eine mesokavale Anastomose durchgeführt wurde?
- A echofreies Lumen der V. mesenterica superior
 - B Strömungsumkehr im Pfortaderstamm und der Milzvene
 - C Strömungsumkehr im Pfortaderstamm und dem distalen Abschnitt der V. mesenterica superior
 - D dreiphasisches Flussmuster in den Lebervenen und hoher Widerstandsindex in der Milzarterie bei Patienten mit hepatopetalem Fluss entlang der V. mesenterica superior
 - E hepatopetaler Fluss in der Milzvene, im Pfortaderstamm und den intrahepatischen Ästen mit phasischem Flussprofil
- 5** Aus welchem Grund sollte man bei einem Patienten mit Zirrhose, der während einer Phase der klinischen Dekompensation stationär aufgenommen wurde, die sonografische Untersuchung des Abdomens wiederholen?
- A Ausschluss eines hepatozellulären Karzinoms (welches häufig den Pfortaderhochdruck kompliziert)
 - B Ausschluss einer inkomplett okkludierenden Thrombose der Pfortader, Milzvene und Mesenterialvene (führt zu plötzlichem Anstieg des Pfortaderdrucks)
 - C Bestimmung der Aszitesmenge
 - D Ausschluss möglicher Herde von intraabdominalen Infektionen
 - E alle zuvor genannten Ursachen
- 6** Die folgenden Befunde einer sonografischen Kontrolluntersuchung bei Patienten mit Zirrhose geben einen Hinweis auf Verschlechterung des Pfortaderhochdrucks bei Patienten mit Zirrhose und sagen die erste klinische Dekompensation voraus:
- A Abnahme der Flussgeschwindigkeit der Pfortader $\geq 5\%$ nach 6 Monaten
 - B Milzvergrößerung ≥ 1 cm und mehr nach 12 Monaten
 - C Zunahme des Pulsatilitäts-Index der A. mesenterica superior $\geq 10\%$ nach 6 Monaten
 - D Abnahme des Widerstandsindex der Nierenarterie $\geq 10\%$ nach 12 Monaten
 - E Zunahme der respiratorischen Durchmesserdiffferenz der Milzvene $\geq 10\%$ nach 6 Monaten
- 7** Welche der folgenden Aussagen über die Doppler-Untersuchung von Patienten mit Zirrhose ist falsch?
- A Erhöhte Impedanz-Indizes der Milzarterie deuten auf eine KSPH hin.
 - B Verlust der Pulsatilität der Lebervenen ist mit einer höheren Sterblichkeit assoziiert.
 - C Der hepatofugale Fluss (Flussumkehr) im Pfortadersystem ist kein Hinweis auf KSPH.
 - D Erhöhte Impedanz-Indizes der Nierenarterie sind unabhängige Prädiktoren für eine Nierenfunktionsstörung.
 - E Ein erhöhter Congestion-Index der Pfortader ist ein unabhängiger Prädiktor für eine erste Varizenblutung innerhalb der folgenden 6 Monate.
- 8** Welche der folgenden Aussagen über die Nachsorge von Patienten mit Betablocker bei Pfortaderhochdruck trifft zu?
- A Patienten unter chronischer Betablockertherapie können mit Ultraschall überwacht werden, da eine Abnahme des HVDG genau mit der Abnahme der Flussgeschwindigkeit und des Flusses in der Pfortader übereinstimmt.
 - B Das Ansprechen des Pfortaderdrucks auf chronische Betablockergabe kann nicht durch Ultraschall überwacht werden, da eine Abnahme des HVDG nicht genau durch die Veränderungen der untersuchten US-Parameter wiedergegeben wird.
 - C Patienten unter chronischer Betablockerbehandlung können durch US überwacht werden, da eine Abnahme des HVDG sehr genau mit der Zunahme des Strömungsmusters in den Lebervenen übereinstimmt.
 - D Patienten unter chronischer Betablockergabe können durch US überwacht werden, da eine Abnahme des HVDG sehr genau mit dem Anstieg des Pulsatilitäts-Index der A. mesenterica superior übereinstimmt.
 - E Patienten unter chronischer Betablockergabe können nach der ersten Medikamentengabe durch US überwacht werden, da eine Abnahme des HVDG sehr genau mit der im Doppler-US beobachteten Abnahme des Pfortaderflusses nach akuter Betablockergabe übereinstimmt.
- 9** Nur eine der folgenden Therapien bei Pfortaderhochdruck-Patienten sollte routinemäßig sonografisch nachuntersucht werden:
- A nicht kardioselektive Betablocker
 - B endoskopische Gummibandligatur bei Varizenblutung
 - C Terlipressin
 - D transjugulärer intrahepatischer portosystemischer Shunt
 - E Somatostatin oder Somatostatin-Analoga
- 10** Nach TIPS-Anlage wegen Varizenblutung tritt folgende Veränderung normalerweise nicht auf:
- A intrahepatische Flussumkehr in den Pfortaderästen
 - B Zunahme der Flussgeschwindigkeit in der Pfortader
 - C hohe Flussgeschwindigkeit innerhalb des Stents
 - D Rückbildung der portosystemischen Kollateralen
 - E Rückbildung des Aszites

CME-Questions **Ultrasound in Portal Hypertension – Part 2**

- 1** **Ultrasound examination is accurate for assessing the presence of most causes of portal hypertension. Which of the following cannot be detected by US and needs to be investigated by appropriate invasive diagnostic means?**
 - A liver cirrhosis
 - B portal vein thrombosis
 - C hepatic vein thrombosis
 - D idiopathic portal hypertension
 - E intrahepatic arterio-portal fistula
- 2** **Which are the essential sonographic parameters to be reported in a patient with a recently diagnosed chronic liver disease evaluated for the first time in a primary referral center?**
 - A presence or absence of signs of cirrhosis and ascites
 - B portal vein patency, diameter and direction of flow, and presence/absence of porto-systemic abdominal collaterals
 - C hepatic vein patency
 - D spleen size
 - E all of the above
- 3** **Which are the sonographic parameters to be reported in addition to the essential ones in patients with diagnosed chronic liver disease evaluated in a secondary referral center?**
 - A Portal vein: portal vein blood velocity; patency of its intrahepatic main and segmental branches, and, in the case of thrombosis, assessment of the extension of the clot (partial or total; percentage of lumen occupied by thrombosis).
 - B Hepatic veins: course, semi-quantitative assessment of diameter and pattern of blood flow.
 - C Splenic vein and superior mesenteric vein: patency, diameter and its respiratory variation, and blood flow direction.
 - D Ascites: semi-quantitative assessment of the amount (minimal, mild, moderate, massive).
 - E All of the above
- 4** **Which of the following Doppler US patterns indicates shunt patency in a patient receiving a surgical meso-caval shunt?**
 - A Anechoic appearance of the superior mesenteric vein lumen.
 - B Reversal of the flow direction in the portal trunk and splenic vein.
 - C Reversal of the flow direction in the portal trunk and distal tract of the superior mesenteric vein.
 - D A triphasic flow pattern in the hepatic veins and a high resistance index in the splenic artery in patients with hepatopetal flow all along the superior mesenteric vein.
 - E Hepatopetal flow in the splenic vein, portal trunk and intrahepatic portal branches, with a phasic flow profile.
- 5** **Which of the following is a reason for repeating abdominal ultrasound examination in a patient with cirrhosis hospitalized for an episode of clinical decompensation?**
 - A rule out hepatocellular carcinoma (often complicates portal hypertension)
 - B rule out portal vein, splenic vein and mesenteric vein patency thrombosis (induce sudden increases in portal pressure)
 - C assess the amount of ascites
 - D rule out possible foci of intra-abdominal infections
 - E all of the above
- 6** **Which of the following findings in the follow-up sonographic evaluation of patients with cirrhosis was shown to suggest worsening of portal hypertension and predict first clinical decompensation?**
 - A decrease $\geq 5\%$ in portal vein velocity after 6 months
 - B spleen enlargement ≥ 1 cm or more after 12 months
 - C increase $\geq 10\%$ in superior mesenteric artery pulsatility index after 6 months
 - D decrease $\geq 10\%$ in renal artery resistance index after 12 months
 - E increase $\geq 10\%$ in respiratory variation of splenic vein diameter after 6 months
- 7** **Which of the following statements about Doppler examination in patients with cirrhosis is false?**
 - A Increased splenic artery impedance indexes suggest CSPH in patients with cirrhosis.
 - B Loss of pulsatility of hepatic veins is associated with a higher mortality.
 - C Hepatofugal flow (reversal of flow) in the portal vein system is not a sign of CSPH.
 - D Increased renal artery impedance indexes are an independent predictor of renal dysfunction.
 - E Increased congestion index of the portal vein is an independent predictor of first variceal bleeding in the following 6 months.
- 8** **Which of the following statements about the follow-up of patients on beta-blockers for portal hypertension is true?**
 - A Patients on chronic beta-blockers can be monitored by US, since the decrease in HVPG strictly correlates with decreases in portal blood velocity and flow.
 - B Portal pressure response to chronic beta-blockers cannot be monitored by US since the decrease in HVPG is not accurately reflected by the changes in any of the US parameters.
 - C Patients on chronic beta-blockers can be monitored by US, since the decrease of HVPG strictly correlates with increase in flow oscillations in the hepatic veins.
 - D Patients on chronic beta-blockers can be monitored by US, since the decrease in HVPG strictly correlates with the increase in the superior mesenteric artery pulsatility index.
 - E Patients on chronic beta-blockers can be monitored by US after first drug administration, since the chronic decrease in HVPG strictly correlates with the decrease in portal vein blood flow observed in Doppler US after acute beta-blocker administration.
- 9** **Which one of the following treatments available for portal hypertensive patients should be routinely followed-up by ultrasound?**
 - A non-cardioselective beta-blockers
 - B endoscopic variceal band ligation
 - C Terlipressin
 - D transjugular intrahepatic porto-systemic shunt
 - E somatostatin or somatostatin analogs
- 10** **After TIPS placement for variceal bleeding, which of the following usually does not occur?**
 - A reversal of intrahepatic flow in the portal branches
 - B increase in portal vein velocity
 - C high velocity flow within the stent
 - D disappearance of porto-systemic collaterals
 - E disappearance of ascites

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Die Fortbildungspunkte der Ultraschall in der Medizin werden gemäß der Novellierung der DFP-Richtlinien vom 23.6.2005 (§26 Abs.3) auch von den österreichischen Ärztekammern anerkannt.

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Die Fortbildungspunkte der Ultraschall in der Medizin werden gemäß der Richtlinien der SGUM/SSUM anerkannt. Die Kontrolle der Fortbildung durch die SGUM/SSUM erfolgt im Auftrag der FMH (Foederation Medicorum Helveticorum) im Rahmen der Fortbildungsordnung.

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The EFSUMB Guidelines and Recommendations on the Clinical Practice of Contrast Enhanced Ultrasound (CEUS): Update 2011 on non-hepatic applications

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DOI <http://dx.doi.org/10.1055/s-0031-1281676>

Published online

August 26, 2011

Ultraschall in Med 2011; 32:

33–59 © Georg Thieme Verlag

KG Stuttgart · New York ·

ISSN 0172-4614

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List of Abbreviations

AAA = Abdominal Aortic Aneurysm
 AUC = Area Under the Curve
 CE = Contrast Enhanced
 CECT = Contrast Enhanced Computed Tomography
 CEMRI = Contrast Enhanced Magnetic Resonance Imaging
 CEUS = Contrast Enhanced Ultrasound
 CE-TCCS = Contrast Enhanced Transcranial Colour-Coded duplex Sonography
 CE-EUS = Contrast Enhanced Endoscopic Ultrasound
 CT = Computed Tomography
 DCE-US = Dynamic Contrast Enhanced Ultrasound
 EFSUMB = European Federation of Societies for Ultrasound in Medicine and Biology
 EUS = Endoscopic Ultrasound
 HCC = Hepatocellular Carcinoma
 NFS = Nephrogenic systemic fibrosis
 GIST = Gastrointestinal Stromal Tumour
 MI = Mechanical Index
 RECIST = Response Evaluation Criteria in Solid Tumours
 PET = Positron Emission Tomography
 RI = Resistance Index
 ROI = Region of Interest
 TIC = Time Intensity Curve
 UCA = Ultrasound Contrast Agent
 US = Ultrasound
 VUR = Vesico-ureteral Reflux
 WFUMB = World Federation of Societies for Ultrasound in Medicine and Biology

1. Introduction

The first studies on the clinical use of ultrasound contrast agents (UCAs) with contrast specific imaging techniques were published at the beginning of this century using Levovist® as UCA [1, 2]. A couple of years later sulphur hexafluoride (SonoVue®, Bracco, Milan) was marketed in Europe, opening the era of real time low mechanical index (MI) contrast enhanced ultrasound (CEUS). The European Federation of Societies for Ultrasound in Medicine and Biology (EFSUMB) released the first Guidelines on the use of CEUS in 2004 [3]. This document, which focused mainly on liver applications, contributed to the rapid expansion of CEUS and sanctioned the acronym "CEUS". CEUS was felt to be a revolutionary technique and many new applications, besides those in the liver, were developed in the following years. Therefore, in the update of the Clinical Recommendations on the use of CEUS by the EFSUMB, published in 2008 [4], applications in some other organs were described. Since then, there has been exponentially increasing interest in the clinical applications of CEUS and new fields have been investigated, so that nearly all organ systems have now been subjected to some kind of CEUS study. More than half of the approximately 900 original investigative articles (editorials and letters excluded) found in PubMed® under the search term "Contrast Enhanced Ultrasound" by the end of 2010 were published after 2008, after the last update of the EFSUMB guidelines [4]. Therefore, in 2010 EFSUMB felt it was the right time to start preparing a new update of the Guidelines. In the light of the expansion in CEUS usage, it was felt that a new update on CEUS for liver applications would be more beneficial to the clinical community if endorsed on a worldwide basis. Therefore, an agreement was reached with the World Federation of Societies for Ultrasound in Medicine and Biology (WFUMB) to prepare joint guidelines with EFSUMB exclusively for liver applications, taking advantage of its previous experience and of the previously published document [4]. These are expected to be issued as double simultaneous publications in *Ultraschall in der Medizin*/European Journal of Ultrasound and in *Ultrasound in Medicine and Biology*. At the same time the EFSUMB Executive Bureau decided that non-liver applications would be covered by a dedicated EFSUMB document under the guidance of a steering committee. The steering committee chose a panel of authors on the basis of their publication records in the various fields of interest and their reputation as international experts in research and teaching CEUS. By necessity, this list of co-authors could include only a limited number of persons and we acknowledge that many other highly qualified CEUS operators are active throughout Europe and have published valuable scientific articles on different CEUS topics. EFSUMB regrets not being able to include all of them in this process.

These Clinical Recommendations on the use of CEUS are based on comprehensive literature surveys including results from prospective clinical trials. In the case of topics for which no or little significant study data were available, evidence was obtained from expert committee reports or was based on the views of experts in the field during a consensus conference held in Frankfurt in April 2011.

As with the previous editions, these recommendations provide general advice for the use of UCAs. They are intended to create standard protocols for the use and administration of UCAs and improve the patient management. Individual cases must be

managed on the basis of all clinical data available for that specific patient.

A few points are worth special mention. Many applications included in this article continue to be off-label. UCAs registered in Europe are licensed only for cardiac or, in the case of SonoVue®, for liver, breast and vascular applications. Levovist® is also registered for vesico-ureteric studies, but is practically no longer marketed, and is expected ultimately no longer be available. The current legal requirements for registration of pharmaceutical products in Europe are strict. In order for a new indication to be registered, the manufacturer must provide data on safety and efficacy, with a dedicated phase III trial specifically designed to obtain that registration approval. Diagnostic agents, including contrast microbubbles, are not exempt from this rule, which is designed to protect patients from misuse of drugs or diagnostic agents but, on some occasions, may limit the potential benefit to patients. In fact, applications for indications not only follow clinical or scientific needs, but also the financial expectations of the producer. Similarly, for some products, the marketing forecast for income from additional indications is lower than the cost of a registration trial, so that new indications, especially for some organs, are highly unlikely to appear. However, lack of registration does not mean lack of efficacy of a marketed compound. Having said that, we must not forget that UCAs continue to be off-label for many non-liver indications detailed in the present recommendations. This means that patients should be informed and must consent to the investigation, and this is the responsibility of the operator. Indeed, non-liver CEUS is frequently performed on demand, to address specific questions raised in the individual patient. This explains (and justifies!) why it is not simple to write definitive guidelines and recommendations for the extrahepatic applications of CEUS.

CEUS has a number of distinct advantages over CT and MRI. It can be performed immediately, without any preliminary laboratory testing, and it can be carried out in a variety of scenarios (bedside, operating room, CT suite, etc.). Importantly also, it operates in real time so that rapid changes can be captured.

What then is the role of the current document? Firstly, it explains rationale for proceeding with the investigation, both to patients and clinicians, since for most situations the benefits are clearly outlined in this article. Secondly, it reports on the extremely rare and limited risks to which patients are exposed when they undergo a CEUS examination. These two points together facilitate and expedite the explanation of the risk/benefit ratio for the specific investigation to which a patient may be asked to consent. One example of this is in paediatric applications, for which the EFSUMB officers have already expressed a similar point of view [5].

Finally, based on the literature and the experts' consensus, an attempt was made to provide a recommendation level for each indication. The British guidelines for reporting on this topic have been used, as found at http://www.essentialevidence-plus.com/product/ebm_loe.cfm?show=guidelines, accessed in March 2011, in which the more detailed criteria of the Centre for Evidence Based Medicine in Oxford have been incorporated after slight adaptation (● Table 1).

A: There is good research-based evidence to support the recommendation.

B: There is fair research-based evidence to support the recommendation.

Grade level	Type of evidence (adapted from the modality of the Centre for Evidence Based Medicine, Oxford)	
1a:	Systematic review of level 1b studies	
1b	Prospective independent blind comparison (separate readers) of an <i>appropriate</i> spectrum/number of <i>consecutive</i> patients, all of whom have undergone both the diagnostic test and the reference standard	
2a	Systematic review of level 2b or level 4 studies	
2b	Study performed in a set of <i>non-consecutive</i> patients or confined to a <i>narrow</i> spectrum/number of patients all of whom have undergone both the diagnostic test and the reference standard	
3	Systematic review of case-control studies (no intra-individual comparison)	
4	Reference standard was not valid (unobjective, unblinded or not independent) or study was performed in an <i>inappropriate</i> spectrum /number of patients	
5	Expert opinion	
This scale will be also translated into a synthetic judgement of strength of recommendation using the following scale:		
A	Recommendation based on good evidence	At least one multicentre level 1 or 2 study or ≥ 3 monocentric level 1 or 2 studies
B	Recommendation based on moderate evidence	One of the following: <3 monocentric level 1 or 2 studies 1 level 3 study (systematic review) 1 multicentre level 4 study ≥ 3 monocentric level 4 studies
C	Recommendation based on experts opinions	Consensus of experts not supported by sufficient data of evidence level A or B.
0	No indication	
X	Contraindication	

Table 1 Criteria for the assessment of the level of evidence for the EFSUMB non-liver CEUS guidelines. Adapted from: Centre for Evidence Based Medicine, Oxford (http://www.essential-evidenceplus.com/product/ebm_loe.cfm?show=oxford).

C: The recommendation is based on expert opinion and panel consensus.

X: There is evidence that the intervention is harmful

0: We added level 0 for situations in which not enough information was available to provide a recommendation.

In addition to the level of the recommendation (A, B, C, X or 0), we reported the strength of the recommendation based on the study with the highest quality supporting the recommendations, according to the classification detailed in **Table 1**.

2. General Considerations



Any CEUS examination should be preceded by careful assessment of the target with conventional B-mode US and, when appropriate, with Doppler (spectral and/or colour/power). Before starting any CEUS examination, all relevant clinical information, including laboratory tests and previous imaging investigations, useful for reaching the expected final diagnosis, should be reviewed. This also helps to explain the expected benefit of the proposed CEUS study to the patient, an important step in obtaining consent.

Four transpulmonary UCAs are currently approved by the European Medicines Agency for use in European countries. The products and indications may vary on other continents.

- ▶ Levovist® (air with a galactose shell and palmitic acid as a surfactant) (Bayer-Shering Pharma AG, introduced in 1996). Production of Levovist has been discontinued and its use is not considered in these Recommendations.
- ▶ Luminity® (perflutren) (octafluoropropane with a phospholipid shell) (Lantheus Medical Imaging, inc., introduced in 2006). Sole European indication to date is cardiac which is outside the scope of these recommendations.
- ▶ Optison® (octafluoropropane – perflutren with an albumin shell) (GE Healthcare Inc., introduced in 1998). Sole European indication to date is cardiac which is outside the scope of these recommendations.

- ▶ SonoVue® (sulfur hexafluoride with a phospholipid shell) (Bracco Spa, introduced in 2001). Registered indications in Europe are cardiac, macrovascular, liver and breast lesions.

This is the main agent in general use.

The composition, packaging, storage, indications and contraindications of these agents are detailed in the respective web-pages of the manufacturers, whose addresses can be reached following the informations reported in Appendix 1.

Other UCAs are approved outside Europe and several more are under investigation.

Dose of contrast agent and data storage. For SonoVue®, which is the focus of the current document and which is the UCA used in almost all of the referenced articles, the recommended dose is 2.4 mL. This can be increased to 4.8 mL or decreased to 1.0 mL or less depending on the sensitivity of the equipment used, the type of transducer and the organ under investigation. When using higher frequency transducers, a dose of 4.8 mL performs better. A real-time videoclip should be recorded, preferably digitally, for review and documentation. The clip should include at best the whole examination or at least the most relevant parts, usually corresponding to the initial 10–40 seconds starting at the onset of enhancement with additional shorter clips taken at 2–3 minutes. Finally, either the entire clip (preferred choice) or at least various selected most relevant frames should be stored permanently [6–9].

3. Equipment



Contrast-specific US modes are required and are generally based on the cancellation and/or separation of linear US signals from tissue and the utilisation of the non-linear response from microbubbles.

The non-linear response from microbubbles arises from two different mechanisms:

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

Non-linear harmonic US signals also arise in tissues themselves from distortion of the sound wave during its propagation through the tissue. The extent of this tissue harmonic response increases with the acoustic pressure, which is proportional to the MI. The precise unit of measurement for acoustic pressure is the Pascal, but the most common reference unit is the MI. Minimisation of bubble disruption is the main reason for using low MIs for real time imaging but it also reduces tissue harmonics and artefacts, thus facilitating the separation of signals from UCAs from those of tissue. Low MI is typically below 0.3, but most equipments work well at MIs much below this (for details see manufacturers' recommendations or contact the manufacturers' representatives). For the purpose of this document, CEUS is defined as low MI real time contrast specific imaging, unless otherwise specified. This is in agreement with the terminology of the vast majority of the literature.

Technical information on US equipment capable of CEUS imaging can be accessed via the respective webpages reachable through the web address reported in Appendix 1. Updating this information is the responsibility of the companies.

EFSUMB is unable to express any judgement on the quality of particular scanners or transducers. However, the following features should be kept in mind, as they characterise the quality of the equipment used for CEUS examinations:

Sensitivity reflects the ability of a system to detect extremely small amounts of microbubbles. Good sensitivity extends the duration of useful enhancement.

When using high frequency probes, higher doses of UCA may be needed to achieve a sufficient enhancement level, as these frequencies are higher than those at which current UCAs resonate most strongly.

The ability to image small differences in local contrast concentration is a component of sensitivity. It reflects the dynamic range of contrast performance.

Tissue suppression is mandatory to differentiate contrast enhancement from tissue echoes. Strongly reflective structures such as vessel walls, the abdominal wall and gas-filled structures can break through and appear on the CEUS part of the screen.

Resolution. As in B-mode, temporal and spatial resolution are important for CEUS imaging. Temporal resolution is defined by the frame rate at a given line density, depth and width. A high frame rate allows visualisation of the flow direction in arteries. It may also produce more rapid destruction of bubbles within the acoustic field. Spatial resolution mainly refers to the ability to display bubble echoes with optimal detail. Additionally, the image should be homogeneous throughout.

Like all imaging techniques, CEUS has artefacts, mainly caused by incorrect machine settings or UCA dosages [10]. The MI is the most important setting for CEUS and gain is the second one. Adequate training allows knowledge, recognition and prevention of artefacts.

4. Investigator Training

Competence ensured by adequate training is a prerequisite to achieve correct diagnoses when using ultrasonography and

especially CEUS. EFSUMB has defined three levels of training in its minimal training requirements [11] (EFSUMB Appendix 14) [12] and recommends that CEUS should be performed by operators at a competence level higher than Level 1. To ensure adequate training, EFSUMB started a new initiative to organise dedicated Euroson Schools on CEUS in 2009 [13].

EFSUMB advises that investigators intending to start using CEUS spend some time under the supervision of an expert, who is preferably at Level 3. It is important that there is a sufficient number and variety of examinations in their own department. Investigators should also consult the manufacturers to ensure that their scanner is optimised for CEUS examinations. The practice of CEUS also requires knowledge of UCA administration and contraindications and the skill to handle possible side effects within the medico-legal framework of their country.

5. Terminology

UCAs were initially developed to enhance Doppler US and any scanner with Doppler facilities can be utilised for this. Conventional Doppler US operates at a higher acoustic power than real-time contrast-specific modes. Consequently microbubble disruption occurs at a high rate and the enhancement does not last long (a few minutes) after bolus injection. Moreover, the injection of contrast as a bolus often produces an initial "blooming" effect (proportional to the amount of contrast utilised), so that either smaller amounts or a continuous infusion (1–2 ml per minute) may be preferable. This technique has few applications nowadays since CEUS can provide information either more accurately or in an easier way in most organs.

During CEUS, the screen should show only a few signals from intensely reflective structures, such as signals generated by the large difference in acoustic impedance between the lung and the diaphragm (overload of the tissue suppression software). This applies both to single-screen contrast-only displays and to the split-screen display, where the CEUS image is shown alongside a low MI version of conventional B-mode image. In some equipment a single panel mixed mode is used. In these cases, the underlying conventional B-mode image is seen, with the CEUS overlay displayed in a different colour, potentially with the addition of colour Doppler information.

The description of the behaviour of tissue or lesion under examination should be in terms of its enhancement, taking into consideration its temporal behaviour, degree of enhancement, and contrast distribution.

1. As regards the **timing** of enhancement, two phases are apparent for most organs:

- a) the arterial phase, starting from the first arrival of contrast (usually in 10–20 seconds) until around 30–45 seconds, during which the degree of enhancement increases progressively.
- b) the venous phase which starts from approximately 30–45 seconds after contrast injection, during which the degree of enhancement shows a plateau and then decreases progressively until microbubble signals have disappeared completely or fallen to the noise level. Most organs have a single blood supply with a single inflow (namely arterial) phase, the exceptions being the liver, which is supplied by its artery and the portal vein, leading to two distinct inflow phases (arterial and portal venous) and the lungs, which are supplied by pulmonary and bronchial arteries with different arrival times.

The liver and spleen are also exceptions in that they tend to retain microbubbles longer than other organs, probably due to the trapping of microbubbles in their unique microcirculations after clearance from the remainder of the macrovasculature. Consequently, the wash-out phase in most organs is shorter than in the liver and spleen, whose prolonged retention is termed the late phase. There is no precisely definable event that allows an exact distinction between the arterial and venous and late phases.

The time of contrast arrival is usually 10 to 20 seconds after i.v. injection, but factors such as a slow injection of microbubbles in very peripheral small veins or cardiac diseases may prolong it, whereas intracardiac or pulmonary shunting or a hyperdynamic circulation may shorten it.

2. The **degree** of enhancement is difficult to assess, unless measurements are made using in-built or off-line software, for example, in the assessment of tumour response to antiangiogenesis treatment [14]. Generally, when the target of the study is a focal region in a parenchymal organ, the degree of enhancement should be compared to the surrounding parenchyma or to the paired organ when available. The lesion might be relatively hyperenhancing, isoenhancing, hypoenhancing or non-enhancing and the pattern should be described separately for the arterial and venous phases. The transition from hyper- or iso-enhancement to hypoenhancement is commonly referred to as "wash-out". The use of this term for other enhancement patterns creates confusion and should be avoided. EFSUMB recommends that reports on CEUS are made in terms of the degree of enhancement. For targets that have no background tissue to describe the relative enhancement (studies of large vessels, endocavitary administration, or when a mass occupies an entire organ, etc), it is important to describe the presence or absence of enhancement and its distribution (e.g. in septa within a complex cystic mass or a fluid-containing structure, or blood flow where this is not expected to be present, for instance outside an organ) whereas the degree of enhancement is more difficult to assess.
3. Contrast **distribution**. When enhancement is seen, its distribution should be described. The relevant terms have not been predetermined and should be chosen with the aim of characterising the tissue and reaching a diagnosis. The description of whether the enhancement is homogeneous or heterogeneous and, in the latter case, if non-perfused regions exist, should be included. Any further description of the enhancement pattern is left to the operator inspired by the recommendations for each organ. In general terms, the CEUS depiction of non-perfused (potentially necrotic or liquid) areas might be relevant prior to any US-guided biopsy in order to better identify the target.

6. Safety

In general, UCAs are very safe with a low incidence of side effects. They are not nephrotoxic and do not interact with the thyroid gland and it is therefore not necessary to perform laboratory tests before their administration. The incidence of severe hypersensitivity or anaphylactoid reactions is lower than with current X-ray agents and is comparable to that of MR contrast agents. UCAs are not licensed in pregnancy. Breastfeeding is a contraindication in some countries.

Life threatening anaphylactoid reactions have been reported with a rate of less than 0.002% [15, 16]. Previous allergic/anaphylactoid reaction to X-ray iodinated contrast agents does not necessitate the prophylactic use of steroids or antihistamines prior to UCA injection since the two types of agent are completely different.

There is a theoretical possibility that the interaction of diagnostic US and UCA could produce bioeffects. *In vitro* cellular effects that have been observed include sonoporation, haemolysis and cell death. Although observed *in vitro*, such bioeffects may have relevance for the *in vivo* situation as they result from interactions between gas bodies and cells. Data from small animal models suggest that glomerular capillary haemorrhage and other microvascular rupture could occur when microbubbles are insonated at high MI [16]. This could be injurious in specific situations in which such vascular damage would be clinically important such as in the eye and brain. This potential for non-thermal bioeffects exists with all modes, including conventional 2D imaging and 3D methods. The MI provides a useful, albeit very rough, on-screen indicator of the potential for non-thermal effects. Changes have been observed *in vivo* in mammalian tissue models for diagnostic US exposures with an MI greater than ~0.4 in the presence of UCAs. In addition, premature ventricular contractions have been described when high MI end systolic triggering is used in echocardiography [17, 18].

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

Some general recommendations are:

- ▶ Resuscitation facilities should be available.
- ▶ Caution should be exercised for off-label use of UCA in tissues in which damage to the microvasculature may have serious clinical implications, such as in the eye, the brain and in the neonate.
- ▶ As in all diagnostic US procedures, the operator should be mindful of the desirability of keeping the displayed MI low and of avoiding unduly long exposure times. Caution should be exercised when using UCAs in patients with severe coronary artery disease and pulmonary hypertension. Unstable ischaemic heart disease in the 7 days prior to administration is a relative contraindication. Caution with respect to the use of UCAs in these cardiac instances derives from an anecdotal temporal, but unproven causal, association between contrast injection and death in severely compromised cardiac patients. However, in very large patient cohorts, the use of UCAs for acute cardiac patients has been shown to be associated with a decreased, not increased risk of death, thanks to the efficacy of the modality [19, 20].

7. Paediatrics

The current use of CEUS in paediatric work-up in Europe is peculiar. Two UCAs are registered for clinical non-cardiac use, Levovist® and SonoVue®. However only Levovist® is approved for use in children and adolescents and only for the indication of vesico-ureteral reflux study. At the same time production of Levovist® has ceased and it is no longer available. SonoVue®, performs equally well for this particular indication, but has to be used off-label, as previously mentioned.

CEUS in paediatric applications remains of critical importance, because of its obvious benefits compared to alternative imaging modalities, which in most cases necessitate exposure to ionizing radiation and the use of potentially harmful contrast agents. The benefit of avoiding ionizing radiation is clearly far more important in children and adolescents than in adult patients. This important question was addressed recently in a Letter to the Editor of *Ultraschall in der Medizin/European Journal of Ultrasound*, with a reply from the EFSUMB Executive Board [5]. There is no easy solution to this problem as strict rules and regulations apply to the official registration of medical drugs, which is of course for the safety of patients and thus to the benefit of all, including the medical community and pharmaceutical producers. In some situations, however, strict regulations may inhibit use of the most beneficial and simple techniques or drugs, and CEUS is one such example.

8. Pancreas



8.1 Background

CEUS is not indicated for the detection of focal solid or liquid pancreatic lesions, but can be utilised for the characterisation of sonographically detected lesions [21–23]. The use of CEUS improves the diagnostic accuracy of US in the study of pancreatic pathologies.

8.2 Study Procedure

CEUS is an accurate imaging method, superior to Doppler techniques, for the visualisation of intrapancreatic vessels and microvessels [24]. Enhancement of the pancreas begins immediately after aortic enhancement. After this early arterial phase (10 to 30 sec), there is a transient venous phase (30 to approximately 120 sec), as with other dynamic imaging modalities [4].

The CEUS study of a pancreatic mass should aim at its characterisation and the evaluation of its relationship with the peripancreatic arteries and veins [21, 22, 25, 26]. After completion of the pancreatic study, the liver should be assessed in the late phase, exploiting the same contrast injection, searching for metastases [22].

8.3 Pancreatic Masses

8.3.1 Image interpretation for lesion characterisation

The enhancement pattern of focal pancreatic lesions is usually compared with the adjacent pancreatic tissue. Therefore, the field of view should include the mass under investigation together with a portion of surrounding pancreatic parenchyma.

8.3.2 Adenocarcinoma

Ductal adenocarcinoma, the most common primary malignancy of the pancreas, is typically hypoenhancing in all phases, presumably because of the desmoplastic reaction and low mean vascular density [27–29]. This pattern is reported in about 90% of cases [23, 27, 30]. Lesion size and margins as well as the relationship with peripancreatic vessels are better visualised with CEUS than with conventional US [25, 26].

CEUS can demonstrate changes in pancreatic tumour vascularisation during chemotherapy [31, 32] raising a hope for future use in clinical practice.

8.3.3 Neuroendocrine tumours

Neuroendocrine tumours typically present as hyperenhanced masses in the arterial phase, owing to their abundant arterial vascularisation, even when the Doppler study is negative [21, 33, 34]. In larger tumours necrotic avascular areas result in inhomogeneous enhancement [33, 34].

8.3.4 Mucin-producing cystic tumours

CEUS improves the ultrasonographic differential diagnosis between pseudocysts and cystic tumours of the pancreas by accurately revealing vascularisation of intralésional septa or nodules [22].

Mucinous cystadenoma is a potentially malignant lesion that may transform into cystadenocarcinoma. Usually unilocular, it appears as a round macrocystic lesion, with particulate content, irregular thick walls and internal inclusions which enhance on CEUS [30, 35]. In general, mucinous cystic pancreatic tumours have vascularised septa and parietal nodules [22, 35]. Intraductal papillary mucinous neoplasms (IPMN) are divided into main-duct and side branch-duct types. CEUS is helpful for differentiating between perfused (nodules) and non-perfused (clot) regions [36]. Magnetic resonance imaging (MRI) and endoscopic US (EUS) are the imaging methods of choice for the study of this tumour to demonstrate the communication of the cystic lesion with the pancreatic ducts [37, 38]. CEUS can be employed in the follow-up of borderline cystic lesions of the pancreas, if well visualised on US, in order to reduce the use of MRI.

8.3.5 Serous cystadenoma

Serous cystadenoma is a benign cystic lesion, typically with a lobulated microcystic appearance with thin and centrally oriented septa, which are vascularized on CEUS [22]. When the cysts are minute, microcystic serous cystadenoma may mimic a solid lesion, both on conventional US and CEUS. They are hyperenhanced on CEUS [38].

8.3.6 Pseudocysts

Pseudocysts typically contain non-vascularised material (debris), with the exception of transversing vessels, which are typically found in the early stages. Pseudocysts do not show any signal on CEUS and remain completely non-enhancing in all phases, even when they are heterogeneous on US [30, 35]. The reported sensitivity and specificity of CEUS in characterising pseudocysts is up to 100% [35].

8.4 Pancreatitis

In severe acute pancreatitis, CEUS may help identify and delineate necrotic areas, which do not enhance [39]. If the pancreatic region is clearly visible on US, CEUS can be used in the follow-up of acute pancreatitis after CT staging, in order to reduce the number of CT examinations [39].

Focal mass-forming pancreatitis and autoimmune pancreatitis have been reported to have similar enhancement to that of the normal pancreatic parenchyma [27].

8.5 Recommended uses and indications

Focal pancreatic lesions identified with US can be studied with CEUS in order to improve:

1. Characterisation of ductal adenocarcinoma. (Recommendation Level: A;1b)

2. Differential diagnosis between pseudocysts and cystic tumours. (Recommendation Level: A;1b)
3. Differentiation of vascular (solid) from avascular (liquid/necrotic) components of a lesion. (Recommendation Level: A;1b)
4. Defining the dimensions and margins of a lesion, including its relationship with adjacent vessels. (Recommendation Level: B;2b)
5. Management of the lesion with a better distinction between solid and cystic lesions, thus providing information for the choice of the next imaging modality (i.e. MRI and/or Endoscopic US for cystic lesions). (Recommendation Level: C;5)
6. Diagnosis in cases that are indeterminate on CT (vascularisation of solid pancreatic lesions; differential diagnosis between pseudocysts and pancreatic cystic tumours, especially mucinous cystic tumour). (Recommendation Level: C;5).

9. Contrast Enhanced Endoscopic US (CE-EUS)



9.1. Background

Contrast enhanced endoscopic ultrasound (CE-EUS) is a newly established method which combines the advantage of high resolution US of internal organs with the administration of UCAs [38]. CE endoscopic Doppler US works at high MI that does not require specific software and uses the UCA as a Doppler enhancing medium [40, 41]. Low MI CE-EUS has been introduced recently using the same contrast-specific modes as for transabdominal CEUS [42–44].

EUS will be performed first and CE-EUS can be added to characterise internal vasculature, to differentiate benign from malignant masses, and to improve staging and real-time guidance of diagnostic and therapeutic procedures.

9.2. Study procedures

9.2.1. Contrast enhanced high mechanical index EUS

In CE endoscopic Doppler US the colour Doppler window should include the whole tumour if possible. The Doppler frequency should be as high as possible, depending on the distance to the tumour. The Doppler scale should be between 3 and 8 cm/s assuming an insonation angle of 0° if directional colour Doppler is used [45]. The gain should be as high as possible without inducing artefacts. The flow velocity range (pulse repetition frequency, PRF) should be 5–15 cm/s if pulsed wave Doppler is used. The technique is the same as for transcutaneous US. CE endoscopic Doppler US scanning takes an extra 3–4 min [46].

9.2.2. Contrast enhanced low mechanical index EUS (low MI CE-EUS)

The technique is the same as described for the transcutaneous route. However, there are various settings that should be checked in accordance with the manufacturer. The MI used in published feasibility articles was variable [42, 43, 47], ranging from 0.08 to 0.3.

9.3. Image interpretation for pancreatic lesions

9.3.1 Discrimination of adenocarcinoma

CE endoscopic Doppler US can be used to differentiate between pancreatic neoplasms, mainly the hypoenhancing ductal adenocarcinoma and the iso- or hyperenhancing neuroendocrine tumours but also pseudo-solid lesions like serous microcystic cystadenoma [21, 37, 48]. The differential diagnosis

between ductal adenocarcinoma and mass-forming focal pancreatitis can be improved since adenocarcinomas mainly contain arterioles and hardly any venules whereas in focal pancreatitis both arterioles and venules are detectable during CE endoscopic Doppler US [45, 49–51]. The method can be improved further by estimation of the resistance index (RI) of the arterioles. The cut-off RI for suspected malignant lesions is >0.70 versus <0.70 for non-malignant, inflammatory lesions [52]. As for all other US applications, the limitations of CE endoscopic Doppler US are extensive calcifications and poor B-mode depiction of the lesion.

Low MI CE-EUS seems to be more powerful, but there is currently only minimal published data [53–55]. Analysis of the microvessel architecture seems to be an advantage over transcutaneous CEUS, e.g., the central feeding artery in serous cystadenoma [21]. The technique can be used in cases in which significant artefacts impede transcutaneous visualisation, especially for characterisation and follow-up of focal pancreatic lesions. The accuracy for the differential diagnosis of pancreatic adenocarcinoma is reported to be over 85% [53, 55, 56].

9.3.2 Discrimination of pancreatic pseudocysts from cystic tumours

Low MI CE-EUS can be also used for differential diagnosis in cystic pancreatic lesions [57] as described in the transcutaneous section. EUS has a clear advantage in small cystic lesions and in patients with impaired transcutaneous visibility.

9.4 Differential diagnosis of autoimmune pancreatitis

Both focal and diffuse autoimmune pancreatitis show hyperenhancement. Low MI CE-EUS is able to visualise hyperenhancement to discriminate ductal adenocarcinoma (which does not hyperenhance) from autoimmune pancreatitis [58] but experience is limited. 3D reconstruction might have a higher impact because of better visualisation of vessel patterns [58].

Recommended uses and indications

CE-EUS can be recommended for:

1. Discrimination of hypoenhancing ductal adenocarcinoma of the pancreas from other iso- or hyperenhancing lesions. Experience is mainly based on CE endoscopic Doppler US. (Recommendation Level: A;1b)
2. Discrimination of mass-forming chronic pancreatitis from ductal adenocarcinoma in patients with chronic pancreatitis. (Recommendation Level: A;1a)
3. Improved discrimination of cystic tumours from pancreatic pseudocysts. (Recommendation Level: A;1b)

10. Gastrointestinal Tract



10.1 Background

When examining the intestines, it is preferable to use frequencies above 7.5 MHz to enable optimal visualisation of wall layers, thickened bowel walls and lesions. Higher contrast doses (e.g. 2.4–4.8 ml SonoVue®) should be used. The arrival time in the intestinal capillaries is usually 10–20 sec after injection, particularly in the submucosal layer [59]. Peak enhancement is reached after 30–40 sec and this arterial phase is followed by a venous phase that lasts from 30 to approximately 120 sec.

10.2 Study procedure

Before i.v. UCA administration, the intestines must be examined in B-mode and Doppler US to detect any pathology. The difference in bowel wall microvasculature between healthy and diseased intestines can be recognised by CEUS [60].

10.3 Inflammatory Bowel Disease (IBD)

10.3.1 Image interpretation and evaluation

CEUS allows the quantification of bowel wall vascularity in patients with Crohn's disease [61] and correlates well with MRI of the intestinal wall [62, 63]. Additionally, CEUS visualises the microvasculature of the tissue surrounding the intestines. Time Intensity Curve (TIC) analysis may further help to quantify disease activity.

10.3.2 Disease activity

US can be used to study disease activity in IBD using bowel wall thickness and Doppler measurements as a marker of inflammation [64–66]. Adding a UCA improves reliability in estimating disease activity in Crohn's disease [67, 68]. Enhancement in different wall layers can be evaluated and quantified in Crohn's disease and correlates to clinical activity indices with good sensitivity and specificity [69–71]. Quantitative measurements of bowel enhancement obtained by CEUS also correlate with endoscopic severity [72] and histopathologic findings [71]. Furthermore, ultrasonographic evaluation of the changes of bowel wall enhancement during biological therapy (e.g. antiTNF agents) promises to be a useful and relatively cheap imaging modality for the clinical monitoring of the activity of Crohn's disease [73].

10.3.3 Distinguishing between fibrous and inflammatory strictures

Preliminary studies indicate that the use of UCAs is effective for the recognition of predominantly cicatricial stenoses in patients with Crohn's disease [74]. In patients with bowel stricture and resultant obstruction, it is important to determine whether there is active inflammation at the site of stricture or if the stenotic segment is fibrotic. Using CEUS, the active inflammatory components enhance strongly whereas a fibrotic stricture enhances poorly [75].

10.3.4 Abscesses

Distinguishing abscesses from inflammatory infiltrates is an important clinical task in the management of Crohn's disease. If areas of a significant size close to or within an affected bowel wall are completely devoid of microbubble signals, these lesions likely represent abscesses rather than inflammatory infiltrates, particularly if adjacent tissue shows hyperenhancement [61]. Similar findings also apply to abscesses caused by other diseases, e.g. diverticulitis [76].

10.3.5 Fistula

Injecting a UCA into one of the orifices of a fistula improves visualisation of the course of the fistula in Crohn's disease [77]. The UCA can be diluted manyfold with sterile saline before injection into orifices (see section on intracavitary applications).

10.4 Limitations

It is impossible to visualise all bowel segments using transabdominal US. Intestinal peristalsis can impair image quality and

the repeatability of quantitative measurement of bowel enhancement patterns. More studies are needed to establish the exact role of CEUS in the imaging of GI pathology [78].

Recommended uses and indications

CEUS is indicated in the following clinical situations:

1. Estimation of disease activity in inflammatory bowel disease. (Recommendation Level: B;1b)
2. Discerning between fibrous and inflammatory strictures in Crohn's disease. (Recommendation Level: C;4)
3. Characterisation of suspected abscesses. (Recommendation Level: C;4)
4. Confirming and following the route of fistulas. (Recommendation Level: C;4)

11 Spleen



11.1 Background

The indication for CEUS investigation of the spleen, other than in trauma (see section 15), is the characterisation of focal lesions [79]. Solid splenic lesions may be occasional incidental US findings in asymptomatic subjects. In this setting and when they are single or scanty, especially if they are hyperechoic on conventional US, they are benign in the large majority of cases. However, in cancer patients, especially when lesions are multiple, hypoechoic and of recent onset, they tend to be malignant. Unfortunately, the clinical information and US findings are not usually sufficient to provide a reliable distinction between benign and malignant masses. Fine needle biopsy of splenic masses may have complications, especially peritoneal bleeding, making a noninvasive diagnosis highly desirable. CEUS may increase confidence in suggesting a benign nature.

11.2 Study procedure

The peculiar splenic vascularisation [80] leads to a rapid and transiently inhomogeneous enhancement pattern, especially in congestive splenomegaly, resembling the "zebra" pattern seen on dynamic CECT or CEMRI. About 1 minute after injection, the parenchyma becomes homogeneous, showing strong and persistent late phase enhancement that lasts longer than 5 minutes [81].

11.3 Image interpretation

CEUS is useful for characterising ectopic splenic tissue (accessory spleens and post-splenectomy splenosis) [82]. Splenic hilar lymph nodes, adrenal lesions, pancreatic tail tumours, metastatic deposits, and other lesions show less enhancement than the normal splenic parenchyma in the late phase. Accessory spleens usually exhibit a typical location and appearance and further imaging is necessary only in a minority of cases. CEUS shows an enhancement pattern exactly paralleling that of the adjacent spleen [83], i.e. more intense than that of other organs in the late phase.

In splenic infarction, CEUS accurately demonstrates the shape and extent of the lesion as a wedge-shaped, non-enhancing area based on the spleen capsule and pointing towards the hilum [84].

A splenic abscess is a poorly- or completely non-enhancing lesion, best recognised in venous phase images, with an enhancing rim and septa. No contrast enhancement is seen within

the internal fluid, debris, or necrotic components. Intermediate and early stage lesions show mixed patterns, like those in the liver [85].

Typical findings for benign splenic lesions include either no contrast enhancement or rapid wash-in, followed by persistent enhancement in the late phase. If CEUS findings are consistent with a benign splenic lesion, CT seems to be of limited additional value [86]. In contrast, the combination of contrast enhancement (diffuse or peripheral) in the arterial phase followed by rapid and marked wash-out is typical for malignant lesions (metastases or lymphoma) [87–90]. However, the behaviour of malignant and some benign lesions partially overlap, since haemangiomas, hamartomas, as well as other uncommon splenic abnormalities, may show some degree of wash-out, mimicking a malignant pattern [90, 91].

11.4 Differential diagnosis and limitations

In patients with left upper quadrant pain and splenic inhomogeneity on conventional US, CEUS allows visualisation of the underlying splenic abnormalities [84] increasing operator confidence in establishing a diagnosis [92]. CEUS is particularly helpful when an infarcted region is barely recognisable on US or it is spherical and simulates a focal lesion. Additionally, CEUS can diagnose splenic tumour infiltration mimicking infarction on conventional US. Differentiating splenic abscesses from necrotic lymphomatous lesions remains a challenge, since both conditions may occur in the immunocompromised patient.

CEUS may be helpful when a splenic cyst with ill-defined margins and/or inhomogeneous content is identified with US. Echogenic splenic tumours incidentally found on US and assessed by CEUS can be diagnosed as haemangiomas and can be managed with follow-up examinations.

11.5 Splenic tumour detection

CEUS may aid in detecting focal lesions in the spleen [79]. Lesions that are not seen on baseline US can be revealed by CEUS, which has been found to be 90% sensitive and 100% specific compared to CT with respect to lesion detection in lymphoma patients [93]. In a retrospective study on splenic metastases, CEUS increased the detection rate by 38% [94]. Lesions found in patients with solid organ or haematological malignancies require whole-body imaging using CT and/or PET [95], but CEUS can be useful if they are inconclusive, particularly to rule out lesions when PET shows “non-specific uptake”. Finally, CEUS can be used in patients with splenic malignancies to monitor their response to treatment. When chemotherapy is successful, the lesion becomes almost non-enhancing on CEUS with absence of any intra-nodular vessels or microcirculation. These findings are seen early, paralleling the PET response. Long-term follow-up shows progressive disappearance of the lesions.

Recommended uses and indications

CEUS can be utilised:

1. To characterise splenic parenchymal inhomogeneity or suspected lesions on conventional US. (Recommendation Level: B;1b)
2. To confirm suspected splenic infarction. (Recommendation Level: B;2b)
3. To characterize suspected accessory spleens or splenosis. (Recommendation Level: B;2b)

4. To detect splenic malignant lesions in oncologic patients when CT and/or MRI and PET are contraindicated or inconclusive. (Recommendation Level: B;1b)

12. Kidney



12.1 Background and vascular anatomy

In most centres, ultrasonography is the preferred first imaging modality in patients with known or suspected renal disease. The main objectives are to measure renal size, to detect focal lesions and obstruction of the collecting system and to look for vascular disorders. However, US is not reliable in distinguishing between different types of tissue and benign and malignant lesions may be difficult to distinguish. Doppler helps to characterise renal blood flow, with limitations because of attenuation, poor sensitivity for very slow blood flow, and angle dependency.

12.2 Study procedure

Kidneys enhance quickly and intensively after microbubble administration. The arterial pedicle and main branches enhance first, followed within a few seconds by complete fill-in of the cortex. Unlike with Doppler US, signals from microbubbles are independent of the angle of insonation, and depiction of renal perfusion is excellent even at the renal poles. Medullary perfusion follows cortical perfusion, with the outer medulla enhancing first, followed by gradual fill-in of the pyramids [96]. There is no microbubble excretion into the urinary tract. As contrast concentration in the general circulation decreases, enhancement fades. The expert opinion is that contrast enhancement is less intense and fades earlier in patients with chronic renal disease.

12.3 Renal ischaemia

Several investigations, both in animal studies and in humans, have shown excellent diagnostic performance in the detection of renal parenchymal ischaemia, similar to that of CECT [97] and superior to colour Doppler US, making CEUS a recommended technique in case of suspicion of infarction. Infarcts appear as wedge-shaped non-enhancing areas within an otherwise enhanced kidney. The excellent spatial resolution of CEUS allows confident differentiation between renal infarction and cortical necrosis, which appears as non-enhancing cortical areas with preserved hilar vascularity [96, 98].

Another important application of CEUS in patients with renal ischaemia is differentiation between non-perfused, infarcted tissue and hypoperfused parenchymal regions. On Doppler US, both appear as areas lacking colour signal, but only infarcted areas completely lack contrast enhancement after microbubble injection.

12.4 Renal artery stenosis

UCAs can be injected to improve the sensitivity of conventional colour Doppler US in identifying the renal arteries, with an improvement of approximately 10% [99]. This allows correct positioning of the sample volume for the detection of Doppler spectral tracings with the aim of screening for renal artery stenosis. Routine use of UCA offers no significant advantage [99].

12.5 Renal focal lesions

12.5.1 Differential diagnosis between cystic and solid lesions

Thanks to its excellent sensitivity, CEUS is more sensitive than CECT in detecting blood flow in hypovascularized lesions [100] and can be utilised in the few cases in which the distinction between solid hypovascular tumours (showing enhancement, even if there is very little flow) and atypical cystic masses (no contrast perfusion at all) remains unresolved after CT and colour Doppler US.

12.5.2 Differential diagnosis between solid renal masses and pseudotumours

The enhancement in renal tumours differs from the surrounding parenchyma, with a difference in degree or distribution of enhancement in at least one vascular phase, in the majority of cases. This helps differentiation between tumours and pseudotumours, since the latter have the same enhancing characteristics as the surrounding parenchyma in all phases [96, 101]. Solid renal tumours do not show diagnostic perfusion patterns on CEUS, which is thus usually not able to differentiate between malignant and benign solid renal masses (e.g. carcinoma versus angiomyolipoma).

In expert hands, CEUS may help identify renal vein invasion by cancers with an accuracy comparable to CECT [102]. In addition, in the opinion of the experts, the arterial vascularisation of the thrombus in the renal vein promises to differentiate bland thrombus (non-enhancing) from tumour invasion (enhancing thrombus), but further studies are necessary.

12.5.3 Characterisation of complex cystic renal masses

CEUS allows the characterisation of renal cystic lesions as benign or malignant with at least the same accuracy as CECT. It is more sensitive than CT in detecting enhancement of the cystic wall, septa, and solid components [103–106]. Nonetheless, CT remains the reference method for staging patients with malignant cystic lesions. CEUS is very well suited for the follow-up of non-surgical lesions and might replace CT, in light of its lack of contraindications, wide availability and lack of ionizing radiation, all of which are particularly welcome in this setting.

12.5.4 Renal infections

Following the European Urology Association guidelines, diagnosis of acute uncomplicated pyelonephritis is based on the clinical picture and laboratory findings. Conventional B-mode US is used to rule out urinary obstruction and renal stones. Additional investigations should be considered if the patient remains febrile after 72 h of treatment. These recommendations have a low level of evidence, and are made despite the absence of directly applicable clinical studies of good quality. As a consequence, the role of CEUS and of imaging itself in patients with uncomplicated pyelonephritis is debated and no clear indications exist, despite the finding that CEUS depicts renal abscesses as non-enhancing regions and can be used to monitor their course [96].

12.6 Assessment of percutaneous ablation therapies

Percutaneous ablation plays an increasing role in the management of patients with renal tumours. Diagnostic imaging in these patients includes CECT and/or CEMRI imaging during pre-treatment work-up and at distinct time points during follow-up after treatment. Unenhanced US can be used to guide

ablation, but does not provide enough information about the outcome of ablation treatments. There is increasing evidence that, CEUS overcomes many of these limitations in patients undergoing renal tumour ablation [107]. It provides important information on lesion vascularity, and may improve visualisation of lesions that are poorly demonstrated on the baseline US scan. Guidance of the ablation needle into the lesion and assessment of the therapeutic results are improved [108, 109]. Similarly to the liver, the intra-procedural assessment must be delayed by 5–10 minutes after the end of the ablation to allow the heat-generated gas and the related artefacts to dissipate. Any contrast enhancement within the ablation zone is conventionally regarded as residual tumour. Larger vessels surrounding the ablated region may be misinterpreted as residual tumour. Meticulous comparison with pre-procedural examinations and evaluation of lesion morphology are therefore important to avoid misdiagnosis, since residual tumour presents as nodular or crescent-like enhancing regions, with enhancement remaining similar to what observed in the tumour before treatment [110]. In two recent series of 28 [111] and 66 [110] renal tumours with sufficiently long follow-up, CEUS provided similar overall accuracy to that of CT/MRI in confirming the adequacy of treatment.

Recommended uses and indications

CEUS is recommended in the following clinical situations:

1. Suspected vascular disorders, including renal infarction and cortical necrosis. (Recommendation Level: A;1a)
2. Differential diagnosis between solid lesions and cysts presenting with equivocal appearance at conventional US. (Recommendation Level: B;2b)
3. Differentiation between renal tumours and anatomical variations mimicking a renal tumour ("pseudo-tumours") when conventional US is equivocal. (Recommendation Level: B;1b). However, both CEUS and CECT have limitations in rare very small iso-enhancing tumours.
4. Characterisation of complex cystic masses as benign, indeterminate or malignant to provide information for the surgical strategy. (Recommendation Level: A;1b)
5. Additional aid, when necessary, in the follow-up of non-surgical complex masses. (Recommendation Level: C;5).
6. Identification of clinically-suspected renal abscesses in patients with complicated urinary tract infection. (Recommendation Level: C;5)
7. In patients undergoing renal tumour ablation under US guidance, CEUS may be used to improve lesion visualisation in difficult cases and to detect residual tumour either immediately or later after ablation. When CEUS is planned, pre-ablation assessment of lesion vascularity is important. (Recommendation Level: B;1b)

13 Vesico-Ureteric Reflux (VUR)



13.1 Background

In addition to intravascular use, UCAs are suitable for intracavitary administration. The intravesical administration of UCA for the diagnosis of vesico-ureteric reflux, voiding urosonography, has become a routine option that can completely replace reflux examinations using ionizing radiation (i.e. voiding cystourethrography) in girls. Comparative studies between voiding urosonography and cystourethrography have revealed sig-

nificantly higher sensitivity for urosonography in detecting reflux [112, 113].

Levovist® is licensed for VUR. SonoVue®, seems to perform at least as well [114] although it is not licensed for this indication.

13.2 Study procedure

The basic steps of voiding urosonography [112] are:

- (a) US evaluation of the kidneys and bladder;
- (b) intravesical administration of UCA diluted in normal sterile saline and
- (c) repeated scanning of the bladder and kidneys at low MI during and after bladder filling and, finally while voiding. During the last step, urethrosonography (transpubic and/or transperineal) is added in some centres.

UCAs can be administered via a transurethral bladder catheter or via suprapubic puncture (0.1–0.5 mL SonoVue® in 500 mL 0.9% saline [112, 115]), by slow instillation during CEUS monitoring, until strong enhancement of the bladder content has been achieved. The dose can be adjusted if there is excessive shadowing or insufficient signal. A full bladder is necessary for suprapubic puncture, and it is advisable to apply an anaesthetic plaster to the puncture site about one hour prior to the examination.

13.3 Diagnosis of vesico-ureteral reflux

Reflux is diagnosed when microbubbles appear in one or both ureters and/or the pelvicalyceal system. The severity of reflux is graded using 5 degrees (grade I–V) [116] comparable to the international reflux grading system of voiding cystourethrography. The US scan is continued during and after voiding with the child supine, prone, sitting, or standing, always scanning the kidneys alternately and also the bladder, if the patient's position allows [112].

13.4 Voiding urosonography

Voiding urosonography is also helpful for studying the urethra [117]. However, further studies on this application are needed. Voiding urosonography can be considered the method of choice for the initial study of suspected VUR in girls, in whom information about the urethra is less important, whereas voiding cystourethrography continues to be the first choice in boys, though voiding urosonography also shows potential in this setting [117]. Conventional cystography remains the reference technique in patients with abnormal urethral findings and/or to plan surgery.

13.5. Limitations

Voiding urosonography is not recommended as the primary imaging modality for reflux, if the bladder or one of the kidneys is not depicted on ultrasound and for specific urethral and/or bladder functional and anatomical evaluation [113].

Recommended uses and indications

Voiding urosonography is recommended in the following clinical situations:

1. First examination for vesicoureteral reflux in girls. (Recommendation Level: A;1a)
2. Follow-up examinations for vesicoureteral reflux in girls and boys after conservative or surgical therapy. (Recommendation Level: A;1a)
3. Screening high-risk patients for reflux (e.g. siblings, transplanted kidney). (Recommendation Level: A;1a)

4. The CEUS assessment of urethra in boys appears feasible and accurate, but not enough experience has been gained yet to recommend it in routine clinical practice. (Recommendation Level: 0;4)

14 Scrotum



14.1 Background

Ultrasonography is the imaging modality of choice for examination of the scrotum. Occasionally, however, sonographic findings are equivocal and this may be important as a misinterpretation can result in an unnecessary orchiectomy. A particular conundrum is the unequivocal differentiation between hypovascular and avascular lesions, presuming that an avascular lesion implies benign disease: this may be impossible using colour Doppler US. CEUS provides a practical solution by increasing the confidence of the interpretation of lesion vascularity and of scrotal cord vessels, allowing for appropriate clinical management.

14.2 Study procedure

A full B-mode and colour Doppler examination of the lesion with linear high frequency transducers should be performed and recorded to relate to the subsequent CEUS findings. The arterial phase at CEUS is the most important aspect of the examination. The testis and epididymis enhance rapidly but the arrival time varies between individuals. The arteries enhance first, followed within seconds by complete parenchymal enhancement. The scrotal wall tends to enhance to a lesser degree than the contents. There is no accumulation of microbubbles in the parenchyma of the testis and the enhancement declines over a variable period of time such that there is minimal residual enhancement by 3 minutes.

14.3 Patterns of disease

14.3.1 Torsion of the spermatic cord

CEUS may be used as a problem solving technique in children with small testes where conventional Doppler imaging methods provide suboptimal assessment of flow. There is no firm data currently to inform the use of CEUS in spermatic cord torsion. In a small series of men with torsion, CEUS confirmed absence of vascularisation, but failed to add any clinically significant information to unenhanced colour Doppler US [118].

14.3.2 Segmental infarction

The appearance of acute segmental testicular infarction on conventional B-mode and colour Doppler US is variable. Often the benign nature of the lesion is established by its wedge shape with markedly diminished or absent colour Doppler flow [119]. The main concern is the differentiation of a segmental infarct with a rounded configuration from a poorly vascularised tumour [120]. CEUS improves the characterisation of segmental infarction by showing one or more ischaemic parenchymal lobules separated by normal testicular vessels [121]. Subacute segmental infarction characteristically exhibits a perilesional rim of enhancement, which diminishes over time and is eventually lost with changes in lesion shape and shrinkage [121].

14.3.3 Trauma

Conventional B-mode and colour Doppler assessment of the testis in trauma is well established, but they under-estimate

the extent of injury. Besides integrity or interruption of the tunica albuginea, the most important information for the surgeon is the extent of viable testicular tissue. CEUS adds to the colour Doppler assessment with clear delineation of fracture lines, intratesticular haematomas, and the amount of viable testis [122].

14.3.4 Inflammation

Epididymo-orchitis is a clinical diagnosis and is usually easily confirmed on colour Doppler US. CEUS may be able to determine the development of an abscess (appearing as a non-enhancing region) at an earlier stage, or the extent of a large abscess, and allow for prompt treatment [118]. CEUS may be utilised in selected cases to increase the sensitivity in detecting thrombosis of the spermatic cord vessels, especially in funiculitis, and in detecting post-inflammatory parenchymal ischaemic changes.

14.3.5 Tumours and complex cysts

The current understanding is that testicular tumours with a diameter of less than 1.5 cm may not show flow on colour Doppler US and thus may be misinterpreted as a benign lesion, the purported hallmark of malignancy being an increase in vascularity. Simple testicular cysts are usually benign, but any wall irregularity or echogenic debris may be suggestive of a (rare) cystic testicular tumour [123, 124]. It is thought that virtually all testicular tumours display vascularisation on CEUS, with the exception of any cystic component and regions of necrosis [125]. Experience suggests that CEUS is able to confirm the absence of vascularity in benign complex and epidermoid cysts [126]. There is currently no evidence in the literature with regards to these findings.

Recommended uses and indications

CEUS for the testis can be currently recommended for:

1. Discrimination of focal testicular lesions into those that are vascular and those that show no enhancement, potentially identifying lesions without malignant potential. (Recommendation Level: B;2b)
2. Discrimination of areas of non-viable tissue in cases of testicular trauma. (Recommendation Level: B;4)
3. Detection and characterisation of segmental infarction. (Recommendation Level: B;2b)
4. Discrimination of abscess formation in severe epididymo-orchitis. (Recommendation Level: C;4)

15. Abdominal Trauma



15.1 Background

CECT is the modality of choice for the rapid detection and grading of neurological, skeletal, and thoraco-abdominal injuries in all cases of high-energy multitrauma. However, there is a wide range of severity among trauma patients who are admitted to an emergency unit, and the rate of positive findings on CT decreases with lower energy trauma. This should be weighed against the negative aspects of CT, including exposure to ionizing radiation and injection of iodinated contrast media. US is sensitive in detecting free peritoneal fluid as an indirect sign of injury (Focused Assessment with Sonography in Trauma – FAST) but it has poor sensitivity in detecting solid organ trauma and is even less useful for hollow viscus trauma.

CEUS can increase the conspicuity of traumatic injuries, with a closer correlation with CT [87, 127, 128]. In a large, multicentre study [129], CEUS was more sensitive than US and provided sensitivities of 69% (renal), 84% (liver) and 93% (spleen) compared to CT in the detection of solid organ injuries with very high specificity (over 90%).

15.2. Study procedure

Contrast enhancement lasts long enough to allow an adequate exploration of all parenchymal organs in the trauma patient. The kidneys have the earliest and most transient enhancement and the spleen is inhomogeneous initially and then becomes persistently and homogeneously enhanced. Consequently the examination sequence usually starts with the kidneys, then moves to the liver, and finally examines the spleen. An alternative is to split the contrast dose in two, using the first to explore the right kidney and then the liver, and the second for the left kidney and the spleen. However, in many instances the CEUS study directly targets the organ suspected or known to be injured.

15.3 Image interpretation of abdominal injuries

CEUS demonstrates the injuries as non-enhancing defects, sharply demarcated from the intensely enhanced, undamaged tissue, particularly during the venous phase. Contusion appears as an ill-defined area of subtle hypoenhancement. Lacerations are depicted as markedly hypoechoic bands, usually oriented perpendicular to the organ surface; sometimes the torn organ capsule is seen as a discontinuity. A haematoma is recognisable as a non-enhancing area without internal enhanced vessels. CEUS can detect changes that are not apparent on conventional US, such as infarcts, perilesional hyperaemia, pseudoaneurysm formation, as well as contrast extravasation, which appears as a pooling or as a jet of contrast enhancement outside blood vessels. The spread of contrast enhanced blood into the parenchyma, the peritoneal cavity, or the retroperitoneum is an important finding since it indicates on-going haemorrhage and the need for surgery. As shown both by experimental and clinical studies, CEUS can detect ongoing bleeding from a variety of traumatic and also non-traumatic sources [87].

Emergency CT scans of trauma patients can have artefacts and CEUS may be useful for better assessing unclear findings. Furthermore, CEUS may be used in patients not ideal for CECT, such as children (see section 7). CEUS may decrease the number of repeat US examinations and expedite patient discharge. Several published series have demonstrated that CEUS allows a confident exclusion of major abdominal injuries. Hence, many patients with minor trauma can be discharged after a period of observation, without being submitted to CT at all.

15.4 Limitations

Since UCAs are not excreted in the urine, CEUS cannot be used for detecting damage to the urinary excretory system.

Recommended uses and indications

CEUS can be employed consistently in trauma imaging, considering the wide spectrum of scenarios encountered in clinical practice.

1. As an alternative to CT in stable patients with isolated blunt moderate-energy abdominal trauma to rule out solid organ injuries, especially in children (Recommendation Level: A;1b)

2. To further evaluate uncertain CT findings (Recommendation Level: C;2b)
3. For the follow-up of trauma managed conservatively, because it may make it possible to reduce in the number of CT scans or increase confidence when the situation does not strictly require a CT scan. (Recommendation Level: B;1b)

16. Lung and Pleural Lesions



16.1 Background

US imaging of the healthy lung is impossible because the US beam is totally reflected at the lung surface. Consolidations can be visualised when they reach the pleura, are accessible via an acoustic window, and there is no subcutaneous emphysema or pneumothorax [130]. CEUS assessment of the lung is therefore addressed to lung consolidations.

Because of its dual arterial supply, the lung has similarities to the liver and CEUS allows the differentiation of the pulmonary from the systemic bronchial arterial supply of consolidations by assessing the timing and extent of enhancement [131].

16.2 Study procedure

For lung consolidation, a conventional convex abdominal transducer is most commonly used. Before injecting the UCA, the best probe position to visualise the consolidation should be determined using B-mode and colour Doppler US and then observed for at least the first 30 s after contrast administration [132].

16.3 Image interpretation

Contrast arrives in the right heart between 1 and 5 sec after injection and immediately thereafter enters the pulmonary artery (indicating the beginning of the time window of pulmonary arterial enhancement), and between 8 and 11 sec enters the left heart (determining the start of systemic bronchial arterial enhancement immediately thereafter) in healthy subjects. An arrival time in the consolidation under study of less than 10 seconds ("early arterial enhancement") indicates pulmonary arterial supply and a delayed arrival time over 10 seconds ("late arterial enhancement") indicates supply by the bronchial arteries. In patients with cardiac and/or pulmonary disease, the arrival time for pulmonary arterial supply may be longer than 10 seconds [131].

16.3.1 Pneumonia

Contrast arrives early in pneumonia (10 sec) and enhancement is marked [131] followed by a plateau caused by a combined supply from pulmonary and bronchial arteries [132]. In addition, CEUS allows demarcation of necrosis or abscess formations in the infiltrated lung tissue as regions of absent enhancement [131].

16.3.2 Pulmonary embolism

In embolic pulmonary infarcts, the arrival time is delayed and the degree of enhancement is minimal [131] within the first 30 seconds after UCA administration [132]. Such a decrease in enhancement is most evident early after pulmonary embolism and progressively recovers, so that infarctions are more clearly recognisable early after their onset. Quantification of contrast enhancement using dedicated software may provide more consistent information. Pleurisy or pneumonia can be

clearly differentiated from pulmonary embolism by early and intense pulmonary artery enhancement [131–133].

16.3.3 Pulmonary carcinoma and metastasis

The value of CEUS for lung cancer is the improved delineation of viable from non-viable tissue before biopsy compared to colour Doppler US [134]. Lung tumours may behave very variably as regards contrast distribution on CEUS, but on average the time of arrival is late arterial as the arterial supply is from the bronchial system and not from pulmonary arteries [131, 132].

16.3.4 Atelectasis

In atelectasis, the CEUS pattern is similar to pneumonia with early and marked enhancement (<10 sec) followed by a plateau [132]. An underlying central tumour may be better differentiated from the atelectasis by late enhancement [134].

Recommended uses and applications (applicable only to peripheral lesions visible on US)

1. CEUS is useful in differentiating inflammatory from embolic lung consolidation, especially in patients with equivocal CT findings. (Recommendation Level B;2b)
2. CEUS may be used in equivocal cases to diagnose lung abscesses within pneumonia, since CEUS appears better than conventional B-mode US or X-ray. (Recommendation Level C;5)

17. Vascular



17.1 Background

There are two major extracerebral vascular systems with common indications for CEUS. One is the cervical carotid artery and the other the abdominal aorta. Conventional US techniques are limited in demonstrating slow flow, especially in small vessels such as vasa vasorum or collaterals and flow in critical stenoses. UCAs help to overcome some of these limitations and might be used also in other extracerebral vascular districts, but such usage is less well established and is not reported herein.

17.2 Study Procedures

As for conventional investigations, CEUS of the carotid artery is carried out with linear probes working in the range of 5–10 MHz and the abdominal aorta with convex probes at 2.5–5 MHz.

17.3 Carotid artery

17.3.1 Stenosis

Duplex US is the first line imaging modality for suspected carotid artery disease [135–138]. CEUS improves the sensitivity of Doppler US and can be used for distinguishing occlusion from tight sub-occlusive stenosis, even with conventional US equipment. However, when a contrast-specific modality is available, low MI CEUS can be utilised to further improve the delineation of the endovascular border in difficult cases, making it possible to detect the shape of pre-stenotic, intra-stenotic and post-stenotic segments, especially in elongated vessels [139, 140]. This is also facilitated by the fact that high velocity and low-velocity flow phenomena are registered at the same time with CEUS without aliasing and blooming artefacts and without any angle dependence, which all affect Doppler US

19.3 Image interpretation

19.3.1 Arthritis and synovitis

Microscopic examination of synovial biopsies shows angiogenesis from the earliest stages of inflammatory disease. Proliferation of hypervascularised pannus can be detected before joint destruction. It correlates with disease activity and appears to be crucial to its invasive and destructive behaviour [180]. Moreover, the development of novel biological therapies (e.g. tumour necrosis factor-alpha inhibitors), which target the microvasculature, have created a demand for more sensitive vascular imaging in order to assess response to treatment [180–184]. The addition of UCAs to Doppler US significantly improves the detection of vascularity in active rheumatoid arthritis [185, 186]. Following CE Doppler US, therapy was modified in up to 24% of patients in a dedicated study [185]. There is also evidence that CE power Doppler US helps to differentiate between active and inactive disease in subclinical juvenile rheumatoid arthritis of the knee [187]. CE Doppler US correlates with the findings of CEMRI, indicating the degree of inflammation in patients with synovitis [188]. CE Doppler US is also more useful in the diagnosis of sacro-iliitis than conventional unenhanced Doppler US [182, 189]. Overall, improved diagnostic accuracy in assessing the degree of inflammation can be achieved by the addition of UCA in large and small joints.

19.3.2. Differentiation between synovial pannus and fluid

MRI studies have demonstrated that the presence and amount of synovitis is a prognostic factor for bone damage [190]: no bone damage occurs in joints without synovitis. Therefore, early detection of vascularised synovia is a primary goal in assessment of inflammation. CE Doppler US improves the differentiation between active synovitis and other articular thickenings such as fibrotic pannus and articular fluid [191, 192].

19.3.3. Bursae and tendons

Contrast administration can highlight peripheral enhancement on Doppler US corresponding to the vascularised synovial lining of an inflamed bursa and can better differentiate between fluid, fibrous and hypervascular synovial thickening in comparison to non-enhanced Doppler US [193, 194].

19.3.4 Therapeutic follow-up

Successful treatment results in a decrease in synovial thickening and necrosis of the pannus with reduction of vascularity and thus of Doppler signals. The distinction between fibrous pannus and active synovial proliferation is one of the most important questions during follow-up, because the volume of the synovium itself is not clinically significant, as it may contain varying amounts of fibrous tissue [190]. On unenhanced power Doppler US, fibrotic pannus shows no vascularity as also after addition of UCA into fibrotic pannus shows no vascularity, as it also does after the addition of UCA and, with CEUS, lacks enhancement [195–199].

Recommended uses and indications

Contrast enhanced colour/power Doppler US:

1. Can be utilised for further assessment of the degree of vascularisation in joints of patients with rheumatoid arthritis. (Recommendation Level: C;2b)
2. Repeat contrast enhanced Doppler US may provide useful information on the response to treatment, to guide therapeutic

strategy. The technique has the potential to be utilised within dedicated centres using standardised methodology. (Recommendation Level: C;2b)

20. Intracavitary Uses



20.1. Introduction

Reports on numerous off-label extravascular or intracavitary administrations of SonoVue® have been published and those considered of more general use and most consistent are reported. Other potential applications have been occasionally described as case reports and congress abstracts.

20.2. Study procedure

To date, no standard dosage of UCA has been established for intracavitary injection. The reported range is 0.1 mL–1 mL SonoVue® (most commonly just a few drops) diluted in 10 mL or more of 0.9% saline; a higher content of SonoVue® may be needed for high frequency US probes.

20.3 Injection into Physiological Cavities

20.3.1 Voiding US for vesicoureteral reflux

This topic is described in section 13.4.

20.3.2 Imaging of tubal patency – contrast enhanced hystero-salpingo-contrast-sonography (CE-HyCoSy)

Originally performed using shaken saline infused into the uterine cavity, hystero-salpingo-sonography suffers from a false negative rate of patency of about 12% [200]. CEUS with SonoVue® provides better results [200–202] with higher specificity, but the positive predictive value for the diagnosis of “occluded tube” remains low [200]. The high negative predictive value of conventional hystero-salpingo-contrast-sonography leads authors to suggest performing contrast enhanced hystero-salpingo-contrast-sonography only if conventional hystero-salpingo-contrast-sonography does not show patency.

20.3.3 Detection of peritoneo-pleural communication for the diagnosis of hepatic hydrothorax

The detection of direct communication between the abdominal and pleural cavities is the main indication reported so far [203, 204]. Confirmation of the suspected diagnosis of hepatic hydrothorax can be established in cirrhotic patients by injecting SonoVue® into the peritoneal cavity, at best early (<2 days) after thoracentesis and demonstrating its passage into the pleural cavity.

20.3.4 Bile ducts

CEUS-guided percutaneous cholangiography was first described in 2009 [205]. A later case report on UCA injection into a surgically placed T-tube followed [206]. It is expert opinion that the advantage of CEUS-guided percutaneous cholangiography and drainage is that external drainage for biliary obstruction in patients with severe cholangiosepsis can be performed in the intensive care unit without X-ray guidance. UCA for endoscopic retrograde cholangiography has been reported [207].

20.3.5 Salivary glands

UCA injected into the main duct of a salivary gland could become a supplementary diagnostic method added to sialogra-

phy to classify obstructive diseases of the salivary glands. The salivary gland is cannulated with appropriate dilators and the plastic tube of a peripheral vein catheter is inserted [208].

20.4 Injection into Non-Physiological Cavities

20.4.1 CEUS for imaging of fistula

CEUS detection and classification of fistulas, whatever the initial disease, has been proven to be effective. The following conditions have been reported: rectovaginal fistulas via a transvaginal approach [77], vesicointestinal fistulas via a transabdominal approach [209] and anal fistulas via the transrectal approach [210].

20.5 Other intracavitary indications for CEUS

In principle, UCAs can be instilled into any sonographically accessible physiological or pathological body cavity to assess morphology of the cavity and potential communications with adjacent structures or organs. Clinical applications include: abscesses, pancreatic pseudocysts and other complications of pancreatitis, intestinal and other fistulas, gastro-oesophageal reflux, gastric lumen and intestinal stenoses.

Recommended uses and indications

No definite recommendation can be made for these indications. Use of CEUS must be decided on a case-by-case basis, usually resorting to CEUS because of inconclusive standard diagnostic techniques or when patients are not suitable for these or because they have higher risks (for instance, use of ionizing radiation on sensitive organs, or moving the patient out of intensive care units) or more complex logistic situations.

21 Lymph Nodes



21.1 Background

The differential diagnosis of superficial lymphadenopathy in cancer patients has been the object of various studies with high-resolution US. Their shape, appearance and vascular pattern have been analysed to discriminate benign from malignant nodes, with a wide range of sensitivities and specificities [211, 212]. CEUS has been shown to increase the accuracy of the analysis of the vascular pattern (angioarchitecture) [213]. Contrast enhanced investigations were first performed with high MI US using Doppler and later with low MI CEUS.

21.2 Study procedure

The same probes as for conventional B-mode US are utilised but with contrast-specific modalities and a full vial of SonoVue®, as for other superficial applications.

21.3 Image interpretation and differential diagnosis of benign and malignant lymph nodes

Demonstration of malignant neovascularisation, seen as vessels penetrating the node's capsule away from the hilum, has been used in most reports as the characteristic feature of metastatic lymph nodes. Confirmation of the reactive nature of lymph nodes relies on their preserved morphology and vascular anatomy, with a single vascular pedicle at the hilum containing arteries and veins vessels, regularly branching towards the periphery of the lymph node. Display of vascular anatomy can be facilitated by the addition of UCAs during colour Doppler US. Conventional CEUS using low MI can improve on the results

of Doppler US with a sensitivity, specificity and accuracy rate of up to 84%, 79% and 80% [214–223].

However, the US study of lymph node vascularisation has limitations. Most studies were made in special clinical settings (known head and neck or gynaecologic cancer). Vessel distribution analysis is usually satisfactorily informative if the whole lymph node is involved. This is not always the case, because of the possibility of focal cancer metastases or necrosis. Lymphoma must be considered separately because there is evidence that the vascular pattern of lymphoma lymph nodes resembles that of non-malignant nodes [224, 225].

21.4 Sentinel lymph nodes

CEUS can be used for detecting sentinel lymph nodes in cancer patients. One mL of SonoVue® is injected subcutaneously near the tumour site and the enhanced lymphatics are traced to the sentinel node [226–231]. Initial experiences indicate that the method is not toxic and performs as well as the blue dye or radioisotope methods [231].

Recommended uses and indications

1. CEUS appears to be capable of discriminating benign from malignant superficial lymph nodes only in special clinical settings. Therefore, despite some positive publications, it is the opinion of the experts that CEUS is not recommended for routine discrimination of benign from malignant lymph nodes. (Recommendation Level: C;5)
2. CEUS with subcutaneous injection of contrast agent to identify the sentinel lymph node is a field of ongoing research and can therefore not be recommended for clinical practice to date. (Recommendation Level: C;5)

22. Tumour Response Assessment



22.1 Background

The advent of novel therapies targeting tumour angiogenesis and vascularity has highlighted the need for accurate and reproducible quantitative techniques to assess early changes in tumour vascularity [232]. However, as these therapies are predominantly cytostatic, current response assessment which is based on interval evaluation of the tumour size using the *Response Evaluation Criteria In Solid Tumours* (RECIST) [233] is inadequate as it reflects only late changes and is unable to identify non-responders at an early time-point [234].

22.2 Study procedure

Dynamic contrast enhanced US (DCE-US) can be performed using two different approaches with different results and evidence produced so far:

- (a) bolus injection of UCA with TIC analysis; single plane imaging is usually performed at 10–20 frames per second for the duration of the enhancement. The average intensity within a region of interest (ROI) can be displayed as a function of time, i.e. a TIC which describes the wash-in and wash-out of the UCA in the ROI [235]. In addition, a second ROI can be placed in a reference tissue for comparison purposes [236]. The majority of clinical studies to date are based on this method.
- (b) intravenous infusion of UCA with disruption-replenishment analysis. The UCA is administered using a pump or drip over 5 to 20 minutes. UCA is first imaged without being disrupted at a low MI, then the MI is increased for a few frames, causing

bubble disruption. Immediately after that, the MI is returned to the non-disrupting level to observe the replenishment of the microbubbles into the ROI. Various models describe the echo-signal dynamics during the UCA-replenishment phase, which can be used for flow analysis [237].

Initially monitoring for tumour response with UCAs relied on qualitative analyses [238], but new methodologies have been developed to produce more robust and semi-quantitative indices. Analyses of the TIC, including wash-in and wash-out times, can be performed with curve fitting to determine functional indices [239]. The main indices include: peak intensity (PI); area under the curve (AUC); area under the wash-in (AUWI); area under the wash-out (AUWO; all corresponding to blood volume); time to peak intensity (TPI); slope of the wash-in (SWI; both corresponding to blood flow); and mean transit time (MTT). No permeability information can be obtained because of the pure blood pool nature of microbubbles. A more extensive EFSUMB introduction to quantitative enhancement indices is being prepared.

22.3 Clinical application of DCE-US

Early clinical trials employed qualitative analysis in the assessment of the response of different tumours such as gastrointestinal stromal tumour (GIST) or renal cell carcinoma [240–243]. More recently, there have been studies using semi-quantitative techniques with UCA bolus injection in renal cell carcinoma, hepatocellular carcinoma (HCC) and GIST [244–246]. Studies from the French group showed that two indices representing blood volume correlated with the RECIST response. For one study on renal cell carcinoma the authors demonstrated a correlation of such indices with Progression Free Survival and Overall Survival [244]. The same results could not be reproduced in a Canadian study using the disruption-replenishment technique tested versus Progression Free Survival assessed by the RECIST method [237].

A French multicentre study of various types of tumours, approximately half of which were located outside the liver (including more than 400 patients), such as metastatic renal cell carcinoma, GIST, colon cancer, melanoma, breast cancer and HCC, treated with anti-angiogenic therapies has been running, but not yet reported in its complete form. The preliminary results found that the AUC is one of the features correlated to response at 6 months in good and poor responders [247], but the full results of the data set are not yet available. There is now emerging evidence that DCE-US may be used with appropriate tools to differentiate between responders and non-responders at an earlier stage than conventional methods and this potentially allows tailoring of the treatment regimen, particularly changing treatment for non-responders. DCE-US has been endorsed by the European Medical Oncology Society to assess response under biological therapy for GIST [248].

Recommended uses and indications

1. DCE-US can be utilised to assess response to biologic therapy in metastatic GIST and other metastatic tumours, e.g. renal cell carcinoma, in dedicated centres with appropriate software for contrast signal quantification. (Recommendation Level: A;1b)

23. Breast



The application of CEUS to the differential diagnosis of breast masses was one of the first [249] and the initial results were very encouraging. Sadly, this early promise has not been fulfilled, despite numerous studies using modern methods [250] (summarised in [251]) including temporal accumulation methods (microvascular imaging) [252]. No specific pattern indicating malignancy has been identified. Thus, CEUS of the breast remains an important topic for research but cannot be recommended for routine clinical use. Among the different fields of research, that on contrast quantification appears the most promising [253].

24. Adrenal Glands



So far, no CEUS criteria that can reliably differentiate between benign (endocrine tumours and adenomas) and malignant adrenal masses are known and indeed, the specificity of CEUS in the diagnosis of malignant adrenal masses was reported to be below 70% [254]. Malignant adrenal tumours may infiltrate and occlude the adrenal vein. The vascularity of a tumour thrombus can be shown by UCA and thus its character be demonstrated.

CEUS may demonstrate characteristic hypervascularity of some adrenal gland tumours, e.g. pheochromocytoma, which typically also have necrotic regions with no contrast enhancement [255].

25 Emerging Perspectives and Potential Future Applications for CEUS



25A. Obstetrics and Gynaecology

25A.1 Obstetrics

The use of UCAs in obstetrics is not indicated because of lack of testing and underlying fears of toxicity. There is older literature in humans on the topic but none that is recent in animal models. It is unknown whether the microbubbles pass through the placenta, though this seems unlikely. CEUS to assess a pregnant mother should be balanced against the risk of other modalities. The opportunities seem very limited and the subject is not considered further here.

25A.2 Gynaecology

25A.2.1 Uterus

Research has included uterine and cervical tumours [256], flow differences between endometrial polyps and cancer [257], and CEUS during uterine artery embolisation to treat leiomyomas [258]. So far, no prospective trials confirm the value of CEUS to assess uterine tumours and thus there is no proven clinical indication for its use in examining the endometrium or the myometrium.

25A.2.2 Adnexa

Differentiation of benign from malignant adnexal masses was attempted by visual assessment of contrast distribution and by quantification of enhanced Doppler signals but, despite some difference in average values for some variables, no feature with sufficient clinical potential was obtained [259].

By using CEUS it was demonstrated that adnexal masses without internal enhancement are invariably benign, and this feature was detected with high intra- and interobserver reproducibility [258], but the presence of enhancement is not a specific sign of malignancy [256]. CEUS does not greatly improve the accuracy of colour Doppler US for the diagnosis of malignancy in adnexal masses [260]. A large multicentre study on the diagnosis of malignancy in adnexal masses, including quantitative CEUS features, confirmed that CEUS is not superior to conventional US, despite being statistically more accurate [260]. Both also have difficulty in distinguishing between benign and borderline tumours.

At present, there are no recommended gynaecological clinical indications for the use of CEUS, despite the finding that absence of any enhancement in adnexal masses corresponds to benign lesions. (Recommendation Level: A;2b).

25B. Perineum

CE perineal US is an effective, easily available but so far not well known diagnostic tool. Perineal US is particularly useful if clinical examination, endorectal US or MRI with endorectal coils cannot be performed (e.g., due to severe pain when introducing the probe). CE perineal US requires good knowledge of the anatomy of the pelvic floor and the sphincters. No patient preparation is required. The location of inflammatory and neoplastic lesions should be described in relation to the sphincter apparatus. Fistulas can be further differentiated by US examination into intersphincteric, transsphincteric and extrasphincteric forms. Conventional B-mode perineal US is inadequate for complex fistulas, as its sensitivity for the complex branching structure is poor. However, discrimination of fistulas and abscesses with CE perineal US is possible in most cases, but studies have not been published so far. Additionally, the extent of a fistula can be imaged by instillation of UCA into its external ostium. CE Doppler US has shown a higher resistance index (RI) in neoplasia compared to inflammation, but further studies are needed.

25C. Urinary Bladder

25C.1 Background

In patients with urinary bladder tumours, noninvasive diagnostic imaging may play a role, even though it cannot replace cystoscopy and pathologic staging. The depth of wall invasion, as well as the histological grade and the extension outside the bladder are the three main factors determining prognosis and therapeutic approach.

25C.2 Study procedure

Optimal bladder filling (approximately two thirds of the total bladder volume) is critical [261]. Insufficient filling prevents lesion detection, while excessive distension results in bladder wall thinning and reduced conspicuity of the wall layer and may make it more difficult to differentiate a superficial tumour from an infiltrating lesion.

The layers of the bladder wall can be differentiated after microbubble injection. The mucosa, and especially the submucosal layer, exhibit early and intense enhancement that persists for 1–2 minutes. The muscular layer has lesser and delayed enhancement [261].

25C.3 Image interpretation

25C.3.1 Characterisation of mural masses

CEUS improves the differential diagnosis of intraluminal echoic masses, allowing the detection of tumours, which are vascularised and thus enhance [262], while clots do not enhance [263]. In a group of 35 patients in whom cystoscopic biopsy was the reference standard, CEUS correctly assessed the presence or absence of tumour in 88% of cases [263].

25C.3.2 Bladder tumour staging

CEUS is superior to conventional B-mode US in identifying infiltration of the muscle layer [261], but MRI and CT are the imaging modalities of choice for local staging of bladder tumours. Attempts to predict tumour grading by the pattern of CEUS enhancement is still a research topic [262].

25C.4 Limitations

Similarly to other imaging modalities, the most important limitation of CEUS in bladder tumour detection is the difficulty in identifying subcentimetre lesions. Flat, plaque-like tumours may also be difficult to detect, even when large. Tumour position can affect the quality of depiction at CEUS, and therefore the accuracy of staging. Tumours in the anterior portion of the bladder dome are sometimes difficult to visualise. Columnar hypertrophy of the bladder wall associated with benign prostate hypertrophy can hide or mimic urothelial polypoid projections, as well as prostate hypertrophy itself [261]. Benign tumours and focal cystitis are other uncommon conditions that present with focal bladder wall enhancement and can mimic a malignant lesion. Finally, CEUS is not panoramic as CT and MR are.

To summarize, the most useful application of CEUS is the differential diagnosis of bladder cancer from clots in patients with haematuria when the diagnosis is equivocal on conventional B-mode and Doppler US. (Recommendation Level: C;2b). In patients with anatomical situations leading to poor urinary bladder visualisation, CEUS often does not provide the desired information. (Recommendation Level: X;5).

25D. Transplanted Kidney

Progressive vascular remodelling in the transplanted kidney, from a variety of mechanisms, compromises renal perfusion and accounts for the majority of allograft failures. CEUS has the potential to investigate perfusion abnormalities in renal transplants and to obtain information on blood flow based on the quantification of contrast enhancement or on the depiction of devascularised regions (the latter with the same significance as in native kidneys, so that CEUS use for this indication can be considered as established also in transplanted kidneys). Different quantitative features have been assessed, all related to impaired parenchymal perfusion (e.g. longer time to peak, lower wash-in slopes, longer mean-transit time) and associated with a worse prognosis of graft function and survival [264].

Although these preliminary results are promising, further studies are needed to assess whether detecting haemodynamic changes in renal grafts affects the management of patients with poorly functioning transplants; consequently the quantification of CEUS is still considered a research field in transplant assessment.

25E. Prostate Cancer

Conventional B-mode and Doppler transrectal US imaging have a limited role in the detection of prostate cancer because of poor sensitivity and specificity (approximately 50–60%). However, there is a correlation between microvascular density and the presence of prostate cancer, its stage and survival. Therefore, attempts were made with CE transrectal US with colour-Doppler to improve the detection of additional cancer nodules; with this modality the detection rate of targeted biopsies increased by almost 50% compared to systematic biopsies in some studies [265, 266]. Low MI transrectal CEUS became available only recently when contrast specific modalities were implemented on endocavitary probes. Preliminary single centre results appeared to confirm the findings of CE Doppler US, despite the lack of specificity of enhancing areas and of any other pattern [267–269]. The evidence achieved so far with CEUS modalities is, however, still too limited and not sufficiently confirmed in clinical practice in other centres, so that the role of CEUS in prostate cancer should still be considered a research topic, with hopes of improvements as new techniques are becoming available, such as 4D contrast enhanced transrectal US imaging.

25F. Aorto-Caval Fistula

Perioperative mortality of abdominal aortal aneurysms complicated by aorto-caval fistulas undergoing open surgery is up to 60% and the additional retroperitoneal rupture of the aneurysm considerably raises the mortality [270]. The diagnosis can be made by noninvasive testing, such as US scanning, including CEUS, which improves visualisation of the fistula track and of the number of fistulas, avoiding the aliasing or the overwriting artefacts typical of Doppler US.

25.G Free Tissue Transplants

25G.1. Background

Free flap reconstruction of complex defects after trauma, tumour resection, burns, or wound healing disturbances has revolutionized plastic, reconstructive, and microsurgery, giving the unprecedented potential to provide form, function, and volume for defects in every body region. However, despite refinements in this technique over the last several decades that have resulted in a decreased rate of flap loss of less than 5–10%, in general, the loss of free flaps because of vascular impairment remains a serious complication. Early identification of vascular deterioration and prompt revision could save up to 33–57% of failing flaps. CEUS offers the possibility of earlier detection [271–273].

25G.2 Study procedure

Standard doses (2.4–4.8 mL of SonoVue®) and administration methods are used together with high frequency probes (≥ 6 MHz) to evaluate the microcirculation of the cutaneous, subcutaneous, and deeper layers of free flaps. Beside the standard visual evaluation, improved diagnostic assessment is obtained by contrast specific software working on the acquired information, including the production of TIC in different tissue layers by demarcation of different ROIs to quantify enhancement [274]. Postoperative TIC analysis allows calculation of peak and time to peak of enhancement and regional blood volume. Exported cine-loops allow colour-coded depiction of these features with dedicated software [275, 276].

25G.3 Image Interpretation

25G.3.1 Preoperative planning of tissue transplants

The blood vessels in the transplanted free flap are small (at most 1–2 mm). The surgeon needs to know the precise number, course and position of these blood vessels as well as the flow in order to estimate the proportion with a good blood supply.

25G.3.2 Intraoperative imaging

CEUS enables the identification of perforator vessels intraoperatively, and helps to determine if there are any abnormalities. The surgeon can thus make a more accurate decision as to whether the entire flap is perfused and if the estimated flap size is correct.

25G.3.3 Postoperative monitoring of tissue transplants

The feeding vessels or, if there is a connection to a bypass, the anastomosis, and the transplant's own vessels can also be examined even if the vessel diameter is very small. CEUS can provide valuable information about a vascular compromise (thrombosis, embolism, twisting, kinking, or compression) and demonstrate successful surgical salvage [274, 277].

25G.3.4 Critical microvascularisation of free flaps

A significant difference between normally vascularised and compromised flaps can be observed and the Time to Peak and Regional Blood Flow appear to be the most useful indices [278]. For CEUS and CEMRI, the mean signal increase of the TIC was significantly higher in ROIs of normally perfused flaps compared to compromised flaps [275, 276, 279, 280]. With CEUS, the exact size of the necrotic regions can be evaluated by analysing the entire flap. A haematoma or seroma can be detected early with CEUS, by the absent perfusion.

25G.4 Limitations

The main limitation for the evaluation of flap perfusion is the fact that CEUS does not allow for continuous monitoring after bolus injection. Continuous infusion might be a better method, but remains to be explored.

To summarise, high-resolution CEUS is promising for confirming a clinical suspicion of malperfusion of free tissue transplants as well as for determining the cause. (Recommendation Level: B;2b).

25 H. Biliary disease

25 H.1 Background

The vascular phases of the gallbladder are different from those of the liver because the blood supply is provided entirely by the cystic artery and not by portal vein branches. The arterial phase is followed by the venous phase, which is shorter than that of the liver.

25 H.2. Image interpretation

25 H.2.1 Acute cholecystitis

In acute cholecystitis, the detection or exclusion of abscess formation in the surrounding liver parenchyma is important and can be performed with CEUS, but published evidence is sparse so far. Interruption of the gallbladder wall suggests perforation, which can be confirmed by the absence of enhancement of the perforated wall.

25 H.2.2 Extrahepatic biliary tumours

The absence of enhancement in biliary sludge (whether in the gallbladder or in a dilated biliary tree) allows differentiation from a tumour, which enhances, in almost all cases using CEUS.

Gallbladder carcinomas are typically hyperenhancing in the arterial phase and hypoenhancing in the venous phase. The differentiation between benign and malignant lesions is mainly determined by clinical features and size and enlargement of polyps to >10 mm is an indication for cholecystectomy. More sophisticated classification of the vascular and enhancement pattern of gallbladder lesions, including that provided by CEUS, has not been introduced so far in the clinical routine and CEUS currently has no role in differentiating benign from malignant gallbladder polyps.

The most important task of CEUS and other imaging methods is to detect infiltration of the surrounding liver parenchyma and to exclude liver metastases.

Transabdominal CEUS has no proven role when extrahepatic cholangiocarcinoma is suspected, although promising findings have been observed e.g., determining the depth of wall infiltration and surrounding tissue mainly by using CE-EUS.

Intrabiliary administration of UCA is discussed in 20.3.4.

26. Use of CEUS in Patients with Renal Failure

The use of iodinated/Gadolinium-containing contrast agents for CT and MR, respectively, potentially exposes patients with renal failure to severe complications [281, 282]. Assay of serum creatinine level and calculation of the estimated glomerular filtration rate before injection is mandatory in patients who may have impaired renal function (diabetes mellitus, age >70 years, history suggesting possible reduced eGFR, congestive heart failure, intensive diuretic treatment, dehydration, etc). Recommended guidelines to avoid contrast-induced nephrotoxicity from iodinated contrast agents [281] are available. However, none can guarantee completely successful prevention.

The risk of nephrotoxicity is very low with MRI contrast agents, even in patients with impaired renal function. However, these agents can induce nephrogenic systemic fibrosis (NSF), a rare but severe complication [282]. The risk of NSF depends upon the degree of impairment of the patient's renal function and the type of agent (stability of the Gadolinium bound to chelate).

Thus in patients with renal failure, it is recommended to consider an alternative imaging method that does not use iodinated or Gadolinium-containing contrast media. Since UCAs are not nephrotoxic (and no renal function assessment is required), CEUS should be considered in every case, especially if it offers the possibility of achieving enough diagnostic information, even with off-label CEUS uses. This is particularly the case in patients with severe renal failure, in whom CT or MRI should only be used in case of inconclusive examinations and strong clinical need.

27. Technical Appendices

The number of systems capable of CEUS imaging has increased greatly in recent years and almost all manufacturers have im-

plemented this technique in top level as well as, in many instances, in lower level machines. The technical details of the modalities which produce CEUS imaging are rapidly and continuously evolving so that any written list of information would not be complete. Accordingly, it is preferable that readers access such technical information directly from the websites of each manufacturer who supported this project. The links can be found on the EFSUMB webpage (<http://www.efsumb.org/guidelines/ceus-manufacturers-links.pdf>), but the content remains the responsibility of the respective manufacturers.

Acknowledgements

The authors acknowledge the contribution of Dr. Ralph Faschinger who gave advice for the section on inflammatory joint disease.

The unrestricted financial support provided by the following companies (listed in alphabetical order) to support the preparation of this document is gratefully acknowledged:

B-K Medical, Bracco, Esaote, GE Healthcare, Medical Diagnostics, Hitachi, Lantheus Medical Imaging, Philips, Siemens, SuperSonic Imagine, Toshiba, Zonare.

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Reference No. 5 was modified on September 9, 2011 with respect to the eFirst publication.

Contrast-Enhanced Ultrasound for Imaging Blunt Abdominal Trauma – Indications, Description of the Technique and Imaging Review

Kontrastverstärkter Ultraschall zur Darstellung des stumpfen Bauchtraumas – Indikationen, Beschreibung der Technik und Bildbewertung

Authors

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Key words

- abdomen
- ultrasound
- contrast agents
- CEUS

Zusammenfassung

Patienten mit stumpfem Bauchtrauma werden zunächst mit Ultraschall (US) untersucht, um das freie Bauchwasser zu bewerten. Dabei können allerdings Verletzungen der festen Organe übersehen werden. Obwohl die Computertomografie (CT) die Goldstandardtechnik zur Darstellung von Bauchverletzungen ist, sind deren wohlbekannte Nachteile die zu häufige Anwendung, die ionisierende Strahlung, der nötige Transport des Patienten und mögliche Artefakte. Die kontrastverstärkte Ultraschallsonografie (CEUS) kann als bildgebendes Verfahren zwischen diesen beiden Methoden angesiedelt werden. Sie entdeckt einfach und verlässlich Verletzungen der Bauchorgane bei Patienten mit energiearmen lokalisierten Traumata und verringert die Anzahl der CT-Untersuchungen. Die Durchführung erfolgt sehr schnell am Bett des Patienten, sodass sich ein Transport erübrigt. Es gibt nur sehr wenige Kontraindikationen und äußerst selten anaphylaktische Reaktionen. Insgesamt hat sich CEUS als sehr hilfreich bei der anfänglichen Darstellung traumatischer Läsionen von Leber, Niere und Milz sowie bei der Nachuntersuchung der Patienten erwiesen.

Abstract

Patients with blunt abdominal trauma are initially imaged with ultrasound (US) for the evaluation of free abdominal fluid. However, lacerations of solid organs can be overlooked. Although computed tomography (CT) is the gold standard technique for abdominal trauma imaging, overutilization, ionizing radiation, need to transport the patient and potential artifacts are well known disadvantages. Contrast-enhanced US (CEUS) can be used as an imaging tool between the two methods. It can easily and reliably reveal solid abdominal organ injuries in patients with low-energy localized trauma and decrease the number of CT scans performed. It can be rapidly performed at the patient's bedside with no need for transportation. There are only very few contraindications and anaphylactoid reactions are extremely rare. Altogether, CEUS has proved to be very helpful for the initial imaging of traumatic lesions of the liver, kidney and spleen, as well as for patient follow-up.

received 26.11.2010

accepted 3.5.2011

Bibliography

DOI <http://dx.doi.org/10.1055/s-0031-1273442>

Published online

January 24, 2012

Ultraschall in Med 2011; 32:

60–67 © Georg Thieme Verlag

KG Stuttgart · New York ·

ISSN 0172-4614

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Introduction

Baseline non-enhanced ultrasound (US) is currently the primary imaging examination for detecting blunt abdominal trauma [1–3] and is routinely used on an emergency basis for the rapid evaluation of trauma patients [4]. It is fast, cheap, easy to perform at the patient's bedside and lacks ionizing radiation. Its main utility is the detection of free abdominal fluid as well as pleural and pericardial fluid. It is described by the acronym FAST (Focused Assessment with Sonography in Trauma) [5] and its

sensitivity for detecting free abdominal fluid ranges from 63% to 99% [6, 7].

However, the baseline US sensitivity is significantly lower for imaging abdominal solid organ traumatic lesions [8], while one out of three such lesions can occur in trauma patients without hemoperitoneum [9, 10]. Furthermore, while performing abdominal US, injuries of the dome or lateral segments of the liver can be overlooked, especially in the presence of ileus or an uncooperative patient. Moreover, hepatic lacerations or hematomas may be difficult to detect, especially in the acute phase, when

they are isoechoic to the normal liver [4]. Finally, the value of sonography for revealing a solid organ injury varies greatly with the location of the lesion, the organ size, as well as the presence of overlying bowel and gastric gas. For all these reasons, computed tomography (CT) is still considered the gold standard technique in trauma imaging and is the obvious modality of choice for high-energy multitrauma patients [11]. On the other hand, the fact that modern multislice CT machines have made it possible to scan the whole body in less than a minute has considerably increased the number of CT scans performed worldwide, resulting in overutilization of the modality. Furthermore, cases with localized trauma on one flank may be more common than those with multiple abdominal wounds. Such cases are sports, playground and low-altitude fall injuries [11]. As a result, patients scanned with CT on an emergency basis for abdominal trauma often show no traumatic lesions.

In addition, emergency CT disadvantages are well known: The patient needs to be transferred from the emergency department to the CT suite. Ionizing radiation is a factor to consider, especially since many trauma patients are young people subjected to CT scans of multiple body areas, often before and after intravenous contrast medium injection. A patient in pain often cannot cooperate and assume the best position for performing a CT scan. Thus, non-elevated arms, as well as iatrogenic devices (catheters, tubes and lines) can cause artifacts which decrease imaging quality.

Therefore, there is a need for an imaging modality that is superior to baseline US for detecting blunt abdominal trauma and may serve as a filter for cases being referred to emergency CT.

Emergency imaging and ultrasound contrast agents



In recent years, contrast-enhanced US (CEUS) has shown a potential to fill the gap between cases of severe trauma which warrant a CT scan and cases of minor wounds (where at least initially a CT may not be justified) but in which conventional US has not shown any traumatic lesions, in spite of strong clinical suspicion. It can reveal solid organ traumatic lesions that are not visible on baseline sonography, permitting better definition of traumatic lacerations, thereby reaching levels of sensitivity, specificity and positive and negative predictive values up to 96.4%, 98%, 98.8% and 94.1%, respectively [12].

CEUS has been shown to be more sensitive than US for the detection of solid organ injuries [13]. Although CEUS cannot completely replace CT for the time being, it may reduce its use as a screening method. In our department stable patients with severe generalized abdominal traumas undergo contrast-enhanced CT. However, in patients with a low-energy trauma history, complaining of only unilateral pain, CEUS is performed initially. Moreover, in cases in which abdominal trauma has already been detected by CT, CEUS is used to follow up conservative treatment, thus minimizing the patient's radiation exposure.

The technique is practical on an emergency basis. Although the majority of CEUS examinations (usually focusing on focal liver lesion characterization) are scheduled in advance, many patients are imaged under emergency conditions during off-hours. Most of these cases apply to blunt abdominal trauma. In experienced hands, a CEUS examination is easy to perform and is not time-consuming. If an intravenous catheter has already been inserted (which is the usual case in emergency de-

partments), a study can be completed in less than 10 min, thus not prolonging evaluation time.

In this article we describe the basic physics of ultrasound contrast agents, as well as their indications and contraindications. We also outline the technique for performing a CEUS examination for imaging blunt abdominal trauma and present examples of selected cases compared to CT and magnetic resonance (MR).

Basic knowledge of US contrast agents



These agents consist of gas microbubbles coated with a protein, lipid or polymer shell [14]. Their diameter ranges from 1 to 10 μm . This is about the size of a red blood cell. As a result, microbubbles are too large to pass through the vascular endothelium and are considered pure intravascular agents [15]. After several minutes in the blood vessels, they dissolve, the gas is exhaled, and the shell is metabolized, mainly in the liver [16]. They are not excreted by the kidneys. Therefore renal insufficiency is not a contraindication for their injection. However, they do not accumulate in the pelvicalyceal system, which thus cannot be visualized as in intravenous urography or contrast-enhanced CT.

US contrast agents have overcome the limitations of color and power Doppler US [17–19], enabling imaging of parenchymal microvasculature in vessels too small and with too low a velocity to be detected by Doppler. Their enhancement patterns are similar to contrast-enhanced CT and MR. However, these methods are not equivalent [20], since CT and MR contrast agents are cleared from the blood pool into the extracellular space, while US contrast agents remain in the vessels. When subjected to a US wave, microbubbles size alters. They expand and contract and, like every oscillating system, they have a natural frequency (the resonance frequency) at which their response is maximal. By coincidence, this frequency is very close to the frequencies used for diagnostic US imaging, accounting for the contrast agents' high reflectivity. Bubble expansion during rarefaction exceeds contraction during compression. This asymmetric oscillation produces a returning signal (echo) containing harmonics [21]. These are sonographic signals with frequency peaks at multiples of the insonation frequency and are characteristic for the microbubbles [14].

Besides their capacity to detect blood flow which color Doppler US is unable to image, microbubbles do not need to be moving at all to be detected. Thus, US contrast agents have the ability to detect enhancement in real-time continuously for up to 5 min with higher temporal resolution in comparison to contrast-enhanced CT and MR (where only still images in certain time periods can be obtained). The most common radiological CEUS indications (besides cardiac studies) are the detection and characterization of focal liver lesions. In this field, CEUS has proved to be as reliable as MRI for differentiating and specifying newly discovered liver tumors [22], of equal rank to CT [23], and excellent for clarifying liver lesions that remain unclear after baseline ultrasound [24]. Although still not used very often worldwide for various reasons [25], contrast agents can be administered for imaging practically all organs of the body, including the kidneys, spleen, breast, large vessels, scrotum, etc. Anaphylactoid reactions to ultrasound contrast agents are extremely rare, about 1:10000 patients. They do not affect renal function, contrary to CT and MR agents. In practice, their administration should be avoided as

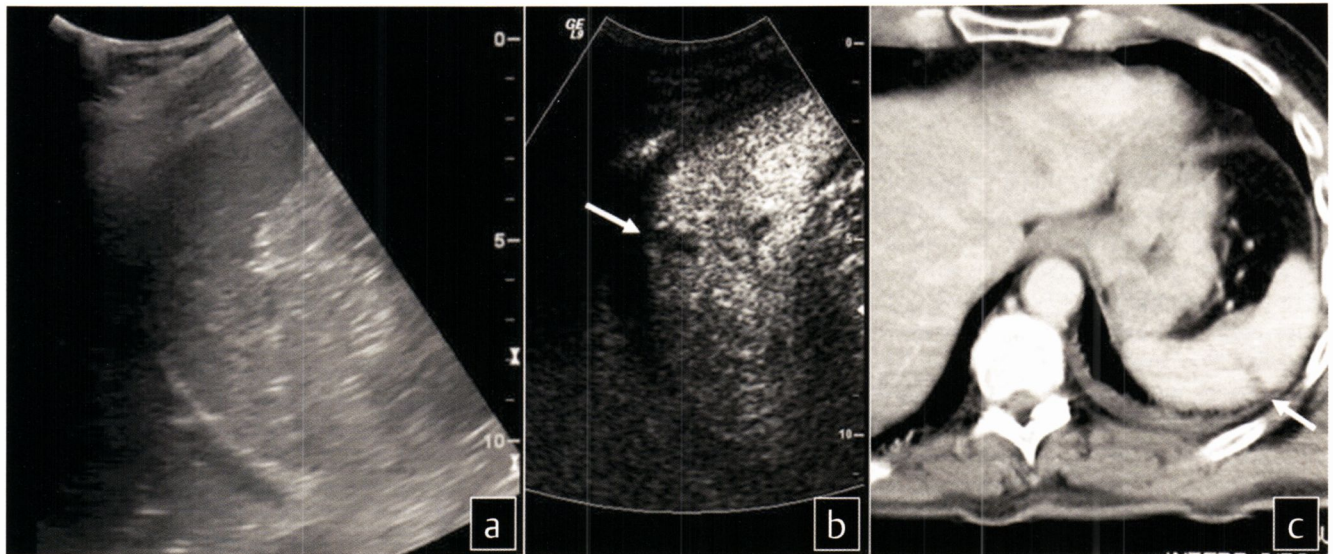


Fig. 1 Splenic laceration of a 34-year-old man who fell from a height. On B-mode US **a** a perisplenic collection is noted. However, no discrete lesion is observed in the spleen. At 23 sec post-contrast injection **b**, a linear filling defect is evident in the peripheral part of the spleen (arrow) consistent with trauma. Contrast-enhanced CT **c** confirms the finding (arrow).

Abb. 1 Milzlaceration bei einem 34-jährigen Mann nach Sturz aus großer Höhe. Im B-Bild **a** wurde eine perisplenische Ansammlung festgestellt, allerdings ohne diskrete Läsion der Milz. 23 s nach Kontrastinjektion **b** ist im peripheralen Bereich der Milz ein linearer Füllungsdefekt ersichtlich (Pfeil) in Übereinstimmung mit dem Trauma. Die kontrastverstärkte CT **c** bestätigt diesen Befund (Pfeil).

a precaution in patients with a recent history of cardiopulmonary pathology (myocardial infarction and ongoing angina or chest pain, recent coronary artery intervention or electrocardiogram changes, frequent and/or repeated angina/chest pain in past week, heart failure, severe lung disease and shortage of breath, etc.) [26]. Altogether, US contrast agents are well tolerated [22].

Although conventional US is able to detect microbubbles in high concentrations, it is mandatory for contrast-specific imaging modes to be installed in a US machine in order to detect contrast enhancement [20]. For this reason, various imaging techniques exist. The most common is based on the principle of phase inversion. In this technique, two US pulses, 180° out of phase, are sent sequentially. Returning echoes are added up by the US machine [27]. Linear tissue echoes nullify each other, while non-linear microbubble echoes produce a detectable signal. This allows almost complete tissue cancellation, while a strong signal is obtained from the contrast agent. In this way, bubbles are not destroyed, allowing continuous real-time sonography with high spatial resolution and sensitivity. This is possible due to the use of a low mechanical index (MI) technique which combines adequate tissue annulment and optimal agent detection for a satisfactory period of time before bubble destruction. A useful feature used in CEUS imaging available in most scanners today is a technique which simultaneously shows contrast enhancement side by side with the baseline grayscale image. By using this split-screen presentation, we can keep the baseline US reference image during contrast scanning. At our institution, we administer a blood pool sonography agent, consisting of stabilized aqueous suspension of sulfur hexafluoride microbubbles with a phospholipid shell [22]. The agent is administered intravenously as a bolus injection via an upper extremity vein. An at least 20-gauge needle is used in order to minimize mechanical damage of microbubbles during injection. When injection begins, the machine's chronometer is switched on. A 10 mL saline flush through a 3-way tap follows.

Description of CEUS technique and trauma imaging findings

Contrary to CEUS assessment of focal liver lesions, where hemodynamic behavior can be observed during the different uptake phases and the probe is focused on a specific part of the organ, abdominal trauma may not be evident on baseline US. Therefore, the examiner is required to scan the organ in question multiple times in order to image the suspicious region, which occasionally can be overlooked. In general, traumatic lesions usually do not enhance (due to a complete lack of blood flow [11]) with strong contrast to the adjacent intact parenchyma of the liver, kidneys or spleen. Some hepatic and splenic lacerations may show minor circulation due to contusion with edema. Altogether, scanning should begin as soon as the parenchyma of the organ in question shows even enhancement throughout its volume. The time from this even enhancement to the deterioration of the contrast agent is considered the late enhancement phase [11].

In all cases of abdominal trauma assessment, the patient should be initially scanned using the FAST protocol for free abdominal and pericardial fluid [28, 29]. Then, conventional US and CEUS imaging of the liver, spleen and kidneys should be performed on the patient's side of trauma. Technical details are important for imaging these organs.

Spleen

It is the most common site of blunt abdominal trauma, the liver being second [30]. The spleen has a longstanding irregular arterial phase, due to different uptake rates between the red and white pulp ("zebra appearance"), disappearing 40–60 sec post-injection. Therefore, special care should be taken in order to differentiate a laceration (which appears as a filling defect – **Fig. 1**) from this inhomogeneous early enhancement (**Fig. 2**). The spleen's late phase is also very long, up to 6 min or longer. The splenic vein and its branches show con-

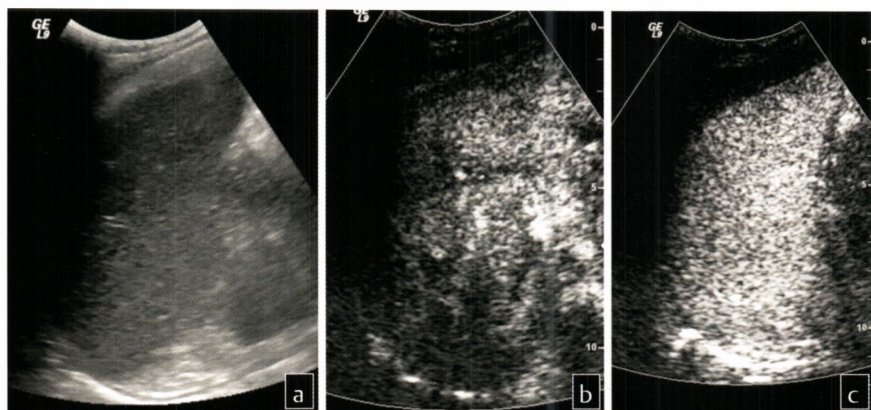


Fig. 2 The “zebra appearance”. The spleen shows normal echogenicity on B-mode US **a**. On CEUS, inhomogeneous enhancement (zebra pattern) is evident 40 sec post-injection **b**. At 75 sec post-injection **c**, there is homogeneous uptake throughout the splenic parenchyma.

Abb. 2 Das „Zebra-Erscheinungsbild“. Die Milz zeigt im B-Bild normale Echogenität **a**. Durch CEUS ist 40 s nach Injektion eine inhomogene Kontrastverstärkung (Zebra-Muster) sichtbar **b**. 75 s nach Injektion **c** erfolgt die homogene Aufnahme durch das Milzparenchym.

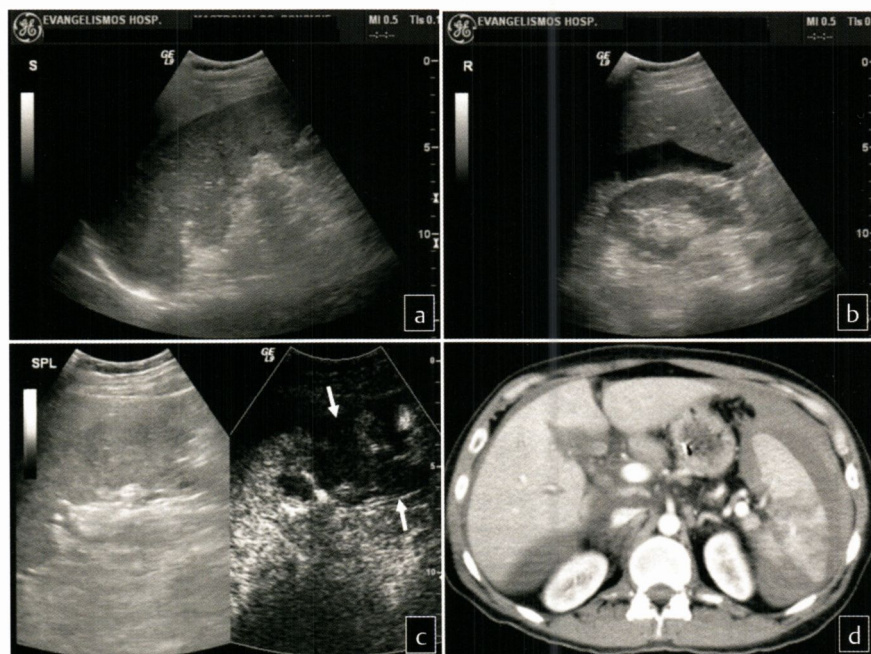


Fig. 3 Splenic rupture of a 22-year-old motorcycle accident victim. On B-mode US **a** the spleen appears inhomogeneous, but no focal lesion is evident. However, fluid collection is seen in Morison's pouch **b**, in the right part of the abdomen. CEUS with dual view mode **c** reveals extended filling defects (arrows) due to rupture, confirmed on contrast-enhanced CT **d**, where blood in multiple abdominal compartments is noted.

Abb. 3 Milzriss bei einem 22-jährigen Motorrad-Unfallopfer. Im B-Bild **a** erscheint die Milz inhomogen, aber es sind keine fokalen Läsionen nachweisbar. Sichtbar ist allerdings eine Flüssigkeitsansammlung in der Morison'schen Tasche **b**, im rechten Bereich des Abdomens. CEUS mit Dual-View-Modus **c** erkennt durch den Riss verursachte, ausgeprägte Füllungsdefekte (Pfeile), bestätigt in der kontrastverstärkten CT **d**, bei der Blut in vielen Bauchabschnitten beobachtet wird.

trast washout in late images (about 2–3 min post-injection) because the spleen acts as a microbubble filter [11]. Thus, there is little enhancement in the vein due to splenic trapping. This hypoechoic appearance of the splenic vein should not be confused with lacerations: vessels have a tubular shape and some microbubbles can be seen in their lumen, while lacerations have irregular shapes with no microbubbles running through them. The spleen's subdiaphragmatic area may be (as in the liver's case) difficult to image because of the superimposed gas-containing lung base or left colonic flexure. In cases of a shattered spleen, there is complete architectural derangement of the organ along with perisplenic (and possibly left pleural) collection (● Fig. 3). Suggested doses for SonoVue in the literature range between 0.6 mL and 25–50% of the liver dose for adults or calculated as follows for children: age in years/20 in mL.

Liver

Among the abdominal solid organs, the liver presents the most difficulties for imaging trauma, due to its large size and the shadowing effects of overlying lung and ribs. It can be challenging to assess its deeper parts, where the sound beam may be attenuated, especially in patients with fatty infiltration. The

liver should be scanned in the longitudinal, transverse and oblique direction with extra attention to the subdiaphragmatic area, where the lung base may obscure imaging. The liver's arterial phase lasts for up to 40 sec, followed by the portal phase (up to 2 min) and the late phase, which lasts for about 4–5 min. Traumatic areas appear as non-enhancing lesions and are much more evident on CEUS than on baseline US (● Fig. 4, 5). Large concave areas extending from the liver capsule towards the medial parts are consistent with hematomas (● Fig. 6). CEUS can also be used to differentiate traumatic lacerations from lesions of a non-traumatic nature (● Fig. 7). The administered contrast agent dose ranges between 50% and 100% of the amount given for imaging focal liver lesions. If SonoVue is used, the adult dose ranges between 1.2 and 2.4 mL. For children, the dose is calculated as follows: age in years/10 in mL. As a general rule, it is advisable that a dose smaller than that used for focal liver lesions is administered for trauma assessment in order to avoid obscuring thin lacerations.

Kidneys

The renal cortex enhances early with the medulla (pyramids) following approximately 10–20 sec later with less intense en-

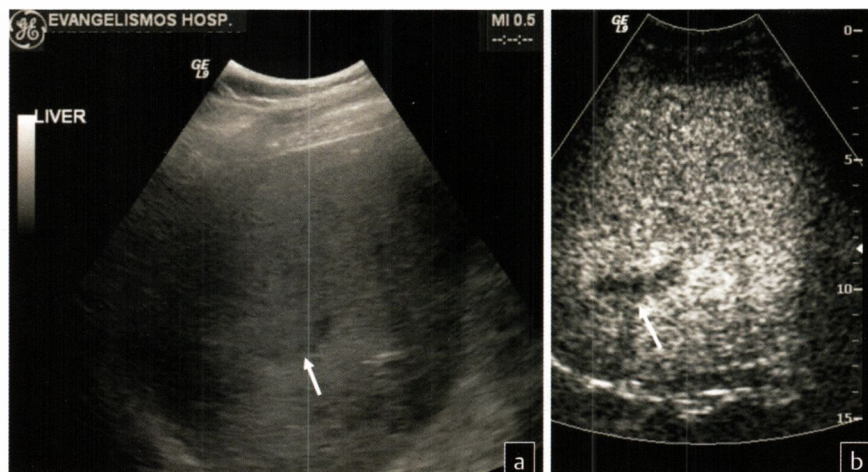


Fig. 4 Hepatic laceration. A linear echopoor area (arrow) is faintly noted in the right lobe of the liver on B-mode US **a**. By 1:32 min post-contrast injection, a laceration is clearly seen (arrow in **b**).

Abb. 4 Leberlazeration. Eine lineare echoarme Region (Pfeil) am rechten Leberlappen ist im B-Bild schwach auffällig **a**. 1:32 min nach Kontrastinjektion ist eine Lazeration deutlich sichtbar (Pfeil bei **b**).

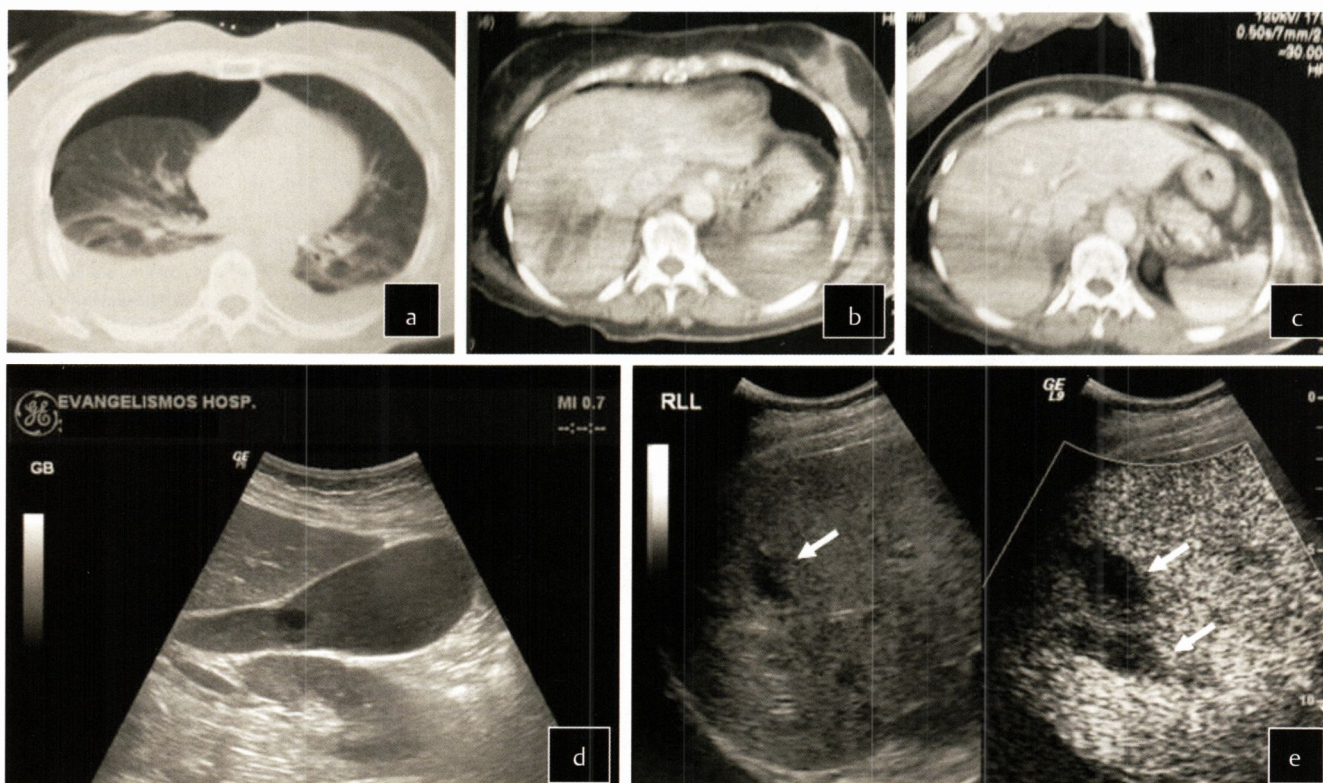


Fig. 5 Hepatic lacerations. Contrast-enhanced CT **a–c** shows hydropneumothorax and hypoattenuating areas in the right lobe of the liver. Artifacts are evident due to the patient's inability to raise his arms. Hemobilia is also present in the gallbladder **d**. CEUS 4:05 min post-injection **e** clearly confirms lacerations (arrows). Note that on this dual view mode image, traumatic areas evident with contrast (right part of image) are underestimated without contrast (left part).

Abb. 5 Leberlazerationen. Die kontrastverstärkte CT **a–c** zeigt Hydropneumothorax und gering abgeschwächte Bereiche am rechten Leberlappen. Artefakte sind sichtbar aufgrund des Unvermögens des Patienten, die Arme zu heben. Hämobilie besteht auch in der Gallenblase **d**. CEUS 4:05 min nach Injektion **e** bestätigt eindeutig die Lazerationen (Pfeile). Zu beachten ist, dass in dieser Dual-View-Modus-Darstellung die traumatischen Bereiche, die mit Kontrast nachweisbar sind (rechtes Teilbild), ohne Kontrast unterschätzt werden (linker Teil).

hancement. Pyramids show contrast uptake from the periphery to the center for 30 sec. The kidneys' maximum enhancement phase lasts for 2–2.5 min. Therefore, imaging should be finished by that time, since contrast wash-out begins thereafter. The dose used is the same as in the spleen. Similar to the rest of the abdominal organs, traumatic areas show no contrast uptake (● **Fig. 8**). Subcapsular or perirenal hematomas also appear anechoic post-contrast injection.

Assessment of multiple abdominal organs

Although CEUS is generally used in cases of low-energy localized abdominal trauma, it is feasible to image more than one abdominal organ. In this case a full vial dose (e.g. 4.8 mL of SonoVue) can be divided into two or three doses of 2.4 mL or 1.6 mL, respectively, making it therefore possible to scan the liver, spleen and kidneys. On both sides, the kidneys should be scanned first following contrast agent injection, in order not to miss their short peak enhancement phase. The



Fig. 6 Hepatic contusion and hematoma. CT of a 65-year-old female fall victim reveals complete hepatic architectural derangement of the right lobe **a**. On B-mode US performed 4 days later **b**, normal architecture is seen in only a small part of the organ. Most of the liver appears echopoor. CEUS on the same day as **b** (**c**) notes partial hepatic enhancement at 22 sec post-injection, while the rest of the liver shows no uptake. This finding is consistent with a hematoma and was confirmed by MR **d**. A year later, CEUS (26 sec post-injection) revealed that the hematoma size had diminished **e**.

Abb. 6 Leberprellung und Hämatom. CT eines 65-jährigen weiblichen Sturzoepfers zeigt die vollständige architektonische Störung des rechten Leberlappens **a**. In dem 4 Tage darauf durchgeführten B-mode-US **b** ist nur in einem kleinen Bereich des Organs eine normale Architektur zu sehen. Der Großteil der Leber erscheint echoarm. CEUS am gleichen Tag wie **b** (**c**) bemerkt 22 s nach Injektion eine partielle Kontrastverstärkung der Leber, während der übrige Teil der Leber keine Aufnahme zeigt. Dieser Befund spricht für ein Hämatom und wurde durch MR **d** bestätigt. Ein Jahr später zeigt sich in der CEUS (26 s nach Injektion) eine Verringerung der Hämatomgröße **e**.

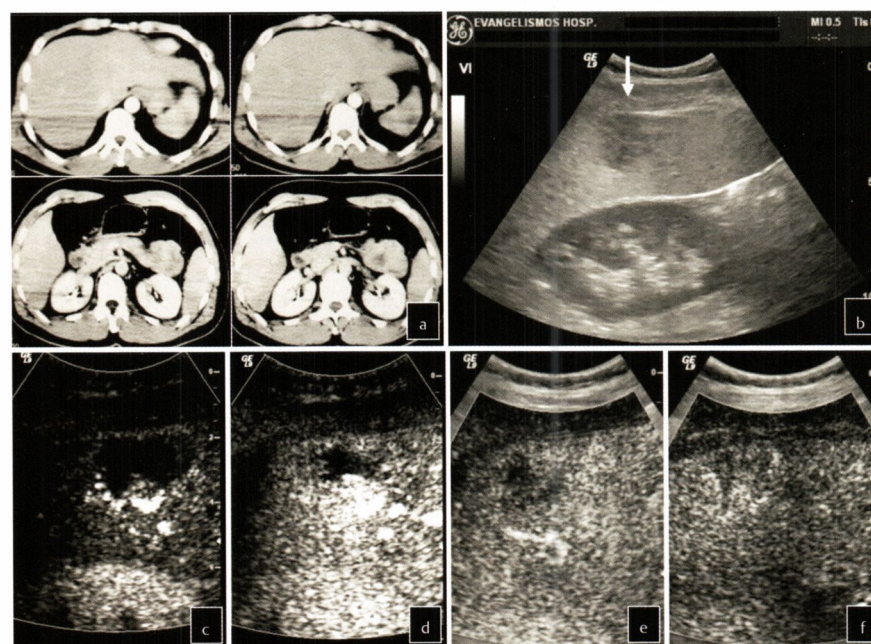


Fig. 7 Hepatic hemangioma. A 42-year-old man complained of right flank pain after a car accident. The contrast-enhanced CT **a** image quality was compromised by artifacts. However, a right hepatic lobe laceration was reported. On B-mode US **b**, an echopoor lesion is noted in segment VI (arrow). Post-contrast injection, this lesion showed arterial peripheral nodular enhancement at 25 sec **c**, with centripetal filling in the portal (**d** 45 sec) and late phase (**e** 2:23 min, **f** 3:14 min). This behavior is consistent with a hemangioma.

Abb. 7 Leberhämangiom. Ein 42-jähriger Mann beklagte sich über Schmerzen in seiner rechten Flanke in Folge eines Autounfalls. Die Bildqualität der kontrastverstärkten CT **a** wurde durch Artefakte beeinträchtigt, dennoch wurde eine Laceration des rechten Leberlappens gefunden. Im B-Bild **b** wurde im Segment VI eine echoarme Region beobachtet (Pfeil). Nach der Kontrastinjektion zeigte diese Läsion eine arterielle periphere knotige Kontrastverstärkung bei 25 s **c**, mit zentripetaler Füllung in der portalen (**d** 45 s) und späten Phase (**e** 2:23 min, **f** 3:14 min). Dieses Verhalten spricht für ein Hämangiom.

first dose can be used to image the left kidney and spleen with the patient in a supine or right decubitus position. The first 2 min should be dedicated to the kidney, which can be scanned repeatedly in the transverse and longitudinal plane from the beginning of pyramid enhancement throughout the maximum uptake phase. Sufficient time (2–4 min) is then left to examine the spleen in the same position. For the second dose, the patient assumes a left decubitus position, allowing the examination of the right kidney (for the first 2 min) and the liver (for the next 2–3 min) [11, 20, 31].

Ongoing hemorrhage

In cases of traumatic and non-traumatic (e.g. in a suspected aneurysm or tumor rupture) ongoing hemorrhage, as well as in patients with a post-operative leak, it is possible to image blood extravasation with CEUS, provided that an adequate window between the overlying tissues is available. CEUS can image blood flow better than color and power Doppler, where a critical limitation is the inability to differentiate blood flow from signals arising from vessel walls [32]. Perivascular collections, depending on the quantity of blood extravasation, can appear on CEUS as a hyperechoic pool or as a fountain-like, hyperechoic jet [33, 34].

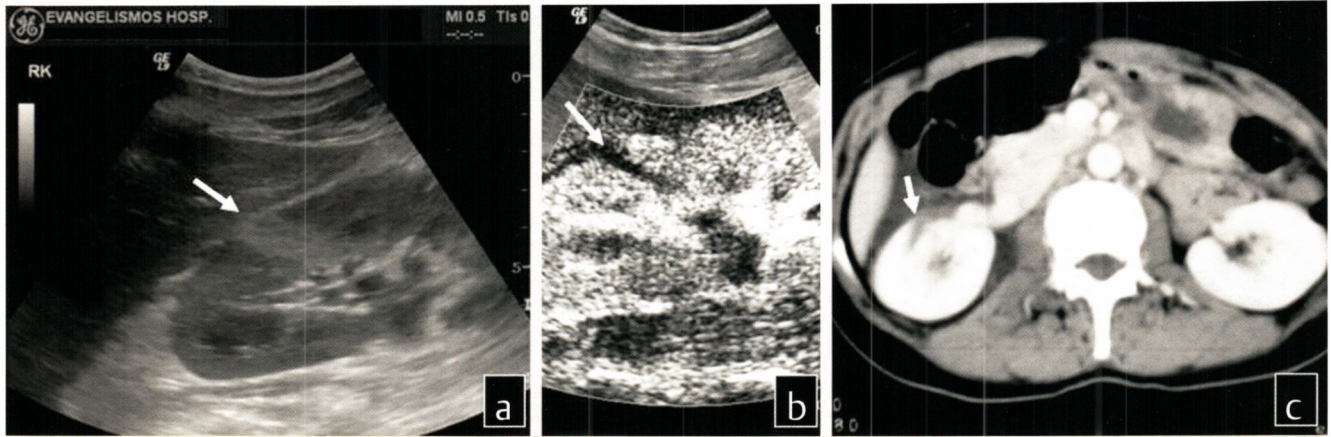


Fig. 8 Renal trauma. B-mode US **a** reveals an echogenic area in the cortex of the right kidney (arrow). CEUS 30 sec post-injection **b** shows that this finding clearly corresponds to a laceration (arrow). Contrast-enhanced CT **c** confirms right kidney trauma (arrow).

Abb. 8 Nierentrauma. Das B-Bild **a** zeigt echodichte Bereiche im Kortex der rechten Niere (Pfeil). CEUS 30 s nach Injektion **b** zeigt, dass dieser Befund deutlich mit einer Laceration übereinstimmt (Pfeil). Die kontrastverstärkte CT **c** bestätigt das Trauma der rechten Niere (Pfeil).

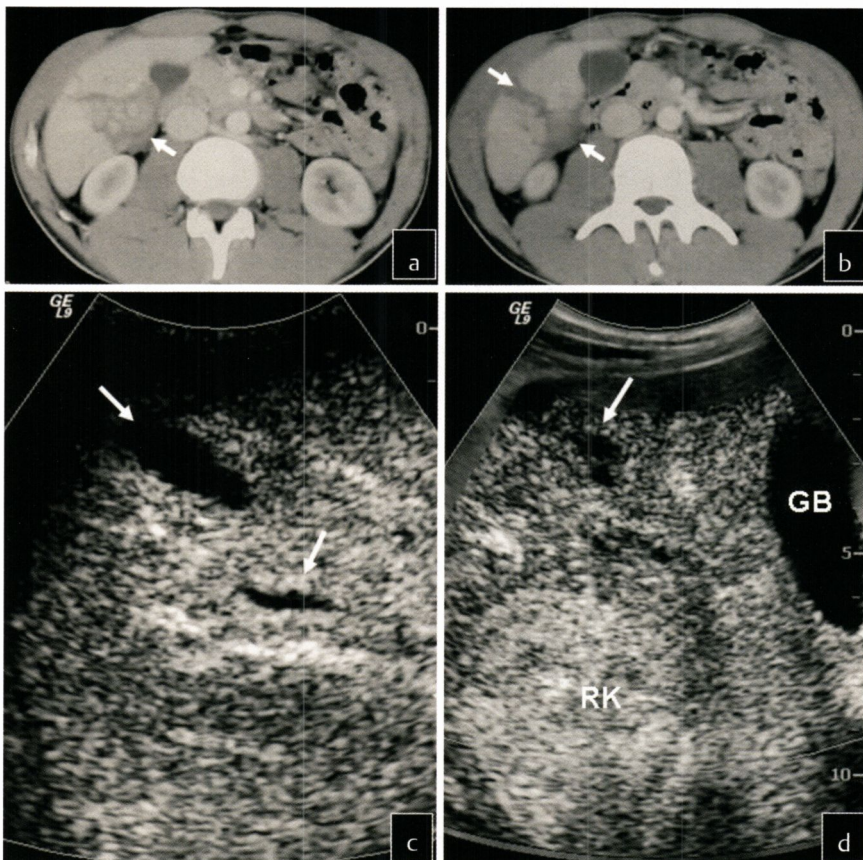


Fig. 9 Hepatic laceration. A 31-year-old man was subjected to contrast-enhanced CT **a, b**, which revealed a large laceration (arrows), extending from the lateral to the medial surface of hepatic segment VI abutting the right kidney and gallbladder. The patient was treated conservatively. Six days later CEUS (**c** 33 sec, **d** 1:13 min post-injection) shows that the traumatic area (arrows) has diminished in size, not reaching the right kidney (RK) and gallbladder (GB). No additional CT was performed.

Abb. 9 Leberlazeration. Ein 31-jähriger Mann durchlief eine kontrastverstärkte CT **a, b**, die eine große Laceration (Pfeile) enthüllte, die von der seitlichen bis zur mittleren Oberfläche des VI. Lebersegments, angrenzend an die rechte Niere und Gallenblase verlief. Der Patient wurde konservativ behandelt. 6 Tage später in der CEUS (**c** 33 s, **d** 1:13 min nach Injektion) zeigte sich, dass die verletzten Bereiche (Pfeile) an Größe abgenommen haben und nicht mehr die rechte Niere (RK) und die Gallenblase (GB) erreichen. Es wurde keine zusätzliche CT durchgeführt.

CT or CEUS for trauma?

Although CEUS has proved to be very useful in imaging patients with blunt abdominal trauma, it should not be considered as a replacement for contrast-enhanced CT. Patients should initially be scanned following the FAST sonographic protocol, along with full abdominal US scanning, if possible. If abdominal fluid is detected, suggesting trauma in a certain organ, or if a contusion is seen, it is legitimate to further assess a hemodynamically stable patient with CEUS. If an intravenous catheter is already inserted, the delay in the US department

can be less than 10 min, while the benefit for the patient is major: a CT scan may be avoided, reducing exposure to ionizing radiation and saving time and money.

However, multiple trauma cases as well as patients in a serious clinical condition are not suitable for CEUS. In these cases, immediately after FAST assessment, patients should be transferred to CT (if stable) or to surgery (if unstable) with no further delay [11, 12].

Finally, patients with abdominal solid organ trauma, initially imaged with CT, who have followed an uneventful course, can be followed up with CEUS [19]. In our department, many pa-

tients with traumatic lesions on the initial CT scan are further imaged with CEUS during follow-up – if this is needed – or before discharge (● Fig. 9). Thus, repeated CT scans can be avoided.

Conclusion

CEUS is a very useful method for imaging patients with blunt abdominal trauma. Although it cannot completely replace CT, it may reduce its use as a screening method. CEUS is fast, easy to perform and clearly reveals traumatic lesions in abdominal solid organs as filling defects with excellent contrast to the adjacent normal tissue. Moreover, in cases in which abdominal trauma has already been detected with CT, CEUS can be used for conservative treatment follow-up, thus minimizing further exposure to ionizing radiation.

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Quality Indicators for the Development and Didactics of Ultrasound Courses in Continuing Medical Education

Qualitätsindikatoren für die Konzeption und Didaktik von Ultraschallkursen in der ärztlichen Fort- & Weiterbildung

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Key words

- QA/QC
- abdomen
- ultrasound
- teaching
- assessment

Zusammenfassung

Ziel: Basierend auf Evaluationsdaten aus Teilnehmerrückmeldungen sollte stufenweise ein, in Hinsicht auf Lernerfolg pro Zeit, optimiertes Ablaufkonzept für mehrtägige Sonografiegrundkurse des Abdomens entwickelt werden.

Material und Methoden: Dieses Konzept ist nach den Erkenntnissen der Lehr-/Lernforschung und den Erfolgen in abschließenden Kursprüfungen im OSCE-Format [2] über mehrere Jahre mithilfe detaillierter Rückmeldungen von ca. 2000 ärztlichen Kursteilnehmern jährlich modifiziert und so stufenweise optimiert worden. Dazu wurden die letzten 1005 konsekutiven Teilnehmer-rückmeldungen analysiert.

Ergebnisse: 1005 Teilnehmerrückmeldungen ergeben die Empfehlung eines modularen Kursaufbaus mit nur kurzen Theorievorträgen (optimale Dauer 20 Min., SD 9,6 Min.), im alternierenden Wechsel mit längeren praktischen Schallübungen (60 – 90 Minuten, insgesamt mindestens 50 – 60% der Kurszeit), vertiefenden Zeichenübungen und Wechselpausen. Als ideale Gruppengröße in den praktischen Übungen geben 51% der ärztlichen Kursteilnehmer fünf und 43% sogar nur vier Teilnehmer pro Gruppe an. Die Diskussion stellt zehn konkrete Qualitätsindikatoren für effiziente Ultraschallkurse vor, beleuchtet die Machbarkeit und logistischen Voraussetzungen dieses Modells und vergleicht es mit anderen Grundkurskonzepten. Flankierend wird ein Modell für eine kurskonzept- und ausbilderbezogene Evaluation und ein Trainingsprogramm für Ausbilder inklusive Kostenanalyse vorgestellt.

Schlussfolgerungen: Die Teilnehmer bewerten das entwickelte Kursdesign als ausgereiftes Konzept, das seine Machbarkeit und hohe Akzeptanz unter ärztlichen Kollegen unter Beweis gestellt hat.

Abstract

Purpose: Based on evaluation data from participant feedback, a concept was to be developed for introductory abdominal ultrasound courses lasting several days. This approach was to be developed incrementally with the intent of maximizing the learning effect per time.

Materials and Methods: This concept has been modified annually over several years based on the findings of educational research and the scores on final examinations in OSCE format. It has been modified with the aid of detailed questionnaires completed by approximately 2000 participating physicians and has thus undergone incremental optimization.

Results: Analysis of the most recent 1005 questionnaires has shown that participants recommend a modular course design with only brief lectures on theory (average optimal duration of 20 min., SD 9.6 min.). These should alternate with longer practical "hands-on" ultrasound exercises (60 – 90 min., accounting for at least 50 – 60% of the course time), consolidating drawing exercises, and breaks. 51% of the physicians specified 5 participants as the ideal group size for practical exercises, while 43% specified only 4. The discussion presents 10 specific quality indicators for efficient ultrasound courses. It elucidates the feasibility and logistical prerequisites of this model, and compares it with other basic course concepts. Furthermore, this article presents a model for an evaluation covering the course concept and tutors as well as discussing a training program for tutors including a cost analysis.

Conclusion: In summary, the participants estimate the course design to represent a mature concept that has demonstrated its feasibility and broad acceptance among physicians in CME.

received 8.4.2011
accepted 19.6.2011

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DOI <http://dx.doi.org/10.1055/s-0031-1281649>
Published online
September 5, 2011
Ultraschall in Med 2011; 32:
68 – 75 © Georg Thieme Verlag
KG Stuttgart · New York ·
ISSN 0172-4614

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Introduction

An increasingly interdisciplinary tool, diagnostic ultrasound, has become a well established imaging modality in both routine clinical and emergency settings. A survey of 1000 physicians preparing for their specialty board certification examinations has shown that most specialists regard ultrasound examining skills as particularly relevant. At the same time they feel that the teaching of these skills is particularly in need of improvement [1]. Standardized practical examinations in OSCE format have currently been developed for ultrasound and may be included in model curricula in medical schools (for example as a component of "internship examinations"). They are also being discussed within the scope of continuing medical education where they are being considered as possible supplementary components of specialty board certification examinations or health insurance colloquiums [2]. The importance of professionalizing ultrasound courses becomes apparent in this setting. It would increase the learning effect among course participants and improve ultrasound tutors' teaching methods. This in turn would partially address the frequently criticized lack of structure in continuing medical education [3–5] in many specialties with respect to this key skill.

Objective

The main purpose of this study was to develop an adaptive model for the didactic optimization of ultrasound courses for continuing medical education that reflects the current state of research regarding learning and memory processes. The intent was to maximize the course participants' practical examination proficiency while striving for a high level of long-term retention of theoretical background knowledge and of the cross-sectional anatomy of the abdomen.

A further goal was to develop a catalog of criteria to help innovative ultrasound course providers to develop their own course designs. These criteria could then be used to examine the specific methodological or didactic potential for improvement of such course designs. This in turn would allow them to make appropriate modifications and, in applicable cases, to optimize the qualifications of their tutors and instruction methods.

Methods

In cooperation with the Marburger Bund Foundation, the Medical Education Group Düsseldorf has offered introductory abdominal ultrasound courses since 1992. Held under the supervision of radiologists and internists, these courses were originally designed for about 80 physicians per year and currently accommodate 120. To date, over 2000 physicians have participated in our 3–5 day ultrasound courses. Approximately 60% of these participants were hospital staff physicians receiving CME (increasing over time), approximately 30% were interns (decreasing over time), and about 10% were specialists and physicians in private practice. A total of 116 tutors completed the tutor qualification and training program, with an annual fluctuation rate of 2–6 tutors.

A modular course was developed to include lectures, interactive quizzes, live demonstrations with single and synchro-

nous double projections of magnified transducers, and practical exercises in small groups with five participants per ultrasound workstation and tutor. The course was supplemented by consolidating drawing exercises for each of 12 standardized imaging planes [6]. The small groups rotated with each new module from one tutor to the next. This gave them the opportunity to give comparative feedback about the efficiency of the practical exercises and instructional styles. In 2010, standardized preparatory assignments based on the literature [7] were added to the course and sent to the participants about two months prior to the course.

The tutor qualifications included a 3D abdominal topography training session and practical teaching and drawing exercises within increasingly shorter time limits, followed by video feedback. Participants trained for the role of examiner in standardized OSCE examinations and difficult course situations with role-play exercises. These included moderating typical conflicts and explaining matters such as the physical origins of artifacts or the fundamentals of image optimization, all within a brief time frame. A coach discussed the potential for improvement and for shortening with the participants. Initially the tutors invested four full days of training and eight 90-minute training sessions. Later the advanced tutors only participated in this training sporadically as trainers for new tutors or as required, depending on their evaluation.

Standardized questionnaires were used to survey all course participants about the quality criteria for the general course design, the learning points, the weighting of the various course phases and breaks, and the potential for improvement. The latter also included the delivery techniques of the tutors, who were evaluated individually and by name.

The results were jointly reviewed and discussed by the team of tutors and lecturers immediately after each ultrasound course and viable options for optimization were identified. Each year changes were made to the method of delivery of theory, the practical exercise phases, and the methodical design of preparatory and consolidating exercises. The effectiveness of these changes was then verified with new evaluation data and standardized OSCE examinations at the end of each respective course [2]. The detailed evaluation results were entered into a chronological trend analysis, which was made available to the tutors shortly after the course along with the participant comments. They also received an anonymous comparison of the results of all tutors.

The frequency of participant comments in the last 1043 consecutive participant evaluation questionnaires was used to rank course characteristics and criteria deemed by participants to contribute to an optimal learning effect in ultrasound courses. Additionally, the results of the participant survey were summarized as relative frequencies and/or mean values and standard deviations (SD). The participants' votes were evaluated in total and analyzed according to the respective survey period (2000–2004, 2005–2007 and 2008–2010).

The evaluation results were compared with a total of 60 external basic abdominal ultrasound courses (2 × 30 courses each in the years 2005–2007 and 2008–2010) offered by third parties with respect to group size, course design (block structure vs. alternating structure) and the duration of theoretical presentations. All external courses were attended incognito and scored with the same evaluation form used for the internal courses of our study. The differences between the concepts desired by the participants and those offered by the 60 external

Agenda: Training formats

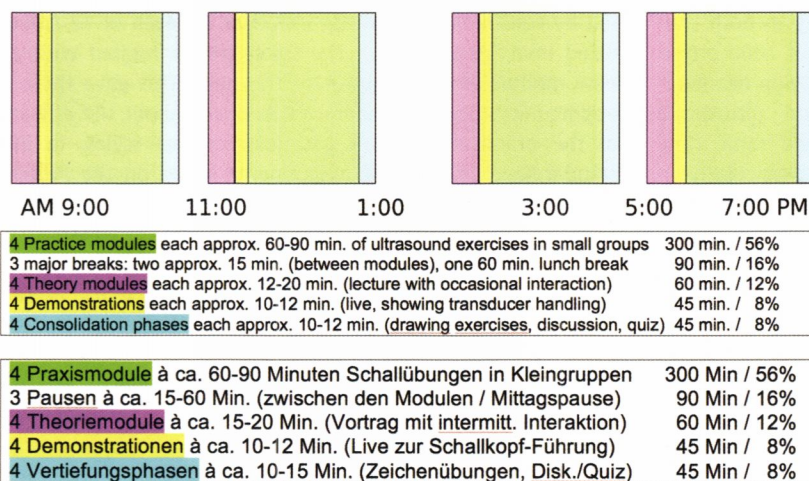


Fig. 1 Flow diagram of a full day of training showing the time weighting of the various modules. Introductory lectures are shown in purple, live demonstrations in yellow, practical ultrasound exercises in small groups in green, and consolidating drawing exercises in blue. Breaks are shown in white.

Abb. 1 Ablaufschema mit zeitlicher Gewichtung eines vollen Trainingstages mit modularem Wechsel zwischen Einführungsvorträgen (violett), Live-Demos (gelb), praktischen Schallübungen in Kleingruppen (grün) und vertiefenden Zeichenübungen (blau) sowie intermittierenden Pausen (weiß).

courses were analyzed using a one-sample t-test (length of theory lectures, optimal group size) or binomial test (course concept). All tests were two-sided and assessed at the 5% significance level. Statistical analyses were preformed with the use of SAS®, V9.2 (SAS Institute Inc., Cary, NC, USA).

Inclusion criteria

Only questionnaires that were over 85% complete and contained no contradictory statements were included in the evaluation.

Results

A total of 38 of 1043 questionnaires from the years 2000 through 2010 fell under the exclusion criteria so that 1005 questionnaires (96%) were evaluated. Nearly all course participants favored the following mix of methods for a 9-hour training day for their subjective and objective learning effect in the OSCE examinations (● Fig. 1).

For retention of the abdominal cross-sectional anatomy, 94.8% of the participants regarded the assisted drawing exercises for the 12 standard imaging planes as "very helpful" or "helpful." Consolidating drawing exercises were not observed in any of the external courses.

Items emphasized as particularly helpful to learning included the brief intervals for changing among the participants actively performing imaging (usually 7–10 minutes) and for tutors changing between the individual imaging modules as well as the frequent involvement of participants not actively performing imaging. This included content, quiz, and repetition questions. Passive participants were also asked to give imaging instructions and to operate equipment. Of the participants queried, over 99% supported frequent alternation between brief theory modules and longer practice phases. They explicitly decided against a course designed in blocks with several successive lectures (for example in the morning) followed by practical exercises. Only 0.7% favored a longer theory block followed by a practice block (● Table 1).

The design of the 60 visited external courses has the opposite structure (75% block structure with 25% alternating structure). In the early survey period (2005–2007), the percentage of courses with a block structure was 88%; in the second survey period (2008–2010), it dropped down to 2/3. In these time periods 99% of participants desired an alternating structure, while 0.37% and 0.82%, respectively, favored a block structure (● Table 1). The design of the external courses in both survey periods thus differed significantly ($p < 0.0001$) from the wishes of the participants we surveyed. The optimal length of theory lectures (● Table 1) was specified on average as 20.0 minutes (SD 9.6). With four theory modules planned, their total desired duration represents 15% of the course time. This desired value differs significantly ($p < 0.0001$ in each case) from the lengths of the theory lectures in the external ultrasound courses. In the early survey phase 2005–2007, these lectures averaged 56.3 minutes (SD 13.5; 72% of total course time); in the second survey period 2008–2010, they averaged 46.8 minutes (SD 11.2; 67% of total course time).

The optimal average group size for practical exercises was specified as 4.5 (SD 0.69) per workplace and tutor in both survey periods. In our courses the number of participants per group was 5. This value differed significantly ($p < 0.0001$ in each case) from the group size of the external ultrasound courses, which in the early survey period was on average 8.1 (SD 1.0) participants per group and in the second survey period 6.9 (SD 1.2). Of our participants, 54.34% stated they were willing to pay higher course fees for groups smaller than 5, while 45.66% rejected this proposal and felt that a group size of 5 was optimal.

The course participants specified 9 items as essential quality indicators for the maximization of their learning effect, which are listed in descending order in ● Table 2.

Discussion

Prior to any interpretation of the results, it should be considered that some constellations of increasing clinical workload coupled with problems in acquiring qualified staff are not con-

Table 1 Results of participant survey (percentage and mean (SD)) according to survey period.

		Survey period			Total
Item		2000 – 2004 n = 359	2005 – 2007 n = 275	2008 – 2010 n = 371	2000 – 2010 n = 1 005
<i>Training background</i>					
n = 966 (349/266/351)	Student/intern	58.17%	26.69%	8.55%	31.47%
	Resident	37.25%	65.79%	76.92%	59.52%
	Hospital staff specialist	2.87%	6.39%	9.97%	6.42%
	Private practice	1.72%	1.13%	4.56%	2.59%
<i>Age</i>					
n = 996 (254/273/369)	20 – 25	7.06%	12.09%	7.05%	8.43%
	26 – 30	59.89%	47.25%	42.55%	50.00%
	31 – 40	6.84%	31.50%	32.52%	30.22%
	> 40	6.21%	9.16%	17.89%	11.35%
<i>Concept</i>					
n = 994 (354/272/368)	In blocks	0.85%	0.37%	0.82%	0.70%
	Alternating	99.15%	99.63%	99.18%	99.30%
<i>Time allotment</i>					
n = 965 (333/268/364)	Optimal	19.82%	21.27%	31.04%	24.46%
	Pleasant	41.44%	45.52%	45.33%	44.04%
	Strenuous	38.14%	32.09%	23.35%	30.88%
	Very strenuous	0.60%	1.12%	0.27%	0.62%
<i>Drawing exercise</i>					
n = 996 (357/272/367)	Very helpful	52.66%	54.78%	58.31%	55.32%
	Helpful	40.90%	39.34%	38.42%	39.56%
	Not very helpful	5.88%	5.15%	2.45%	4.42%
	Not helpful	0.56%	0.74%	0.82%	0.70%
<i>Group size = 5</i>					
n = 992 (350/274/368)	Optimal	42.00%	55.11%	55.16%	50.50%
	Acceptable	50.57%	39.42%	38.04%	42.84%
	Too large	7.43%	5.11%	6.25%	6.45%
	Far too large	0.00%	0.36%	0.27%	0.20%
<i>Higher costs for smaller groups?</i>					
n = 968 (346/269/353)	Yes	55.49%	56.13%	51.84%	54.34%
	No	44.51%	43.87%	48.16%	45.66%
<i>Prior mailing of textbook and assignment</i>					
n = 115 (–/–/115)	Very helpful	–	–	69.57%	69.57%
	Helpful	–	–	29.57%	29.57%
	Not very helpful	–	–	0.87%	0.87%
<i>Optimum lecture duration</i>					
n = 925 (334/255/336)	Minutes	20.8 (SD 9.3)	19.9 (SD 10.0)	19.4 (SD 9.6)	20.0 (SD 9.6)

Table 2 Quality indicators for optimal learning effect in ultrasound courses from the participants' perspective.

Course emphasis on long practical ultrasound exercises
Increasingly brief and only intermittent theory phases (lectures)
Small practice groups of at most four to five participants
Experienced tutors and lecturers with specialized training in the subject and in didactic methods
Frequent change of media in the theory phases (PPT slides, films, live demonstrations, quizzes)
Active participation constantly required in the form of: drawing exercises, quizzes, consolidating questions
Tangible consideration of the needs of the participants and their learning effect
Opportunity for systematic preparation (mailing literature and assignments)
Sufficient length and number of breaks

ductive to implementing all of the recommendations outlined below for ultrasound courses. However, that was never a premise of this study. On the contrary, this long-term study is intended to develop an adaptive model based on continual re-

evaluation from which each course director can apply those elements that are feasible and expedient in the respective setting.

The model presented here is based on course experience with a specific group of participants consisting of hospital staff physicians. Their needs are not necessarily applicable to ultrasound refresher courses for general practitioners in private practice for example. However, the current situation is favorable for measures to improve the quality of CME courses as hospitals compete for qualified staff and increasingly assume the expenses of their residents' CME courses. As a result, there are now new opportunities for improving the tutor-participant ratio, which leads to higher course fees. In this regard it is interesting to note that 54% of participants are explicitly willing to pay higher course fees for groups of 4 in the practical exercises.

Our observations have also shown that evaluations rarely cover both the course concept and the individual tutors. It is also rare for them to request participant feedback about specific persons and to make this information available to the tutors shortly after the course in the form of their personal chrono-

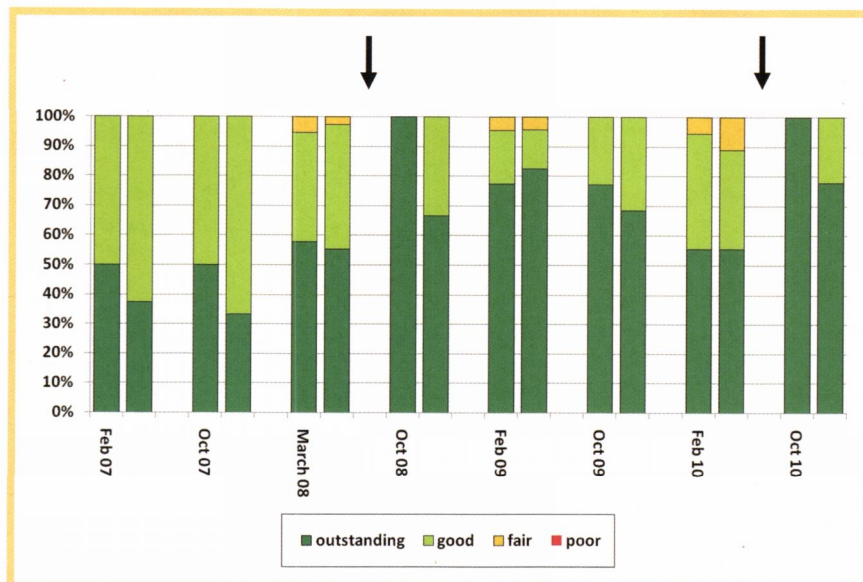


Fig. 2 Example of a chronological trend in a tutor's evaluation results. Participants evaluate the tutor's qualifications with respect to subject matter (left bar) and didactic presentation (right bar). The original is supplemented by participant comments about the tutor. The typical wave-like progression reflects the interplay of "fatigue effects" and performance improvements following training sessions (↓).

Abb. 2 Beispiel eines zeitlichen Trends in den Evaluationsergebnissen eines Ausbilders zur fachlichen (jeweils linke Säule) und didaktischen (jeweils rechte Säule) Qualifikation aus Teilnehmersicht, im Original ergänzt durch den Ausdruck der ausbilderbezogenen Freitextkommentare. Typisch sind wellenförmige Verläufe durch "Ermüdungserscheinungen" und verbesserte Bewertungen nach Schulungsintervention (↓).

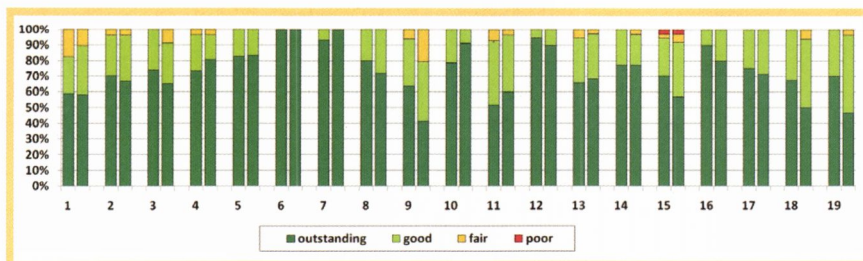


Fig. 3 Example of an evaluation comparison of proficiency with respect to content (left bar) and didactic presentation (right bar) among the 19 tutors of an ultrasound course. The respective tutor is shown only his or her own ID number. The other 18 tutors remain anonymous for that tutor. The tutor's own position within the teaching team is still readily apparent.

Abb. 3 Beispiel eines Evaluationsvergleichs zu den fachlichen (linke) und didaktischen Kompetenzen (rechte Balken) innerhalb der 19 Ausbilder eines Sonografie-kurses: Rückgemeldet wird dem Ausbilder nur die eigene Kennziffer. Die anderen 18 Ausbilder bleiben somit für den Einzelnen anonym. Dennoch wird die eigene Position innerhalb des Ausbilderteams transparent.

logical trend (compared with previous courses, ● Fig. 2) and as an anonymous comparison to the other tutors (● Fig. 3). This sort of data and the culture of candid reflection that they foster make it easier for the respective tutors to reflect upon and, if applicable, modify their instructional technique in the hands-on exercises. The course directors are more readily able to optimize their own course concept in the interest of quality while providing their tutors with specific training with respect to content and didactic approach. Although the course director received the best evaluation scores on average in our study, several tutors came close to or sometimes even exceeded his ratings, which might provide a challenging motivational aspect among the teachers and tutors.

Therefore, a first step might be to develop a detailed participant course evaluation that is specifically tailored to the individual tutors. It can be helpful to have participants fill out the questionnaires before the end of the course, e.g. prior to the final practice module.

In our concept, the costs per course of such an evaluation and digital feedback to the tutors via email are approximately 20 student assistant hours at €8.56 for a total of about €200 including copying costs. This is about €3.50 per participant or about 1% of the course fee. At a calculated hourly rate of €40 over five work days, the costs of training tutors in our concept

totalled approximately €1600 per tutor (distributed over several years). Assuming that a tutor remains on the team for an average of five years and teaches two courses per year, this would represent only fictitious costs of €160 per tutor per course. Our tutors receive no remuneration for their preparation time but voluntarily invest in their own qualifications. They are compensated for this by subsequent tutor salaries. The results of the present study indicate that the opinion of a majority of the physicians participating in ultrasound courses correlates to a high degree with the results of research regarding teaching, learning, and memory processes [6]: These results indicate that brief theory modules alternating frequently with longer practice phases in small groups should be required. At the same time the survey over two time periods shows that the actual course reality still deviates significantly from this course design in many places. However, its prevalence has doubled from one-sixth originally to one-third in our most recent analysis.

From the course organizers' perspective there are understandable reasons for preferring a long theory block in the morning, i.e., this requires significantly less personnel than an alternating concept with a higher proportion of practical exercises in small groups. The latter requires the constant presence of all tutors and therefore leads to higher personnel costs. Constella-

tions in which the practical exercises are supervised in the afternoon by the course director's clinical assistants, however, will not permit the course design recommended here. This poses the question of whose needs should be given greater emphasis in quality management. Unfortunately, the "convenient" method with its lower labor costs for the course organizers conflicts with the needs of the course participants.

In spite of this, the course fees of our more labor-intensive model at €350 per participant including catering and preparatory literature are below the average fee for a 3-day ultrasound course in Germany. However, the introductory course design presented here dispenses with ultrasound examination subjects for cost reasons. The participants examine each other under supervision, and upon registration give their consent to let others perform ultrasound examinations on them. For this reason the intermediate and advanced courses with patient presentations requiring more elaborate logistics are more cost-intensive.

Although the block concept warrants critical re-examination from an educational standpoint, relevant improvements in the learning effect can be achieved even without "radical" changes. In particular, mailing literature to course participants beforehand has significantly improved their professional preparation for the course. The literature contains specific preparatory assignments, including exercises such as drawing 12 standard planes from memory, to facilitate pattern recognition and quick orientation within the three-dimensional abdominal space. This helped participants to better handle the drawing exercises (designed as memory aids) and significantly increased their average point score in the subsequent OSCE parcourses [2]. The apparent low ranking of participant comments (Table 1) is attributable to the very recent introduction of this systematic preparation. Since then, this criterion has become the one that is most frequently mentioned.

According to course participant feedback, the frequent active integration of participants even in the "passive" or observational learning phases has the effect of minimizing fatigue despite the compact, strenuous course structure. This important quality criterion is consistent with findings of educational re-

search, which indicate that a high proportion of practical exercises in small groups leads to the best and most sustainable learning effects [9–11].

Practical exercises in audiovisual synchronization are among the techniques that have proven effective in the specific didactic training of the tutors. Using a trackball to move a high-contrast arrow over the frozen or moving image, the tutors practice pointing out the respective structure while simultaneously delivering a verbal explanation. Consequently, they avoid one of the cardinal errors (Table 3), namely pointing out a key structure only intermittently on the monitor with their own hand. Often the tutor's hand will block the view of the relevant parts of the image for those participants who are not performing the ultrasound examination. Unfortunately, most course participants never object to this lack of clarity. This is attributable in part to a lack of familiarity with the more illustrative instructional method, and in part to the risk of subjective embarrassment in having to admit one's own lack of knowledge ("Now, where is the pancreas?").

Table 3 Overview of most frequently observed educational mistakes made by ultrasound tutors.

"High-speed" monologues and self-demonstrations (instead of pauses, interactive discussions and support of the participants' hands-on performance)
Verbal explanations only without synchronized visualization of sectional anatomy
Showing of specific structures with own hand in front of monitor, thus blocking participants' view (instead of using the trackball and a well-contrasted arrow to highlight the relevant pixels)
Lack of awareness of the listening (non-active) course participants (instead of activate tasks to involve them all, e. g. by commands to the sonographer, mental or image quizzes, multitasking)
Use of too many words for circumstantial or complicated explanations (instead of precise verbalization according to KISS principle: keep it short and simple)
Lack of balancing-out of the hands-on time between participants of one group

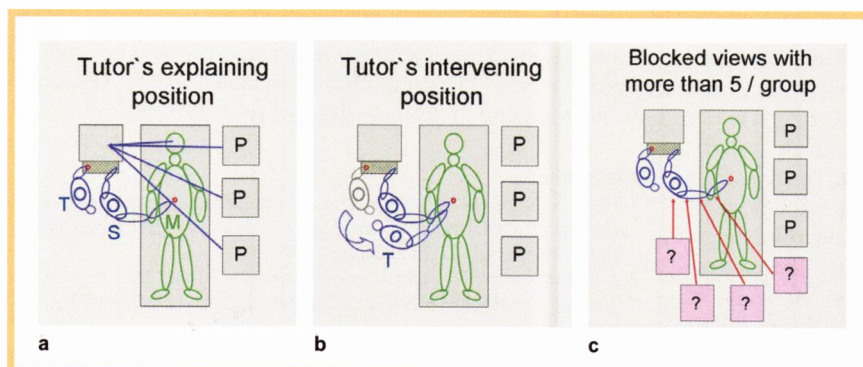


Fig. 4 Optimized position of the tutor (T) in practical exercises: The left hand operates the unit and trackball for explanations on the ultrasound image (a). Taking one step forward allows the right hand to help the current sonographer (S) correct the transducer position (b). This largely avoids blocking of the line of sight of the remaining participants (P). If more than 3 to 4 passive participants are present, their view of the monitor would be impaired by the sonographer's arm and shoulder (c). Adequate rotation and tilt of the monitor is also important for the participant acting as the ultrasound examination subject (M).

Abb. 4 Didaktisch optimierte Standposition des Ausbilders (T) bei praktischen Übungen: Die linke Hand übernimmt die Gerätebedienung/Trackball für Erläuterungen am Sonobild (a). Mit nur einem Schritt kann bei Bedarf die rechte Hand in die Schallkopf-führung des aktuell schallenden Teilnehmers (S) eingreifen (b). So wird die Blickperspektive der nicht schallenden Teilnehmer (P) am wenigsten beeinträchtigt. Bei mehr als 3–4 passiven Teilnehmern wäre der Blick auf den Monitor durch Arm und Schulter des Schallenden versperrt (c). Eine adäquate Drehung und Kippung des Monitors ist für den als Schallmodell dienenden Teilnehmer (M) wichtig.

This technique also produces an interesting effect (and one conducive to learning), namely it slows the tutor's speech. The left hand (most tutors are right-handed) cannot move the arrow with the trackball fast enough to keep up with the tutor's speech if he or she speaks too quickly (● Fig. 4a). During this procedure, the tutor's right hand remains free to help the course participant correct the transducer position if necessary (● Fig. 4b). In addition, tutor training is focused on repeated practice of precisely formulated task assignments for the participants performing the ultrasound examination. In training our own tutors and observing other tutors, we repeatedly observed initial random scanning taking place without a specific imaging target (an organ or vascular region). The observers generally had the impression, consistent with the findings of educational research [12], that these unstructured ultrasound practice phases tended to reflect a less obvious training effect as opposed to specific, chronologically limited scanning exercises of a complete organ or the task of measuring the width of a vascular lumen. The most effective instruction exercises proved to be those combined with subsequent video analysis. The "aha" effect of tutors seeing themselves as others see them is achieved much faster. Apparently, it also leads to more permanent changes in behavior than without the opportunity of being able to see and analyze oneself from the perspective of others [13, 14].

The option of being able to conclude ultrasound courses with standardized practical examinations in OSCE format with feedback for one's own learning effect [2] also provides a very effective opportunity to shift the participants' attitude to course participation away from one of passive expectation toward a more active, exercise-oriented attitude. Possible deterrent effects with problems of acceptance in the target group need not be feared among hospital staff physicians. Although there are many regional alternatives without final examinations offered for similar prices, our courses, despite practical examinations, have been rapidly overbooked for years with over 100 registrations per course. Course participants are willing to travel longer distances from northern, eastern, and southern Germany and as far as Switzerland (approx. 40% >400 km).

The concept can also be applied to 4-day courses (according to KBV directives and §135 (2) of the German Social Security Code V) as the number of hours per day can be reduced and the breaks extended. The authors also offered 5-day introductory abdominal ultrasound courses under the auspices of the German Federal Chamber of Physicians for several years. The longer course duration had positive effects by giving participants opportunities for additional preparation and further study during the course breaks. It is difficult for many hospital staff physicians to take off more than a Friday plus the weekend for such CME courses. As a result, we have deferred to the participants' wishes and have not expanded the compact 3-day course concept to 4 days. Otherwise, our tutors would increasingly encounter problems with taking time off from their own hospitals. Approval of the ultrasound courses according to DEGUM or KBV directives is of secondary importance for the participants surveyed here (<5%). In Germany, the ultrasound skills required for a particular specialty are usually included in residency skills catalogs, and residents do not normally need to document any additional courses when they later go into private practice.

The present study does exhibit limitations in the comparison with the various external course concepts. Although 30 exter-

Table 4 Ten quality indicators for efficient ultrasound courses.

A tutor-participant ratio conducive to learning: for the hands-on ultrasound exercises, a maximum of 4–5 participants per tutor and ultrasound workplace.
Frequent alternation between brief introductions or theory presentations (each about 20 minutes, < 15% of total course time) and longer practice phases (> 50%).
Frequent, active involvement of participants by means of consolidating questions and quizzes, or by requesting them to give imaging commands or operate the ultrasound equipment.
Change of media in lectures (PowerPoint slides, films, board, live demonstrations with separate projection of the transducer position).
Encouragement of the participants to actively repeat and verbalize key points, instead of listening in a "passive" role.
Drawing exercises to help consolidate knowledge of 3D sectional anatomy.
Systematic course preparation required with specific training assignments.
To increase motivation, the course should conclude with an optional test (OSCE) with feedback about the individual participant's learning effect and/or potential for improvement.
System for evaluating the course concept and individual tutors and lecturers, feedback results made available to the lecturers and tutors shortly after the course.
Regular didactic training tailored to the specific level of experience for lecturers and tutors (with video feedback wherever possible).

nal basic course models were visited per survey period, it is possible that this limited sample may not be representative of the entire palette of available course concepts and didactic methods. The presented course concept is particularly well suited for introductory courses. At least in its present form it is not readily applicable to intermediate or advanced courses. Future studies with the use of common evaluation forms with comparable quality indicators (items), which should be common-sense among the ultrasound course providers of the national society of ultrasound, are desirable.

Conclusion



Based on the participant' statements, our course design represents a mature concept that has demonstrated its feasibility and broad acceptance among physicians in continuing medical education. From the perspective of the participants and tutors, 10 major quality indicators have emerged (● Table 4).

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Endocavitary Contrast Enhanced Ultrasound (CEUS) – Work in Progress

Endokavitäre Kontrastsonografie (CEUS) – Work in Progress

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Key words

- abdomen
- thorax
- drainage
- ultrasound
- abscess

Zusammenfassung



Ziel: Darstellung der diagnostischen Möglichkeiten der endokavitären Anwendung von Ultraschallkontrastmittel über Drainagen, im biliären System sowie bei oraler Gabe zur Untersuchung des GI-Traktes.

Material und Methoden: Kochsalzlösung unter Zumischung eines Tropfens SonoVue® wurde über die Drainage bzw. pro-/retrograd in das biliäre System eingebracht. Bei der oralen Anwendung wurden unterschiedliche Mischungsverhältnisse von Wasser mit SonoVue® verabreicht.

Ergebnisse: Die Kontrastmittelzumischung in Kochsalzlösung erleichtert die Lagekontrolle der Drainage und liefert zusätzliche Informationen zur Ausdehnung des zu drainierenden Prozesses. Komplikationen wie Fisteln zu den Gallengängen, Gefäßen, Darmschlingen, anderen Organen oder in die freie Bauchhöhle sind sensitiv erkennbar. Das biliäre System lässt sich gut darstellen. Bei der Gabe per os lässt sich das Kontrastmittel im Gastrointestinaltrakt verfolgen. Auch lassen sich Anastomoseninsuffizienzen und Perforationsstellen erkennen.

Schlussfolgerung: Die Gabe eines verdünnten Ultraschallkontrastmittels über eine Drainage bringt wertvolle Informationen über Lage, die Ausdehnung und Kommunikation des drainierten Prozesses zur Umgebung. Das biliäre System ist darstellbar. Die Gabe von Ultraschallkontrastverstärker per os ist möglich und kann Anastomoseninsuffizienzen und Perforationsstellen darstellen.

Abstract



Purpose: To demonstrate the benefit concerning localisation, measurement and visualisation of complications of drained fluid collections in the abdomen by applying ultrasound contrast agent via drainage catheters. In addition, to investigate the usefulness of CEUS in applying the agents in the biliary tract or when given orally.

Materials and Methods: A single drop of SonoVue® was added to 0.9% saline solution and instilled via drainage catheters. Location, dimensions and complications of drained fluid collections were recorded and compared to the results of sonographic examination using saline solution alone and fluoroscopic examination using iodinated contrast agents. The biliary system was visualised by applying the solution via nasobiliary drains or via ERC catheterisation. Orally administered solutions consisted of one drop of SonoVue® in 50 ml aqua.

Results: Admixture of an ultrasound contrast agent to saline solution facilitates position monitoring of the drains in fluid collections and provides reliable information on the dimensions of the drained collection. Complications like fistulae to the biliary system, blood vessels, small or large intestine or to the peritoneal cavity are precisely displayed. The biliary system is shown in detailed description. Orally administered, the contrast agent is visible after intake long into the colon. Insufficient anastomoses or spontaneous perforations become detectable.

Conclusion: The application of ultrasound contrast agents via drainage catheters provides substantial information on location and dimensions of drained fluid collections and their communication with surrounding organ structures. The biliary system can be visualised. Oral administration is feasible and provides important additional information.

received 20.8.2011

accepted 22.9.2011

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DOI <http://dx.doi.org/10.1055/s-0031-1299056>
Published online:
December 19, 2011
Ultraschall in Med 2011; 32: 76–84
© Georg Thieme Verlag KG
Stuttgart · New York ·
ISSN 0172-4614

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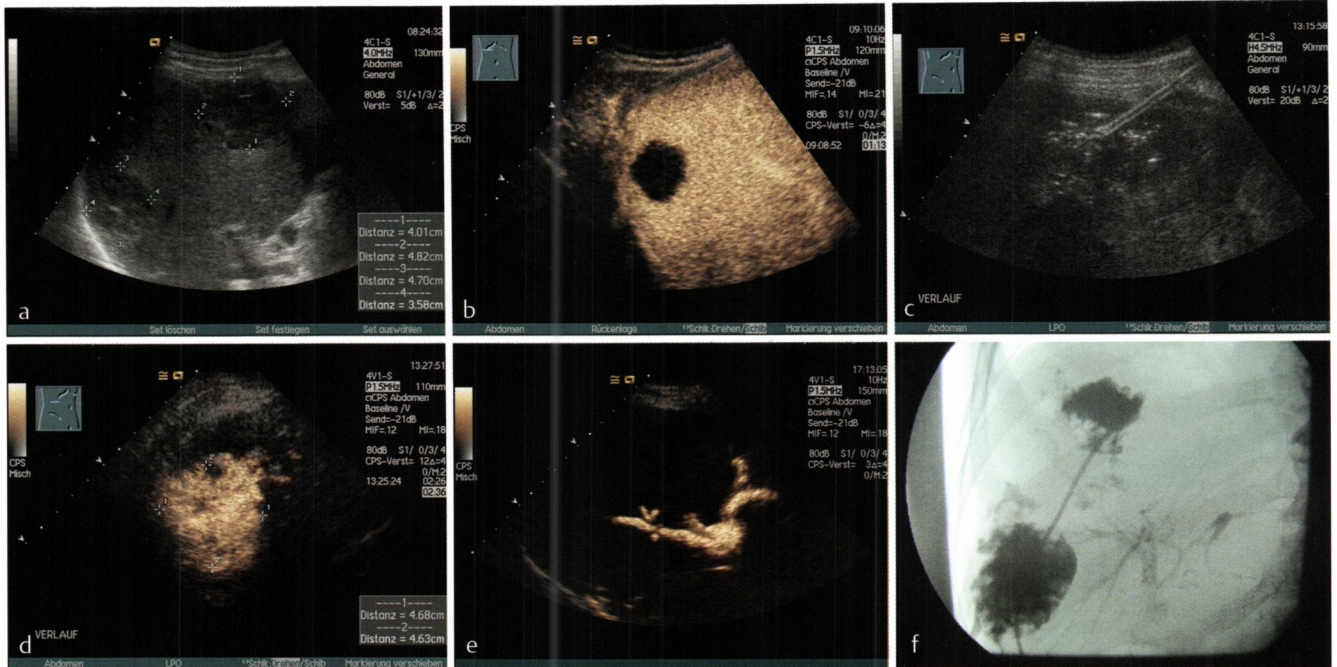


Fig. 1 **a** A Patient with a history of biliodigestive anastomosis after resection of caput pancreas, now admittet presenting fever and the shivers. The figure shows two hypoechoic, ill-defined lesions in the right hepatic lobe. **b** CEUS was performed on suspicion of a hepatic abscess. Already in early arterial phase, the dorsal lesion is depicted by complete filling defect of the CEUS-agent (2,4 ml of SonoVue®, i. v.). Diagnostic puncture confirmed the abscess. **c** Drainage (10 french, pigtail drain) of both abscesses guided by ultrasound, then confirmation of their location by instillation of 10 ml of saline solution. Distribution of the saline solution as well as dimension of the abscess are shown quite well in B-mode. However, only for a short period of time. **d** After admixture of CEUS-agent (1 drop of SonoVue®), the abscess is illustrated much longer and rich of contrast. Some of the bubbles appear in the biliary tract after having left the site of abscess. This crucial information was not shown by saline solution alone. **e** CEUS-agent appearing in the biliary tract, even in its branches. Outlet via the biliodigestive anastomosis is demonstrated. **f** X-ray with usual iodinated contrast agent shows the biliary tract and the biliodigestive anastomosis.

Abb. 1 **a** Patient mit biliodigestiver Anastomose nach Pankreaskopfresektion, jetzt Aufnahme mit Fieber und Schüttelfrost. Darstellung zweier fokaler, echoarmer, unscharf begrenzter Herde im Bereich des rechten Leberlappens. **b** Unter der Verdachtsdiagnose Leberabszess erfolgte die Kontrastsonografie. Nach Gabe von 2,4 ml SonoVue® intravenös lässt sich der dorsale Herd schon früharteriell als Kontrastmittelaussparung darstellen. Die diagnostische Punktion bewies den Abszess. **c** Unter sonografischer Sicht Drainageeinlage (10F-Pigtaildrainagen) in beide Abszesse. Zur Lagekontrolle Instillation von 10 ml Kochsalzlösung. Die Verteilung der Kochsalzlösung und die Ausdehnung des Abszesses sind im B-Bild gut, allerdings nur kurzfristig, erkennbar. **d** Nach Kontrastmittelzumischung (SonoVue® 1 Tropfen) lässt sich der Abszess deutlich länger und kontrastreicher darstellen. Einzelne Kontrast-Bubbles verlassen den Abszess-Bereich und erscheinen im biliären System. Diese für den Patienten wichtige Zusatzinformation war mit Kochsalzlösung allein nicht erkennbar. **e** Das Ultraschallkontrastmittel erscheint im biliären System und lässt sich bis in

die Seitenäste darstellen. Der Abfluss über die biliodigestive Anastomose ist nachweisbar. **f** Die biliodigestive Fistel und die Gallengänge sind im Röntgenkontrast erkennbar.

Video 1 Patientin mit schmerzlosem Ikterus. In der ERC konnte eine Stenose im mittleren Gallengangsdrittel erkannt werden, eine nasobiliäre Sonde wurde eingelegt. Nach Ultraschallkontrastmittelgabe über die nasobiliäre Sonde wurde das erweiterte intrahepatische Gallengangssystem bis in die peripheren Äste dargestellt.

Video 2a Bei einer Patientin mit Verdacht auf Gallenblasenperforation erfolgte die Anlage einer Drainage in die Gallenblase und Gabe des Ultraschallkontrastmittels über die Drainage. Man kann die Perforationsstelle deutlich erkennen. **Video 2b** Hier erkennt man das Ausmaß der Perforation. Man erkennt eine Verteilung des Kontrastmittels um die rechte Niere.

Video 3 Nach Anlage einer Thoraxdrainage und Gabe von Kochsalzlösung mit Ultraschallkontrastmittel kommt der komplette Pleuraraum zur Darstellung. Die komprimierte Lunge erscheint vom Kontrastmittel umspült. Es sind keine Kontrastmittelaussparungen und damit Septierungen erkennbar, die erfolgreiche Drainagen-Behandlung ist damit zu erwarten.

Video 4 Bei einem Patienten mit Verdacht auf Ösophagusperforation erkennt man nach oraler Gabe des Kontrastmittels den Übertritt des Kontrastmittels vom distalen Ösophagus in den Pleuraraum und anschließend die Verteilung im Pleuraerguss. Die Perforationsstelle im Ösophagus ist hier direkt dargestellt. Der Patient wurde operativ versorgt.

Video 5 Bei einem Patienten war, bei in das Duodenum einbrechendem Pankreaskarzinom, eine duodenale Stent gelegt worden. Jetzt war es zu rezidivierendem Erbrechen gekommen. Der Verdacht auf ein Stentverschluss war gestellt worden. Nach oraler Gabe von Ultraschallkontrastmittel sieht man die Verteilung des Kontrastmittels im Magen. Der Stent wird nicht passiert. Der Verdacht des Stentverschlusses konnte endoskopisch nicht bestätigt werden. Wohl aber das Passagehindernis. Das Stentende lag im Jejunum direkt auf der Wand.

Introduction

In recent years, numerous studies have demonstrated the value of contrast enhanced ultrasound (CEUS) mainly for the characterization of focal liver lesions [1–17] and with increasing interest in other fields [18–34]. EFSUMB guideline updates were last published in 2008 [35] and 2011 [36]. Earlier, it had been shown that fluid collections barely detectable in conventional B-scan

could be successfully punctured and drained performing i.v. CEUS [37]. Little has been published on endocavitary applications – apart from imaging of vesicourethral reflux or the passage of the fallopian tube [38–41].

Here, we demonstrate the feasibility of visualizing abdominal and thoracic fluid collections by instillation of the diluted ultrasound contrast media (USCM) SonoVue® via the drainage and in this way to determine their size as well as complications. We also

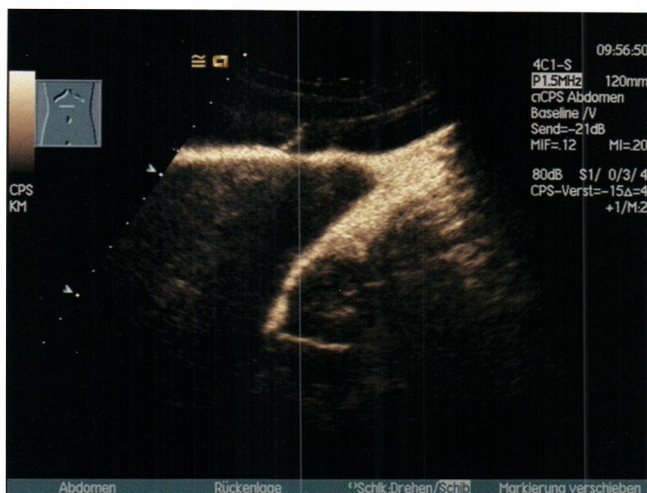


Fig. 2 On clinical suspicion of dislocation of a drain previously applied during a PTHC, saline solution with admixture of CEUS-agent was administered via the drain. The contrast medium can be seen subcutaneously and also forming an inverted contrast of the liver by surrounding it, thus proving complete dislocation.

Abb. 2 Nach einer PTHC (perkutane transhepatische Cholelithdrainage) bestand klinisch Verdacht auf Dislokation der Drainage. Nach Gabe von Kochsalzlösung mit Ultraschallkontrastmittel (SonoVue® 1 Tropfen) über die Drainage lässt sich die Drainage im subkutanen Verlauf als zartes Kontrastmittelband erkennen, das Kontrastmittel umspült die Leber, entsprechend zeigt sich ein Negativkontrast der Leber als Beweis für die komplette Dislokation.

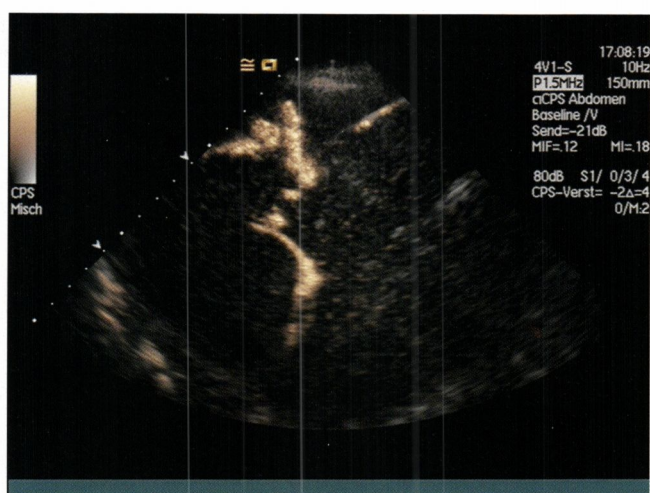


Fig. 3 A fistula of a drained hepatic abscess towards the right hepatic vein and the vena cava is revealed by the CEUS-agent. Complications like these are disclosed highly sensitively by the CEUS-procedure.

Abb. 3 Nach Anlage einer Leberabszessdrainage erkennt man eine Fistel zur rechten Lebervene mit Abfluss des Kontrastmittels über die rechte Lebervene und in die V. cava (dorsal der Leber). Die Drainage ist oben rechts im Bild zu erkennen. Derartige Komplikationen sind hochsensitiv mit einem Ultraschallkontrastmittel erkennbar.

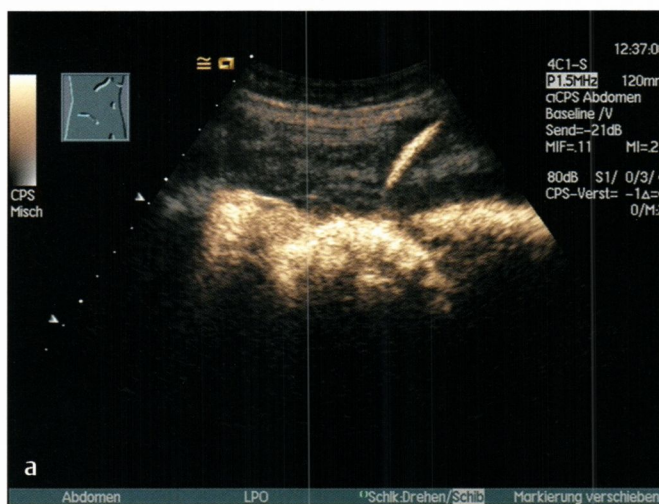


Fig. 4 a Visualization of a necrotic cavity in the right middle abdomen by CEUS-agent applied via drain in a case of necrotizing and ongoing abscess-forming pancreatitis. The whole extension of the abdominal necrosis with its smallest fistulae can be detected highly sensitively. **b** Transit of the ultrasound contrast agent from the retroperitoneal necrosis towards the colon transversum. This finding was also seen in a CT scan with usual iodinated contrast agent applied by the drainage. The fistula was managed surgically.

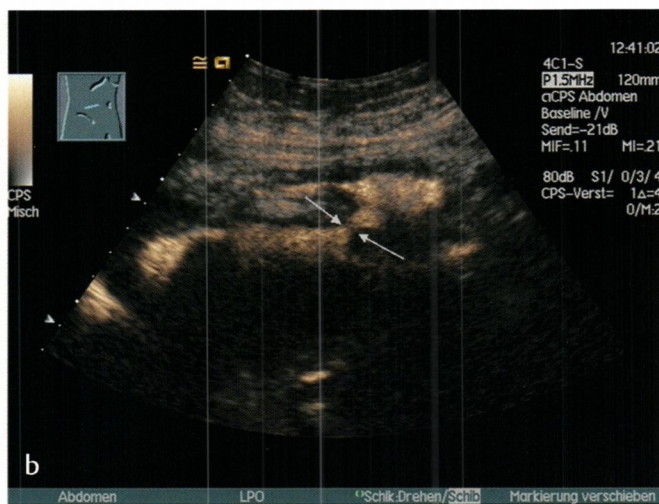


Abb. 4 a Bei einer Patientin mit nekrotisierender und nicht abheilender abszedierender Pankreatitis Kontrastmitteldarstellung einer Nekrosehöhle im rechten Mittelbauch über die Drainage. Die gesamte Ausdehnung der intraabdominellen Nekrose einschließlich von kleinsten Fistelungen können hochsensitiv erfasst werden. **b** Man erkennt einen Kontrastmittelübertritt (Pfeile) aus der retroperitoneal gelegenen Nekrose ins ventral gelegene Colon transversum. Dieser Befund wurde im CT mit Kontrastgabe über die Drainage bestätigt. Die Fistel wurde operativ verschlossen.

investigated the behaviour of SonoVue® in the biliary tract or when administered orally. We demonstrate the usefulness of these applications for daily clinical practice.

Methods

After drainage of an abdominal or thoracic fluid collection, a single drop of SonoVue® was added to 10 – 20 ml of (0.9%) saline solution and then instilled via the drain. US examinations were performed with Siemens' Sequoia CEUS technology CPS in low MI

mode. Whenever possible, results were compared to those of saline solution alone or to X-ray after instillation of iodinated contrast agents.

To picture the biliary tract, we applied the USCM either retrogradely via a nasobiliary tube, or during endoscopic retrograde cholangiography (ERC), or progradely via a percutaneous transhepatic cholangiogram (PTHC).

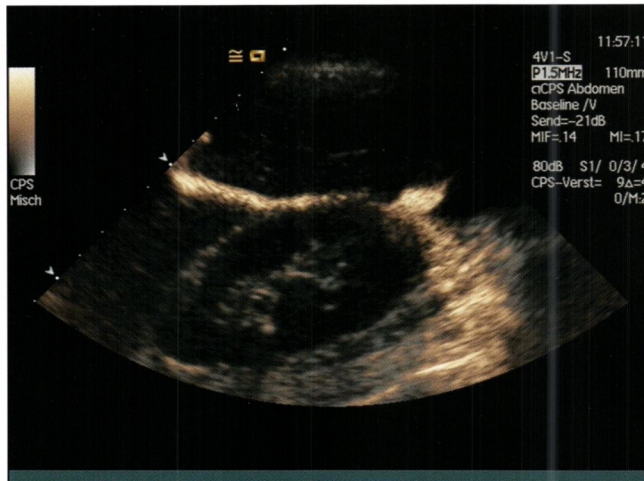


Fig. 5 Drained gallbladder in a patient with suspected perforation of the gallbladder. After administering CEUS-agent via the drain, not only was proven its perforation, but also was revealed its dimensions, e.g. communication around the right kidney.

Abb. 5 Bei einer Patientin mit Verdacht auf Gallenblasenperforation erfolgte die Anlage einer Drainage in die Gallenblase und Gabe des Ultraschallkontrastmittels über die Drainage. Damit konnte nicht nur die Perforation bewiesen, sondern auch das Ausmaß der Perforation dargestellt werden. Man erkennt eine Verteilung des Kontrastmittels um die rechte Niere.

For the investigation of the gastrointestinal tract, we orally administered tap water with USCM (one drop of SonoVue® in every 50 ml of water). The dilution of the contrast medium may be varied according to the clinical question and need.

Results

Application via abdominal or thoracic drains

Abscesses are the most common indication for aspiration and drainage of the abdomen. CEUS facilitates the identification of abscesses and their drainage (● Fig. 1a, b). Tubes and drains are easily detected in common B-mode because of their high differences in impedance but hardly seen in their full length; the tip's position is sometimes difficult to locate. Application of saline solution alone can usually confirm the correct positioning of the drain (● Fig. 1c) but gives only a vague impression of the collection's dimension. Adding a drop of USCM in the low MI mode, the site of the drain and the dimensions of the abscess can be evaluated with marked contrast and much longer – up to 20 minutes (● Fig. 1d). Mishandled or dislocated drainages are easily and reliably detected, also after a PTHC (● Fig. 2).

Complications of liver abscesses like fistulae to the biliary tract (● Fig. 1e) or blood vessels (● Fig. 3) are detected with high sensitivity. X-ray with iodinated contrast agent provides no additional information (● Fig. 1f).

As in the liver, abscesses (or necrosis) within the abdominal cavity or in the retroperitoneal space are identified and measured more precisely with diluted USCM applied via the drain (● Fig. 4a). Here, complications like fistulae towards the intestine can be revealed (● Fig. 4b). The fistulae to the intestine following a perforation, e.g. of the gall bladder, are visualized (● Fig. 5). Also, we detected fistulae towards other organs and hence could explain their etiology (● Fig. 6a, b).

The procedures described above may be easily transferred to the thorax. Here as well, instillation of diluted USCM via the drain is

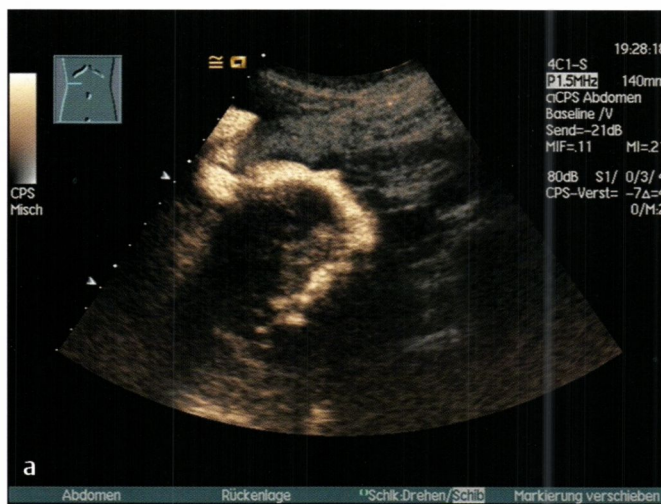


Fig. 6 a A Patient presenting with recurrent subhepatic abscess of unknown genesis. Once more, a drainage was inserted, but now, by applying CEUS-agent via the drain, communication with the retroperitoneal and perirenal space is demonstrated. **b** After applying even more volume of saline solution with CEUS-agent (meaning increased pressure to spread out), contrast medium can be detected also in the renal pelvis unto the calices. An ongoing history of nephrolithiasis had preformed this fistula.



Abb. 6 a Patientin mit Rezidiv eines subhepatisch gelegenen Abszesses, dessen Genese bisher ungeklärt war. Nach erneuter Drainageanlage und erstmaliger Gabe von Kontrastmittel zeigt sich eine Kontraststraße nach dorsal ins Retroperitoneum in den perirenal Raum. **b** Nach Instillation des Kontrastmittels mit erhöhtem Volumen und damit erhöhtem Verteilungsdruck erkennt man einen Kontrastübertritt bis ins Nierenbecken. Das gesamte Nierenbecken war bis in die Kelche darstellbar. Bei langjähriger Nephrolithiasis war es zu dieser Fistelstraße gekommen.

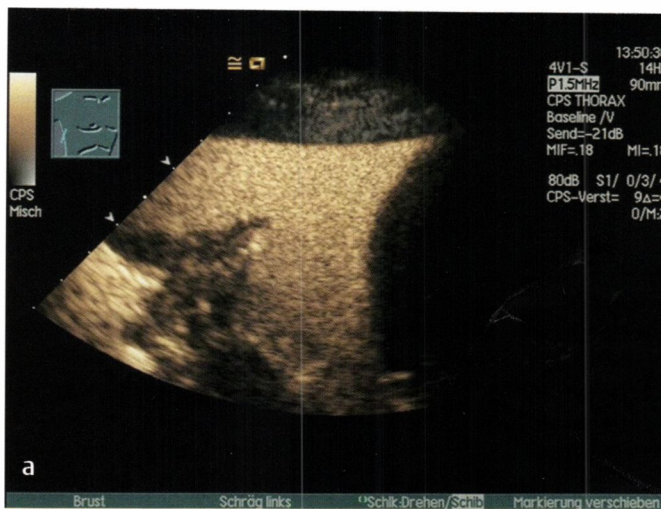


Fig. 7 a Saline solution with an admixture of CEUS-agent was applied via a pleural drainage, and the whole pleural space is contrasted. The compressed lung is surrounded with contrast medium, and no filling defects (representing septums) can be seen. Thus, effective drainage therapy can be expected. **b** When the drain turned down output, CEUS-agent was applied again. A subcutaneous depot of contrast medium is depicted, but not a single bubble in the effusion, thus proving complete dislocation.

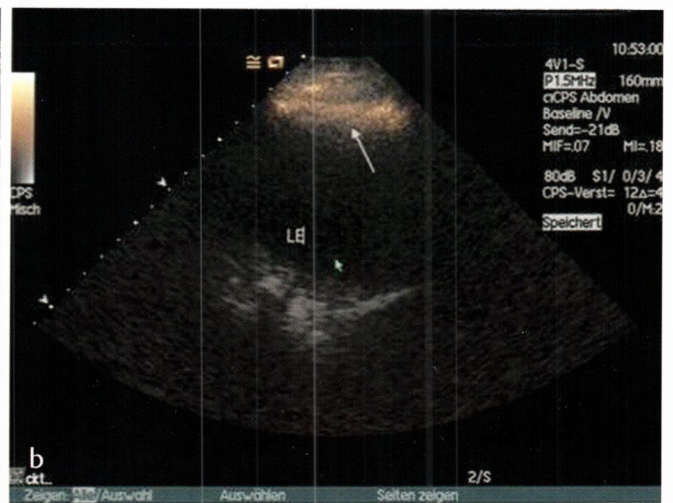


Abb. 7 a Nach Anlage einer Thoraxdrainage und Gabe von Kochsalzlösung mit Ultraschallkontrastmittel kommt der komplette Pleuraraum kontrastiert zur Darstellung. Die komprimierte Lunge erscheint vom Kontrastmittel umspült. Es sind keine Kontrastmittelaussparungen und damit Septierungen erkennbar, die erfolgreiche Drainagenbehandlung ist damit zu erwarten. **b** Eine erneute Lagekontrolle mit Kontrastmittelgabe ist erfolgt, als die Drainage kaum noch förderte. Man erkennt ein subkutan gelegenes Kontrastmitteldepot und keine Kontrastmittel-Bubbles im Erguss als Beweis der kompletten Dislokation.

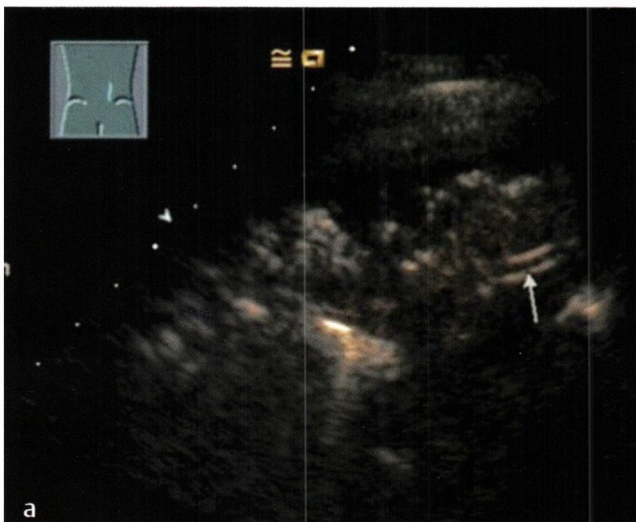


Fig. 8 a Multiple septations are seen in this patient with a parapneumonic effusion. A thoracic drain was installed (arrows). The CEUS-agent is spreading just around its tip. **b** Forced rinsing via the drain led only to a local deposit of contrast medium (arrow). We then proceeded to intrapleural lysis by Urokinase, four times.

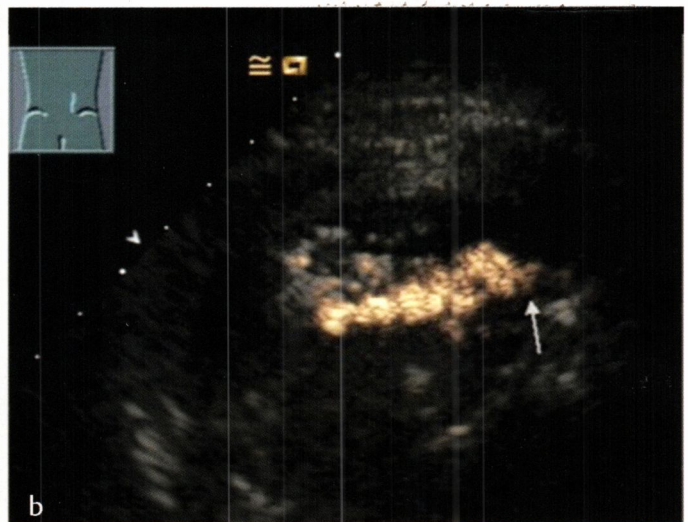


Abb. 8 a Patient mit parapneumonischem septiertem Pleuraerguss. Anlage einer Thoraxdrainage (Pfeile). Das Kontrastmittel verteilt sich nur minimal um die Drainagenspitze. **b** Auch eine forcierte Kontrastspülung führte nur zu einem lokalen Depot (Pfeil). Es erfolgte eine viermalige intrapleurale Urokinaselyse.

useful to confirm the drain's position (● Fig. 7a) as well as its misplacement, dislocation (● Fig. 7b) or insufficient draining (e.g. due to septations) (● Fig. 8a, b). The USCM is detectable in the thoracic cavity for up to 20 minutes.

Demonstration of the biliary tract by pro- and retrograde instillation of USCM

By instillation of diluted USCM via the nasobiliary tube, bubbles sensitively illustrate (in a thread-like manner) the drain's lumen – and their dispersal its tip. With ongoing instillation, the biliary tract is depicted up to its smaller branches (● Fig. 9a). In this field, nevertheless, the resolution of today's CEUS-technology is

not yet acceptable compared with techniques of current radiology. A stenosis is shown quite well, whereas more subtle alterations of the bile ducts, e.g. in primary sclerosing cholangitis, are not depicted sufficiently. Gallstones in the choledochus are seen only as an imperfect negative contrast (● Fig. 9b). They are identified more sensitively in the B-mode, possibly in combination with the twinkling artefact of the colour-mode.

By combining endocavitary and intravenous administration, new fields of application emerge. E.g., tumours of the bile duct, which have been enormously difficult to reveal, can now be illustrated precisely:

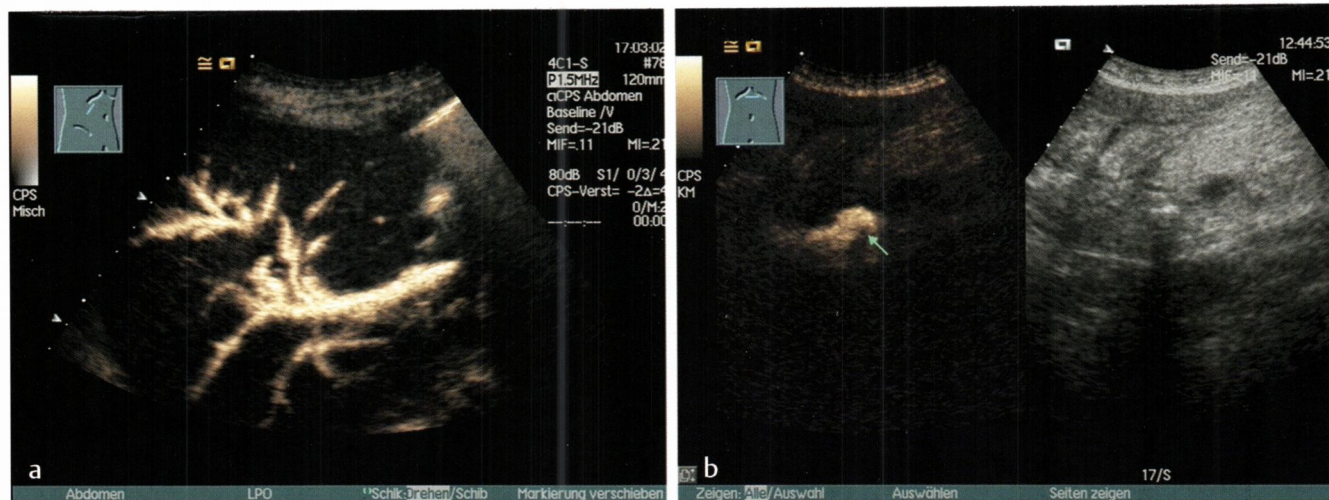


Fig. 9 **a** Patient on the ICU with suspected dislocation of a nasobiliary tube. Via bed-sided CEUS, correct positioning of the tube and the intrahepatic biliary system are shown. **b** A bile duct cholelith is demonstrated by provoking a filling defect while applying contrast medium via the tube. However, this cholelith was detected much better in the B-scan.

Abb. 9 **a** Auf der Intensivstation war der Verdacht auf eine Dislokation einer nasobiliären Sonde gestellt worden. Es zeigte sich bei der Bedside-Sonografie mit Kontrastmittel eine korrekte Sondenlage mit Darstellung der intrahepatischen Gallenwege. **b** Bei Anspritzen der nasobiliären Sonde erkennt man einen Gallengangsstein als Negativ-Kontrast (Pfeil). Dieser Stein war allerdings im B-Bild deutlich besser darstellbar.

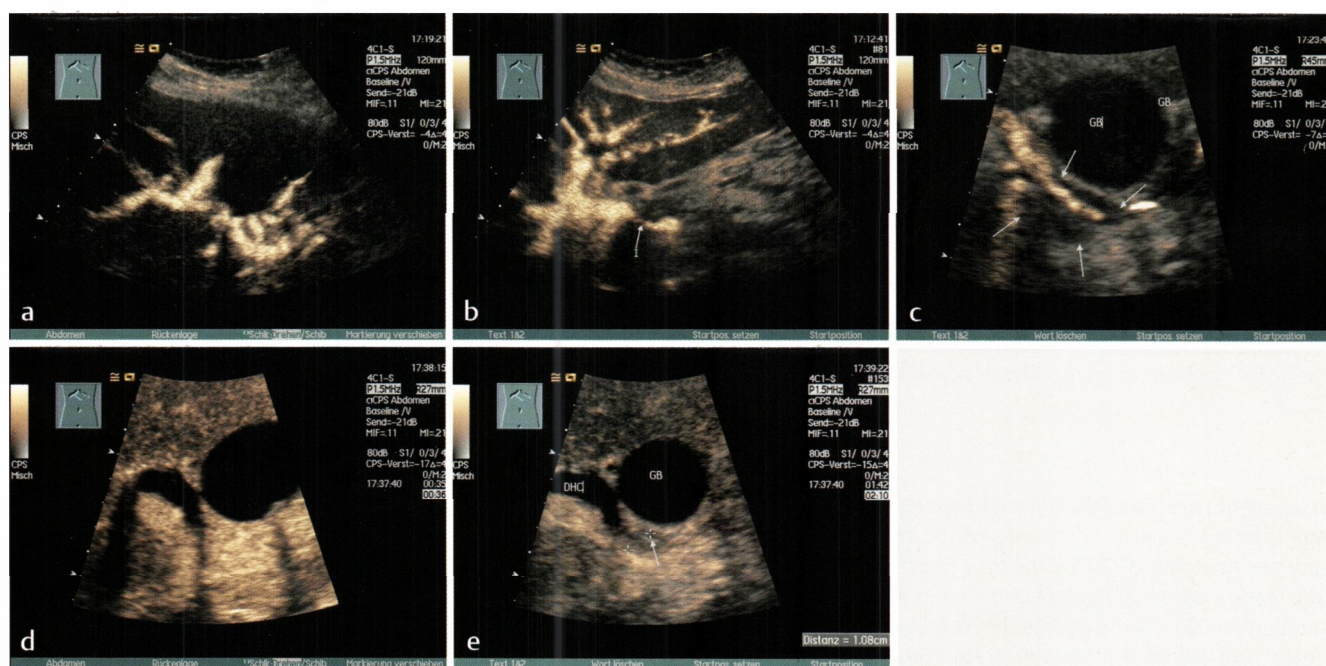


Fig. 10 **a** A Patient presenting jaundice without pains. The ERC revealed stenosis in the middle third of the common bile duct, and a nasobiliary tube was inserted. Application of CEUS-agent via the tube illustrated the widened intrahepatic system of bile ducts with all of its branches. **b** Representation of dilated intra- and extrahepatic bile ducts. The stenosis found in the ERC (in the middle third of common bile duct) is revealed highly sensitively by CEUS as well (arrow). **c** Enlarged picture of the stenosis: a tumorous mass is seen in the overlaid B-scan (arrows). **d** By administering SonoVue® i. v., the common bile duct and its stenosis are represented in inverted contrast. The tumor shows enhancement. The nasobiliary tube is detectable by its echoic signal followed by acoustic shadowing (left). **e** The suspected tumor forming the stenosis shows wash-out in the „late phase“, hence a malignancy is most probable. A carcinoma of the common bile duct was proven intraoperatively.

Abb. 10 **a** Patientin mit schmerzlosem Ikterus. In der ERC konnte eine Stenose im mittleren Gallengangs-Drittel erkannt werden, eine nasobiliäre Sonde wurde eingelegt. Nach Ultraschallkontrastmittelgabe über die nasobiliäre Sonde wurde das erweiterte intrahepatische Gallengangssystem bis in die peripheren Äste dargestellt. **b** Man erkennt ein intra- und extrahepatisch dilatiertes Gallenwegssystem. Die in der ERC gesehene kurzstreckige Stenose im mittleren Bereich des Gallengangs ist auch im Kontrast-Ultraschallbild hochsensitiv erfassbar (Pfeil). **c** Die Stenose ist in Vergrößerung dargestellt, eine „Tumormass“ ist im überlagerten B-Bild (Mischmodus) erkennbar (Pfeile). **d** Nach Gabe von SonoVue® intravenös stellt sich der DHC samt Stenose als Negativkontrast dar. Die „Tumormass“ nimmt das Kontrastmittel auf. Die nasobiliäre Sonde ist links im Bild als hochamplitudiger Reflex mit Schallschatten erkennbar. **e** Der tumorverdächtige Bezirk um die Stenose zeigt ein Auswaschen des Kontrastmittels in der „Spätphase“, damit ist ein Tumor hochwahrscheinlich. Operativ wurde das Gallengangskarzinom bewiesen.

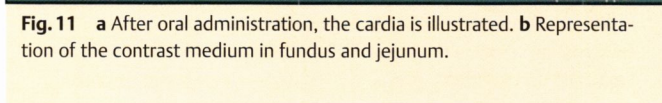


Fig. 11 **a** After oral administration, the cardia is illustrated. **b** Representation of the contrast medium in fundus and jejunum.

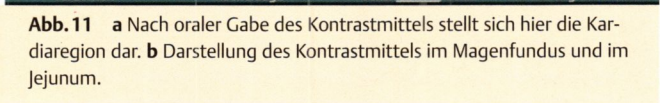


Abb. 11 **a** Nach oraler Gabe des Kontrastmittels stellt sich hier die Kardiaregion dar. **b** Darstellung des Kontrastmittels im Magenfundus und im Jejunum.

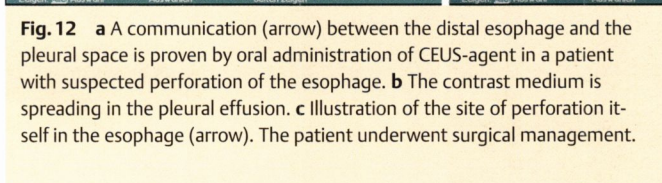


Fig. 12 **a** A communication (arrow) between the distal esophage and the pleural space is proven by oral administration of CEUS-agent in a patient with suspected perforation of the esophage. **b** The contrast medium is spreading in the pleural effusion. **c** Illustration of the site of perforation itself in the esophage (arrow). The patient underwent surgical management.

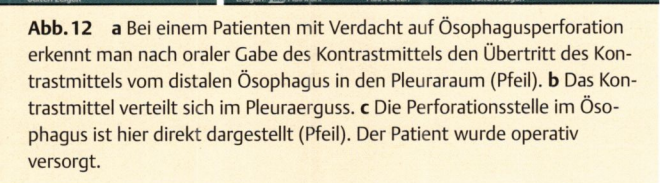


Abb. 12. **a** Bei einem Patienten mit Verdacht auf Ösophagusperforation erkennt man nach oraler Gabe des Kontrastmittels den Übertritt des Kontrastmittels vom distalen Ösophagus in den Pleuraraum (Pfeil). **b** Das Kontrastmittel verteilt sich im Pleuraerguss. **c** Die Perforationsstelle im Ösophagus ist hier direkt dargestellt (Pfeil). Der Patient wurde operativ versorgt.

Oral administration

We administered diluted Sonovue® orally as well. Swallowed, it can be easily detected on several predefined points as the proximal and distal oesophagus (○ Fig. 11a), the stomach (○ Fig. 11b) and the duodenum. Visualization of the overall length of the small intestine is hardly possible.

In the given example, we depicted a perforation of the distal oesophagus by an ulcer in a patient suffering from reflux oesophagitis (● **Fig. 12a–c**). Crossing of the USCM from the oesophagus towards the pleural space is demonstrated after oral administration.

Conclusions

The application of ultrasound contrast agents via drainage catheters provides substantial information on the location and dimensions of drained fluid collections and their communication with surrounding organ structures. The biliary system can be visualized pro- and retrogradely. Oral administration is feasible and provides important additional information.

Table 1 Fields of application

Approved indications	- Application via abdominal or thoracic drains – position and localization of the drain – dimensions of the drained fluid collection – insufficient draining (e.g. due to septations) – fistulae to the biliary tract – fistulae to the blood vessels – fistulae to the intestine – fistulae into other organs - Demonstration of the biliary tract by pro- and retrograde instillation of USCM – position of the tube - Administration via a catheter of the bladder – detecting reflux, sacculated bladder - Reliable inspection of the position of gastric, duodenal or jejunal tubes as well as PEG/PEJ to avoid unnecessary ionizing radiation, particularly in children.
Possible indications	- Administration via a catheter of the bladder – detecting malignant infiltration - Oral administration – anastomotic insufficiencies of the digestive tract – spontaneous perforations of the digestive tract
Questionable indications	- Demonstration of the biliary tract by pro- and retrograde instillation of USCM – to depict the biliary tract unto its smaller branches – to reveal a stenosis – to detect gallstones in the common bile duct - Oral administration – Identification of space-occupying gastric lesions such as polyps, tumours or gastric balloons – stenosis of the gastric outlet tract - Administration during a colonoscopy for the depiction of diverticula or stenosis by a tumour

Anmerkung



1. Preis auf dem 3-Ländertreffen in Mainz 2010 für Inhalt, wissenschaftlichen Nutzen, Aktualität sowie Qualität der Präsentation.

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Prenatal Ultrasound Diagnosis of a Multiple Atypical Right Atrial Cardiac Fibroma

Pränatale sonografische Diagnose eines multiplen atypischen rechts-atrialen Fibroms

Introduction

Congenital cardiac tumors are very rare with an incidence at birth of approximately 0.0017–0.28% (Holly DG et al. *J Am Coll Cardiol* 1995; 26: 516–520). The majority of cardiac tumors in children are benign, with only approximately 10% being malignant. The manifestations of a cardiac tumor in fetal life include congestive heart failure, arrhythmias, hydrops and sudden death (Allan L. In *Textbook of Fetal Cardiology*: Greenwich Medical Media, London, 2000; 358–365; Atallah J et al. *Pediatr Cardiol* 2006; 27: 493–496).

We report a case with an atypical form of cardiac fibroma located in the right atrium. To the best of our knowledge a cardiac fibroma located in the right atrium has not previously been reported in the literature. The prenatal diagnosis was made at 36 weeks of gestation.

Case report

A 34-year-old woman, gravida 2, para 1, was referred for obstetric care at Hvidovre Hospital because of a previous preterm birth (33+2 weeks of gestation) and subsequent medically treated postnatal depression (Citalopram 20 mg×1). This treatment was stopped during the first trimester of the current pregnancy. This pregnancy was further complicated by group B streptococcal cystitis, treated with oral penicillin, and diet-controlled gestational diabetes, diagnosed at 34+5 weeks of gestation.

During the current pregnancy, ultrasound examinations at 13+5 and 22+0 weeks of gestation were interpreted as normal. Because of the previous preterm birth, the patient was followed with ultrasound examinations for growth and cervical length until 36 weeks of gestation. These were unremarkable.

At 36+0 weeks of gestation, an ultrasonographer found that the fetus had marked ascites and scrotal edema and the patient was referred for further investigations. A semi-urgent fetal echo

was performed and showed a hyper-echogenic tumor (15×17×20 mm) in the right atrium, almost fully obstructing the tricuspid valve (● Fig. 1). The fetal heart was otherwise normal. Doppler flow studies revealed a large negative A-wave from the ductus venosus (PIV 2.70) as a sign of compromised flow. A normal profile was revealed from the umbilical artery. Furthermore fetal bradycardia with a fetal heart rate of 105 bpm at spectral Doppler was observed.

Because of the compromised flow and an expected need for postpartum cardiac surgery, the woman was transferred to Rigshospitalet for a subacute caesarean section. A male infant, birth weight 3575 g, with an Apgar score of 9/1, 10/5, was delivered.

Neonatal echocardiography showed an 18×20 mm tumor in the right atrium almost fully obstructing the tricuspid ostium, indicating the need for surgical removal. ECG showed bradycardia and second degree AV block. The infant was

operated on two days after delivery. At operation the tumor was found to originate in the interatrial septum (● Fig. 2). Two further small tumors were found in the right atrium. They were completely excised. Because the extensive involvement of the interatrial septum, radical excision of the largest tumor was not possible without a major risk of subsequent permanent third degree AV block. Histopathological findings were consistent with a cardiac fibroma (● Fig. 3).

At 1½ months of age, the infant was hospitalized with an upper respiratory tract infection. At this time his ECG showed progression to intermittent third degree AV block and an epicardial pacemaker in VVI¹ mode with a lower limit of 100 bpm was inserted.

Discussion

According to the literature, the incidence of primary cardiac tumors is very low and prenatal diagnosis is rare. Most cardiac tumors tend to appear between 20 and 30 weeks of gestation, although some, if small in size or intramurally located, will not be detected prenatally (Allan L. In *Textbook of Fetal Cardiology*: Greenwich Medical Media, London, 2000; 358–365; Zhou QC et al. *Ultrasound Obstet Gynecol* 2004; 23: 165–171).

Early diagnosis of fetal and neonatal tumors is important for allowing early intervention and improving fetal outcome,



Fig. 1 Cardiac fibroma in right atrium.

Abb. 1 Kardiales Fibrom im rechten Vorhof.



Fig. 2 Tumor excised from right atrium.

Abb. 2 Der Tumor nach Entfernung aus dem rechten Vorhof.

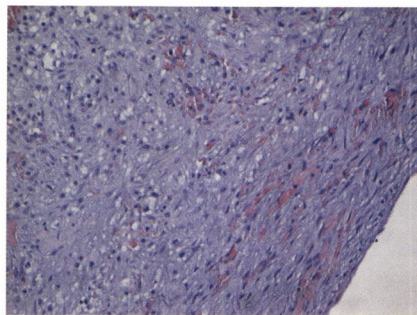


Fig. 3 A view of the architecture in the cardiac fibroma. Note the bundles of spindle cells replacing the normal myocardium.

Abb. 3 Darstellung der Zellarchitektur des kardialen Fibroms. Man beachte die in Bündeln gelagerten Spindelzellen, die das normale Myokard verdrängen.

as these tumors can cause hemodynamic compromise and heart block in fetal life which can lead to fetal hydrops and sudden death (Muñoz H et al. *J Ultrasound Med* 1995; 14: 479–481). Possible neonatal manifestations include cardiomegaly, cardiac murmurs, arrhythmias, congestive heart failure, cyanosis and sudden death (Holly DG et al. *J Am Coll Cardiol* 1995; 26: 516–520; Allan L. In *Textbook of Fetal Cardiology*: Greenwich Medical Media, London, 2000; 358–3659; Isaacs Jr H. *Pediatr Cardiol* 2004; 25: 252–273).

Rhabdomyomas are the commonest cardiac tumor (60%) in children followed by cardiac fibromas and teratomas (12–15%) (Allan L. In *Textbook of Fetal Cardiology*: Greenwich Medical Media, London, 2000; 358–365; Uzun O et al. *Orphanet J Rare Dis* 2007; 2: 11; Zhou QC et al. *Ultrasound Obstet Gynecol* 2004; 23: 165–171). Prenatal diagnosis depends on the appearance, size, number and location of the tumor(s) (Zhou QC et al. *Ultrasound Obstet Gynecol* 2004; 23:

165–171; Geipel A et al. *Ultrasound Obstet Gynecol* 2001; 17: 17–21). Rhabdomyomas are often nodular and multiple, located in the ventricles, septum or atrial wall. Sonographically they have a homogeneous echogenicity.

About 50% of cardiac rhabdomyomas are associated with tuberous sclerosis and cardiac rhabdomyomata observed in utero are the most striking feature of tuberous sclerosis (Zhou QC et al. *Ultrasound Obstet Gynecol* 2004; 23: 165–171; Geipel A et al. *Ultrasound Obstet Gynecol* 2001; 17: 17–21). These tumors may regress spontaneously (Muñoz H et al. *J Ultrasound Med* 1995; 14: 479–481). Cardiac fibromas are connective tissue tumors and are most often solitary with their origin in the interventricular septum or ventricular wall. Other locations are rare (Allan L. In *Textbook of Fetal Cardiology*: Greenwich Medical Media, London, 2000; 358–3659; Isaacs Jr H. *Pediatr Cardiol* 2004; 25: 252–273). Fibromas have a tendency to grow (Muñoz H et al. *J Ultrasound Med* 1995; 14: 479–481). So-

nographically cardiac fibromas have a complex echogenicity, sometimes with a cystic appearance or central calcification. Teratomas are generally of variable size located in the right ventricle, right atrium or more unusually, in the pericardium. Sonographically they have a heterogeneous appearance with lobulated, solid and cystic components (Zhou QC et al. *Ultrasound Obstet Gynecol* 2004; 23: 165–171; Allan L. In *Textbook of Fetal Cardiology*: Greenwich Medical Media, London, 2000; 358–3659; Isaacs Jr H. *Pediatr Cardiol* 2004; 25: 252–273).

In the case presented the ultrasound findings were consistent with a rhabdomyoma, due to the homogeneous echogenicity and the location of the tumor. Surprisingly, considering the atrial location and the multiple tumors, the histological findings were consistent with a cardiac fibroma. To the best of our knowledge this is the first report of multiple cardiac fibromas with origin in the right atrial side of the interatrial septum. Cardiac fibromas rarely regress postnatally and surgical excision is most often required. Unfortunately cardiac fibromas are often infiltrative and may only be partially excisable. Due to their infiltrative nature, they can cause severe arrhythmias, some of which can be treated with pacemakers (Holly DG et al. *J Am Coll Cardiol* 1995; 26: 516–520; Allan L. In *Textbook of Fetal Cardiology*: Greenwich Medical Media, London, 2000; 358–3659; Isaacs Jr H. *Pediatr Cardiol* 2004; 25: 252–273). The overall survival rate for cardiac fibromas is low, compared to that of other cardiac tumors (Isaacs Jr H. *Pediatr Cardiol* 2004; 25: 252–273).

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Role of Low-Mechanical Index CEUS in the Differentiation between Low and High Grade Bladder Carcinoma: a Pilot Study

We read with great interest the article by Drudi et al. about the role of contrast-enhanced ultrasound (CEUS) in the differentiation between low and high grade bladder carcinoma, recently published in *Ultraschall in der Medizin* [1]. The authors reported that the sensitivity and specificity of CEUS were 90.9% and 85.7%, respectively. And the sensitivity and specificity of CEUS using Time-intensity curves (TICs) enabled was 95.4% and 85.7%. And our data agree with such a result (unpublished data).

In the study by Drudi et al. a slowly declining curve (shape B) indicating low-grade carcinoma and a rapidly declining curve (shape C) indicating high-grade carcinoma. We recently examined ninety-six patients with ninety-six bladder lesions, including 55 high grade urothelial carcinoma and 41 low grade urothelial carcinoma by CEUS. QLAB quantification software (Philips medical system, Bothell, WA, USA) were used. The arrival time (AT), peak intensity (PI), time to peak intensity (TTP) and washout time

(WT) with the tumors were extracted by the off-line software. Our result are shown in **Table 1**. There were no significant differences in the AT, TTP between high and low grade bladder tumors ($P > 0.05$). The PI of high grade tumors are greater than that of low grade tumors, which is consistent with Drudi et al's results, but the WT of low grade tumors were less than that of high grade tumors ($P < 0.05$), which is completely different from their results. Our study found that 93% (51/55) of high grade bladder tumors showed fast wash-in and slow wash-out enhancement patterns (**Fig. 1**) and 85% (35/41) of low grade bladder lesions showed fast wash-in and fast wash-out enhancement patterns (**Fig. 2**).

Several differences between Drudi et al's study and ours should be addressed. Firstly, Drudi et al's sonographic examination was performed on Technos Mpx, Mylab 70 V_x Gold (Esaote, Genova, Italy), and Toshiba Apliova (Osaka, Japan) using a 2-MHz multi-frequency broadband

convex transducer. In our study, both US and CEUS were performed with Philips IU22 (Philips royal electronic corporation, Holland) system with a 1.0–6.0 MHz probe, the contrast-specific sonographic imaging modes were PI (pulse inversion) and PM (power modulation) at a mechanical index of 0.05. Secondly, the dose of Sonovue in the two studies is differently. Drudi et al's study dose was 2.4 ml, and ours was 1.2 ml, the dose we use was based on our research team's clinical experience, we found that when a bolus of 2.4 ml contrast agent was injected, the perfusion of both high and low grade bladder lesions are saturated, and there is no significant difference on PI (peak intensity) between the two kind of tumors. Thirdly, 36 Italian patients in Drudi et al's study were recruited, and 96 Chinese patients were included in our study. It is generally accepted that bladder urothelial carcinoma incidence is affected by environment factors such as the habits of the nation. In conclusion, we agree with Drudi et al. that CEUS is a reliable noninvasive method for differentiating low and high grade bladder carcinomas. However, to the best of our knowledge, that paper was the first regarding the use of CEUS for bladder cancer characterization. As only limited data are available, it might be inappropriate that we applies these enhancement patterns to the worldwide

TIC parameters	HG	LG	P Value
AT (s)	21.13 ± 1.76	22.44 ± 1.34	0.374
PI (dB)	20.85 ± 12.31	14.87 ± 9.24	0.005
TTP (s)	30.32 ± 2.41	28.06 ± 2.23	0.386
WT (s)	35.37 ± 9.34	21.17 ± 8.37	0.002

Table 1 Contrast parameters of high and low grade urothelial carcinoma (mean ± SD). (AT = arrival time; TTP = time to peak; PI = peak intensity; WT = washout time).

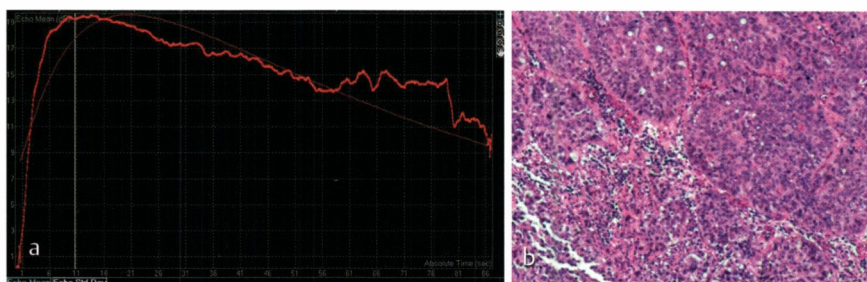


Fig. 1 a 58-year-old man with high grade bladder tumor. Time-intensity curve shows fast wash-in and slow wash-out, and higher PI (peak intensity). b Surgical specimen confirming high grade bladder tumor (hematoxylineosin original magnification × 40).

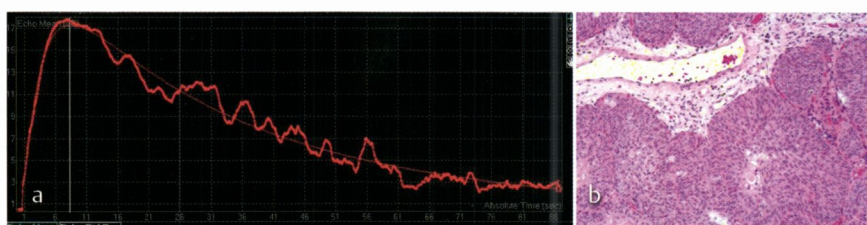


Fig. 2 a 60-year-old woman with low grade bladder tumor. Time-intensity curve shows fast wash-in and fast wash-out, and lower PI (peak intensity). b Surgical specimen confirming low grade bladder tumor (hematoxylineosin original magnification × 40).

population, which has different incidence of bladder carcinoma because of racial, biological, and clinical differences. In our opinion, Further studies involving larger patient populations from different places to confirm these preliminary results is expected.

Reference

- 1 Drudi FM, Cantisani V, Liberatore M et al. Role of low-mechanical index CEUS in the differentiation between low and high grade bladder carcinoma: a pilot study. *Ultraschall in Med* 2010; 31: 589–595

Bibliografie

DOI 10.1055/s-0031-1281690

Ultraschall in Med 2011; 32: 87–89

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ISSN 0939-2661

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Reply

We have with great interest read the letter to the editor published recently in *Ultraschall in der Medizin* (reference) in which the Authors compared our data published in the article "Role of low-mechanical index CEUS in the differentiation between low and high grade bladder cancer: a pilot study" (reference) with their own data.

This comparison shows that we agree on the levels of sensitivity and specificity of CEUS in relation to this application (90.9% and 85.7%, respectively). We also agree that the use of time-intensity curves (TICs) further improves sensitivity, leaving unchanged the specificity of the method (95.4% and 85.7%, respectively). The Authors took the following parameters into account: arrival time (AT), peak intensity (PI), time to peak (TTP) and washout time (WT). In our study, AT was not explicitly expressed but this value was obtained from the TICs (● Fig. 1 and ● Fig. 2), while the other data were expressed; what the Authors denominated peak intensity (PI) was called signal intensity (SI) in our paper and it was expressed as a percentage while "Authors" reported this value in dB. ● Table 1 shows a comparison between the Authors' and our data.

We reported a shorter AT than the Authors (13 seconds versus 21.13 seconds

in high-grade tumors and 13 seconds versus 22.44 seconds in low-grade tumors) but we agree that there is no statistically significant difference between high-and low-grade tumors. Unlike us, the Authors believe that there is also no significant difference related to TTP. This difference is probably due to the fact that the Authors used mean values (30.32 seconds in high-grade tumors and 28.06 in low-grade tumors), whereas our study relied on two ranges of values (>28 seconds in high-grade tumors and <26 seconds in low-grade tumors). This means that a difference of about 2 seconds is not significant in the Authors' study, whereas the same difference acquires a greater statistical significance in our study as it separates two larger groups of values. Despite the different units of measurement used in the two studies (% versus dB), PI/SI is in both cases greater in high-grade tumors. The Authors also reported a disagreement between theirs and our data related to WT, asserting that low-grade tumors show an earlier WT than high-grade tumors. We agree with this comment as evidenced by the data we reported in the legends related to ● Fig. 1, 2 of our article (58 seconds in high-grade tumors and 40 seconds in low-grade tumors). We also noted that the Authors' WT va-

lues were significantly lower than ours (35.37 seconds versus 58 seconds in high-grade tumors and 21.17 seconds versus 40 seconds in low-grade tumors). We believe that this difference may be caused by different methods for measuring time. All our time measurements start from "time 0", i.e. when US contrast agent was injected, but we believe that the Authors' WT value measurements started from a different moment (probably TTP). We arrived at this conclusion as they reported WT of low-grade cancer as 21.17 seconds and therefore apparently earlier than AT, which was 22.44 seconds. This discrepancy between the data can in our opinion only be explained by the use of two different starting points in the measurement of time.

In order to avoid subsequent misunderstandings, we would like to emphasize that all our time measurements started from "time 0" corresponding to the time of injection of US contrast agent, and in our study AT is the length of time preceding the moment in which the time-intensity curve starts rising from the bottom of the chart recording a signal intensity different from 0; PI is the maximum signal intensity reached; TTP is the time elapsed before reaching the peak of the time-intensity curve; WT is the length of time that precedes the moment in which the time-intensity curve signal returns to 0 or a value close to 0.

The most significant differences between the two studies with regard to

	High-Grade		Low-Grade	
AT	13 sec.	21.13 sec	13 sec	22.44 sec
SI or PI	>50%	20.85 dB	<45%	14.87 dB
TTP	>28 sec	30.32 sec	<26 sec	28.06 sec
WT	58 sec	35.37 sec	40 sec	21.17 sec
	Drudi et al.	Authors	Drudi et al.	Authors

Table 1

"Materials and Methods" relate to the equipment, mechanical index, doses of contrast agent and number of patients recruited as well as the different environmental factors to which the patients were exposed because of geographical differences.

Our US study was performed using Technos MPx, MyLab 70VxGold (Esaote, Genoa, Italy), Toshiba Apliova (Osaka, Japan) and multi-frequency convex probes of 2–5 MHz, while the Authors used Philips IU22 (Philips Royal Electronic Corporation, Holland) and a 1.0–6.0 MHz probe.

We furthermore used a mechanical index varying between 0.04 and 0.1, and

we administered 2.4 ml of contrast agent to each patient, while the Authors used a mechanical index of 0.05 and administered 1.2 ml of contrast agent to each patient. Our patient population was smaller than the population studied by the Authors (36 versus 96) and this difference may have affected the statistical significance of some data.

It should also be kept in mind that our quantitative software Qontrast (Bracco, Milan, Italy) requires manual demarcation of the region of interest (ROI); this can lead to possible discrepancies and may be another possible source of statistical differences. In this connection it should be pointed out that we marked

the ROI as the entire area of the lesion including the bladder wall from which it originated.

In conclusion, we believe that the Authors' data and our data are more consistent than stated in the Authors' letter to the editor and we would like to emphasize that CEUS is a useful non-invasive method for differentiating high- and low-grade bladder tumors, although further studies of larger patient populations will be required to confirm the preliminary data emerging from our studies.

Book Review

Contrast-enhanced ultrasound

Weskott HP (Ed.)

Uni-Med Science Verlag Bremen, 1st edition 2011, 200 pp., 230 illustrations, € 39.80, ISBN 978-3-8374-1221-5 (Germany)/ ISBN 978-1-84815-158-1 (rest of the world)

H. P. Weskott published this monograph concerning contrast-enhanced ultrasound (CEUS) together with 18 co-authors. This compact book is based on many years of B-scan and CEUS experience as well as scientific work, workshops and Euroson School meetings. Weskott, who made substantial contributions to the development of CEUS, is responsible for nearly half of the contents, and he was able to almost exclusively recruit renowned colleagues in their areas of specialization for the other half of the manuscripts. P. N. Burns who explains "how ultrasound systems talk to bubbles" should be named as a representative. This small, handy, and well-illustrated book is divided into 8 chapters, with the chapters on the basics and the liver comprising about 50% of the contents.

The clearly arranged structure ensures a high degree of readability. The book includes important tips for the clinical routine as well as precise diagrams and a wide selection of

important and up-to-date references. Among the remaining chapters on the gallbladder, pancreas, spleen, kidney and vessels, the sections concerning the spleen and aorta stand out.

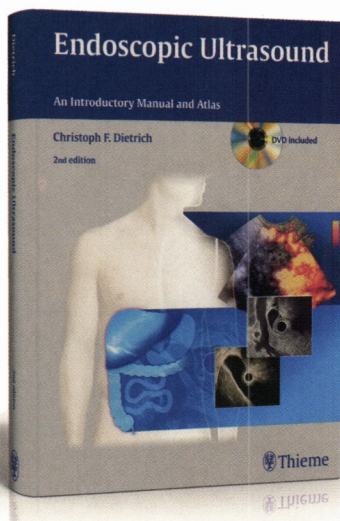
There is little to criticize, i.e., the format necessitates small figures and the contrast of the figures, especially the B-scan images, is slightly low, which may be due to the quality of the paper. I personally only noticed the lack of a diagram about the types of endoleaks in EVAR. Beginners may wish for a CD with video clips because CEUS requires significant training.

This small CEUS monograph contains an impressive amount of CEUS knowledge and due to its excellent price performance ratio, it will hopefully be widely used within the CEUS community. In my opinion, this book is a "must have" for both beginners and advanced US users.

K. Seitz

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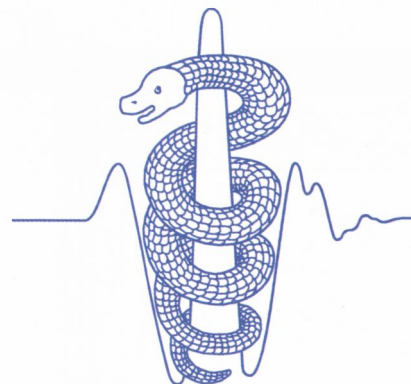
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EFSUMB Newsletter

European Federation of Societies for Ultrasound in Medicine and Biology



EFSUMB Presidential Programme 2012

The Executive Bureau was partially changed, following the election by the Board of Directors during the EUROSON meeting in Vienna in August 2011 and is now made up, for the term 2011–2013, by Dr. Fabio Piscaglia (President), Prof. Christoph F Dietrich (President Elect), Dr. Christian Nolsoe (Past President), Prof. Odd Helge Gilja (Honorary Secretary) and Prof. Diana Gaitini (Honorary Treasurer). The Executive Bureau intends to continue ongoing activities set up by the ExB of the previous term (2009–2011) and also implement new original programs.

A priority of the previous term was to promote Educational Activities. This will remain a priority also for the next term and will be centered on the following activities, developed in conjunction with the EFSUMB Education and Professional Standard Committee (EPSC), chaired by Ass. Prof. Dr J. Tuma.

1. Expansion of the content of the Educational webportal, freely accessible via the EFSUMB website (www.efsumb.org). This portal contains the "case of the month" series, a useful and intriguing education modality, currently coordinated by Dr. P.S. Sidhu, well suited to keep ultrasound operators freshly updated in different fields with usual and unusual imaging patterns. Since the beginning this section has remained among the most visited of EFSUMB web pages. All EFSUMB members are warmly invited to submit their interesting and well documented cases. We would like to take the occasion to remind you that these cases are presented in English as well as translated into other languages.
2. Completion of the EFSUMB Course Book, coordinated by Prof. C.F. Dietrich, whose first chapters are already available online. The chapters making the core of an ultrasound examination will also be printed in a regular book form in 2012 (copies could be ordered online or purchased through booksellers or at EFSUMB Congresses).
3. Postgraduate residential courses in the forms of international Euroson Schools, run on different topics, including Contrast Enhanced Ultrasound, Ultrasound in Gastroenterology and Hepatology, Interventional Ultrasound and others, which are listed in the EFSUMB webpage. From 2012 there will be also the opportunity to attend on a national level EFSUMB endorsed courses, also listed on the portal.
4. Creation of an online video course on CEUS applications derived from recorded lectures of international experts. This goes in line with the program to strengthen the role of e-learning, possibly also with formal recognition, which, in time of economical restrictions and concurrent extension of technology capabilities, might become of greater importance. Prof. O.H. Gilja started to lead this approach while chairman of the Education and Professional Standard Committee and will continue to coordinate it from within the Executive Bureau.
5. For the current term, the EFSUMB Executive Bureau would like to support the use of simple ultrasound scans at bedside in clinical wards. This approach does not replace conventional ultrasound, but may complement the diagnostic capabilities of

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conventional physical examination, facilitate interventions at the bedside or answer simple clinical questions (e.g. does this patient with abdominal enlargement have ascites?). Such exams might easily extend into or be supplied by a complete ultrasound scan, in case of clinical need. If we consider the setting of emergency, a comparable modality has already been established and coded as FAST examination. A similar approach has not been defined for clinical wards in non emergency situation and EFSUMB intends to define it and set up corresponding teaching activities. Our present suggestion is to call this new concept "echoscopy".

In recent years a cooperation with other continental societies was set up and proved successful (e.g. European Society for the Study of the Liver EASL, United European Gastroenterology Federation UEGF) and interactions will be possibly adopted also with other societies. EFSUMB already endorsed and will promote a course on Liver Imaging for young hepatologists, economically fully supported by EASL (Clinical School in Hepatology), whose application forms are reachable from the EFSUMB website.

EFSUMB is a Federation of Societies and not a Society itself. This, together with different knowledge in English language, may contribute to make the contacts of EFSUMB with its members not as strict as desired. Attempts will be made to make closer the possible contact between EFSUMB and its members and among all members by the use of the modern social networks.

In the last decade many substantial innovations became routinely available in the daily practice of ultrasonography. However, its use, despite technically available to any ultrasound user, might generate errors when utilized without a sufficiently technical background. EFSUMB recognized this risk and the need to support all ultrasound users with recommendations. For this reason guidelines and recommendations on the use of Contrast Enhanced Ultrasound were first released in 2004 and subsequently regularly updated. The plan of the ExB is to regularly update these recommendations, and new releases will appear divided into liver and non-liver applications, in *Ultraschall in der Medizin*/European Journal of Ultrasound

during 2012 (the non-liver ones already available online). Plans are to spread as much as possible the knowledge of these new guidelines among European US operators, which should also theoretically imply a more homogeneous terminology in writing reports.

Considering new US applications plans of the ExB are to prepare documents, at least on quantification of contrast enhancement, elastography and strain imaging techniques, where recommendations appeared more warranted. The resulting documents will be finalized within 2012 and then submitted for publication. EFSUMB intends, in fact, to identify and drive innovations on a continental level.

Online atlases illustrating the guidelines will also be set up in the future in the Educational EFSUMB web portal, starting from the CEUS guidelines in 2012.

A project will start to prepare documents on how an optimal report has to be written in different fields of applications. The first one to be released will be on how to investigate and make reports for patients with a suspicion of portal hypertension.

All these and other activities included in the program of the ExB for the next two years, aside from regular activities, including the annual EFSUMB congress, are hoped to increase the awareness about the benefits of being or becoming an EFSUMB member. Moreover, we hope that these initiatives will continue to enhance the level of ultrasound education and underline the importance of ultrasound in the European medical community.

EFSUMB Executive Bureau

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Rudd

Summary of EFSUMB Reports to the Board of Directors at WFUMB 2011, Vienna, Austria

EFSUMB has a membership of 19595 members from 30 different countries and 2011 has been an active year for us under the helm of Christian Nolsøe's Presidency. EFSUMB's Past Hon Treasurer Ioan Sporea guarded the finances through these uncertain economic times and his financial report indicates that EFSUMB is in a stable financial position to maintain our programme of support of education, safety and publication projects if we continue to balance our budget with our income. Your continued support as EFSUMB members is vital to these projects and we need your support.

Our website www.efsumb.org is a good place to start for anyone unfamiliar with the changes afoot in EFSUMB. The statistics of the website viewing have been increasing dramatically and not just from our member countries but worldwide. The European Course Book has attracted a lot of this interest. There are currently 20 chapters online which can be accessed and downloaded by anyone. These, and other chapters, will be published in spring 2012 for sale at EUROSON 2012, Madrid, Spain and large scientific meetings in Europe. The book will be non profit making and available for purchase at a reasonable price via our website. This book in its entirety will be found on the EFSUMB Educational Portal which has recently been launched on our website. The intention is

to offer educational material to anyone with access to the internet. The successful Case of the Month, Guidelines, Recommendations, teaching videos, EUROSON School presentations, and more, can all be found here.

The EFSUMB Guidelines and Recommendations on the Clinical Practice of Contrast Enhanced Ultrasound (CEUS) Update 2011 on non-hepatic applications has been published in August 2011 and will be of great value to practitioners of CEUS. The joint WFUMB and EFSUMB CEUS Guidelines on liver should be published this year in *Ultraschall in der Medizin/European Journal of Ultrasound*. The 2010 impact factor of the EJU is 3.260, a significant increase. The EFSUMB Newsletter is published in each issue with interviews with member society Presidents, interesting cases and information about EFSUMB Congresses. Last year's Congress was held in August, shared with WFUMB and the Dreiländertreffen Societies and hosted by OGUM, the Austrian Society. We had world class lectures, refresher courses, practical sessions, workshops and a Pioneers' Session which brought together the historic names in Ultrasound in a session that will live on in all our memories.

Education is at the heart of EFSUMB's activities given the rapid changes in knowledge and practice of ultrasonography.

The Education Committee (EPSC) promotes education at an international high level in English through EUROSON Schools, holding a record number of nine schools last year. Highly instructive video presentations of some of these Schools can be found on our website. In 2012 EFSUMB will be endorsing ultrasound courses in Europe that are held in the national language that are of a sufficiently high teaching standard. To sustain high professional standards in ultrasound scanning, the EPSC has worked to complete guidelines in-progress and stimulate new guidelines to be produced. The minimum training recommendations on CEUS (14) was published in 2010 and the latest add-on is a supplement to Musculoskeletal (12) on training level requirements for rheumatologists.

The Safety Committee (ECMUS) review safety related articles and existing safety statements are reviewed annually and revised as necessary. Tutorial articles designed to be teaching articles aimed at the clinical user without a background in physics can also be found on our website. Safety demonstrations and lectures are held at our annual Congress and WFUMB 2011 was no exception.

The Publications Committee continues to produce the Case of the Month which is now translated into Portuguese, Spanish, Italian, French, Arabic and Greek and available online. Our website viewing statistics encourages EFSUMB's belief that the information provided is used and useful, that we are attracting new members, both individual and National Societies which all contributes to building the European ultrasound community.

Abstract

Therapeutic Bubbles'

The Young Investigator Winner, WFUMB 2011,

Klazina Kooiman

Klazina Kooiman¹ Miranda Foppen-Harteveld¹, Antonius F.W. van der Steen^{1,2}, and Nico de Jong^{1,2,3}

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Purpose

Molecular imaging using ultrasound used targeted ultrasound contrast agents that consist of encapsulated gas microbubbles. Until now, targeted microbubbles have only been used for imaging, not for therapy. In this study we investigated whether they could also be used to induce sonoporation, resulting in a transient increase in cell membrane permeability so that therapeutics can enter the cell.

Methods and materials

CD31-targeted microbubbles were made and allowed to adhere to human umbilical vein endothelial cells. Microbubble-cell behavior upon insonification at 1 MHz (10 cycle sine-wave bursts) was studied with the Branda 128 high-speed camera (frame rate ~ 13 MHz). Microbubble diameter (D) – time curves were extracted from the recordings and the relative vibration amplitude, $D_{\max} - D_{\min}$ normalized to the resting diameter D_0 , was calculated. Propidium iodide (PI; 25 µg/ml) was used as indicator for sonoporation.

Results

Thirty-one cells were studied that all had one microbubble attached per cell. After insonification at 80 kPa (MI 0.08), 30% of the cells had taken up PI, while this was 20% at 120 kPa (MI 0.12), and 83% at 200 kPa (MI 0.20). Irrespective of the ap-

Young Investigator award

Klazina Kooiman (1977) studied Bio-Pharmaceutical Sciences at the University of Leiden, the Netherlands, from 1995–2000 and graduated cum laude. She did her main traineeship at the department of Pharmaceutical Technology of the Leiden/Amsterdam Center for Drug Research (LACDR) under supervision of Prof. dr. H.E. Junginger. Subsequently, she started to work as a PhD student at the Radboud University Nijmegen Medical Centre, the Netherlands. Due to the Epstein Barr virus she could not finish the project. From 2005–2010 she was a PhD student at the Department of Biomedical Engineering of the Erasmus MC, the Netherlands. The research was performed under the supervision of Prof. dr. ir. N. de Jong and Prof. dr. ir. A.F.W. van der Steen. Her project focused on using ultrasound contrast agents (microbubbles) as local drug delivery systems. Both the simultaneous administration of drugs and microbubbles and the incorporation of drugs into microbubbles were studied. The results were presented at national and international conferences. Two of her poster presentations were awarded with a poster prize and two of her oral presentations were awarded with the best student presentation. On January 19, 2011 she obtained her PhD on 'therapeutic bubbles'. The research described in her thesis aids in understanding how to utilise ultrasound and bubbles for therapy in the most optimal way. She currently holds a postdoc position at the Department of Biomedical Engineering focusing on targeted microbubble imaging of vasa vasorum in atherosclerosis. She participates in the European FP7 Sonodrugs project focusing on ultrasound-triggered drug delivery systems and supervises two PhD students. She is (co)author of seven peer reviewed articles and has an h-index of six. At WFUSMB 2011 in Vienna she won the EFSUMB Young Investigator award.



plied peak negative acoustic pressure, uptake of PI was observed when the relative vibration amplitude of the targeted microbubbles was larger than 0.5. No relationship was found between the position of the microbubble on the cell and induction of sonoporation.

Conclusion

This study reveals that vibrating targeted microbubbles can induce sonoporation. This feature may now be used in molecular imaging, thereby combining ultrasound imaging and therapy.



EFSUMB Endorsed Course

All (preferentially young) EFSUMB members interested in Liver Imaging might consider participating in the EFSUMB Endorsed **EASL Clinical School in Hepatology on Liver Imaging**, to be held in Bologna, Italy, 7-9 June 2012 (application deadline 28th March 2012). Nearly all the costs for those selected participants on this residential course will be supported by EASL, making it a unique occasion to apply. More information can be found using the following link on our website www.efsumb.org



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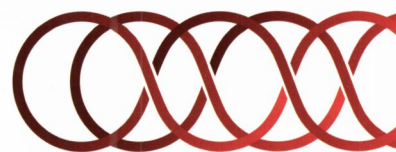
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Sonoporation: Why Microbubbles Create Pores

Ultrasound contrast agents are commonly added to the blood stream in ultrasonic imaging: contrast-enhanced ultrasound (CEUS). They consist of microscopically small bubbles (microbubbles) encapsulated by elastic shells. The most common shell materials are phospholipids. During an ultrasound cycle microbubbles oscillate, i. e., they expand and subsequently contract. Depending on their elastic properties, on the local conditions, and on the acoustic settings, they move in the direction of the sound field, coalesce with other microbubbles, fragment, jet, cluster, release their contents, and dissolve in the surrounding liquid [1]. The diverse behaviour of encapsulated microbubbles in different acoustic regimes has triggered the idea to use them as ultrasound-controlled vehicles to facilitate the delivery of therapeutic agents to a site of interest. Such a noninvasive, localised, side-effect-free method would revolutionise drug delivery as we know it.

Cellular uptake of drugs and deoxyribonucleic acid (DNA) is increased when the region of interest is under sonication, and even more so when an ultrasound contrast agent is present [2]. This increased uptake has been attributed to the formation of transient porosities in the cell membrane that have diameters up to $0.1\text{ }\mu\text{m}$, i. e., big enough for the transport of drugs into the cell. The pores reseal themselves within one minute. The ultrasound-assisted transient permeabilisation of a cell membrane is called sonoporation. Understanding the physics underlying sonoporation is of uttermost importance for the development of ultrasound-activated therapeutic agents.

There are five non-exclusive hypotheses for explaining the sonoporation phenomenon from a physics point of view [3]. These have been summarised in **Fig. 1**. It is noted that fragmenting microbubbles cannot create pores in cells, since fragmentation costs energy.

(a) Push

During its expansion phase, a microbubble might touch a cell membrane surface.

The pushing motion would then cause the cell membrane to be locally disrupted. The pushing mechanism would occur within half an ultrasound cycle. However, under typical sonication conditions, microbubble excursion amplitudes are low. Also, typically, microbubbles are much more flexible than cells. Our current understanding of microbubble physics does not support the push mechanism if the microbubble is not attached. However, if the microbubble is already attached to the cell membrane whilst expanding, pushing under influence of radiation forces might cause the membrane to rupture. The latter mechanism might occur over multiple cycles.

(b) Pull

During the contraction phase of an oscillating microbubble, the plasma filling the void left by the contracting bubble might pull the cell membrane towards the microbubble. This pulling motion would

then cause the cell membrane to be locally disrupted. The pulling mechanism would occur within half an ultrasound cycle. However, under typical sonication conditions, microbubble contractions do not result in an inertial collapse. Moreover, the replace mass of a contracting microbubble is much lower than the fluid supposedly causing the pull. Therefore, this mechanism is less plausible than the push mechanism in non-attached conditions. However, if the microbubble is attached to the cell membrane, a similar mechanism might occur as described under (a), where pulling under the influence of radiation forces might cause the membrane to rupture.

(c) Jetting

Jetting is the asymmetric collapse of a bubble, creating a funnel-shaped protrusion through the bubble that is directed towards a boundary. This spectacular phenomenon has actually been optically observed on a microscopic scale through cell [4]. The jetting phenomenon occurs within half an ultrasound cycle. However, jetting exclusively occurs when using high acoustic amplitudes, at the upper end of clinical settings. Also, there has not been any proof yet of cell survival after jetting.

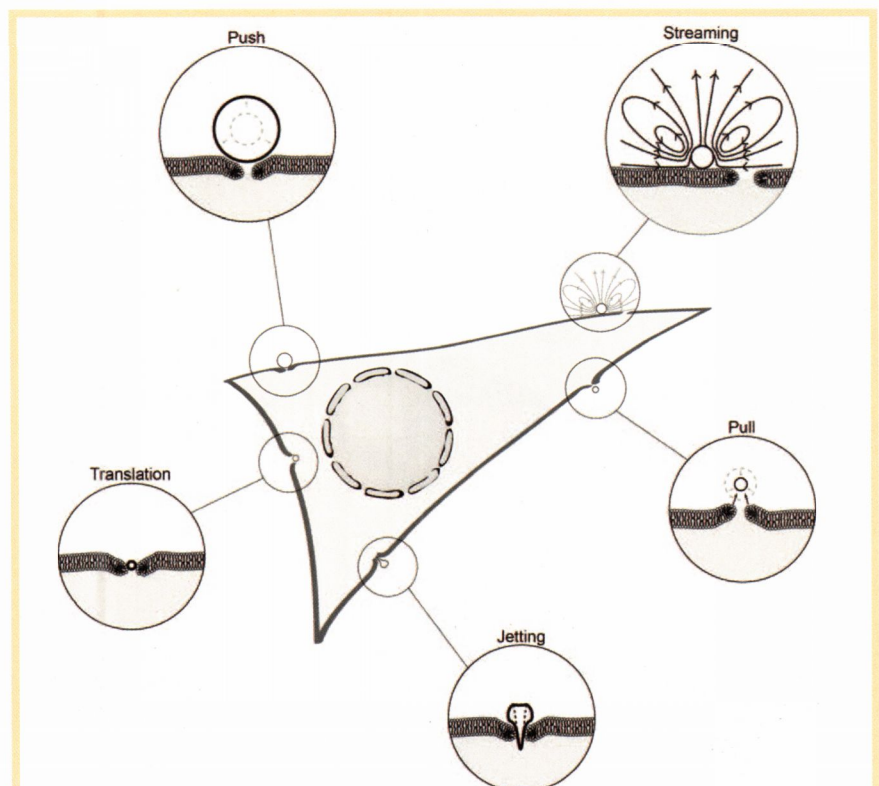


Fig. 1 Schematic representation of the five physical mechanisms supposedly involved in sonoporation.

Based on empiric studies that relate jet length to pore size, we excluded the role of jetting as a dominant mechanism involved in sonoporation [5].

(d) Streaming

If a microbubble is fixed to a membrane, the fluid streaming around the oscillating bubbles creates enough shear to rupture the membrane [6]. Here, long pulse lengths are required to set the fluid in motion. However, low acoustic amplitudes should suffice to create the rupturing shear of a typical cell membrane. Existing research has proven the feasibility of the streaming mechanism in bound conditions, so this mechanism should work for targeted contrast agents that attach to cells. Further research will show whether streaming around weakly-attached microbubbles creates enough shear for cell membranes to rupture.

(e) Translation

Owing to radiation forces, lipid-encapsulated microbubbles may translate through cell membranes or channels in the cell membrane. The microbubble may lose part of its shell whilst passing through the cell membrane. As a result, the gas will dissolve after entry. **Fig. 2** shows a gra-

phic representation of the translation mechanism. In case of therapeutic loading, the load would be delivered directly into the target cell. This mechanism requires long pulse lengths and low acoustic amplitudes. Very recently, fluorescence-coated ultrasound contrast agent microbubbles were observed to move into HeLa cells at a low mechanical index (MI) of 0.15, using high-speed video footage under confocal microscopy [7]. The microbubbles dissolved after entering the cells. The cells survived the sonoporation treatment, confirming the transient character of sonoporation.

All five of these mechanisms require the presence of a microbubble in the vicinity of the cell. Yet, increased drug uptake has also been reported without the use of any ultrasound contrast agent, but merely an ultrasound field itself. Despite speculations about the role of inertial cavitation in the latter, clinical ultrasound scanners do not generate fields strong enough to create such spontaneous microbubbles in blood. Recently, it was found that (bilayer) cell membranes themselves act as cavitation nuclei [8]. Even at modest acoustic pressures, cell membranes might rupture due to the building up of gas cavities inside the bilayer. This important finding would explain the sonoporation in the ab-

sence of ultrasound contrast agent microbubbles. Moreover, it explains why bubbles are attracted to cells that are not in the travel path of the ultrasound wave. However, given the low MI at which cells attract microbubbles, more study is required regarding the safe use of ultrasound contrast agents in long-pulse-length imaging.

In conclusion, in current clinical settings, four non-exclusive mechanisms are plausible for the physical explanation for sonoporation with the aid of ultrasound contrast agent microbubbles.

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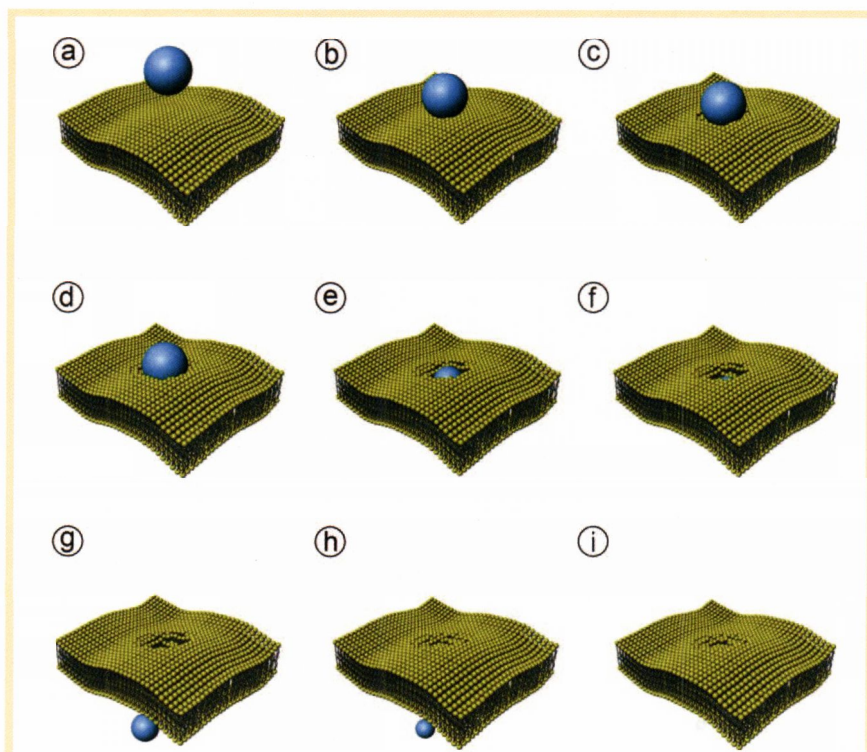


Fig. 2 Schematic representation of a lipid-encapsulated microbubble translating into a cell owing to radiation forces (frames a-g) and subsequently dissolving (frames h-i).

Nicht invasive Behandlung von chronischen neurologischen Erkrankungen

Der globale Marktführer¹ im Bereich MR-geführte fokussierte Ultraschalltechnologie gab letztes Jahr bekannt, dass ein vom Unternehmen für Forschungszwecke entwickeltes System² in klinischen Studien für die Behandlung von 30 Patienten mit chronischen neurologischen Erkrankungen eingesetzt wurde. Diese klinischen Studien^{3–5} wurden von Spezialisten für funktionelle Neurochirurgie, Neurologen und Neuroradiologen in der Schweiz durchgeführt und sollen die Sicherheit und die initiale Wirksamkeit bei der Behandlung von essenziellem Tremor, neuropathischem Schmerz und Parkinsonkrankheit analysieren. Das System soll nur für Forschungszwecke eingesetzt werden.

Millionen Menschen auf der ganzen Welt sind von neurologischen Erkrankungen betroffen; diese Erkrankungen können zu wesentlichen Funktionsverlusten und Medikamentenabhängigkeit führen. Die Patienten leiden, und ihre Lebensqualität sowie die der Personen, die sich um sie kümmern, werden beeinträchtigt. Patienten, die nicht auf Medikamente reagieren, können mit tiefer Hirnstimulation, Hochfrequenzablation oder Radiochirurgie behandelt werden; diese Verfahren sind entweder invasiv oder mit ionisierender Strahlung verbunden. Die Risiken der letztgenannten Behandlungsmethode sind bekannt: hohe Strahlendosen oder hohes Risiko von Komplikationen und Nebenwirkungen.

Es handelt sich um das erste klinische System, das MR-geführten fokussierten Ultraschall durch den intakten Schädel einsetzt. Hierbei werden tiefliegende Hirnbereiche schnittlos und ohne ionisierende Strahlung mit einer Kombination aus fokussiertem Ultraschall und MR-Führung in Echtzeit behandelt.

„Die Möglichkeit der Nutzung fokussierten Ultraschalls für nicht invasive Behandlung von Hirnerkrankungen ist seit Jahren bekannt, doch damit diese Möglichkeit umgesetzt werden konnte, mussten beträchtliche technische Hindernisse überwunden werden. Um dies zu erreichen, haben wir enorme Energie in die technologische und die klinische Seite des Projekts investiert. Die bisher erzielten klinischen Ergebnisse sind sehr ermutigend“, sagte Eyal Zadicario, Vizepräsident der

Abeilung Forschung und Entwicklung und Leiter des Neuro-Programms des Unternehmens.

Die in dem System integrierte Bildführung während des Eingriffs ermöglicht genaue Kontrolle und exakte Abgabe an den gewünschten Bereich mit kontinuierlichem Feedback in Echtzeit während der gesamten Behandlung.

In laufenden klinischen Untersuchungen wird die Fähigkeit dieser Technologie zur Verringerung von Komplikationen und Nebenwirkungen erforscht. Das System könnte eine Behandlungsalternative für Personen darstellen, die derzeit nicht operiert werden können oder eine Hirnoperation ablehnen.

Nach einer Pressemitteilung (InSightec)

¹ InSightec Ltd., Tirat Carmel, Israel

² ExAblate® Neuro, InSightec

³ Jeanmonod D, Martin E. Neurosurg Focus 2012; DOI: 10.3171/2011.10.FOCUS11248

⁴ Moser D, Zadicario E, Schiff G et al. Neurosurg Focus 2012; DOI: 10.3171/2011.10.FOCUS11246

⁵ Martin E, Jeanmonod D, Morel A et al. Ann Neurol 2009; 66: 858–861

Offener Hochfeld-MRT: Wenn Klaustrophobie zum Fremdwort wird

Mit 1,2 T hat ein Magnetresonanztomograf¹ derzeit die weltweit höchste Magnetfeldstärke eines offenen MRT. Das durch versetzte Säulen völlig offene Gerät ermöglicht dem Patienten einen Rundumblick; zusammen mit der extrabreiten Liegefläche nimmt es zudem das Gefühl des Eingengtseins und baut Klaustrophobien ab. Zudem haben der Arzt und seine Mitarbeiter durch die offene Architektur des Geräts vollen Zugang zum Körper des Patienten. Damit ist das offene MRT eine Option auch für die Patienten, die geschlossene MRT-Systeme bisher nicht benutzen konnten.

Bei den derzeit eingesetzten MRT-Systemen überwiegt die Bauform der geschlossenen oder Tunnel-Kernspintomografen.

Ihr Gewicht liegt in der Regel unter 5 t, womit die baulichen Voraussetzungen keine großen Schwierigkeiten bereiten. Für einen hohen Prozentsatz der Patienten – vermutlich 30% – bringt die Untersuchung in der Röhre Beklemmungsgefühle bis hin zur Klaustrophobie. Offene MRT-Systeme dagegen nehmen den Klaustrophobikern die Angst und bieten auch mehr Bewegungsfreiheit, wovon vor allem Kinder und Adipöse profitieren. Zudem haben sie den Vorteil, dass Assistenzpersonal und Arzt in jeder Stufe des Untersuchungsablaufs Zugang zum Patienten haben. Allerdings liefern sie im Vergleich mit den geschlossenen Tunnel-systemen, die durch ihren Aufbau bessere Bilder liefern können, bislang nicht ganz so brillante Bilddaten.

Seit über 20 Jahren entwickelt der Hersteller² offene MRT mit vertikalem Magnetfeld von 0,3 bis 1,5 T und ist mit der Installation von weltweit 5400 offener MRT-Systeme Marktführer. Das erste offene MRT-System mit einer Magnetfeldstärke von 1,2 T ermöglicht dem Patienten einen Rundumblick von 270° und liefert – trotz der offenen Bauart – eine hochwertige Bildqualität. Allerdings sind die baulichen Anforderungen an das Gerät, das mit seiner komplexen Technik und seinen ca. 15 t Systemgewicht ein echtes Schwergewicht ist, deutlich höher als bei den konventionellen Geräten.

Dr. Carsten Figge setzt seit Ende 2009 zusammen mit seinen Kollegen in der Paderborner Radiologiepraxis den MRT ein. Es war das erste Gerät, das in Deutschland installiert wurde, und inzwischen haben sie damit über 8000 Patienten untersucht. Der Hochfeld-MRT wird von den Paderborner Radiologen universal eingesetzt: von den klassischen Untersuchungen der Gelenke und Wirbelsäule oder des Gehirns, über die Angiografie und die MR-Mammografie bis zur Untersuchung des Bauchraums. Neben den technischen Fakten, wie High-End-Bildtechnik, schnelle Aufnahmezeiten durch parallele Bildgebung bei bis zu 5500 Bildern pro Sekunde oder die Möglichkeiten der interventionellen MRT-Diagnostik, spielen für Figge emotionale Faktoren für die Entscheidung zu dem MRT eine wichtige Rolle, wie er auf einem Pressegespräch³ mitteilte. Dass ein offener MRT den Patienten mehr Komfort bringt, ist für ihn nur ein Pfeiler seiner Arbeitsphilosophie und -strategie, in der er eine emotionale und dem Patienten zugewandte Arbeitsweise für nicht weniger wichtig hält. Und die wirtschaftliche Seite? Trotz hö-

herer Anschaffungskosten habe der offene Ganzkörper-Hochfeld-MRT bei der Akquise neuer Patienten Vorteile. Durch die hohe Patientenzufriedenheit vergrößert er über die Mund-zu-Mund-Propaganda das Einzugsgebiet, insbesondere der informierte Privatpatient habe ein starkes Interesse an modernster Medizintechnologie.

Anne Marie Feldkamp, Bochum

¹ OASIS 1,2 T, Hitachi Medical Systems GmbH, Wiesbaden

² Hitachi Medical Systems GmbH

³ Pressegespräch „Hinlegen und Wohlfühlen“ – Offene Magnetresonanztomografen bieten neue medizinische Dimensionen mit Wohlfühlfaktor“ anlässlich der MEDICA im November 2011 in Düsseldorf; Veranstalter: Hitachi Medical Systems GmbH

Reinigung und Aufbereitung von Medizinprodukten erleichtern

Die aktuelle Praxis in der Instrumentenkonstruktion stellt Sterilisationsverantwortliche vor eine große Hürde: Beim heute üblichen Operationsbesteck werden aus Kostengründen häufig Steckgriffe aus Aluminium oder Kunststoff eingesetzt. Diese werden auf den eigentlichen Instrumentenschaft aus Edelstahl aufgesteckt, aufgepresst oder verstiftet. Dabei bleibt ein mehr oder weniger breiter Spalt zwischen Metall und Kunststoff – für die lückenlose, hygienische Reinigung eine entscheidende Schwachstelle.

Hier kann u. U. bereits bei der Anwendung organisches Material eindringen. Bei der Aufbereitung verziehen sich die unterschiedlichen Werkstoffe darüber hinaus entsprechend ihres jeweiligen Ausdehnungskoeffizienten verschieden stark, wodurch sich dieser Spalt um das 2-Fache vergrößern kann. Die Kapillarwirkung und die durch den Reiniger herabgesetzte Oberflächenspannung des Wassers tragen zusätzlich dazu bei, dass kontaminierte Flüssigkeiten in den Spalt fließen. Bei der Dampfsterilisation entweicht das Wasser zwar, der eingetragene Schmutz aber setzt sich ab. Gewebereste können zudem den Spalt verkleben und so Feuchtigkeit und infektiöse Stoffe im Instrument halten.

Vulkanisierung schließt Hygienelücke

Um das zu verhindern, werden etwa bei den Instrumenten des Medizinprodukteherstellers Orange Spine inzwischen die Griffe in einem aufwendigen Verfahren aufvulkanisiert. Der Edstahlschaft wird dazu chemisch vorbehandelt und vorgeheizt in die Griffform eingelegt, in die dann Silikon eingespritzt wird. Durch die Hitze und den Druck im Herstellungsprozess geht der Griff mit dem Metall eine dauerhafte und v. a. spaltfreie Verbindung ein. Diese widersteht sogar den extremen Temperaturen der Sterilisierung und den zur Lösung von Protein- und Fettrückständen empfohlenen alkalischen Reinigern. Dazu trägt auch bei, dass Silikon gegen Laugen, Salze und verdünnte Säuren sehr beständig ist und Temperaturen von –40 bis 200 °C, kurzzeitig sogar 300 °C, sowie Wasserdampf von bis zu 160 °C aushält. Es kann deshalb anders als die meisten Kunststoffe mit allen derzeitigen Verfahren gereinigt werden, ohne seine Beschaffenheit und Eigenschaften zu verändern. Die Vulkanisierung ist dadurch dauerhaft „dicht“, Fremdstoffe und vor allem möglicherweise infektiöses Material können nicht mehr eindringen.

Information: Orange Spine GmbH, Gewerbegebiet 16, 82399 Raisting; www.orange-spine.de

Handschuhe mit antimikrobieller Technologie am Markt

Das Unternehmen Ansell Healthcare, Brüssel¹, gab aktuell bekannt, dass die OP-Handschuhe „Gammex® Powder-Free with AMT Antimicrobial Technology“ das CE-Zeichen erhalten haben. Durch eine spezielle viren- und bakterienabtötende Beschichtung bietet der neuartige Handschuh im Fall eines Handschuhdefekts Schutz vor gängigen Krankheitserregern und auch resistenten Bakterien. „Wir freuen uns darauf, Chirurgen und dem OP-Personal einen neuen Sicherheitsstandard anbieten zu können“, sagte Peter Dobbelssteijn, Senior Vice President EMEA des Herstellers.

Die Handschuhe aus Naturlatex bieten im Umgang mit Instrumenten die gleichen Eigenschaften – Tastempfindlichkeit, Flexibilität und Tragekomfort – wie herkömmliche OP-Handschuhe. Der ent-

scheidende Unterschied besteht in der antimikrobiell wirksamen Beschichtung, die Chlorhexidylgluconat (CHG) enthält. Diese patentierte Technologie kann einen dauerhaften antiviralen und antibakteriellen Schutz vor HIV, Hepatitis C und infektiösen Bakterien bieten. In klinischen und Labortests tötete der Handschuh mit AMT mindestens 99% aller eindringenden HIV- und HCV-Surrogatviren (HCV = Hepatitis C) ab. Darüber hinaus haben klinische Tests gezeigt, dass der Handschuh mehr als 99,7% von 8 häufig vorkommenden infektiösen Bakterien (grampositive, gramnegative und antibiotikaresistente Bakterien) und mehr als 99,99% von Staphylococcus aureus abtötet. Nicht untersucht wurde der Handschuh auf eine Schutzwirkung gegen durch Blut übertragene Infektionen bei Rissen, Schnitten oder Punktionen der Haut.

Mit der CE-Kennzeichnung ist der Weg frei, diese Technologie auf dem Europäischen Markt einzuführen.

Nach einer Pressemitteilung (Ansell)

¹ Ansell GmbH, München; www.anselleurope.com/ansell_de

Nach Angaben der Industrie

DEGUM-Mitteilungen

Deutsche Gesellschaft für Ultraschall in der Medizin



DEGUM-Ausschreibung

Wissenschaftspreis 2012

1. Die Deutsche Gesellschaft für Ultraschall in der Medizin vergibt Förderpreise für hervorragende wissenschaftliche Arbeiten auf dem Gebiet des medizinischen Ultraschalls. Die Förderpreise bestehen aus einer Urkunde und einem Geldbetrag.
2. Im Jahr 2012 werden 3 Preise ausgeschrieben: Der 1. Preis ist mit 2500,-€ dotiert, der 2. mit 1500,-€, der 3. mit 1000,-€. Die Preise können geteilt werden, wenn mehrere gleichwertige Bewerbungen vorliegen.
3. Für den DEGUM-Wissenschaftspreis 2012 können Originalarbeiten in deutscher oder englischer Sprache berücksichtigt werden, die nach dem 31.12.2009 publiziert bzw. zur Publikation angenommen wurden. Übersichtsarbeiten können keine Berücksichtigung finden.
4. Sind an der prämierten Arbeit mehrere Autoren beteiligt, erhält jede Person eine Urkunde, der Geldbetrag wird entsprechend geteilt.
5. Da der Preis der Förderung des Nachwuchses dienen soll, sind Habilitationsschriften sowie Arbeiten von leitenden Ärzten von der Einreichung als Erstautor ausgenommen.
6. Jeder Bewerber (auch Mitautor) kann nur eine Arbeit einreichen.

7. Der Vorstand der DEGUM ernannt ein Kuratorium, bestehend aus mindestens 3 Mitgliedern der DEGUM, von welchen einer als Vorsitzender fungiert. Alle Arbeiten werden nach einem vorher festgelegten Score beurteilt und von mindestens 2 externen Fachgutachtern bewertet. Die Entscheidung des Kuratoriums ist endgültig und unanfechtbar.
8. Bewerbungen um den DEGUM-Wissenschaftspreis 2012 sind in 6-facher Ausfertigung (6 Sonderdrucke oder entsprechende vollständige Manuskriptkopien) einzureichen und müssen am 15.04.2012 in der DEGUM-Geschäftsstelle, Ermekeilstr. 1 in 53113 Bonn vorliegen.

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1. Die Deutsche Gesellschaft für Ultraschall in der Medizin vergibt Förderpreise für hervorragende Dissertationen auf dem Gebiet des medizinischen Ultraschalls. Der Promotionspreis 2012 ist mit 1000,-€ dotiert und kann 2-mal vergeben werden.
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Heidelberg im Dezember 2011

Prof. Dr. S. Delorme, Präsident der DEGUM
Dr. H.-P. Weskott, Sekretär der DEGUM

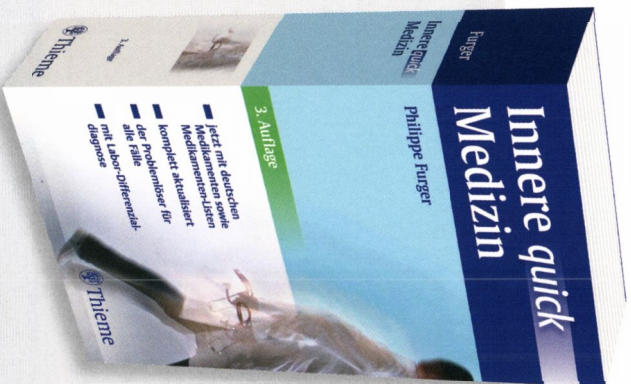
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Stellungnahme der DEGUM zu medizinischem Assistenzpersonal in der Ultraschalldiagnostik

Die DEGUM hat sich in mehreren Vorstandsitzungen 2010 sowie in einer erweiterten Vorstandssitzung am 17.01.2011 ausführlich mit dem Thema von Assistenzpersonal in der Sonographie auseinandergesetzt. Zu der ganztägigen Sitzung des Erweiterten Vorstands wurden Vorträge von Experten, auch aus dem Ausland, zum Thema gehört und diskutiert. Ferner fand eine Befragung aller Arbeitskreise und Sektionen statt.

Danach nimmt die DEGUM bereits seit 2007 eine klare Position zu diesem Thema ein. Die fachlichen Anforderungen an das nicht-ärztliche Assistenzpersonal sind in den vergangenen Jahren gestiegen und erfordern eine höhere Qualifikation. Die DEGUM wird diesem Umstand in zunehmendem Maße Rechnung tragen und auf

Ihren Veranstaltungen und Kongressen Fortbildungsangebote auch für medizinisches Assistenzpersonal anbieten.

Hingegen wurde eine Übernahme der sonographischen Diagnostik durch Assistenzpersonal – wie z.B. in den angelsächsischen Ländern, in denen ein solches Berufsbild („Sonographer“) seit langer Zeit besteht – mit einer überwältigenden Mehrheit abgelehnt. Die DEGUM sieht die Sonographie nicht als eine rein technische Leistung an, sondern versteht sie als klinisches Werkzeug in der Hand des Arztes („klinische Sonographie“): Zielgerichtete Anamnese und Einordnung der erhobenen Befunde in das Krankheitsbild durch den untersuchenden Arzt zum Zeitpunkt der Untersuchung machen den Wert dieser Untersuchungsmethode aus.

Eine Delegation an nicht-ärztliches Personal würde wie in den USA oder Großbritannien eine mehrjährige Ausbildung dieser Berufsgruppe erfordern. Im Übrigen bleibt die Verantwortung für erhobene Befunde unteilbar und liegt mit Hinblick auf die daraus erwachsenen klinischen Konsequenzen weiterhin beim Arzt. Damit wäre eine abschließende ärztliche Befundkontrolle weiterhin unabdingbar, so dass insgesamt keine relevante Zeiterparnis resultieren würde. Die DEGUM betont zugleich, dass eine gute Ausbildung sonographisch tätiger Ärzte unabdingbar ist, und macht darauf aufmerksam, dass diese vielerorts bereits heute nicht mehr ausreichend gewährleistet ist. Eine Verlagerung sonographischer Leistungen auf spezialisiertes Assistenzpersonal würde die Ausbildung von Ärzten in verstärktem Maße gefährden und den klinischen Wert der Sonographie in vielen Fachdisziplinen marginalisieren.

*Für den Vorstand der DEGUM
Prof. Dr. S. Delorme, Präsident
Dr. H.-P. Weskott, Sekretär*

ÖGUM-Mitteilungen

Österreichische Gesellschaft für Ultraschall in der Medizin



Ultraschall wird lesbar

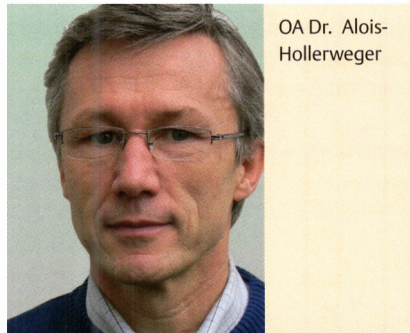
„Ultraschall wird lesbar: Standardisierte Dokumentation in der Sonografie des Abdomens“ war die Überschrift des Buches von H. Czemberek (Springer 1989) und somit einer der ersten Schritte, für eine Standarddokumentation einzutreten.

Auszug aus der Buchbewerbung: „Es wird erstmalig der Versuch unternommen, die dynamische Information der Ultraschalluntersuchung auf standardisierten Schnittebenen zu dokumentieren. Bis jetzt war es in den meisten Fällen üblich, einen pathologischen Befund in Form eines Bildes zu dokumentieren. Die Vorschläge zur standardisierten Schnittführung in der Ultraschalldiagnostik des Abdomens beruhen auf der Dokumentation der anatomischen Leitstrukturen, wodurch ein Zurechtfinden auf den vorliegenden Bildern durch den Untersucher selbst oder durch einen Zweitbetrachter ermöglicht wird.“

Dieses Konzept wurde fortgesetzt im ersten ÖGUM-Poster zur standardisierten Dokumentation mit insgesamt 12 Standardschnitten (4 Längsschnitte bzw. Schrägschnitte durch Leber, Gallenblase, Lig. hepatoduodenale und linken Leberlappen mit Aorta; 2 Subkostalschnitte mit Lebervenenstern und Leberhilus; 2 Schnitte durch das Pankreas und die Milz mit dem Pankreasschwanz; 4 Schnitte durch die Nieren: je ein Längs- und Querschnitt auf beiden Seiten)

Nachdem das bisherige Poster zur Standarddokumentation schon in die Jahre gekommen war, ist nun mit dem Weltultraschallkongress 2011 in WIEN die Neuaufgabe präsentiert worden.

Das neue Poster zeigt leichte Abänderungen der bisher schon verwendeten 12 Standardschnitte und wurde um Retroperitoneum und kleines Becken (männlich +weiblich je 2) auf insgesamt 18 Schnitte



OA Dr. Alois Hollerweger

ergänzt (d. h. pro Patient 16 Schnitte für das gesamte Abdomen).

Schnitt 1 (Längsschnitt rechter Leberlappen) wurde ersetzt durch einen Subkostalschnitt durch den rechten Leberlappen, da dieser mehr die Untersuchungstechnik der Leber widerspiegelt, die doch überwiegend in Subkostalschnitten und nur tws. in Längsschnitten erfolgt. Ansonsten wurden die Schnitte beibehalten und sind nur in der Reihenfolge etwas abgeändert wiedergegeben (ein A4-Bild zum Download gibt es unter: www.oegum.at Reiter: Ausbildung/Poster).

Die beiden neuen Schnitte durch das Retroperitoneum mit Aorta / Cava längs und quer und die beiden Schnitte durch das kleine Becken ergänzen die Dokumentation, da generell der Trend in die Richtung zur Untersuchung des gesamten Abdomens geht und gezielter „Organultraschall“ immer nur eine Teiluntersuchung darstellt und nur bei Verlaufskontrollen bzw. ganz gezielten Fragestellungen durchgeführt werden sollte.

Standardschnitte können nie eine qualitativ gute Untersuchung ersetzen, die durch entsprechende Untersuchungstechnik eine räumliche Erfassung der verschiedenen Organe beinhaltet. Sie können aber ein Anhaltspunkt sein für das Ausmaß einer guten Dokumentation und die Reproduzierbarkeit und Vergleichbarkeit eines

Untersuchungsergebnisses verbessern. Pathologische Befunde außerhalb der Standardschnitte sind selbstverständlich gesondert zu dokumentieren. Außerdem sind Standardschnitte für den Anfänger und Lernenden eine gute Richtlinie, um zu erlernen, wie verschiedene Schnitte in der richtigen Ebene eingestellt werden. Man lernt dabei auch, dass „Standardschnitte“ sich letztlich doch bei jedem Individuum in der räumlichen Ebene leicht unterscheiden.

Alois Hollerweger

ÖGUM-Sekretariat

ÖGUM-Sekretariat
Neutorgasse 9/2a, AT-1010 Wien
Tel.: +43 (0)1 535 13 05
Fax: +43 (0)1 535 70 37
E-Mail: geschaeftsstelle@oegum.at
Öffnungszeiten: Mo–Fr, 9:00–13:00 Uhr
Homepage: www.oegum.at

Beiträge/Kursinfo für ÖGUM-Mitteilungen an:

Ass. Prof. Dr. Christian Kollmann
Zentrum f. Medizinische Physik & Biomedizinische Technik, Medizinische Universität Wien
Währinger Gürtel 18–20, E 4L
A-1090 Wien
Tel: ++43 (0)1 40400 73730
Fax: 0043 (0)1 40400 3988
E-Mail: christian.kollmann@meduniwien.ac.at

WWW.OEGUM.AT – eine Adresse, die gefragt ist

Unsere Webseiten scheinen gefragt zu sein: Mit fast 528 000 Zugriffen für das Jahr 2011 haben wir einen steten Zuwachs zu verzeichnen. Durchschnittlich greifen pro Tag 40 unterschiedliche User 1446-mal auf unsere Seiten zu. Dabei ist immer noch die Homepage die Einstiegsseite, aber auch einige andere Seiten werden als Erst-Einstiegsseite verwendet, sodass hier wohl direkte links gesetzt worden sind.

Die TOP-5-Seiten, die größtes Interesse gefunden haben, 2011 sind: 1. Homepage, 2. Eventkalender, 3. AK Gynäkologie & Geburtshilfe, 4. AK Abdomen, 5. Richtlinien/Standards.

Vielen Dank an alle, die unseren Webserver mit „Content“ gefüttert haben!

Auch 2012 geht die Steigerung der Attraktivität des ÖGUM-Webangebots weiter durch Ausbau und Optimierung, da nicht nur aus eigenen Landen und aus Europa zugegriffen wird, sondern auch aus exotischen Regionen, wie z. B. den Kocos-Inseln oder Ghana. Die ÖGUM scheint auch international gefragt zu sein !

Christian Kollmann

Do you have a HCU and perform HPDI ?

If you are worried now and did not understand anything, have a look to the latest list of medical ultrasound abbreviations OeGUM has been published (Acronym/US [Vers.2]). More than 400 abbreviations have been collected as fast reference on tablets or e-readers (www.oegum.at [Technique|Guidelines]).

Sonografiekurse nach den Richtlinien der ÖGUM

Detaillierte Infos unter www.oegum.at

Abdomen

- ▶ 22.02.–24.02.2012, Baden: Ultraschall-Grundkurs „Abdomen“
- ▶ 20.06.–22.06.2012, Baden: Ultraschall Fortgeschrittenkurs Abdomen
- ▶ Nov. 2012, Wien: Ultraschall-Grundkurs „Abdomen“
Leitung & Auskunft: Prof. Dr. N. Gritzmann (Sono Seminare), Wien
Tel. und Fax: 01/774747117, E-Mail: norbert.gritzmann@gmail.com; www.sonoseminare.com
- ▶ 11.03.–14.03.2012, Gaschn: Abdomensonografie-Refresherkurs
Leitung: Prof. Dr. G. Mathis; Auskunft und Anmeldung: www.ultraschallkurse.at, organisation@ultraschallkurse.at
- ▶ 21.03.–23.03.2012, Salzburg: Grundkurs Abdomen
- ▶ 20.04.–21.04.2012, Salzburg: Kurs Gastrointestinaltrakt
- ▶ 27.06.–29.06.2012, Salzburg: Grundkurs Abdomen
- ▶ 26.09.–28.09.2012, Salzburg: Fortgeschrittenkurs Abdomen
- ▶ 21.11.–23.11.2012, Salzburg: Grundkurs Abdomen
Leitung: OA Dr. Hollerweger; kontakt@bhb-sonokurse.at
- ▶ 03.05.–05.05.2012, Hohenems: Abdomensonografie
- ▶ 11.10.–13.10.2012, Hohenems: Abdomensonografie
Leitung & Auskunft: OA Dr. Gehmacher; otto.gehmacher@lkh.at

Bewegungsapparat

- ▶ 24.02.–25.02.2012, 22.06.–23.06.2012, Baden: Spezialkurs Gelenke/Weichteile
- ▶ Nov. 2012, Wien: Farb-Doppler-Sonografie-kurs „Halsgefäße & periphere Gefäße“
Leitung & Auskunft: Prof. Dr. N. Gritzmann Tel. und Fax: 01/774747117, E-Mail: norbert.gritzmann@gmail.com
- ▶ 28.06.–30.06.2012, Innsbruck: ESSR Musculoskeletal Radiology Meeting
Leitung: Univ. Prof. A. Klauser; Auskunft: www.essr.org/cms

Gynäkologie/Geburtshilfe

- ▶ 25.02.–03.03.2012, Teneriffa: Gyn Allround
Leitung: Univ. Prof. Dr. Deutinger; Auskunft und Anmeldung: gynallround@conventive.at
- ▶ 27.04.–29.04.2012, Salzburg: Grundkurs Doppler-Sonografie
- ▶ 27.04.–29.04.2012, Salzburg: Aufbaukurs Doppler-Sonografie
- ▶ 27.04.–28.04.2012, Salzburg: Sono-UpDate II./III. Trimenon
- ▶ 28.04.–29.04.2012, Salzburg: Kreißsaalführerschein, Modul 2: Seminar und Update prä- und intrapartaler Überwachungs- und Behandlungsmethoden
Organisation und Auskunft: Univ.-Prof. Dr. H. Steiner, R. Oberascher; Universitätsklinik für Frauenheilkunde und Geburtshilfe der Salzburger Landeskliniken (SALK); Tel. +43/662-4482-2501, Fax +43/662-4482-2513; H.Steiner@salk.at oder R.Oberascher@salk.at

Kopf/Hals/Gefäße

- ▶ 24.03.–25.03.2012, Graz: Fortgeschrittenen-Abschlussskurs Duplexsonografie
Leitung & Auskunft: Univ.-Prof. Dr. Niederkorn; office@niederkorn.at
- ▶ 10.03.2012, Wien: Schilddrüsen Ultraschallkurs
Leitung & Auskunft: Univ. Doz. Dr. Zettinig; zettinig@schilddruesenpraxis.at

Thorax

- ▶ 15.03.–17.03.2012, Gaschn: Lungen- und Pleurasonografie
Leitung: Prof. Dr. G. Mathis; Auskunft und Anmeldung: www.ultraschallkurse.at, organisation@ultraschallkurse.at

Richtig fokussiert



Kursbuch Doppler- und Duplexsonografie

Amann-Vesti/Thalhammer/Huck (Hg.)

1. Halbj. 2012. 3., vollst. überarb. u. akt. Aufl.

Ca. 516 S., ca. 1010 Abb., geb., plus DVD

ISBN 978 3 13 115373 9

Ca. 139,99 € [D]

Ca. 144,- € [A]/ca. 196,- CHF

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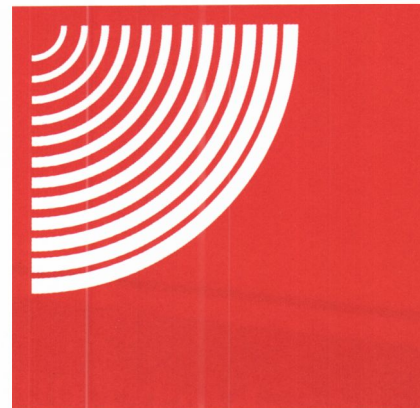
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SGUM/SSUM-Bulletin

Schweizerische Gesellschaft für Ultraschall in der Medizin
Società Svizzera di Ultrasonologia in Medicina
Société Suisse d'Ultrasons en Médecine



Kurse Sonografie des Bewegungsapparates und der Säuglingshüfte:

Alle diese Kurse finden im modernen Csiperkozsa-Konferenz-Centrum in 6135 Csòlyospàlos (Ungarn) statt. Kurssprache ist Deutsch. Die Kurse werden verbunden mit einem lokalen Rahmenprogramm. Alle Einzelheiten zu den Kursen sind auf der Webseite der Sektion Bewegungsapparat www.locomo.ch (Rubrik: Kurswesen) aufgeschaltet. Die Kurse entsprechen den Richtlinien der SGUM und werden testiert.

Grundkurs Sonografie des Bewegungsapparats

- ▶ 6. Sept. – 9. Sept. 2012
Leitung: Dr. med. Beat Dubs

Aufbaukurs Sonografie des Bewegungsapparats:

- ▶ 28. Juni – 1. Juli 2012
Leitung: Dr. med. Beat Dubs

Refresherkurs Sonografie des Bewegungsapparats

- ▶ 1. Juni – 3. Juni 2012
Leitung: Dr. med. Beat Dubs

Refresherkurse Sonografie der Säuglingshüfte nach Graf

- ▶ 4. Mai – 6. Mai 2012
Leitung: Prof. R. Graf
- ▶ 15. Juni – 17. Juni 2012
Leitung: Dr. Raoul Schmid
- ▶ 31. Aug. – 2. Sept. 2012
Leitung: Dr. Markus Renggli

Task Force Tarmed SGUM

Das Bundesamt für Gesundheit bzw. die zuständige Kommission hat die Elastografie zur Diagnostik und Verlaufskontrolle bei Leberfibrose bzw. -zirrhose (z. B. durch virale Hepatitiden, regelmässige Einnahme von Hepatotoxinen) als Pflichtleistung in der Grundversicherung anerkannt. Nähere Spezifizierungen über die Technik wurden nicht vorgenommen. Jetzt gilt es, diese Leistung auch im Tarmed zu verankern. Diesbezüglich werden nun die Parameter ausgearbeitet.

Im Übrigen herrscht momentan relative Funkstille, auch wenn ein weiterer Kumulationsfehler zwischen 2 Leistungen erkannt und gemeldet wurde.

Zum Thema „Verrechnung des Seitenvergleichs bei paarigen Extremitäten-Untersuchungen“ gibt es ebenfalls (noch) nichts Neues zu berichten.

Beat Dubs

Auskünfte: SGUM/SSUM-Bulletin

Dr. med. Luciano Braun,
Specialista FMH medicina interna
Ombudsmann SSUM/SGUM
Via Cantonale 37, 6930 Bedano, Schweiz
Tel. : +41-91/9452183
Mobile: +41-79/2400405
E-Mail: luciano.braun@bluewin.ch

Jetzt zögern und sparen!



Klinische Sonographie und sonographische Differenzialdiagnose

Seitz/Schuler/Rettenmaier (Hrsg.)

2008. 2., kompl. neu bearb. u. erw. Aufl.
1384 S., 3991 Abb., geb.
ISBN 978 3 13 126452 7

Statt 299,95 € [D]

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- Das gesamte Spektrum internistischer Ultraschallanwendungen
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 - Was kann Ultraschall zur Klärung beitragen?
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Flaggermusen

Organ for Norsk Forening for Ultralyd-Diagnostikk (NFUD)



NFUD-symposium 14.–16. mars 2012 i Stavanger

I 2012 arrangerer NFUD sitt årlige symposium i Stavanger fra 14. til 16. mars. Arrangementkomité med Claudia Heien i spissen og styret presenterer her det endelige programmet, som også er lagt ut på foreningens nettsider (www.nfud.no).

Påmeldingsfrist er satt til 1. mars 2012. Som tidligere kommer Gyro Conference til å ha ansvar for påmelding og organisasjon rundt kongressen (www.gyro.no).

Frist for innsending av abstrakt er 1. februar 2012.

Vel møtt!

Onsdag 14. mars

12:30–12:40 Velkommen
Roald F. Havre

12:40–14:00 Fellessesjon

- ▶ Ultrasound in critical care: past, present and future
Erik Sloth
- ▶ Ultralydveiledet leddpunksjon
Moritz Böhme
- ▶ Prenatale og neonatale populasjoner og betydningen av karyotyping
Sturla H. Eik-Nes

14:45–15:30 Frie foredrag

15:30–18:00

Få mer ut av dine ultralyddundersøkelser

- ▶ Billedoptimalisering, bruk knottene!
Jörg Geisler
- ▶ Fysikken bak knottene
Bjørn Angelsen
- ▶ Ultralydmaskinenes tekniske begrensninger
Rune Hansen
- ▶ Powerdoppler vs. Colordoppler
Søren Torp-Pedersen

19:00 Middag

Torsdag 15. mars

09:00–10:30 Fellessesjon

Ultralyd i akuttmedisin

- ▶ Ultrasound in emergency medicine
Dieter Nürnberg
- ▶ The hemodynamic instable patient – why is ultrasound necessary?
Erik Sloth
- ▶ Ultralyd på intensivavdelingen
Nils Peter Ovedal

11:00–12:00 Fellessesjon:

Ultralyd ved behandling av monochorionale tvillinger

- ▶ Complications and management of monochorionic twins
Kurt Hecher

11:30–12:00 Frie foredrag

13:30–15:00 Parallele sesjoner

Muskelskjelett – Inflammasjonskvantifisering i sener og synovia ved CEUS. Fordeler sammenliknet med Doppler

- ▶ Doppler som redskap for identifikasjon av pasienter som har nytte av Biologisk behandling for revmatoid artritt
Søren Torp Pedersen

- ▶ Tolking av Doppler: normalfunn vs. patologi
Lene Terslev
- ▶ Ultralydscoring av artritt
Vivi Bakkeheim
- ▶ Ultralyd ved entesitter
Hilde Berner Hammer

Obstetrikk – Tvillinger og ultralyd i fødsel

- ▶ Monitoring and management of IUGR (TRUFFLE study)
Kurt Hecher
- ▶ Oppfølging av monochorionale tvillinger
Birgitte Kahrs
- ▶ Ultrasound in labor
Torbjørn Moe Eggebø

Indremedisin/radiologi

- ▶ CEUS for adrenal focal lesion evaluation
Dieter Nürnberg
- ▶ Når CT ikke gir svaret: CEUS eller biopsi av leverlesjoner
Beatrice Rüger
- ▶ Nye retningslinjer for CEUS av andre organer enn lever
Odd Helge Gilja
- ▶ Ultralyd ved fokale lesjoner i bryst
Anne Lina Fjellhøy

15:45–17:00 Parallele sesjoner

Muskelskjelett

- ▶ Ultralyd for vurdering av destruktive forandringer ved
Inflammatorisk leddsykdom
Lene Terslev

Styret i NFUD:

Roald Flesland Havre (leder), Claudia Heien (sekretær), Thomas Reiher (kasserer), Rune Hansen, Svein Erik Måsøy, Peter Monzka, Vivi Bakkeheim og Beatrice Rüger
Web-adresse: www.nfud.no

- ▶ Ultralyd ved artrose
Hilde Berner Hammer
- ▶ Diskusjon/spørsmål

Obstetikk – Det føtale sentralnervesystemet

- ▶ CNS hos foster
Harm-Gerd K. Blaas
- ▶ Live demonstrasjon CNS
Harm-Gerd K. Blaas

Indremedisin/radiologi/teknologi – Nye teknikker: Strain og elastisitetsavbildning

- ▶ Strain og elastisitetsavbildning i bløtvev-en oversikt Svein-Erik Måsøy
- ▶ CEUS og elastografi av fokale pankreaslesjoner ved HUS
Roald F. Havre
- ▶ Transrektal ultralyd ved elastografi av rektale svulster
Jo Waage
- ▶ Diskusjon/spørsmål

17:30–18:30 Generalforsamling

19:30 Festmiddag

Fredag 16. mars

09:00–10:30 Fellessesjon

- ▶ Trygg bruk av ultralyd (safety)
Ragnar Sande
- ▶ Usual and non-usual (known and not-so-known use) practice with CEUS in abdominal diseases
Dieter Nürnberg
- ▶ Kan CEUS brukes til å kvantifisere inflammasjon i tarmvegg? Kim Nylund

10:40–11:00 Frie foredrag

11:00–12:00 Parallelle sesjoner

Muskelskjelett

- ▶ Ultralyd for vurdering av bløtdelstomeres i bevegelsesapparatet
Michel Court-Payen
- ▶ Diskusjon/spørsmål

Obstetikk – 1. trimester ultralyd

- ▶ Veke 12 ultralyd - vår nye utfordring?
Sturla H. Eik-Nes
- ▶ Diskusjon/spørsmål

Indremedisin/radiologi/teknologi – Ultralydveilede intervensjoner

- ▶ Ultralyd med praktiske øvelser: punksjon, drenasje, biopsi
Beatrice Rüger, Roald F. Havre

13:00–15:00 Parallelle sesjoner

Muskelskjelett

- ▶ Akillesenen: muskel-, sene- og knokkelenheten
Michel Court-Payen
- ▶ Ultralydvurdering og intervensjon av hofteregionen
Herlof Harstad
- ▶ Postoperativ hoft og nytte av ultralyd
Herlof Harstad
- ▶ Diskusjon/spørsmål, evt. praktisk demonstrasjon

Obstetikk/gynekologi

- ▶ Ultralyd ved assistert befruktning
Peter Montzka
- ▶ Oppdatering om fosterhjerterundersøkelsen
Eva Tegnander
- ▶ Live demonstrasjon, ultralyd uke 18
Claudia Heien
- ▶ Rutinemessig cervixmåling
Torbjørn Moe Eggebo
- ▶ Diskusjon/spørsmål

Indremedisin/radiologi/teknologi

- ▶ Ultralyd av tarmvegg
Svein Ødegaard
- ▶ Ultralyd ved obstipasjon hos barn
Thomas Reiher
- ▶ Intervensjonsmuligheter ved endoskopiske ultralyd
Lars Birger Nesje
- ▶ Ultralydveiledet behandling av invaginasjon
Thomas Reiher
- ▶ Ultralyd ved tarmsykdommer
Beatrice Rüger

15:10–15:30 Avslutning

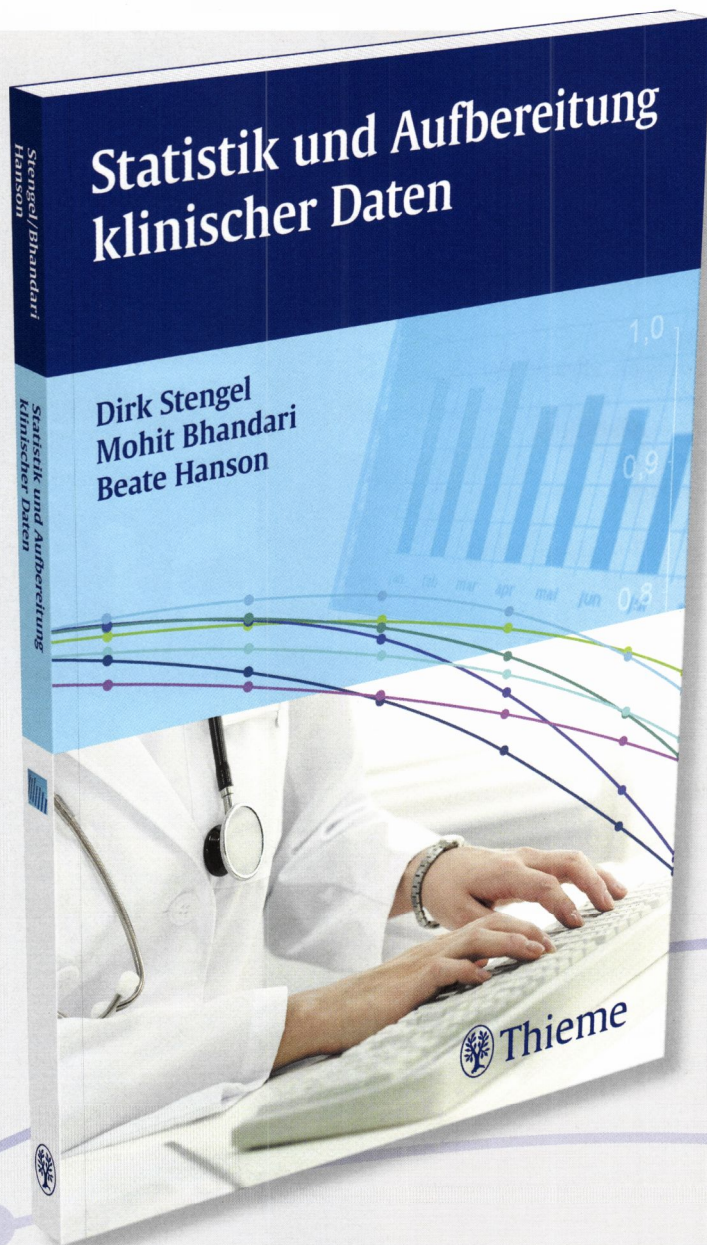
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Statistik und Aufbereitung klinischer Daten
Stengel/Bhandari/Hanson

2010. 150 S., 80 Abb., kart.

ISBN 978 3 13 154791 0

49,95 € [D]

51,40 € [A]/82,90 CHF

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SRUMB Newsletter

Societatea Română de Ultrasonografie

În Medicină și Biologie



SOCIETATEA ROMÂNĂ
DE ULTRASONOGRAFIE
ÎN MEDICINĂ ȘI BIOLOGIE

A XV Conferință Națională de Ultrasonografie și la Conferință de Educație Medicală Folosind Ultrasonografia

Cluj Napoca, 31 mai – 2 iunie 2012

Conferința SRUMB va avea loc anul acesta la Cluj Napoca, în perioada 31 mai – 2 iunie. Intenția organizatorilor este aceea de a schimba paradigma manifestării. În ce constau noutățile?

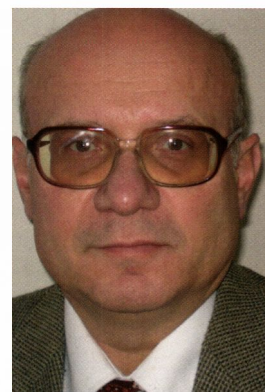
Deși manifestările societății noastre au fost întotdeauna moderne, adaptate la cerințele medicilor practicieni, anul acesta dorim o mai clară separare dintre educație și cercetare. Pentru atingerea acestui obiectiv, ne-am propus organizarea unui număr semnificativ mai mare de cursuri. Acestea vor avea loc în ziua Ia și (parțial) ziua a IIa și se vor adresa principalelor domenii în care ecografia este performantă: terapie intensivă și urgențe, gastroenterologie, patologie vasculară, structuri moi superficiale, ginecologie și obstetrică, nefro-urologie. Dorința noastră este aceea de a conferi un caracter practic și interactiv fiecărui curs. Vom profita de sălile generoase ale Hotelului Grand Hotel Italia, care permit organizarea de sesiuni demonstrative cu echipamentele cele mai noi. Având partener Universitatea de Medicină și Farmacie "Iuliu Hațieganu" din Cluj Napoca, unul dintre cursuri, cel de ecografie intervențională, va putea beneficia de ateliere practice în cadrul Centrului de Abilități nou înființat, folosind Simulatoare. Un punct special al manifestării îl va constitui cursul adresat studenților la medicină. La fel, am invitat colegi de la facultăți de medicină veterinară pentru a ne arăta domenii de graniță cum ar fi cel

al ecografiei pe animale de companie precum și cel al ecografiei experimentale.

Ziua a IIa și a IIIa vor avea structura clasică. Se va începe cu întâlniri cu experți (selecția temelor se va face de către Dvs. on line), se va continua cu mese rotunde paralele, cu sesiuni de prezentări de cazuri clinice și sesiuni științifice. Va exista o sesiune tradițională a Societății de Radiologie din România. Ca de obicei, se vor premia cele mai bune lucrări științifice orale, postere, prezentări de caz clinic. Vom beneficia de prezența unor personalități din străinătate precum și a unor practicieni de excepție.

Activitățile educaționale vor fi discutate separat printr-o masă rotundă dedicată stadiului actual al formării în ultrasonografie pe nivele, începând de la student, continuând cu medicul rezident din diferite specialități și terminând cu specialiștii care urmează cursuri pentru obținerea competenței. Introducerea ecografiei în formarea studenților ca instrument educațional (în ciclul I) și parte a examenului clinic (în ciclul II) vor fi elementele cheie ale simpozionului educațional.

În final, să nu uităm progresele realizate de ultrasonografie în ultimii ani: ecografie cu contrast, elastografie, ecoendoscopie, ecografie tridimensională, telemedicină etc. Toate acestea vor fi demonstrate de



Prof. Dr. Radu Badea

către firmele producătoare de aparatură care vor participa în număr mare la conferința noastră.

Perioada aleasă, sfârșit de mai, început de iunie este foarte bună. Clujul are un farmec deosebit la început de vară, manifestările științifice se combină armonios cu cele cultural-artistice iar programul social va trebui să "facă față acestor provocări".

Vă așteptăm așadar la Cluj, care în perioada 31 mai – 2 iunie va fi o adevărată "Capitală" a ultrasonografiei în țara noastră.

Prof. Dr. Radu Badea (Cluj Napoca)
Președinte SRUMB

HSUMB Newsletter

Hellenic Society for Ultrasound in Medicine and Biology



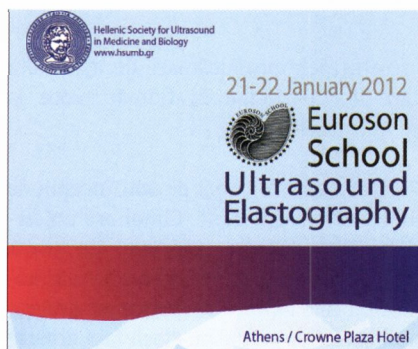
EUROSON SCHOOL

Ελαστογραφία

Το κείμενο αυτό συντάχθηκε το Σάββατο 21/01/2012 στις 23:00 το βράδυ, στο τέλος της πρώτης μέρας του EUROSON SCHOOL που πραγματοποιείται στην Αθήνα στο ξενοδοχείο, Crowne Plaza.

Είναι ήδη εγγεγραμμένοι 212 σύνεδροι εκ των οποίων 28 είναι φοιτητές. Περιμένουμε για αύριο Κυριακή 60 έως 80 νέες εγγραφές. Εγγεγραμμένοι είναι 44 σύνεδροι από άλλες χώρες: Ρουμανία, Κύπρος, Ιταλία, Γαλλία, Τουρκία, Σερβία, Κροατία, Λίβανος, Ισραήλ και Αλβανία.

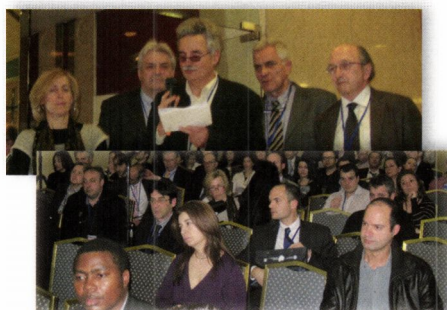
Συνολικός απολογισμός του EUROSON SCHOOL θα πραγματοποιηθεί στα μέσα της επόμενης εβδομάδας.



Η Ελληνική Εταιρεία Μελέτης & Εφαρμογής των Υπερήχων στην Ιατρική & τη Βιολογία οργανώνει το EUROSON SCHOOL στις 21 και 22 Ιανουαρίου, στο ξενοδοχείο Crowne Plaza. Έχουμε σκοπό να εστιάσουμε στις καινοτομίες που έχει να προτείνει η Υπερηχογραφία σήμερα, όπως αυτές εμφανίζονται στις διαφορετικές ιατρικές ειδικότητες που την χρησιμοποιούν.

Παρά τις δύσκολες συνθήκες και τα εμπόδια στην διεκπεραίωση αυτού του επιστημονικού και εκπαιδευτικού στόχου, επιμείναμε στην πραγματοποίηση αυτού του Συνεδρίου και ζητήσαμε την ενεργό παρουσία και συμπαράστασή των μελών της εταιρείας. Η Ελληνική Εταιρεία Υπερηχογραφίας έχει προσκαλέσει στο EUROSON SCHOOL τα περισσότερα επιφανή ονόματα της Υπερηχογραφίας σε όλα της τα διαγνωστικά πεδία και ομιλητές από τα μεγαλύτερα ερευνητικά εργαστήρια στον κόσμο που αναφέρονται

στην Υπερηχογραφική Ελαστογραφία και τη Θεραπευτική Υπερηχογραφία.



Κεντρική θέση στην Ημερίδα έχουν η Ελαστογραφία και η Θεραπευτική Υπερηχογραφία. Σκοπός του EUROSON SCHOOL είναι η εκπαίδευση και πρακτική εξάσκηση των γιατρών που συμμετέχουν ώστε να είναι έτοιμοι για άμεση εφαρμογή των νέων Υπερηχογραφικών μεθόδων. Στο Πρακτικό Μέρος που συνοδεύει κάθε Θεματική Ενότητα του Προγράμματος, έχει δοθεί προτεραιότητα στην παρουσία των Υπερηχογράφων που διαθέτουν τις νέες τεχνολογίες, ειδικευμένων γιατρών στις τεχνικές αυτές και ειδικευμένων στελεχών των εταιρειών που παράγουν τα νέα υπερηχογραφικά μηχανήματα.

Η ευελιξία, η Υπερηχογραφική καθοδήγηση της Ελαστογραφίας και η προσθήκη της νέας Ελαστογραφικής σημειολογίας, ισχυροποιούν την θέση της Υπερηχογραφίας στα διαγνωστικά πρωτόκολλα.

Το EUROSON SCHOOL είναι μια παραγωγική συνάντηση Ιατρών, Φυσικών, Βιο-ιατρικών μηχανικών, που συνθέτουν τη γνώση και την εμπειρία τους στις καινοτομίες της Υπερηχογραφίας.

Το τελικό Πρόγραμμα του Συνεδρίου έχει αναρτηθεί στον ηλεκτρονικό μας ιστότοπο www.hsumb.gr και στο ιστότοπο της Ευρωπαϊκής Εταιρείας Υπερήχων www.efsumb.org.

EUROSON SCHOOL

At the end of the first day of the EUROSON SCHOOL we have already register 212 participants, 28 of them are students. We are waiting for tomorrow Sunday 60 to 80 new registrations. 44 of the participants are from other countries: Romania, Cyprus, Italy, France, Turkey, Serbia, Croatia, Moldavia, Lebanon, Israel and Albania."

The Hellenic Society for Ultrasound in Medicine and Biology organizes a EUROSON SCHOOL entitled Ultrasound Elastography. Aim of the Conference is to summarize today's Ultrasound Elastography and Therapeutic Ultrasound data, how they are applied in all organs of the body and how they are used from doctors of all specialties.

In these difficult circumstances the Board of Directors of the Greek Society of Ultrasound and the Organizing Committee of the EUROSON SCHOOL in co-operation with the European Society of Ultrasound (EFSUMB) persisted in the organization of this Congress. The Greek Society of Ultrasound has invited in the EUROSON SCHOOL most of the prominent scientists of Ultrasound in every diagnostic field and speakers from the biggest labs of the world which specialize in Ultrasound Elastography and Therapeutic Ultrasound.

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Imprint

Ultraschall in der Medizin/European Journal of Ultrasound (Ultraschall in Med)

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Publishers

Georg Thieme Verlag KG
Rüdigerstraße 14, 70469 Stuttgart or
P.O. Box 30 11 20, 70451 Stuttgart
phone +49-711-8931-0
fax +49-711-8931-298
www.thieme.com
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Rüdigerstraße 14, 70469 Stuttgart and
P.O. Box 30 08 80, 70448 Stuttgart
phone +49-711-8931-469
fax +49-711-8931-569
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Printed in Germany

AZ Druck und Datentechnik, Kempten

Typesetting

Reemers Publishing Services GmbH, Krefeld

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phone +49-711-8931-277
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General information

Ultraschall in der Medizin/European Journal of Ultrasound, ISSN 0172-4614, is published in 6 issues per year. Subscribers are asked to inform the publisher immediately in case of address changes in order to ensure correct delivery of the journal. All subscription orders are entered for the calendar year. The rate of subscription is invoiced in advance at the end of the year for the following year and becomes due for payment for the full calendar year. Subscriptions can be started anytime. Subscriptions are automatically extended each year unless notice of cancellation is received from the subscriber prior to September 30 of each year (applies to Germany, Switzerland, Austria only).

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Subscription rates 2012*	Germany	Europe	Global
Postage & Handling	21,40	31,80	38,60
Personal Subscription Rate	340,00	340,00	340,00
Personal Total	361,40	371,80	378,60

Members of the following societies will receive this journal within their membership: German Society of Ultrasound in Medicine and Biology; Austrian Society of Ultrasound in Medicine and Biology; Swiss Ultrasound Society in Medicine and Biology; Danish Society of Diagnostic Ultrasound; Norwegian Society of Diagnostic Ultrasound in Medicine; Flemish Society of Ultrasound

Single issue: 68,00 Euro

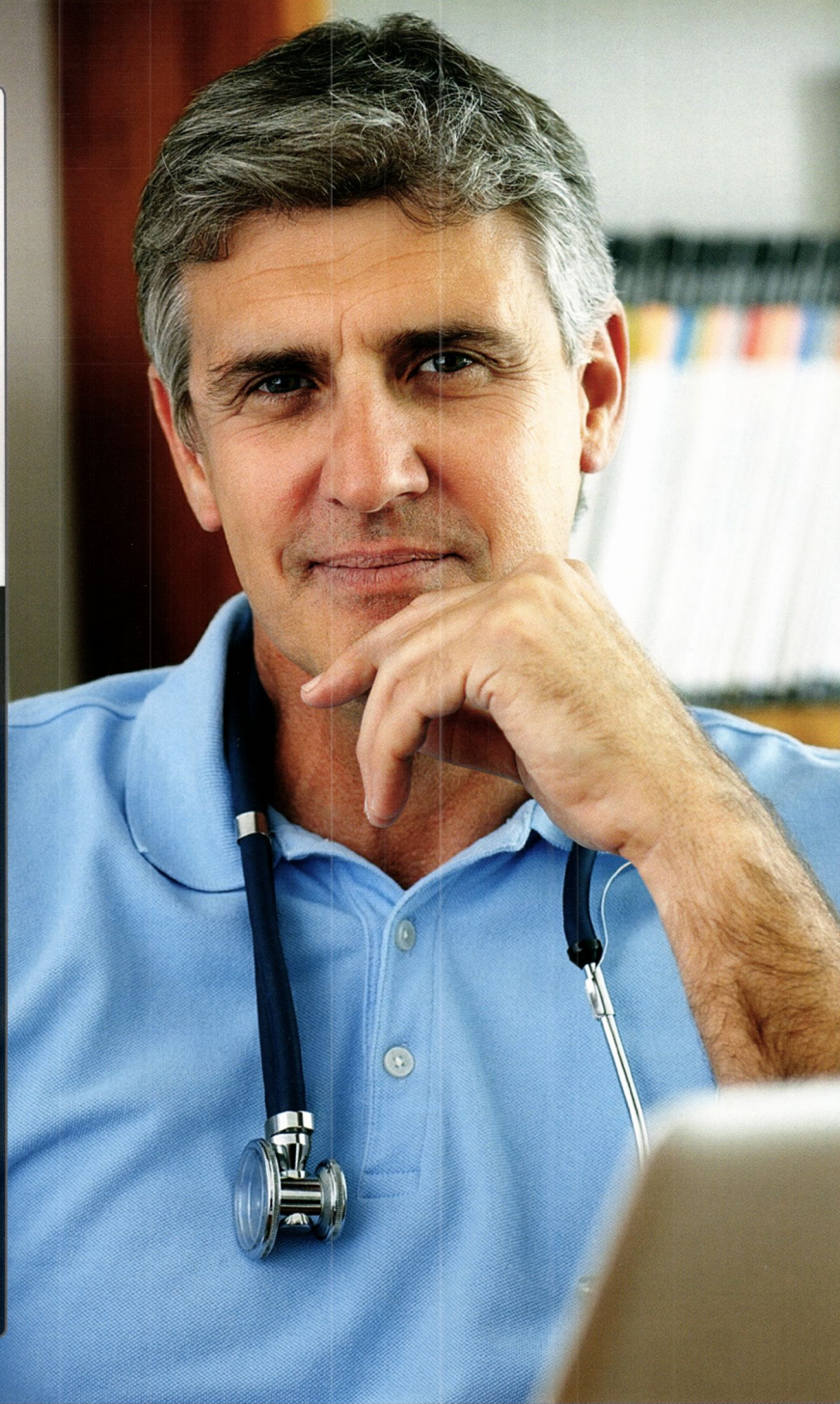
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