EFSUMB Course Book, 2nd Edition

Editor: Christoph F. Dietrich

Interventional Ultrasound

Christian Pállson Nolsøe[1], Torben Lorentzen[2], Bjørn Ole Skjoldbye[3], Michael Bachmann Nielsen[4], Anders Nilsson[5], Luigi Solbiati

[1]Center for Surgical Ultrasound, Department of Surgery, Zealand University Hospital, Denmark. [2]Department of Gastroenterological Surgery, Herlev Hospital, Denmark [3]Department of Radiology, Aleris-Hamlet Hospital, Denmark [4]Department of Radiology, Rigshospitalet, Copenhagen, Denmark. [5]Department of Radiology, Lund University Hospital, Lund, Sweden. [6]Department of Diagnostic Imaging and Interventional Oncologic Radiology, General Hospital of Busto Arsizio, Italy

Corresponding author

Christian Nolsøe MD PhD

Centre for Surgical Ultrasound, Dep of Surgery, Zealand University Hospital, Køge

A/Prof, Copenhagen Academy for Medical Education and Simulation (CAMES)

University of Copenhagen, Denmark

Email: cnolsoe@cnolsoe.dk

Mobile +45 20860880

Introduction

Ultrasound imaging has numerous outstanding advantages recognized by medical professionals throughout a wide range of specialties. However, one of its most versatile features continues to be the capability to visualize, in real time, a handheld needle passing through layers of muscles, fat and organs on its way to a target – decided by you - deep inside the body. Interventional ultrasound as a modality was introduced to clinical medicine in the late sixties and early seventies, and since then the number of applications has been constantly increasing [(1, 2, 3)]. No other imaging modality can compete with ultrasound when it comes to degree of freedom regarding the puncture route and thereby optimize the possibility of placing the needle correctly in the target and at the same time minimizing the risk of complications [(3-7)].

The applications of interventional ultrasound are countless but can be divided into two major groups: Diagnostic and therapeutic intervention. Diagnostic interventions include biopsy of solid tissue, aspiration of fluid and instillation of diagnostic material such as for instance contrast agents through a catheter. Therapeutic interventions comprise drainage of fluid collections like ascites, pleural and pericardial effusions, lymphoceles and abscesses, tubulation of hollow organs as in nephrostomy, gastrostomy and cholecystostomy and tissue ablation by means of heat, frost or radiation.

Regardless of the purpose of the intervention the principles of ultrasound guidance remain the same and can be described as either the “needle guide” or the “free hand” technique. This article describes the basic principles.

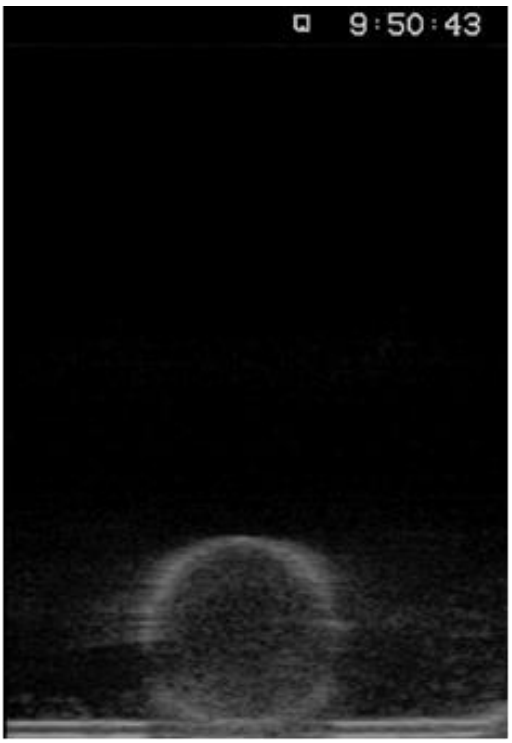
Ultrasound guidance technique

For the inexperienced user it is advisable to practice the technique on a biopsy phantom before doing interventional procedures on patients, even if the first procedures are performed under supervision of an experienced colleague [(8)]. A biopsy phantom can be acquired from manufacturers of ultrasound equipment or it can simply be made of a suspension of gelatin in a small container filled with “biopsy targets” such as grapes or other small organic items [Figure 1].

Figure 1 Biopsy phantom a) Box with gelatin and a grape. Two-dimensional scan-plane of US transducer indicated with grey. b) When transducer is moved to visualize grape, it becomes a perfect biopsy target.

a

b



For a good understanding of the fundamental principle it is furthermore recommended to start doing interventions utilizing a needle guide to familiarize oneself with working the needle with one hand while controlling the transducer - and thereby the scan plane - with the other hand [(9)]. The two hands are not supposed to work independently but on the contrary are to work in a synergy, as were they one piece of equipment. A needle guide is a dedicated device, purpose-made to fit a specific transducer or set of transducers in a way that makes an electronically displayed puncture line on the monitor correspond with the actual path a needle or catheter will take when introduced through the needle canal on the guide [Figure 2].

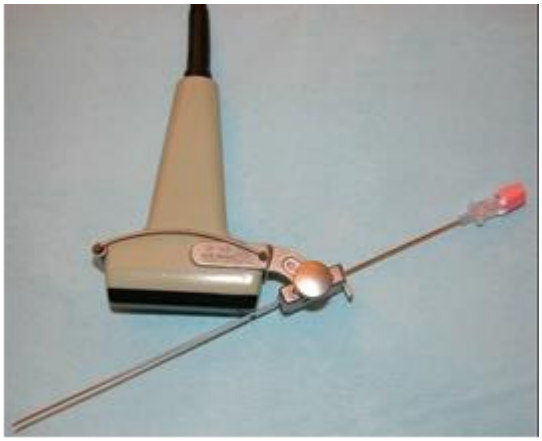
Needle guides are most often disposable utensils. Using a needle guide provides safer control of the needle during insertion, but it is on the cost of lesser flexibility of needle manipulation and limited degree of freedom regarding puncture direction. The transducer produces two-dimensional images of the scanned object. The need to consider the third dimension, i.e. the orthogonal plane, is eliminated, as the guide will keep the needle in the scan plane. The transducer is moved over the area of interest until the scan sector traverses the target, which is then visualized on the scan monitor [Figure 2].

Pressing the needle guide button on the scanner displays the puncture line, which appears on the monitor. The transducer is then moved until the puncture line goes through the target which implies that a needle inserted through the attached needle guide will eventually also be able to hit the target. The point where the needle will penetrate the skin is marked and local anesthesia is applied if needed. The needle guide is mounted on the transducer and depending on the size of the device to be inserted a small skin incision may be necessary. The planned intervention can now be performed and if necessary consecutive needle passes can be made through the same incision.

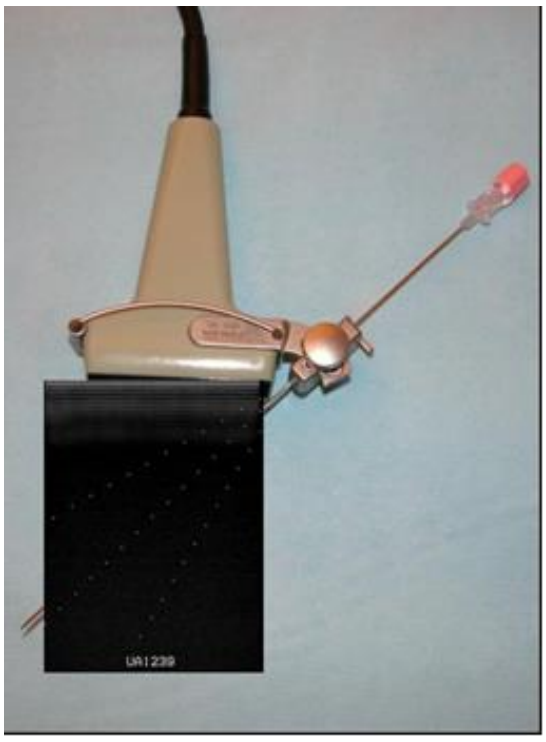
Figure 2 **Needle guide techniques. a) Needle guide attached to transducer and needle inserted. This particular guide has 3 different puncture angels: “horizontal”, “vertical” and “in between”. Image shows “horizontal” angel. b) Ultrasound image displaying all 3-puncture lines is superimposed on picture of transducer to show how the needle follows the predetermined angel. In this case the guide is set to the “in between” angel. c) Ultrasound image of biopsy phantom**

with grape. None of the 3 possible needle paths goes through the target. d) Ultrasound image illustrating that transducer has been moved to allow a needle to be inserted through puncture line "vertical" to hit the target.

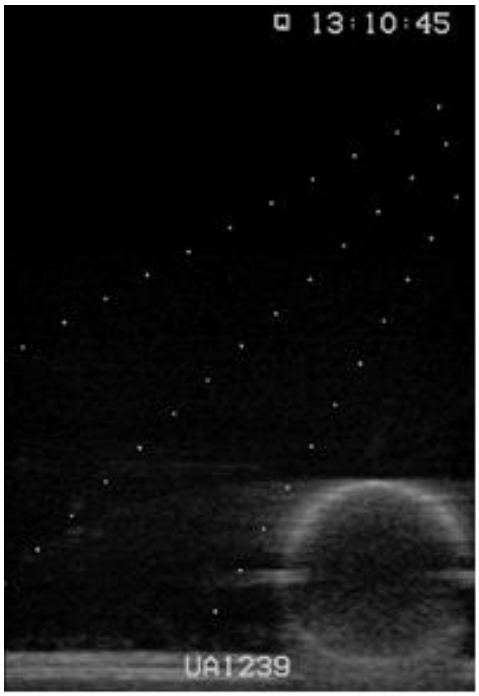
a



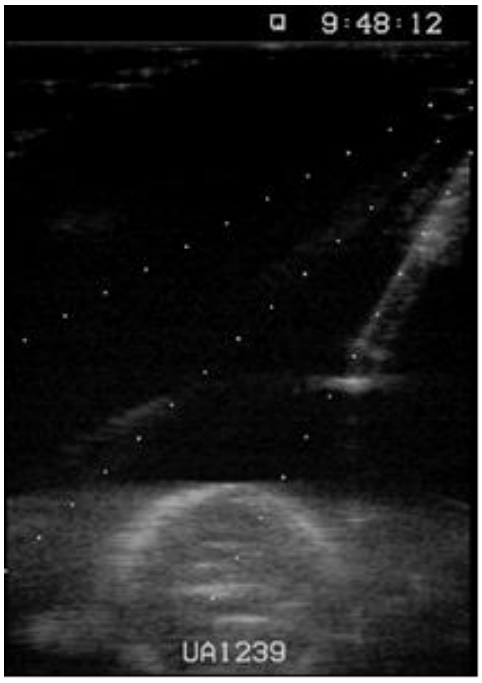
b



c



d



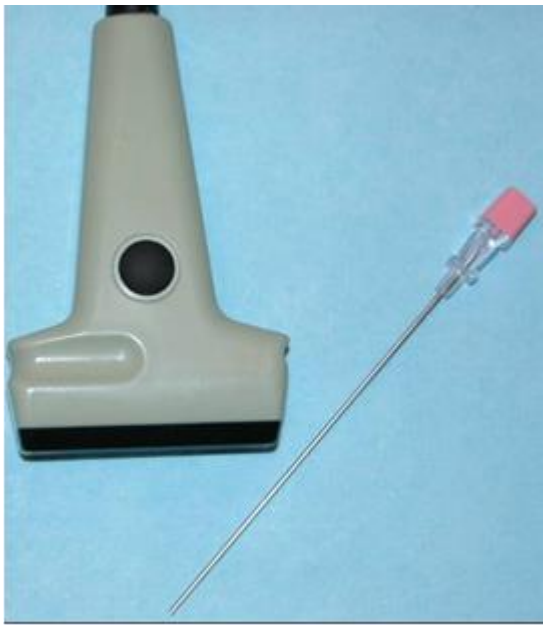
With the “free hand” technique there is no physical connection between needle and transducer and thus no limitations exist regarding point of needle insertion or angel of puncture. There is no puncture line on the monitor and the needle may be inserted from any direction parallel or perpendicular to the scanning plane, whichever solution is most suitable according to the situation at hand [Figure 3]. However, only that particular part of the

needle, which is in the scan plane, can be seen on the monitor. This implies that usually the entire needle shaft should be visualized on the ultrasound image if the needle is inserted from the end of the transducer parallel to the scan plan, whereas, with a needle insertion from the side of the transducer perpendicular to the scan plane the needle is only seen as a single or double dot at the point where it traverses the scan plane. This makes it technically more delicate - and sometimes difficult - to perform a perpendicular “free hand” procedure. If the full path of the needle is not visualized care should be taken that the needle does not traverse any structures that may cause complications.

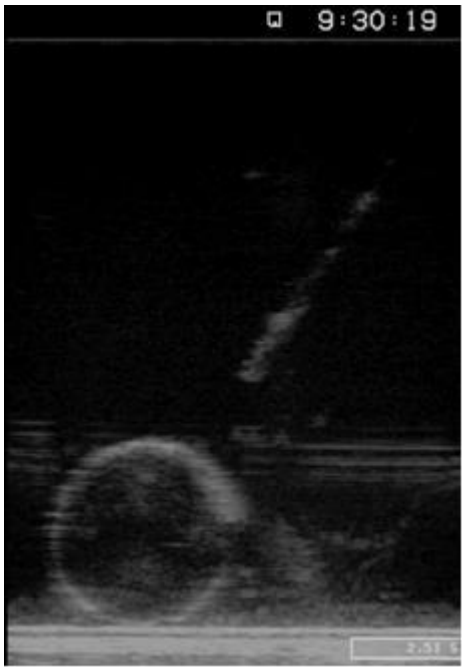
Some interventionists will speak strongly in favor of either the “free hand” or the “needle guide” technique and disregard the other. In our opinion this is a wrong attitude. Both the “needle guide” and the “free hand“ techniques are excellent tools but like everything else in life also both have their advantages and drawbacks. When performing biopsy of a small lesion seated deep in the liver a needle guide is the obvious choice but if the target is a large superficial lesion the “free hand” technique may be just as safe and in addition quicker to use. If the lesion is not only superficial but also small and furthermore placed in a region difficult to access with full contact between transducer and skin – e.g., a lymph node in the supraclavicular region – the free hand technique may be the only option (physically there may not be room for the needle guide or it may be impossible to make the puncture line go through the lesion). Nephrostomy with Seldinger technique, on the other hand, is an example where the needle guide may be useful also for supporting the needle during guide wire insertion. Thus, generally speaking, the two techniques should not be looked on as conflicting with each other but rather as potential alternatives depending on the situation at hand.

Figure 3 **Free hand technique. a) Oblique needle insertion in the correct scanning plane. c) Ultrasound image of biopsy phantom with needle on its way towards grape. Entire needle shaft visualized. b) Oblique needle insertion perpendicular to scanning plane. d) Ultrasound image of grape in puncture phantom with needle tip inside grape. Notice that needle is only visualized as a white dot when it traverses the scanning plane, and one must be sure this dot does represent the needle tip before biopsy is taken.**

a

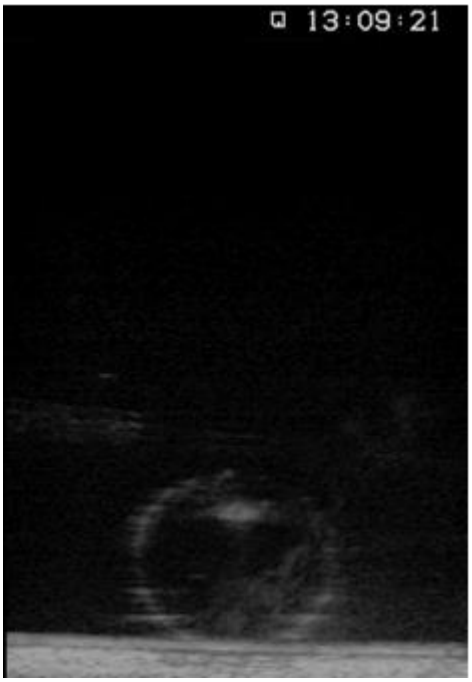


b



c

d



Patient preparation and information

Literature on interventional ultrasound traditionally distinguishes relatively sharply between fine needle and coarse needle interventions with respect to preparation and follow-up of the patient undergoing a procedure. Our knowledge of complications arising from interventional

ultrasound is built on this distinction. The reasons for this may not be evidence based medical practice, but since most of the data accumulated till now relates to this somewhat arbitrary definition so should medical personnel, at least until substantial new evidence is published.

A fine needle is defined as a needle with an outer diameter less than 1 mm and in consequence of this any needle with a diameter equal to or more than 1 mm is defined as a coarse needle.

Information to the patient prior to an interventional procedure as well as preparation and follow up depends on the size of the needle and the nature of the procedure i.e., if it is a simple fine needle aspiration or a case of RF ablation. Specific guidelines for every case cannot be given but below we will give some of the recommendations we have used for a number of years. There may be minor differences between hospitals in the same region and actually the guidelines in different countries could differ substantially from each other, and thus also from those referred to herein. One should always follow the guidelines adopted by the employing institution or national society, or have the guidelines changed before practicing any differences (10). International guidelines and recommendations on interventional ultrasound (including patient preparation and coagulation status) have recently been published [10] and can also be found on some scientific society webpages e.g. www.efsumb.org and www.sirweb.org

In most institutions in Scandinavia, as a general rule, a fine needle biopsy - whether it is a fine needle aspiration biopsy (FNAB) for cytological evaluation or a fine needle core biopsy (FNCB) for histological evaluation - is done without requiring any biochemically tests or having blood available for transfusion. The patient need not be fasting, and post-procedural observation is not required, which implies that the procedure can be done on an outpatient basis. Pre-medication is not required, and the biopsy may be done in local anesthesia or perhaps even without anesthesia in the case of a simple FNAB with one or two needle passes. The patient is informed orally or in writing in accordance with medical legislation about the nature of the procedure and the possible discomfort related to it i.e. a needle is inserted through the skin into the lesion, which may or may not cause minor pain. Importantly, the patient is also informed of the potential risk of complications and how to react in case of unexpected symptoms.

Patients with known coagulation disorders, patients suspected of having a higher risk of bleeding or other conditions predisposing to complications require more restrictive guidelines. This category of patients, aside from coagulative disease, includes patients on anticoagulative medication and chemotherapy, patients with large liver metastases or cholestasis and other causes for liver malfunction. In our institutions the guidelines in such cases for a long time has been: In-hospital patients, fasting for 6 hours, lab tests on coagulative system less than 3 days old with INR < 1.5 and thrombocyte counts > 40,000 per microliter and 6 hours post-procedural observation, but we are aware that a variation of the these rules are used and none of the recommendations appear to be evidence based.

If these laboratory criteria are not fulfilled and the procedure is deemed critical to the patients care, we suggest the administration of 2 portions of thrombocytes or freshly frozen plasma to correct the coagulation parameter in question. The 2 portions should be administered as one before, and one during the procedure.

For the sake of simplicity these recommendations could also apply to patients undergoing coarse needle biopsy (CNB) or procedures requiring the use of large catheters or other utensils.

In a guideline for liver biopsy (whether image guided or not) it was recommended that the prothrombin time (or INR) and platelet count should be checked prior to the biopsy (preferably within 24 hours), but the current data gave no clear consensus as to exact values of the laboratory data at which the biopsy should not be performed [(11)]. An increasing number of liver biopsies for diffuse liver disease now seem to be performed guided by ultrasound [(12, 13)]. Whether biopsy should be performed in in-patients or out-patient, and which type of needle should be used is on on-going debate in the literature [(14-16)]. An out-patient set-up with 18 g coarse needle biopsy in liver and other abdominal organs has been published and reported to be safe [(17)] This implies keeping the patient in the ambulatory for observation 1 hour post biopsy and then performing a FAST scan to rule out bleeding. If no indications of complications the patient is dismissed with written instructions and contact information for the on-call surgeon.

Most procedures can be performed in local anesthesia and without sedation. Some patients may be so nervous that sedation or even general anesthesia is required. Prolonged or complicated cases like for instance most RF ablations are best carried out under some sort of

general anesthesia or conscious sedation because the patient has to lie still in the same position for a long time.

Complications

According to the available literature of large surveys and institutional studies the overall risk of major complications, defined as those complications inducing a significant worsening of the clinical condition and/or requiring substantial care (e. g., blood transfusion, resuscitation, surgery) with delayed hospital discharge or renewed hospitalization, is between 0.05% to 0.4% [(18-20)].

For abdominal biopsies the mortality rates range from 0.001% to 0.038 % in large surveys [(18, 19)], and a large prospective multicenter study of 8172 reported mortality rate of 0.05 % [20]. Cases of death have been reported after biopsy of every abdominal organ, but the highest complication rates and mortality rates are reported after hepatic or pancreatic biopsies [(18)]. In a multicenter study of spleen biopsy, the major complication rate was less than 1% [(21)].

Tumor seeding is a somewhat controversial subject [(22, 23)]. Several casuistic reports have been published which may leave the reader with the impression of a fairly frequent and potentially dangerous complication. Because of the problems with getting complete follow-up the actual number is difficult to determine. In a review of 8 large studies the incidence varied between 0.003% and 0.036% [(19)]. It therefore appears that tumor seeding is rare with a frequency comparable to that of other major complication and this minimal risk obviously must be weighed against the major gain in patient treatment obtained by achieving a biopsy. To avoid seeding, some centers accept the unanimous finding of a suspicious, but resectable tumor in the liver and/or pancreas on 2 different imaging modalities such as CT, PET-CT, MRI and/or CEUS and abstain from biopsy confirmation. If, on the other hand, the diagnosis is still unclear, a multidisciplinary team might ask for a biopsy. In pancreatic tumors, a EUS guided biopsy has been associated with less seeding compared to a percutaneous biopsy (24)

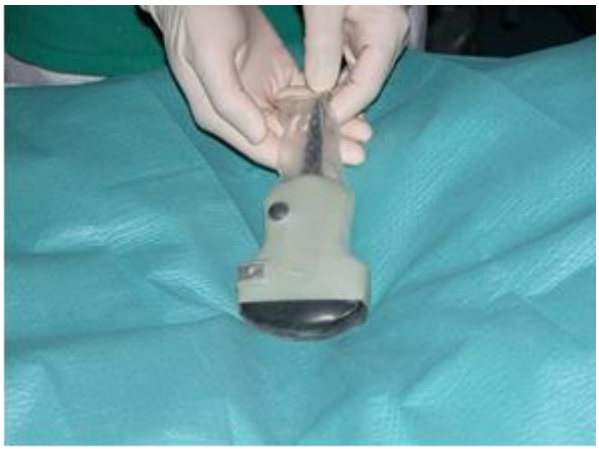
Minor complication such as prolonged pain or discomfort, hematoma formation or minor infection may occur and should be dealt with according to the severity of the symptoms.

Sterility

All interventional procedures should be performed in accordance with the rules of sterility but not all cases need full draping and transducer cover to comply with this concept. A simple FNAB or diagnostic fluid aspiration done with “free hand” technique can be completed without the transducer ever touching the needle. With the transducer in place over the area of interest, the chosen site of skin puncture is cleaned of superfluous gel and sterilized with alcohol. The needle now can be directed to the target without contact with the transducer, but still under full ultrasound guidance. Cases involving multiple needle passes or catheter placement, or cases otherwise more “complicated” and all cases performed with the “needle guide” technique in many institutions require draping of the patient, use of sterile ultrasound gel and sterile transducer surface obtained using a sterile transducer cover. Care should be taken not to do FNAC directly through gel to avoid confusing gel dots on the microscope slide. For procedures involving the use of several utensils a sterile draped working table is needed [Figure 4].

Figure 4 **Sterility. Transducer with sterile cover (a). Transducer soaked in alcohol (b). Working table with sterile draping and utensils (c). Skin disinfection and one piece of sterile draping are sufficient for a free handed FNAB (d). Full draping is recommended for procedures involving several utensils like a Seldinger nephrostomy.**

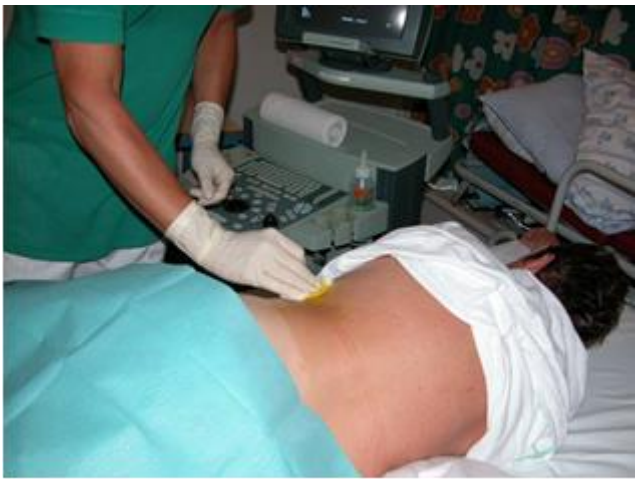
a



b

c

d

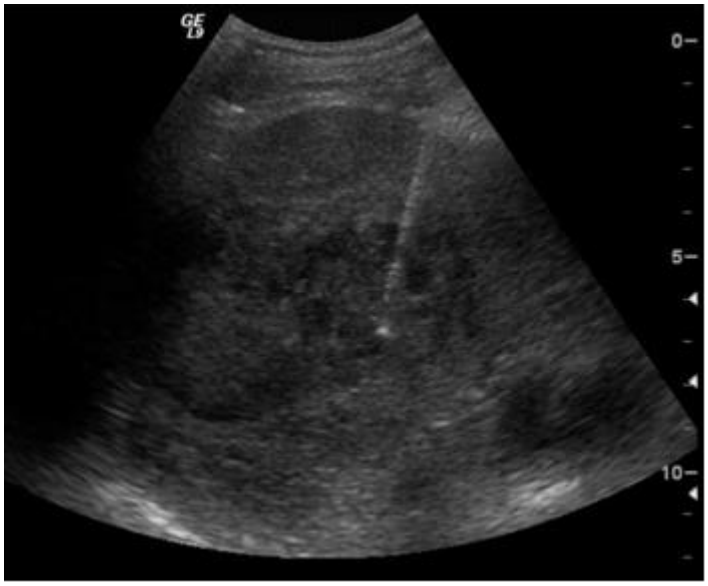


Diagnostic applications

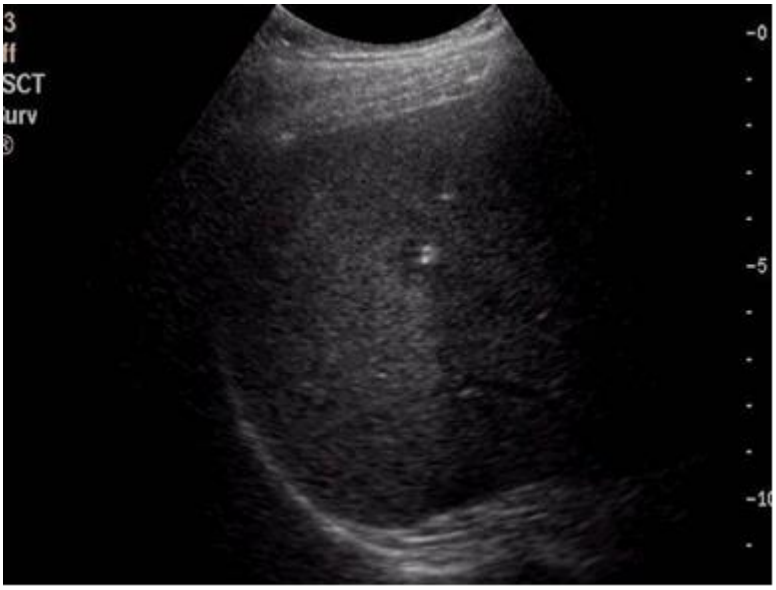
Fine needle biopsy often is indicated when a solid lesion of unknown origin is discovered. If the patient has a history of cancer it usually is sufficient with a FNAB to demonstrate the presence of metastatic deposit. This can be performed with a simple 0.8 mm needle of the same kind used for intramuscular injection. These are available in different lengths and using "free hand" technique and a 10 cm needle most lesions in the upper abdomen can be reached [Figure 5] and a diagnostic aspirate for cytological evaluation obtained with one or two needle passes. The intramuscular needle is mounted on a 10 cc syringe and once the needle tip is seen inside the lesion the needle is gently moved forth and back while at the same time suction is applied by retracting the plunger on the syringe with the thump or index finger. It has, however, been suggested that moving the needle back and forth may increase the amount of blood in the sample and in a situation where an initial aspiration yields too much blood, a technique of holding the needle still but applying suction repeatedly 3 or 4 times may be tried. After tissue sampling the syringe is loosened from the needle, filled with a few cc of air, mounted back on the needle and the air pressed through the needle to allow the aspirate inside the needle to be deposited on a mounting glass for air drying or fixating before further processing by the pathologist.

Figure 5 FNAB with intramuscular needle. a) Large liver metastasis. Good needle monitoring. b) Needle tip visualized in center of 1 cm liver metastasis. Unless patient is very cooperative "needle guide" technique is recommended when target is small and seated deeply.

a



b

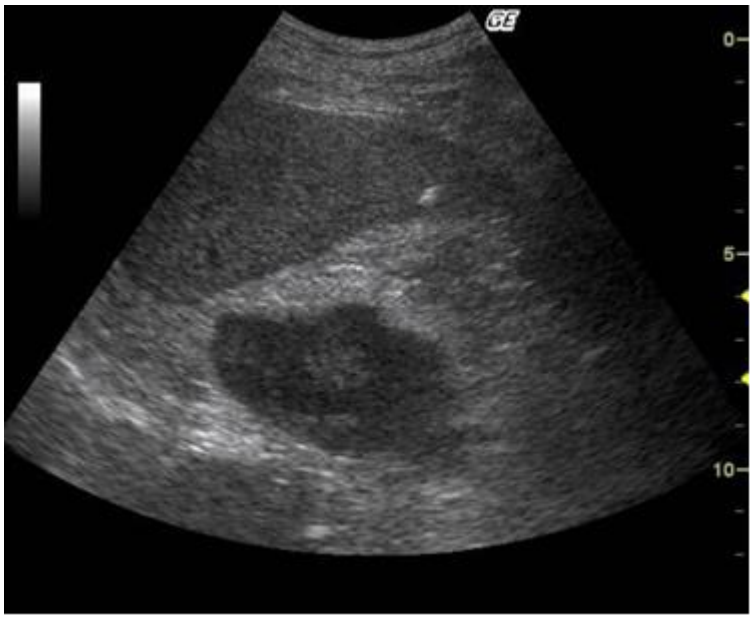


If a needle of greater length is required it may be necessary with an outer needle (e.g., 1.2 mm) to stabilize the thinner biopsy needle during tissue sampling and it is, therefore, also most convenient to use the "needle guide" technique. With the guide mounted on the

transducer a 1.2 mm lumbar needle with stylet in is introduced through the skin, subcutis and abdominal wall muscle layer, but usually not into the organ where the target is seated. The stylet is removed, and the fine needle is introduced through the outer 1.2 mm lumbar needle into the lesion. With this coaxial technique several needle passes including FNCB may be performed through one single skin puncture. Regarding the puncture route a fine needle can safely be inserted through organs overlying the target like the liver, the spleen [(19)] or bowel loops [Figure 6], but it is recommended to check the chosen needle path with color Doppler before the biopsy is actually performed to avoid larger vascular structures [Figure 7]. Also, it should be ensured that the needle does not pass through the liver or spleen too close to the edge to avoid accidently creating a fissure in case the organ moves due to the patient breathing during the procedure.

Figure 6 Puncture route. Fine needle biopsy can safely be obtained through overlying organs as in this case of a "free hand" trans-splenic FNAB from an adrenal mass. a) Needle inserted through spleen in safe distance from the edge with tip just outside tumor. b) Needle tip visualized inside tumor ready for aspiration

a



b

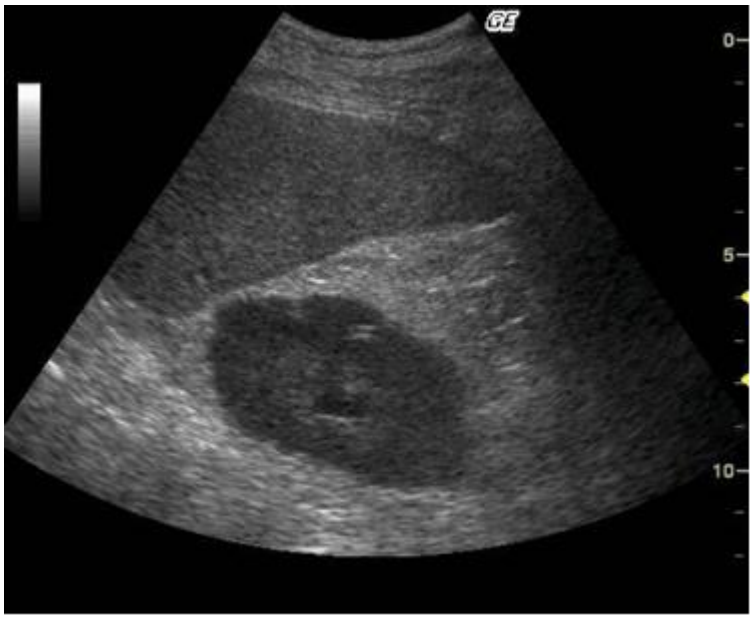
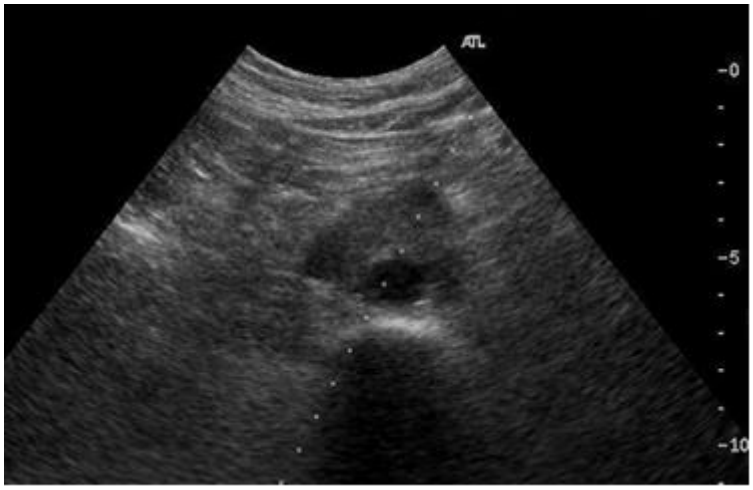
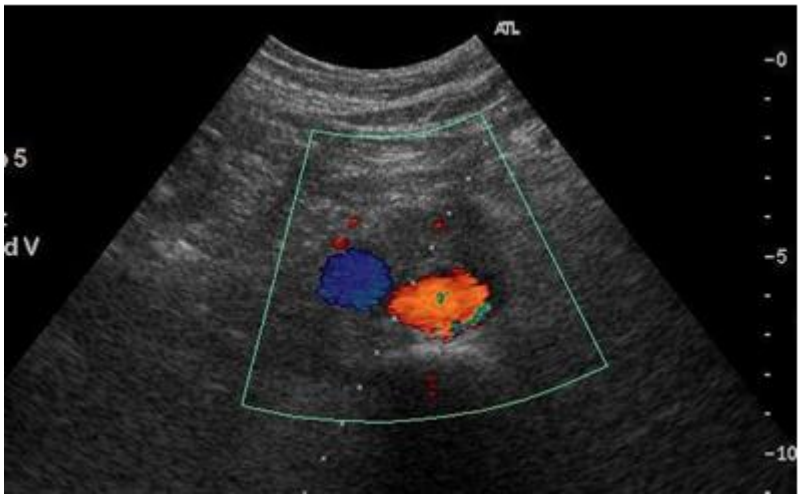


Figure 7 **Color Doppler may help to differentiate a solid mass from nearby vascular structures. a) Retroperitoneal lymph nodes. b) Aorta and IVC are easily identified with color Doppler. A biopsy with "needle guide" technique and puncture line can be performed with the color box on.**

a



b



In case the lesion is extraordinary deep seated the 0.6 mm needle may not be long enough because the outer needle “takes up” 10 cm of the fine needle length and one may be forced to introduce the outer needle into the organ that houses the target. With this scenario it is mandatory the stylet is put back in the outer lumbar needle and the now “loaded” lumbar needle introduced several cm into the organ in order to avoid scratching the capsule of the organ and thereby causing risk of major bleeding. Some institutions however prefer using fine needle and biopsy guidance device regardless of the depth of the target and by performing a quick insertion the problem of needle bending can be negligible.

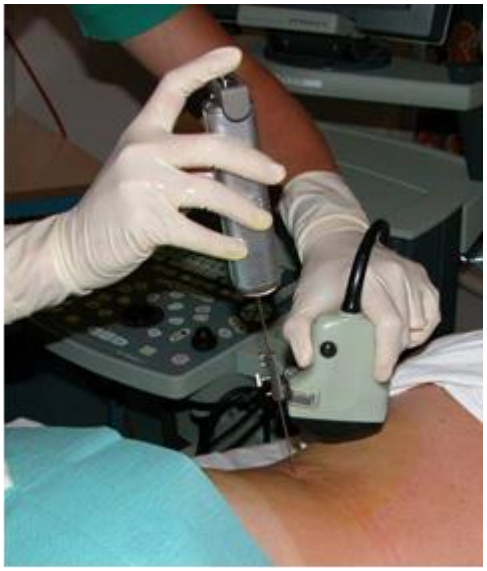
If the patient does not have a history of a malignancy it is always recommended to include both FNCB and FNAC. A FNCB results in a regular tissue core that can be processed with special staining methods or immunohistological techniques which may be of great help in the search for the primary cancer or actually provide the exact organ diagnosis. A FNAC samples from a greater volume when the needle is moved forth and back during aspiration and therefore may have a higher retrieval rate than a core biopsy. The combination of the two thus is a powerful match. Local expertise regarding cytology / histopathology may also influence the choice of method.

Numerous different kinds of core biopsy devices are commercially available. Most are a modification of either the Tru-Cut principle whereby a tissue core is cut with the outer needle and sampled in a slot in the inner needle, or the Menghini principle whereby the tissue core is cut loose with a rotating maneuver and sampled into the needle by suction. Both needle types can be used for several needle passes in the same lesion with the tissue

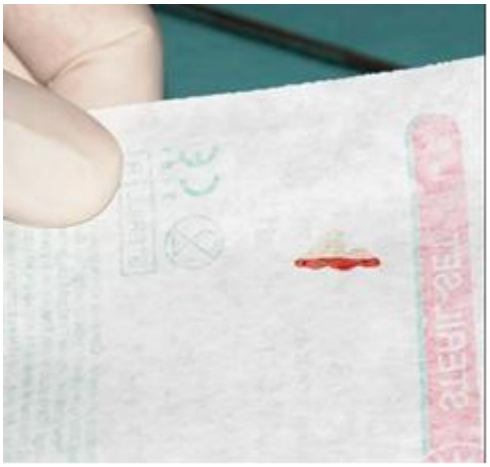
core being deposited on a piece of sterile paper before submerging in a container with fixation fluid [Figure 8].

Figure 8 **Tru-Cut principle and biopsy gun. Top: From left to right shows a) Inner needle with tissue sampling slot is put forward while outer cutting needle is still "on hold". During biopsy both needles move in a split second b) Needle loaded into gun c) Needle tip inserted through skin incision. Picture shows "free hand" procedure with sterile cover on transducer. Bottom: From left to right shows a) Index finger on trigger. "Needle guide" procedure with transducer sterilized by submerging in alcohol b) tissue core deposited on sterile paper c) paper cut with tissue core put in formalin. Needle ready for another biopsy.**

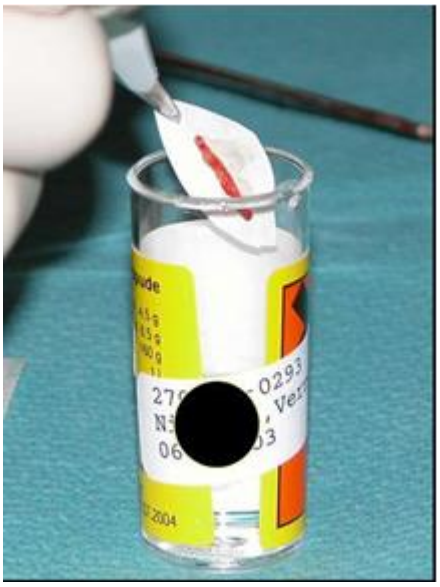
a



b



c



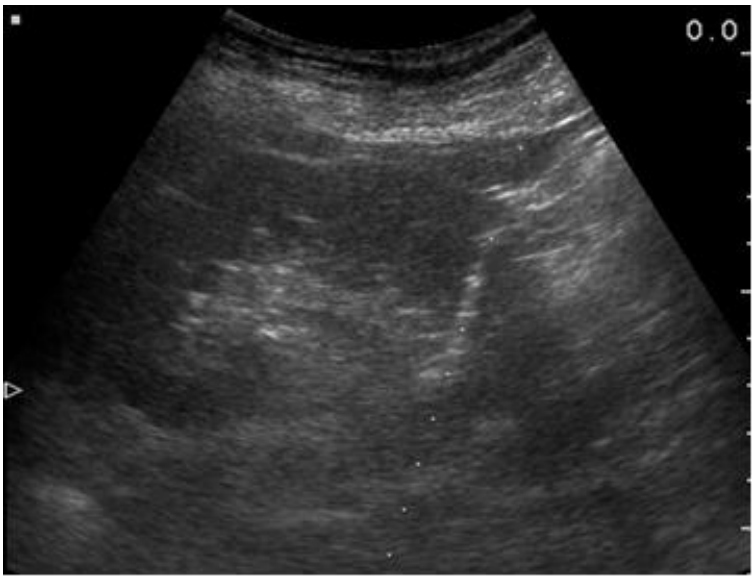
Most core biopsy devices on the market are automatic or semi-automatic and the devices are often referred to as a “biopsy guns” due to the noise they make when sampling the tissue. Guided by ultrasound the needle is inserted to a point just outside the organ capsule, the patient is asked to hold his breath while the needle tip is advanced through the capsule and a few cm into the parenchyma before the “biopsy gun” is “fired” by pressing a trigger on the device [Figure 8]. When activated the inner needle rapidly moves forward and within a fraction of a second the outer needle follows cutting of a tissue core and depositing it in a sampling slot on the inner needle. On some models the size of this sampling slot can be set to different lengths, usually between 1 and 2 cm, by adjusting a control on the device. Changing the length of the sampling slot is paralleled by a change in the length the needle tip advances when fired and thus enables the operator to avoid inadvertent puncture of close nearby structures not supposed to be hit. Other manufactures have approached this need for predetermining the firing length by carrying a selection of needles with fixed different sizes of the sampling slot.

Both reusable and disposable devices are available, and the cost may vary considerably. With the reusable biopsy guns the needles obviously are disposed after use, but the gun itself can be used with different needle sizes usually ranging from fine to coarse needles, and thus the device may be considered having a high degree of versatility.

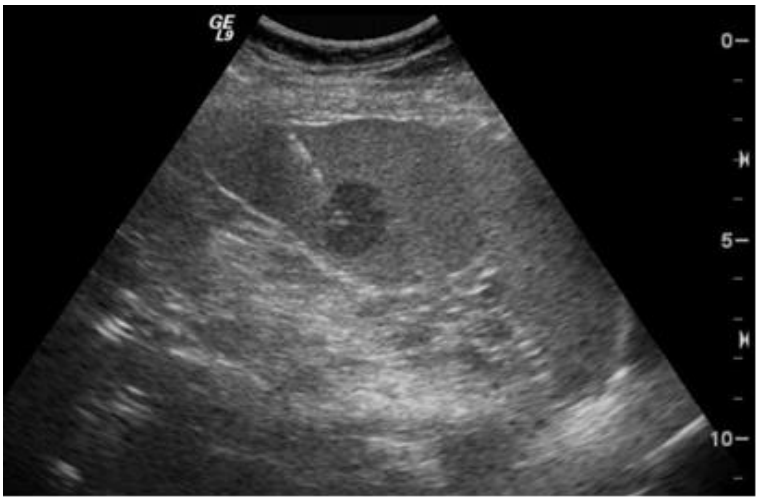
Coarse needle biopsy (CNB) obtains histological material e.g., in the diagnosis of parenchymal liver and kidney disease and in lymphoma [Figure 9]. Usually needles between 1.4 and 2.0 mm are preferred. Intermediary needle size is the term sometimes used to describe the 1.2 mm Tru-Cut type needle that has become increasingly popular. In many institutions it has replaced the use of both FNAB and FNCB, but per definition it is a coarse needle and therefore has to be handled accordingly. The coarse needle biopsy is often preferred in oncologic centers since this type of needle produces a histologic tissue sample usable for advanced techniques such as gen profile and tumor mutation.

Figure 9 Coarse needle biopsy. a) A 2.0 mm kidney core needle biopsy performed with "needle guide" technique. Biopsy correctly taken near the lower pole to minimize risk of bleeding and increase the amount of renal cortex available for microscopy. b) Focal lesion in spleen, lymphoma is suspected. A 1.2 mm core needle biopsy performed with "free hand" technique and good needle visualization.

a



b



Ultrasound guided intra-articular interventions.

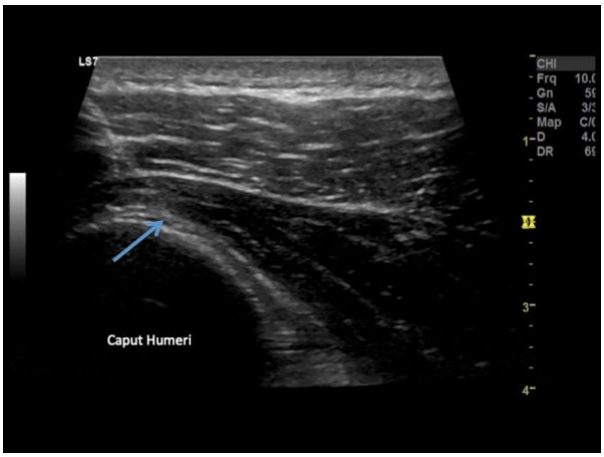
CT- and MR-arthrography requires intraarticular installation of a contrast medium prior to the CT or MR scanning. Ultrasound guided procedures are faster, more precise, provides a higher success rate and less pain score than fluoroscopic-guided techniques (25). The basic principles for US-guided arthrocentesis are identical to other interventional techniques. Most commonly a free hand puncture technique is used - providing the maximum degree of freedom for adjustment during the intra-articular placement of the needle tip, in the relative short distance between the puncture site and the target. Different approaches and choice of puncture needles may have personal or local preferences, especially concerning the gleno-humeral joint, but most important is to ensure the contrast be applied intra-articularily without significant leakage to the surroundings. An approach with an oblique angle to the capsule of the joint, avoiding the labrum, is recommended, both in the hip as well as in the glen-humeral joints. US-guided installation of MR contrast medium with a posterior approach in the gleno-humeral joint is illustrated in Figure 10. The procedure for US-guided steroid injection in joints are similar to the injection of a contrast medium. Ultrasound-guided injections are overall more accurate than landmark-guided injections (26). Interventional procedures in all joints may benefit of ultrasound guidance including the small joins of the fingers (27). A high frequency linear transducer (7-12 MHz), eventually a hockey-stick transducer for small joints, are recommended for intra-articular interventions as well as a Chiba type needle in appropriate length and diameter. A 23 G Chiba needle, 6 cm long, or a 21 G Chiba needle 8 cm long are commonly available standard needles which are

appropriate for free hand US-guided interventions in the hip and shoulder joints. In smaller joints smaller needle length and less diameter should be applied.

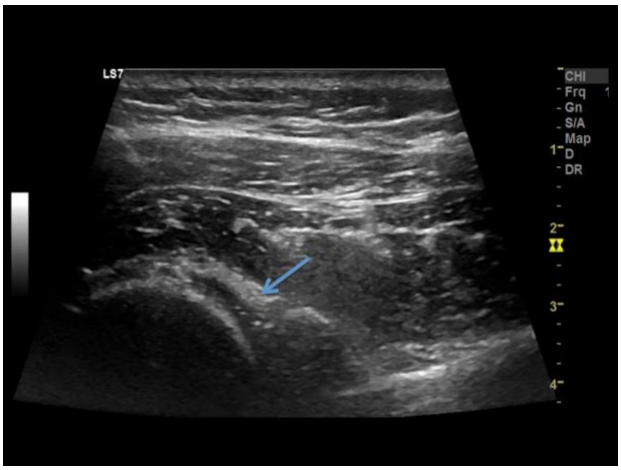
Any contrast medium, steroids, local anaesthetic fluids or other substances to be injected should be known by the operator, and therapeutic effects, risk of side effects and possible complications should be explained to, and accepted by the patient, prior to interventional procedures. The necessary clinical skills, standard emergency gear and antidots should be available for the operator to handle eventually vaso-vagal reactions, acute allergic reactions or cardio-vascular emergency.

Figure 10 US-guided puncture of the gleno-humeral joint. Posterior approach. Needle tip (arrow) seen penetrating the capsule of the joint (a). Intra-articular Fluid (MR-contrast medium) seen filling the left gleno-humeral joint during US-guided arthrocentesis. Labrum (arrow) (b). The gleno-humeral joint with distended synovial capsule containing the anechoic MR-contrast medium before the needle (arrow) is retracted. Posterior approach (c).

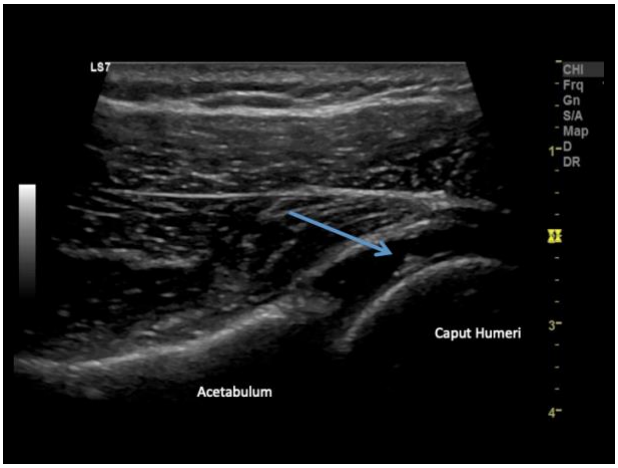
a



b



c



Contrast enhanced ultrasound and biopsy guidance

Lesions in the liver are often better delineated after contrast enhancement and contrast enhancement may also show lesions that were not visible before injection. Even though the effect of contrast enhancement is only temporary - measured in minutes - it is possible to use the contrast-enhanced examination as guidance (28).

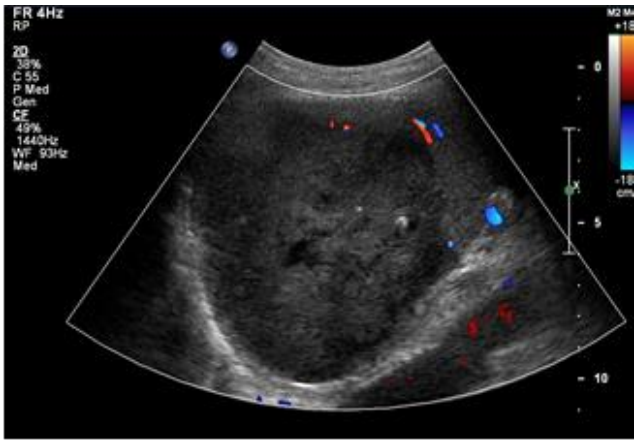
However multiple injections are required. One injection will be necessary to identify and possibly classify the lesion. During this the site for local anesthesia can be marked. When everything is ready for the biopsy including the sterile draping, attachment of steering device for biopsy guidance and skin incision has been made a second injection is given and there will usually be plenty of time to perform several needle passes.

Another useful approach is to use contrast enhancement to avoid the necrotic areas in the tumor and direct your biopsy at the viable (perfused) part of the tumor [Figure 11].

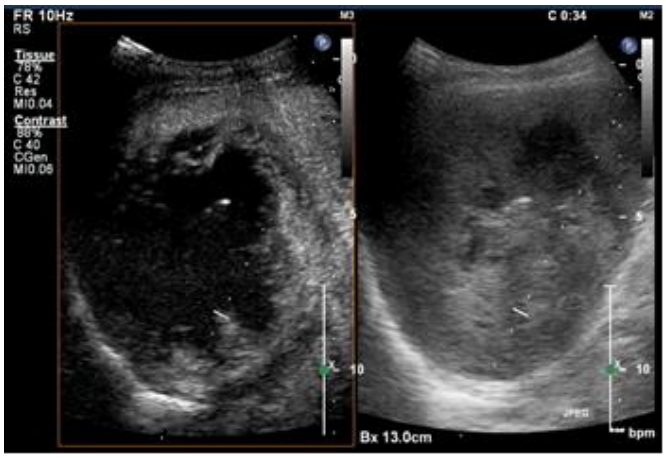
When inserting drainage catheters, the position can be confirmed by injecting contrast agent through the catheter. An example is confirmation of positioning of a nephrostomy catheter. Another example is to inject contrast agent in complicated abscesses to visualize undrained sections and possible fistulas. For this application only a small amount of contrast media is necessary, and it can easily be diluted in saline. Recent publications including the so far sole systematic review of CEUS-guided interventions demonstrate the many benefit of these techniques with ample image documentation (29, 30).

Figure 11 Huge spleen metastasis. Several negative biopsies previous. CEUS guided bx diagnosis mesothelioma. a) Color Doppler demonstrates poorly vascularized tissue. b) In left-sided image CEUS demonstrates a small rim of enhancing and thus viable tissue between the big necrotic center and the surrounding splenic tissue. c) CEUS guided biopsy from the small rim of enhancing tumor tissue gives the diagnosis mesothelioma metastasis.

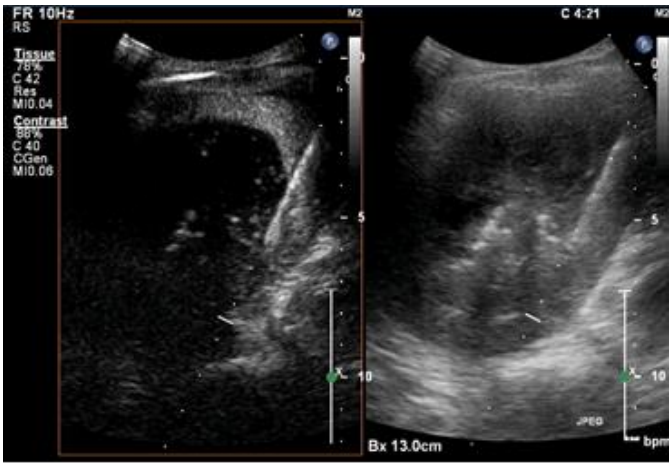
a



b



c



EFSUMB guidelines and interventional ultrasound

EFSUMB - The European Federation of Societies for Ultrasound in Medicine and Biology –has published minimum training recommendations for the practice of medical ultrasound. Three levels of competencies are described for several areas relating to different medical specialties, level 3 being the expert level. In the appendix about gastroenterological ultrasound only simple biopsies (for parenchymal liver disease) are described in level 1, whereas biopsy of focal liver lesions, drainage of fluid collections and tumor ablation are described in relation to level 2 [(31)].

Recently, EFSUMB published guidelines and recommendations of various aspects on interventional ultrasound: www.efsumb.org. We urge you to look at these guidelines and

recommendations since they cover almost all aspects of interventional ultrasound [(10, 32-46)].

Therapeutic applications

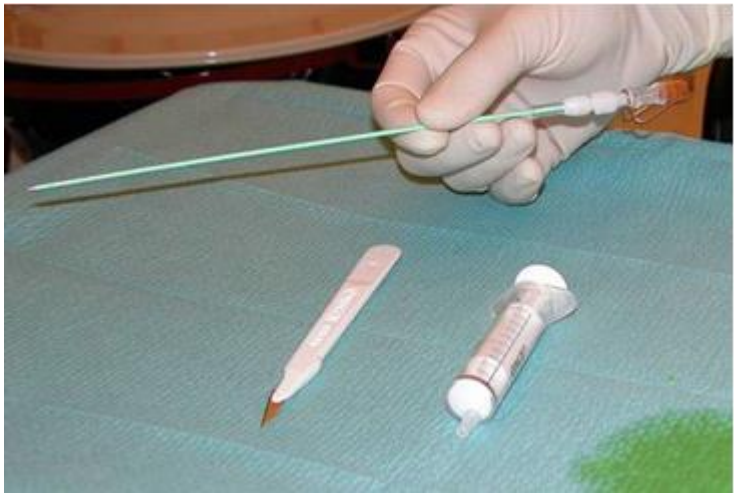
Drainage of fluid collections like ascites and pleural effusion in most cases are easily and safely performed by inserting a one-step catheter under ultrasound guidance. Catheters may be pigtail, have an internal string for internal loop fixation of may use a balloon for internal fixation. The size of one-step catheters, despite the fact that most European countries have adopted the SI units, is still routinely expressed in French (Fr) with the outer diameter indicated by the measure. For ascites and pleural effusions, it usually is sufficient with thin catheters between 5 Fr and 7 Fr and for comparison a 6 Fr catheter has an outer diameter of approximately 2 mm. A one-step catheter consists of an outer non-cutting needle with a trocar stylet for penetration and a catheter pulled over the outer needle. Once the needle tip is seen inside the fluid to be drained, the stylet is withdrawn and, if fluid is coming out freely, the catheter is inserted by gently pushing it forward, while at the same time keeping the needle in a fixed position. If the fluid is not under pressure it may be necessary to use a syringe or a suction system to drain it [Figure 12].

One-step catheters are excellent for drainage but will not penetrate tissue as easily as a lumbar needle and may be difficult to introduce if the tissue is fibrous or for other reasons hard to penetrate. If this problem arises it is possible to convert the procedure to a Seldinger technique using a lumbar needle with the catheter being inserted over a guide wire as the final step. Once correctly in place the catheter should be secured and left in place for several hours to allow the fluid to drain by gravity. If the fluid collection is very small (less than 1,5 cm) it is recommended to use a 1.2 mm lumbar needle for aspiration instead of inserting a catheter [(3)].

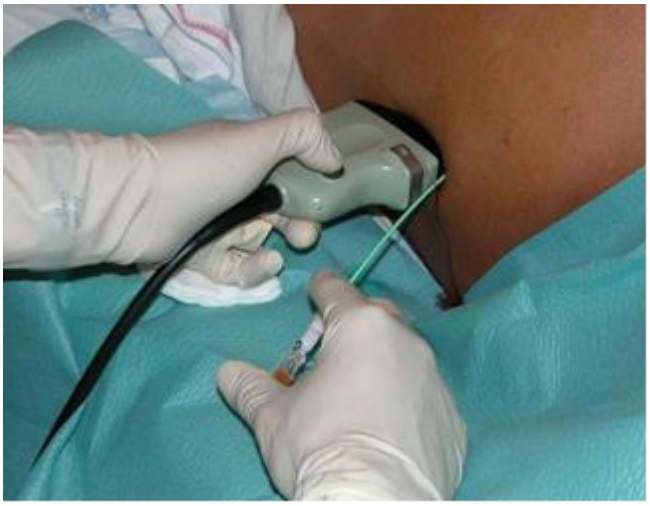
Figure 12 One-step pigtail catheter- ascites drainage. a) One-step device consisting of needle with inner trocar and outer non-cutting shaft with catheter pulled over. Also needed are scalpel for skin incision and syringe for aspiration. b) Procedure done with “free hand” technique. c) When tip of needle is seen

inside fluid on the ultrasound image, the trocar is removed, and aspiration performed with syringe on outer needle to confirm correct position. d) While keeping needle shaft in fixed position with one hand, pigtail catheter is pushed forward and into the fluid collection with the other hand.

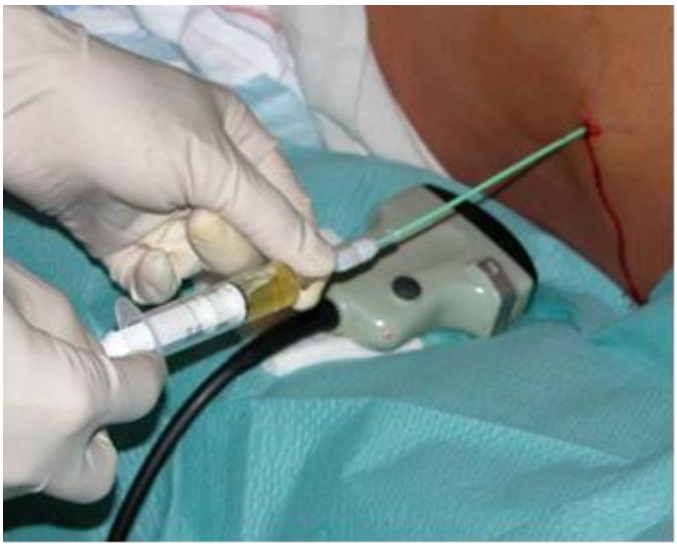
a



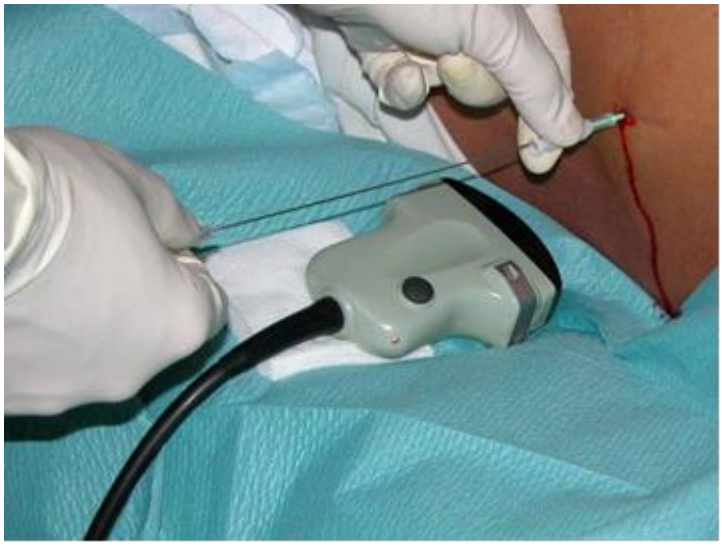
b



c



d

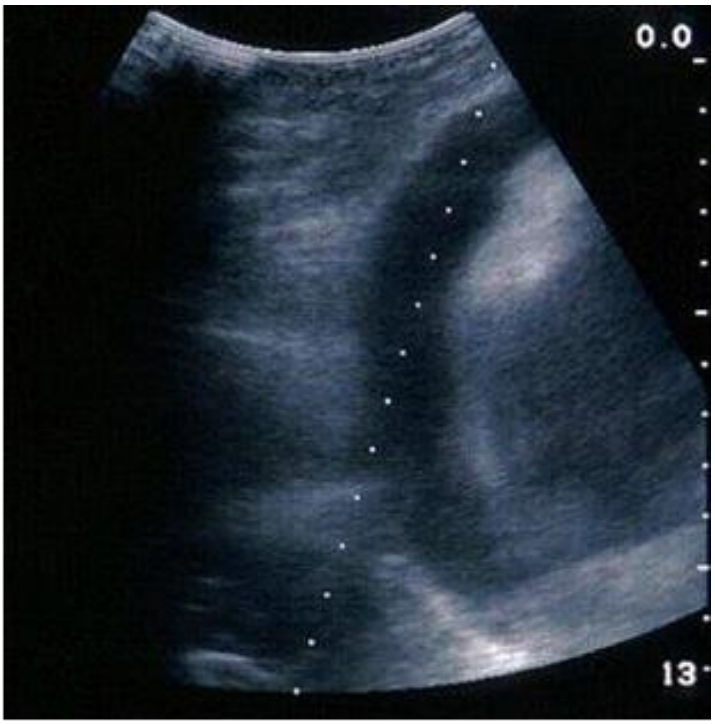


Drainage of pericardial effusion is somewhat more delicate for several reasons. Often the amount of fluid is limited despite severe symptoms and the layer of fluid may not be more than 1-2 cm with the myocardium immediately beneath. The puncture route may be extraordinary hard for the needle to penetrate due to intercostal cartilage or calcifications, and the risk of the needle inadvertently being advanced to far if the hard tissue unexpected gives way, cannot be neglected. Furthermore, the patient may not be able to fully lie down during the procedure due to cardiac constriction symptoms and one may be forced to do the puncture in a somewhat awkward position. For these reasons catheterization of pericardial effusion should as a general rule be performed as a “needle guide” procedure using Seldinger technique. The possible puncture routes may be either subxiphoid or intercostal.

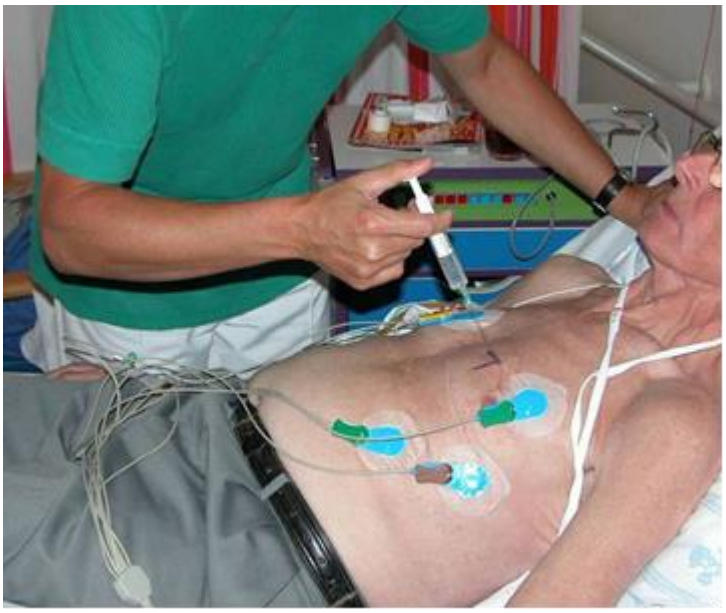
We recommend angulating the needle path in a way that will allow the needle to be inserted parallel to the myocardium to prevent accidental puncturing it if the hard overlying tissue suddenly yields [Figure 13]. In a study of 1127 consecutive ultrasound guided pericardiocenteses a procedural success rate of 97% was found with a total complication rate of 4.7% (major 1.2%; minor 3.5%) [(47)].

Figure 13 Drainage of pericardial effusion. a) Layer of fluid is thin and a puncture route parallel to the myocardium is chosen. b) Patient not able to lie flat on back. Arrhythmia or cardiac arrest may occur during puncture why electrodes are necessary for continuously electro cardiographic monitoring. c) Transducer with needle guide "open" to allow placement and/ or release of needle. d) Needle placed in guide and guide adjusted to secure needle from dropping out but still allowing free up and down movement. e) Needle inserted, inner stylet removed, and guide-wire introduced.

a

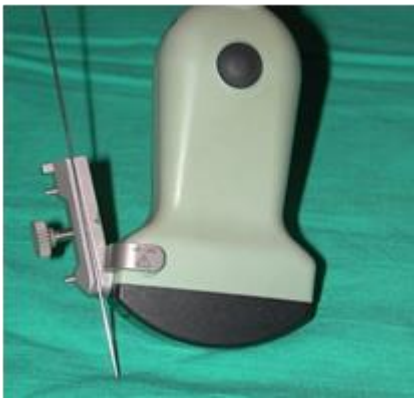


b



c

d

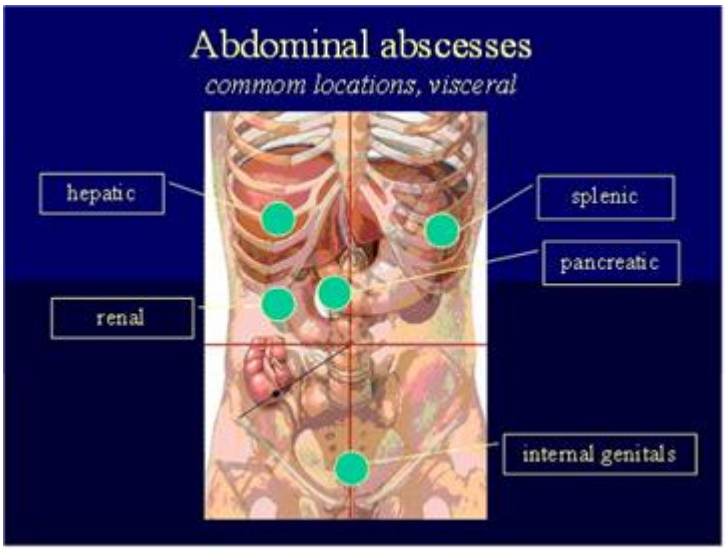


e

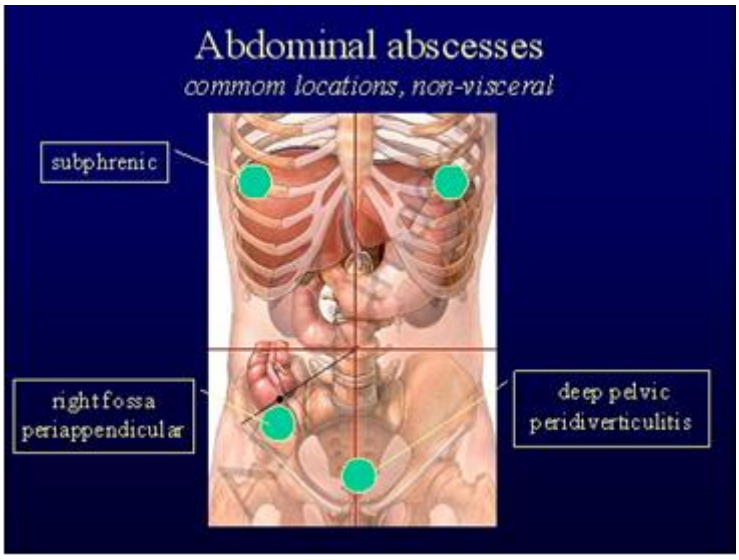
Percutaneous abscess drainage was introduced more than 30 years ago and has since then become the method of choice in abscess treatment [(48, 49)]. An abscess can be defined as a localized collection of pus in a cavity formed by the disintegration of tissue. Pus is a thick whitish-yellow fluid which results from the accumulation of white blood cells, liquified tissue and cellular debris. Most abscesses are formed by invasion of tissues by bacteria, but some are caused by fungi or protozoa or even helminths, and some are sterile. Seventy five % of abdominal abscesses are non-visceral (intra- or retroperitoneal) and 25% are visceral (hepatic, pancreatic, splenic, renal). The most common locations of visceral and non-visceral abscesses are seen on [Figure 14]. There are several factors that predispose to the development of abdominal and extra-abdominal abscesses. These include inflammatory disease (cholecystitis, appendicitis, diverticulitis, pancreatitis, Crohns disease), abdominal surgery, abdominal cancer, trauma (blunt or stab lesion), and immunological deficiency.

Figure 14 Common location of abdominal abscesses a) Abscesses of visceral origin b) Abscesses of non-visceral origin.

a



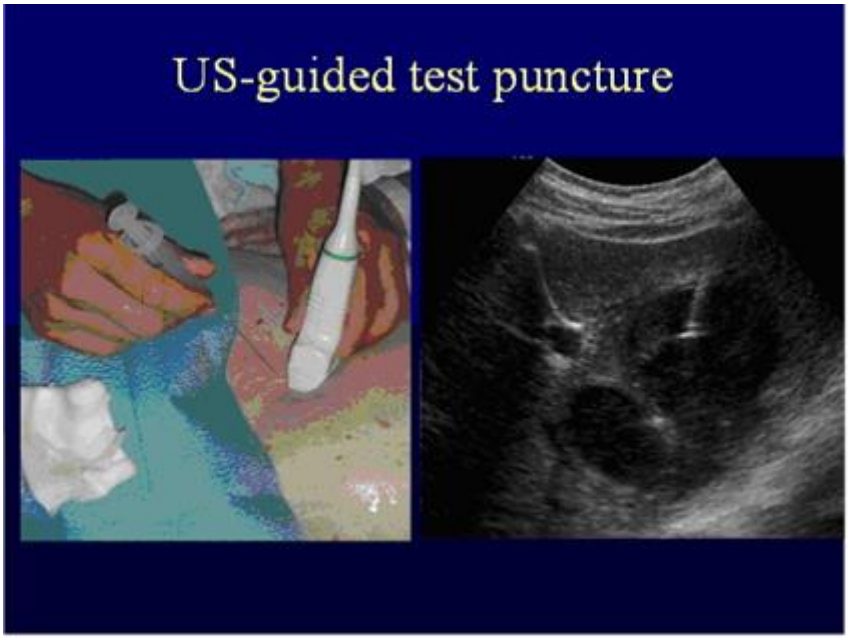
b



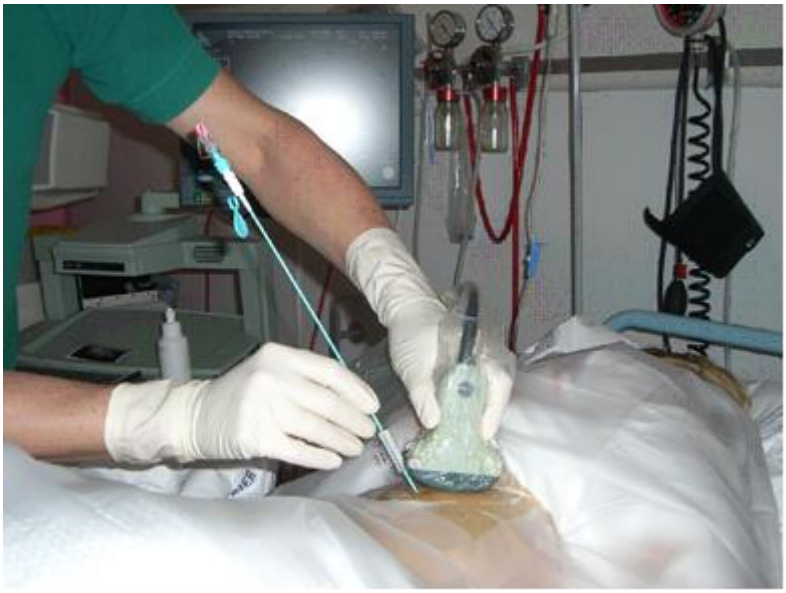
Many abscesses are primarily seen on CT or MRI, however the final diagnosis of an abscess is the test-puncture with a thin needle. Usually one starts with 0.8 mm but if unsuccessful due to thick fluid/pus a thicker needle with a diameter up to 1.2 mm should be used. If pus can be aspirated, the abscess has been successfully diagnosed and a drainage procedure should follow [Figure 15].

Figure 15 a) Test puncture of liver abscess with 0.8 mm needle b) 7 French loop catheter inserted. c) All pus should be aspirated and afterwards irrigation with sterile saline continued till aspirated fluid is clear.

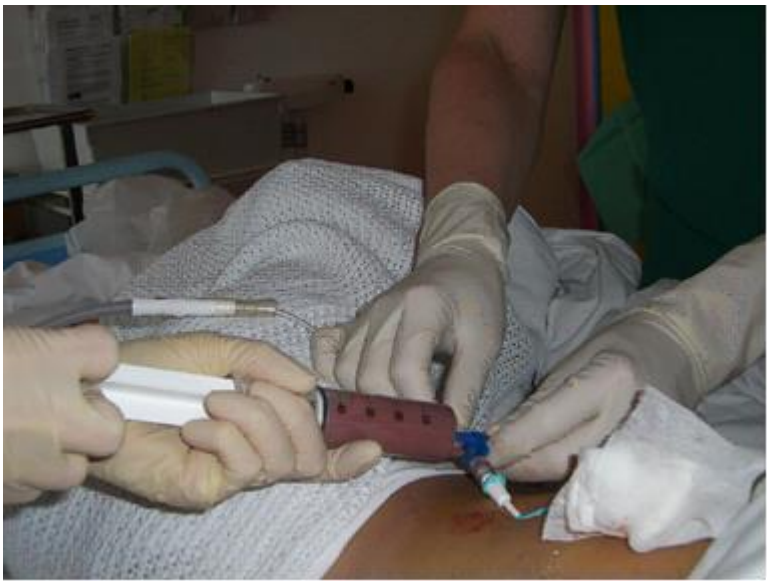
a



b



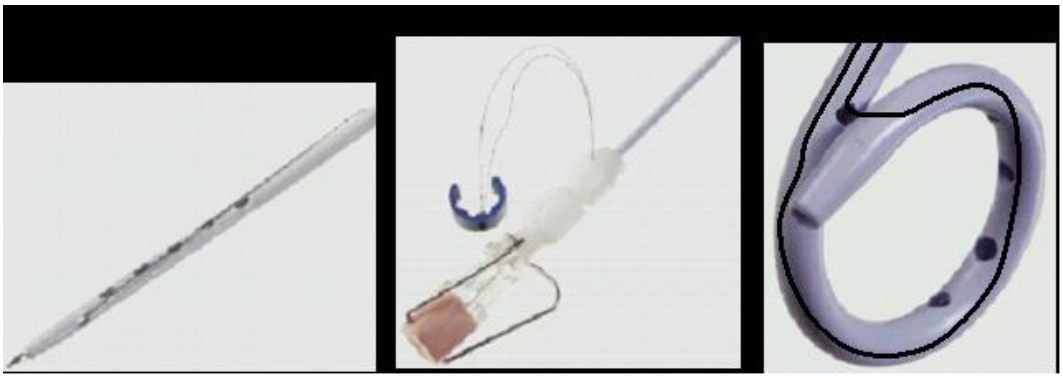
c



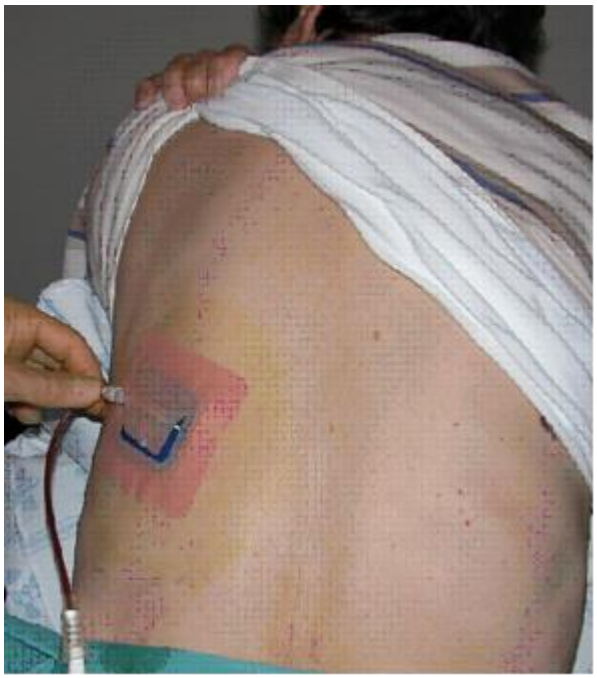
Drainage of an abscess is performed following the same rules as outlined above regarding the ultrasound guidance and the puncture per se. As a general rule an abscess should be treated by inserting a catheter, emptying the pus by suction, and irrigating with sterile saline until the aspirate becomes clear. The procedure of aspirating and irrigating should be repeated 3 times per day till the patient is cured – some abscesses require more frequent irrigation (up to 6 times per day) in case of thick pus and/or septa formation [(3)]. An effective internal catheter fixation (pigtail or balloon or string lock), combined with a thorough external catheter fixation (plaster fixing devices) [Figure 16], can secure the correct catheter position in many days and weeks, if necessary. Routine use of antibiotics is not recommended but should be reserved to patients with severe symptoms and signs of septicemia.

Figure16 Internal and external catheter fixation is important to avoid inadvertent dislodgement. ~~Top~~ a) One example of catheter with internal fixation is the Loop catheter with internal string lock b) External fixation plaster.

a



b

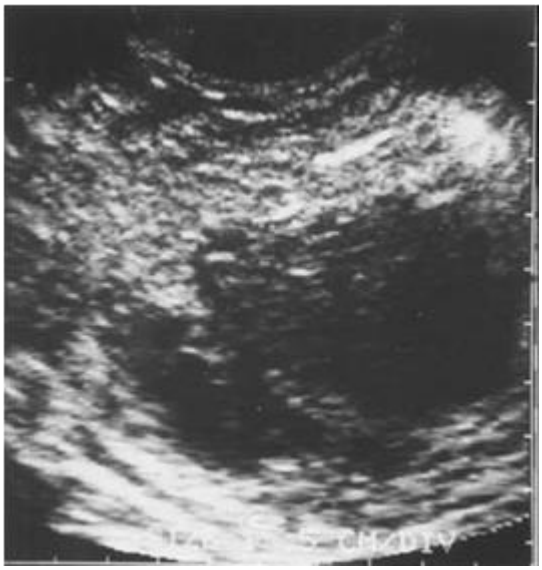


If the abscess is small, i.e., less than 3-4 cm, or if ultrasound scanning cannot rule out overlying bowel loops, the drainage should be performed with a needle by applying the same rules for emptying and irrigation. In case a large abscess is positioned deep to overlying intestines a catheter may be inserted and the aspiration and irrigation performed via this, but the catheter should be withdrawn after the procedure to avoid fistula formation. Follow-up ultrasound scanning should include repeated puncture and drainage if necessary [(3)]. Abscesses located in the lower abdomen including deep pelvic abscesses might be impossible to reach with a percutaneous approach. These abscesses can be treated using a transrectal or a transvaginal access [(50)]. Furthermore, a trans gluteal or a transperineal access can be used in some cases (51). Also abscesses located outside the

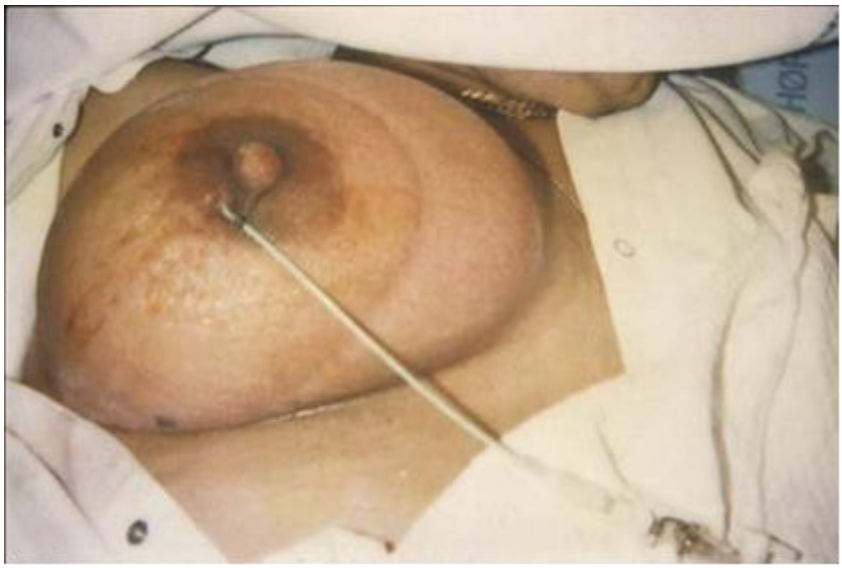
abdominal cavity can be successfully drained with percutaneous US-guided technique. Breast abscesses is one such application [Figure 17] [(52)].

Figure17 Abscess drainage a) Breast abscess with echopoor appearance like most abscesses regardless of organ. b) Drained with pigtail catheter.

a



b



Tubulation of different organs by ultrasonically guided placement of catheters is a well-established application for interventional ultrasound. Cholecystostomy in acute cholecystitis

and short-term nephrostomy in kidneys with marked hydronephrosis can be performed as an ultrasound guided placement of one-step pigtails catheters. In most cases of gastrostomies [(53)], placement of central venous catheters [(54)], nephrostomies on non- or moderately dilated pelvices, the Seldinger technique is preferred due to the limited performance of one-step trocar catheters with regard to the cutting capabilities of the needle, causing deviation from the chosen path, and visualization of the needle tip on ultrasound. Also, these procedures usually involve dilatation of the tract before a catheter can be inserted and thus a guidewire is needed anyway.

Tissue ablation of localized cancer in a variety of organs by means of heat, frost, alcohol or radioactive seeds guided by percutaneous, laparoscopic, endoluminal or endoscopic ultrasound has gained widespread use during the last three decades [(55)].

These techniques are often referred to as minimally invasive therapies but actually differ a lot in their degree of invasiveness as well as with respect to complexity of the equipment, time spent with, and personnel needed for, each procedure and cost related to the treatment.

They range from a simple set up with a needle and a syringe containing a few cc of ethanol used for ablation of hyperparathyroid adenomas to a highly sophisticated scenario where liquid nitrogen under high pressure at a temperature around -200^{o} C is circulated from big tanks into several dedicated needle shaped probes meticulously positioned transperineally in a prostate cancer.

As it can be appreciated each method has its advantages and disadvantages and comparison of the results achieved with the different methods can only be done to a limited degree because the diseases they are used as treatment for are very different.

Anyone with a specific interest in either of these techniques, therefore, is encouraged to search the literature for details.

In general, ethanol has been used for ablation of hepatocellular carcinoma and parathyroid adenoma, brachytherapy mainly for prostate cancer by means of Iodine-125 seeds, cryotherapy for liver metastases, prostate cancer and renal carcinoma and finally, thermal ablation by heat with the use of laser, radiofrequency (RF), microwave or high-intensity focused ultrasound (HIFU) has been used in a range of organs on a variety of indications but, by far mostly in the treatment of colorectal liver metastases.

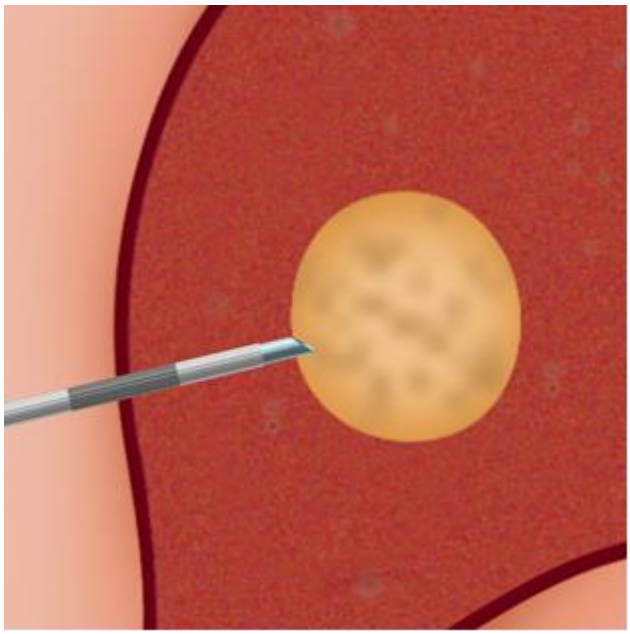
The results of these widespread treatments of course vary considerably but they all have been reported to have some degree of success on selected groups of patients.

One technique, however, seems to be unsurpassed and that is RF ablation. Probably no other ablation technique has experienced even a close increase in popularity measured by the number of articles published and the number of new applications reported.

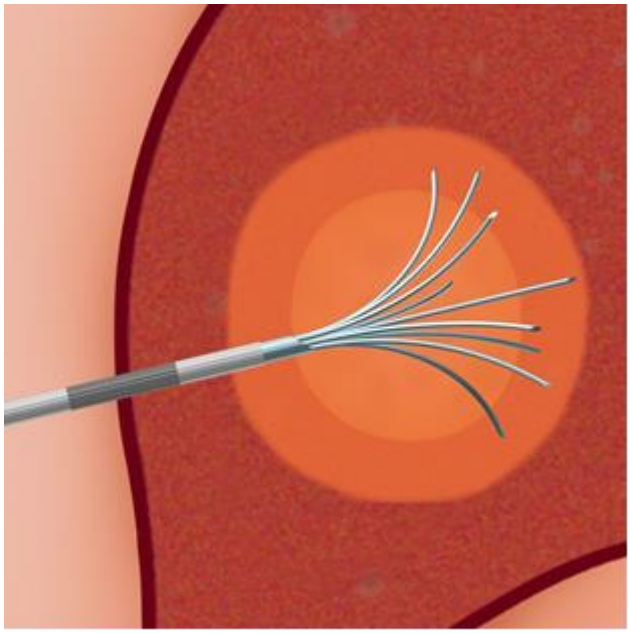
RF equipment dedicated for ablation and with built-in bio-feedback systems are available and despite their high-tech refinements are impressively easy to use. The RF probe is designed like a needle and the procedure resembles any other US-guided intervention where the needle is directed to its target under the guidance of real time scanning [Figure 18]. Once in position, the RF needle has to stay in place for a period of time which is related to the size of the tumor. For each insertion in a definite position, it has been demonstrated that 10-12 minutes are needed to achieve the maximum amount of coagulation necrosis (as an average, 2.5-3.0 cm in axial diameter). If the tumor is larger than 2.5-3.0 cm, more insertions are needed, adequately spaced inside the tumor and therefore the total time for treatment may be much longer. If more tumors (usually up to a maximum of 5-6) are to be ablated, the time spent increases correspondingly, and thus the entire procedure may take 60-90 minutes and necessarily requires that the patient be under general anesthesia.

Figure 18 RF ablation. Several different RF probes are available. Illustrations show deployable type. a) RF needle inserted to margin of metastasis. b) Prongs deployed. Some deliver RF, some measure temperature. c) Liver metastasis with deployed RF needle in. Prongs visible. d) Immediately post RF the metastasis appears hyperechoic.

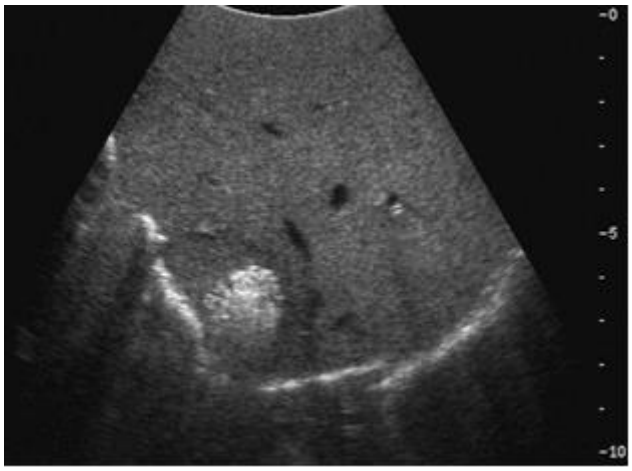
a



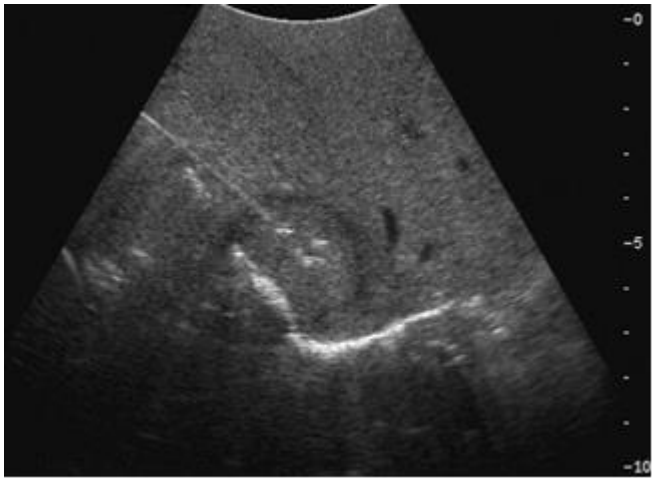
b



c



d



Microwave equipment apparently enabling to overcome some of the limitations of RF ablation have been introduced into clinical practice: with microwaves antennas larger coagulation necrosis volumes can be achieved in shorter time compared to RF and the sink effect due to blood vessels flow (which is a significant limiting factor for RF) is markedly decreased. In addition, if multiple, precisely spaced antennas are simultaneously introduced into the target and activated, ablation volumes with 6-7 cm diameter can be obtained in only 8-10 minutes. If follow-up indicates the presence of residual viable metastatic tissue a repeated RF ablation can be done within a short time, which is often not possible with surgery.

Percutaneous radiofrequency (RF) thermal ablation is an established therapeutic option for hepatocellular carcinomas and liver metastases, which may obviate the need for a major surgery and result in prolonged survival and chance for cure.

Treatment strategies for hepatocellular carcinoma (HCC) are strictly related to the stage of the neoplastic disease and of the underlying chronic liver disease.

For early HCCs, surgical resection, when feasible, is considered the treatment of choice in patients who are not candidates for liver transplantation. This thought is based on the oncological assumption that resection is the most suitable option for obtaining the complete tumor ablation including a layer of tissue surrounding it. Surgical treatment can generally eliminate capsular microinvasion, direct extracapsular invasion, satellite nodules, and neoplastic emboli in small portal branches close to the tumor, and this is the main advantage it offers with respect to non-surgical therapies (NSTs), mostly ablations and transarterial chemoembolization (TACE).

The situation has dramatically changed in the last 10 years and currently NSTs are extensively used not only for patients unsuitable for surgical resection, but in potentially operable cases as well.

The background of chronic liver disease, the characteristics of patients (age, associated diseases) and the variability of presentation patterns of hepatocellular carcinoma (HCC) makes often the choice of the best non-surgical local treatment of HCC very difficult. In addition, the number of therapeutic options available is progressively increasing [percutaneous ethanol injection (PEI), radiofrequency ablation (RFA), laser, microwaves, super-selective trans-arterial chemoembolization (sTACE), ecc..] and the technology of each modality is continuously improving. Consequently, expected efficacy, risks, reported rates of side effects and, last but not least, costs of each modality have to be taken into account before selecting the treatment to perform.

Among NSTs, RFA is currently considered that providing the highest therapeutic efficacy. For this reason, and because two recent randomized trials did not report significant differences in survival rate between surgical resection and RFA [(56, 57)]. RFA is currently widely used as first-line treatment for single HCC nodules less than 3.0 cm in diameter. However, certain tumors are difficult to treat with RFA because of the proximity to anatomic structures that may be damaged by the treatment or to large blood vessels whose flow can cause convectional loss of heat in the ablation zone. These cases are treated by PEI or sTACE. Surgery can be used as salvage therapy in cases of unsuccessful ablation.

In addition, RFA is associated with extremely low rates of mortality and major complications. In contrast, mortality rates reported for surgical resection of HCCs range from 0% to 15%

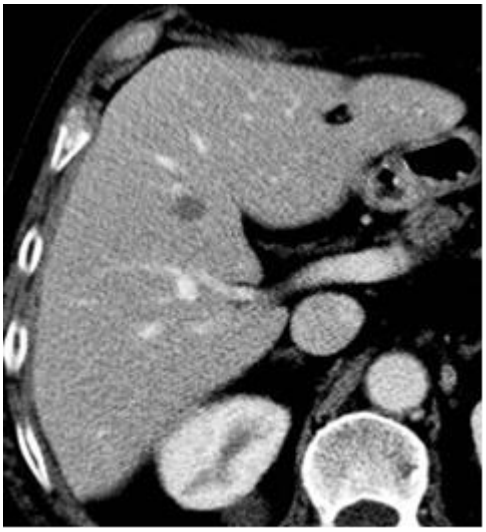
with a mean of 5%. Bilirubin elevations and portal hypertension have been identified as negative prognostic factors for HCC patients who have undergone resection and they are associated with lower survival rate also after ablation.

In conclusion, compared with surgical resection, RFA of small HCCs has a number of advantages that include no loss of non-neoplastic tissue, less invasiveness, repeatability, lower complication rates, and lower costs (reduced treatment time and hospital stays). In addition, our experience shows that RFA is just as effective as surgery in terms of local disease control and survival. These data indicate that RFA can be considered the treatment of choice for patients with single HCC nodules measuring 2.0 cm or less, even when there are no contraindications to surgical resection. The latter approach, along with other treatment options such as PEI or sTACE, can be reserved for those patients whose tumors are not amenable to RFA or used as salvage therapy for the few cases in which RFA was unsuccessful. For HCCs between 2.0 and 3.0 cm RFA still remains a valid therapy, but resection and sTACE must be considered in every patient, particularly at the first presentation of the disease (surgery is usually less indicated for new HCCs after previous resection) and when ablation is either not feasible or technically challenging.

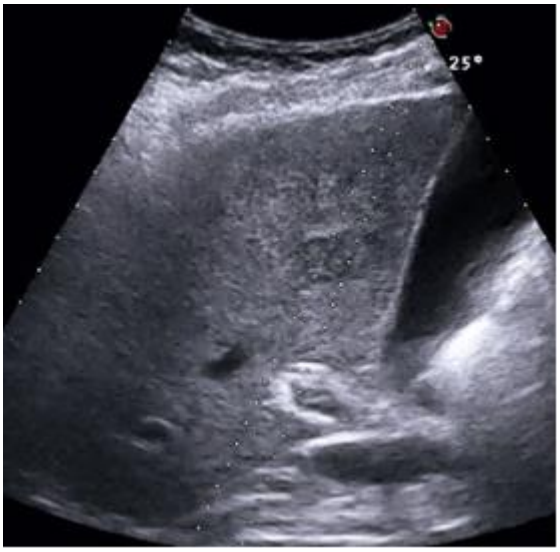
For intermediate HCCs treatment strategies are totally different, given the extremely low possibility to perform liver transplantation and resection. In this stage of the disease, prognosis is highly related to the course of the chronic liver disease and every therapeutic decision has to take into account local advantages and risks to further decrease liver function. Either single-modality treatments (PEI, RFA or sTACE) or combinations of the three therapeutical options (tailored on a case by case basis) can be used, with local control rates ranging from 75 to 90% and very low rates of treatment-related mortality and major complications. Unfortunately, the frequent occurrence of new lesions and the progression of the underlying chronic liver disease account for survival rates not exceeding 25-28% at 5 years. As far as liver metastases are concerned, several clinical studies have reported the excellent results of RFA, which achieved local control and long-term survival rates almost comparable to those reported in literature for surgical resection of metastases from colorectal, breast and endocrine malignancies, but with lower complication rates and costs. However, essential requirement to achieve good results is the size of metastases, with a clear cut-off value of approximately 3.0-3.5 cm [Figure 19].

Figure 19 RF ablation of a 13 mm colorectal liver metastasis in segment 4 a) CT and b) US before ablation. c) US guided and monitored ablation. d) CT at one month shows large complete ablation

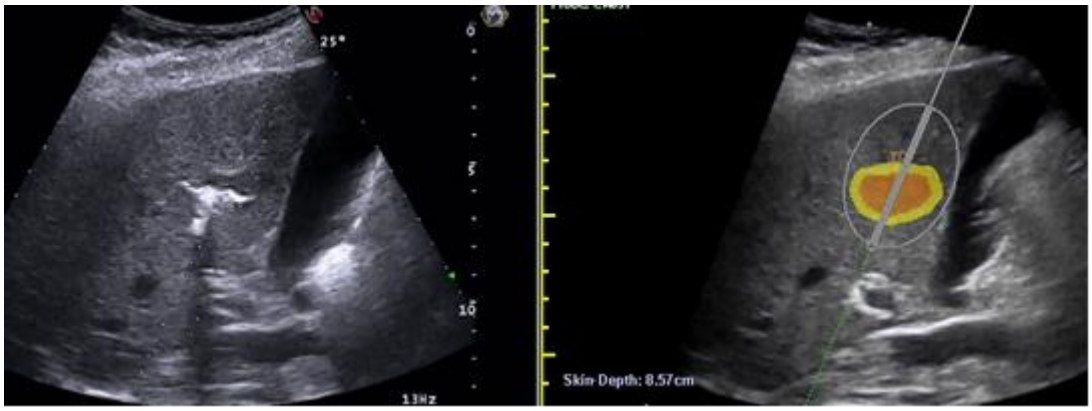
a



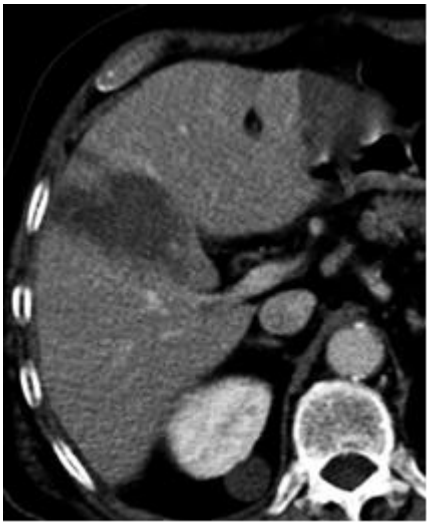
b



c



d



Any new treatment of course has to stand the test of time but with respect to RF ablation of colorectal liver metastases the evidence accumulated so far in the literature beyond reasonable doubt confirms that a 5 years survival rate of between 30% and 40% can be achieved. This is comparable to the results from reports on surgical treatment and ought to imply that any patient diagnosed with colorectal liver metastases be referred to a multi-disciplinary treatment center for evaluation of the optimal treatment strategy.

However, in published series RFA demonstrated significant advantages including a) feasibility of treatment in previously resected patients and non-surgical candidates due to extent of metastatic involvement, age and co-morbidity; b) repeatability of treatment when incomplete and when local recurrence or development of metachronous lesions occur; c) combination with systemic or regional chemotherapy; d) minimal invasiveness with limited complications rate and preservation of liver function; e) limited hospital stays and procedure

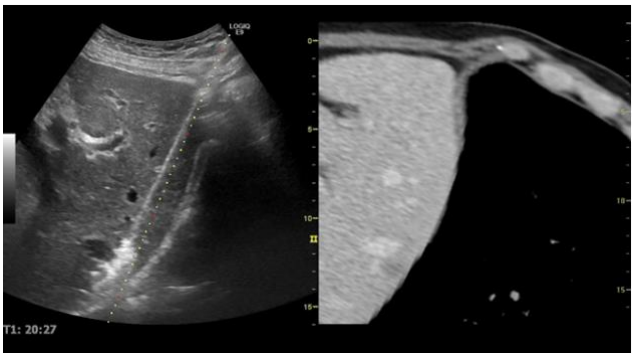
costs [(58-63)]. The constant and progressive improvement of results achieved by percutaneous treatments is also due to the continuous technological improvement of imaging modalities which allow to guide interventional procedures, like contrast-enhanced sonography, contrast-enhanced and diffusion-weighted MRI and real-time image-fusion systems.

Image fusion, ultrasound and interventional procedures

Fusion ultrasound is a new medical application of image fusion, where dynamic ultrasound (US) images are presented simultaneously with corresponding image slices obtained from other imaging modalities, such as computed tomography [(64)]. Image fusion may basically be carried out between all types of image modalities provided their geometrical congruence do not vary considerably. Positron emission tomography (PET)-CT is a known medical example of image fusion based on these principles. The basic advantage of image fusion with ultrasound is the possibility to combine the dynamic features of ultrasound with the virtues of CT and MR imaging. Fusion ultrasound may also facilitate guiding of interventional procedures [Figure 18]. By Fusion ultrasound -CT the ultrasound transducer generates a virtual CT image identical to the US image (or at least intended to be so) from the 3D coordinates using a local electromagnetic field and position sensors fitted to the ultrasound transducer. Prior to the Fusion ultrasound -CT the patient CT images are loaded into the US scanner via the hospital's intranet. Selecting a focal plane with unique anatomical structures in the volume of CT images enables the examiner to identify a corresponding ultrasound image by scanning the patient. When the image planes are identical the CT and ultrasound imaging planes are locked to each other by the examiner. Thus, Fusion ultrasound -CT presents a dynamic ultrasound image alongside a corresponding CT image, or as a composition in which the CT image is superimposed on the active ultrasound image. Biopsies and minimally invasive tumor therapies [(31)], may be performed as Fusion ultrasound -CT or Fusion ultrasound -MR-guided interventions [Figure 20].

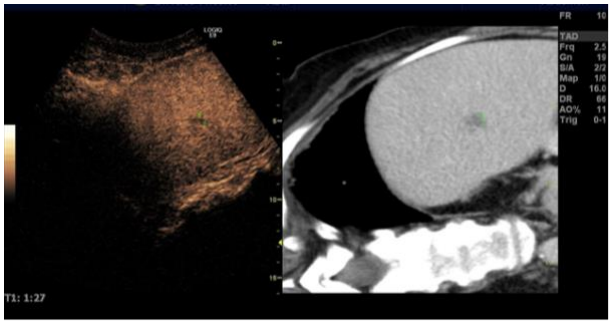
Figure 20 Fusion ultrasound-CT-Guided microwave ablation of a small 10 mm colorectal liver metastasis under the dome of the liver. Both images appear simultaneous

on the US monitor on the left image the microwave needle is seen in the tumor on live US. Right image shows the virtual CT scan that corresponds to the US however both images appear live on the monitor when the transducer is moved around.



In cases where a tumor is indistinct or invisible by ultrasound Fusion ultrasound may provide an alternative to obtain further evaluation or guide interventional procedures. Fusion ultrasound may include the combination of contrast enhanced ultrasound (CEUS) with CT or MR imaging. Furthermore, the position sensors mounted on the transducer provides the advantage of tagging any position (GPS-navigation) in the ultrasound image [Figure 21]. With GPS-navigation, any spatial position may be marked. The marked coordinates remain recognizable by scanning from other angles, by another image modality, or at a later date.

Figure 11 Fusion ultrasound-CT combined with simultaneous CEUS. A small 11 mm liver metastasis is tagged with a position marker on the virtual CT image to the right and simultaneous appears on the live CEUS image to the left. The tagging can also be performed on the CEUS image and as many lesions as one may wish can be tagged and afterwards followed when the transducer is moved



A phantom study with Fusion ultrasound-MR-guided biopsies showed an accuracy comparable to in-vivo biopsies in the abdomen [(65)]. However, the in-vivo conditions are not comparable to the in-vitro condition with regard to establishing consistency between the image planes of two different modalities. Our in vivo experience with FUS, from patients with liver metastases, is that in most patients a versatile alignment between the merged image planes can successfully be obtained, by use of several reference points proximal to the area of interest.

Precise alignment of the ultrasound scan plane and the corresponding plane in a CT or MR volume is crucial for the outcome and the general versatility of FUS. For practical reasons the examiner may choose to sacrifice the general alignment if a suitable local alignment can be obtained for the purpose. Percutaneously as well as intraoperative (open) ablation of liver metastasis may be Fusion ultrasound-CT-guided. Verification of ablation or surgical treatment may be obtained peri-operatively using Fusion ultrasound-CT with contrast enhanced ultrasound (CEUS). In the follow-up Fusion ultrasound may compare the current findings with an earlier ultrasound volume of the same area.

Multi-treated patients with complex metastases, is an imaging challenge. Suspicion of recurrence prevails in a substantial number of the cases where equivocal PET-CT findings generate a significant risk of false positive interpretation error. Ultrasound guided biopsy may introduce a risk of false negative findings. Fusion ultrasound-CT-guided biopsy from such findings may reduce both types of errors. Widespread use of Fusion ultrasound will take place in the near future as the technology becomes available in both the radiological and clinical specialties. In particular musculoskeletal applications seem obvious.

The full potential of this technology is yet to be investigated. However, it is beyond doubt that Fusion ultrasound will redefine the role of ultrasound and its use in guidance of interventional procedures.

Interventional ultrasound has many applications not mentioned in this basic text and, without doubt, in the future will continue to inspire new users to developing new procedures to the benefit of the patients and the medical community [(66-68)].

Reference List

1. Nolsoe CP, Lorentzen T, Skjoldbye BO, Bachmann Nielsen M. The basics of interventional ultrasound. Ultraschall Med 2007;28:248-263; quiz 264, 267.
2. Lutz H: Interventional Ultrasound: Introduction and Historical Background. In: Dietrich CF, Nuernberg D, eds. Interventional Ultrasound: Practical Guide and Atlas: Thieme Publishers., 2014.
3. Holm HH, Cosgrove DO, Pedersen JF: Interventional techniques. In: Meire H, Cosgrove DO, Dewbury K, Farrant P, eds. Clinical Ultrasound: Abdominal and general. 2 ed. London. London: Churchill Livingstone, 2000.
4. Holm HH, Skjoldbye B. Interventional ultrasound. Ultrasound Med Biol 1996;22:773-789.
5. Dodd GD, 3rd, Esola CC, Memel DS, Ghiatas AA, Chintapalli KN, Paulson EK, Nelson RC, et al. Sonography: the undiscovered jewel of interventional radiology. Radiographics 1996;16:1271-1288.
6. McGahan JP. The history of interventional ultrasound. J Ultrasound Med 2004;23:727-741.
7. Otto R. Interventional ultrasound. Eur Radiol 2002;12:283-287.
8. Sites BD, Gallagher JD, Cravero J, Lundberg J, Blike G. The learning curve associated with a simulated ultrasound-guided interventional task by inexperienced anesthesia residents. Reg Anesth Pain Med 2004;29:544-548.
9. Bradley MJ. An in-vitro study to understand successful free-hand ultrasound guided intervention. Clin Radiol 2001;56:495-498.
10. Lorentzen T, Nolsoe CP, Ewertsen C, Nielsen MB, Leen E, Havre RF, Gritzmann N, et al. EFSUMB Guidelines on Interventional Ultrasound (INVUS), Part I. General Aspects (long Version). Ultraschall Med 2015;36:E1-14.
11. Grant A, Neuberger J. Guidelines on the use of liver biopsy in clinical practice. British Society of Gastroenterology. Gut 1999;45 Suppl 4:IV1-IV11.
12. Friedman LS. Controversies in liver biopsy: who, where, when, how, why? Curr Gastroenterol Rep 2004;6:30-36.
13. Malnick S, Melzer E. Routine ultrasound-guided liver biopsy: a time whose idea has come? J Clin Gastroenterol 2005;39:900-903.
14. Spiezia S, Salvio A, Di Somma C, Scelzi C, Assanti AP, Giannattasio F, Varriale M, et al. The efficacy of liver biopsy under ultrasonographic guidance on an outpatient basis. Eur J Ultrasound 2002;15:127-131.
15. Sue M, Caldwell SH, Dickson RC, Macalindong C, Rourk RM, Charles C, Doobay R, et al. Variation between centers in technique and guidelines for liver biopsy. Liver 1996;16:267-270.
16. de Man RA, van Buuren HR, Hop WC. A randomised study on the efficacy and safety of an automated Tru-Cut needle for percutaneous liver biopsy. Neth J Med 2004;62:441-445.
17. Huang C, Lorentzen T, Skjoldbye B, Rosenberg J, Nolsøe CP. Fast-track, ambulatory ultrasound-guided tru-cut liver biopsy is feasible and cost-efficient. Danish Medical Journal 2015;62:1-4.
18. Nolsoe C, Nielsen L, Torp-Pedersen S, Holm HH. Major complications and deaths due to interventional ultrasonography: a review of 8000 cases. J Clin Ultrasound 1990;18:179-184.
19. Buscarini E. Review of interventional ultrasound in the abdomen: safety first. EFSUMB Newsletter p11-15 in Ultraschall Med 2004;24.

20. Strobel D, Bernatik T, Blank W, Will U, Reichel A, Wustner M, Keim V, et al. Incidence of bleeding in 8172 percutaneous ultrasound-guided intraabdominal diagnostic and therapeutic interventions - results of the prospective multicenter DEGUM interventional ultrasound study (PIUS study). Ultraschall Med 2015;36:122-131.
21. Civardi G, Vallisa D, Berte R, Giorgio A, Filice C, Caremani M, Caturelli E, et al. Ultrasound-guided fine needle biopsy of the spleen: high clinical efficacy and low risk in a multicenter Italian study. Am J Hematol 2001;67:93-99.
22. Tarantino L, Francica G, Esposito F, Pisaniello D, Parmeggiani D, Marzullo G, Sordelli IM, et al. Seeding from hepatocellular carcinoma after percutaneous ablation: color Doppler ultrasound findings. Abdom Imaging 2006;31:69-77.
23. Chen I, Lorentzen T, Linnemann D, Nolsøe CP, Skjoldbye B, Jensen BV, Nielsen D. Seeding after ultrasound-guided percutaneous biopsy of liver metastases in patients with colorectal or breast cancer. Acta Oncologica 2016;55:638-643.
24. Micames C, Jowell PS, White R, Paulson E, Nelson R, Morse M, Hurwitz H, et al. Lower frequency of peritoneal carcinomatosis in patients with pancreatic cancer diagnosed by EUS-guided FNA vs. percutaneous FNA. Gastrointest Endosc 2003;58:690-695.
25. Rutten MJ, Collins JM, Maresch BJ, Smeets JH, Janssen CM, Kiemeney LA, Jager GJ. Glenohumeral joint injection: a comparative study of ultrasound and fluoroscopically guided techniques before MR arthrography. Eur Radiol 2009;19:722-730.
26. Daniels EW, Cole D, Jacobs B, Phillips SF. Existing Evidence on Ultrasound-Guided Injections in Sports Medicine. Orthop J Sports Med 2018;6:2325967118756576.
27. Raza K, Lee CY, Pilling D, Heaton S, Situnayake RD, Carruthers DM, Buckley CD, et al. Ultrasound guidance allows accurate needle placement and aspiration from small joints in patients with early inflammatory arthritis. Rheumatology (Oxford) 2003;42:976-979.
28. Nolsoe CP, Lorentzen T. International guidelines for contrast-enhanced ultrasonography: ultrasound imaging in the new millennium. Ultrasonography 2016;35:89-103.
29. Lorentzen T, Nolsoe CP. The Role of US Contrast Agents in US-Guided Biopsy of Focal Liver Lesions: A Pictorial Review. Ultrasound Int Open 2019;5:E11-e19.
30. Nolsoe CP, Nolsoe AB, Klubien J, Pommergaard HC, Rosenberg J, Meloni MF, Lorentzen T. Use of Ultrasound Contrast Agents in Relation to Percutaneous Interventional Procedures: A Systematic Review and Pictorial Essay. J Ultrasound Med 2018;37:1305-1324.
31. Education, Practical Standards Committee EFoSfUiM, Biology. Minimum training recommendations for the practice of medical ultrasound. Ultraschall Med 2006;27:79-105.
32. Lorentzen T, Nolsoe CP, Ewertsen C, Nielsen MB, Leen E, Havre RF, Gritzmann N, et al. EFSUMB Guidelines on Interventional Ultrasound (INVUS), Part I. General Aspects (Short Version). Ultraschall Med 2015;36:464-472.
33. Dietrich CF, Lorentzen T, Sidhu PS, Jenssen C, Gilja OH, Piscaglia F, Efsumb. An Introduction to the EFSUMB Guidelines on Interventional Ultrasound (INVUS). Ultraschall Med 2015;36:460-463.
34. Dietrich CF, Horn R, Morf S, Chiorean L, Dong Y, Cui XW, Atkinson N, et al. US-guided peripheral vascular interventions, comments on the EFSUMB guidelines. Med Ultrason 2016;18:231-239.
35. Dietrich CF, Lorentzen T, Appelbaum L, Buscarini E, Cantisani V, Correas JM, Cui XW, et al. EFSUMB Guidelines on Interventional Ultrasound (INVUS), Part III - Abdominal Treatment Procedures (Short Version). Ultraschall Med 2016;37:27-45.

36. Dietrich CF, Lorentzen T, Appelbaum L, Buscarini E, Cantisani V, Correas JM, Cui XW, et al. EFSUMB Guidelines on Interventional Ultrasound (INVUS), Part III - Abdominal Treatment Procedures (Long Version). Ultraschall Med 2016;37:E1-E32.
37. Fusaroli P, Jenssen C, Hocke M, Burmester E, Buscarini E, Havre RF, Ignee A, et al. EFSUMB Guidelines on Interventional Ultrasound (INVUS), Part V. Ultraschall Med 2016;37:77-99.
38. Jenssen C, Brkljacic B, Hocke M, Ignee A, Piscaglia F, Radzina M, Sidhu PS, et al. Erratum: EFSUMB Guidelines on Interventional Ultrasound (INVUS), Part VI - Ultrasound-Guided Vascular Interventions. Ultraschall Med 2016;37:e1.
39. Jenssen C, Hocke M, Fusaroli P, Gilja OH, Buscarini E, Havre RF, Ignee A, et al. EFSUMB Guidelines on Interventional Ultrasound (INVUS), Part IV - EUS-guided Interventions: General aspects and EUS-guided sampling (Long Version). Ultraschall Med 2016;37:E33-76.
40. Jenssen C, Brkljacic B, Hocke M, Ignee A, Piscaglia F, Radzina M, Sidhu PS, et al. EFSUMB Guidelines on Interventional Ultrasound (INVUS), Part VI - Ultrasound-Guided Vascular Interventions. Ultraschall Med 2016;37:473-476.
41. Sidhu PS, Brabrand K, Cantisani V, Correas JM, Cui XW, D'Onofrio M, Essig M, et al. EFSUMB Guidelines on Interventional Ultrasound (INVUS), Part II. Diagnostic Ultrasound-Guided Interventional Procedures (Long Version). Ultraschall Med 2015;36:E15-35.
42. Sidhu PS, Brabrand K, Cantisani V, Correas JM, Cui XW, D'Onofrio M, Essig M, et al. EFSUMB Guidelines on Interventional Ultrasound (INVUS), Part II. Diagnostic Ultrasound-Guided Interventional Procedures (Short Version). Ultraschall Med 2015;36:566-580.
43. Dietrich CF, Muller T, Bojunga J, Dong Y, Mauri G, Radzina M, Dighe M, et al. Statement and Recommendations on Interventional Ultrasound as a Thyroid Diagnostic and Treatment Procedure. Ultrasound Med Biol 2018;44:14-36.
44. Dietrich CF, Horn R, Morf S, Chiorean L, Dong Y, Cui XW, Atkinson NS, et al. Ultrasound-guided central vascular interventions, comments on the European Federation of Societies for Ultrasound in Medicine and Biology guidelines on interventional ultrasound. J Thorac Dis 2016;8:E851-E868.
45. Mohaupt MG, Arampatzis S, Atkinson N, Yi D, Cui XW, Ignee A, Dietrich CF. Comments and extensions to EFSUMB guidelines on renal interventional ultrasound (INVUS). Med Ultrason 2016;18:351-361.
46. Fusaroli P, Jenssen C, Hocke M, Burmester E, Buscarini E, Havre RF, Ignee A, et al. EFSUMB Guidelines on Interventional Ultrasound (INVUS), Part V - EUS-Guided Therapeutic Interventions (short version). Ultraschall Med 2016;37:412-420.
47. Tsang TS, Enriquez-Sarano M, Freeman WK, Barnes ME, Sinak LJ, Gersh BJ, Bailey KR, et al. Consecutive 1127 therapeutic echocardiographically guided pericardiocenteses: clinical profile, practice patterns, and outcomes spanning 21 years. Mayo Clin Proc 2002;77:429-436.
48. Gronvall J, Gronvall S, Hegedus V. Ultrasound-guided drainage of fluid-containing masses using angiographic catheterization techniques. AJR Am J Roentgenol 1977;129:997-1002.
49. vanSonnenberg E, Wittich GR, Goodacre BW, Casola G, D'Agostino HB. Percutaneous abscess drainage: update. World J Surg 2001;25:362-369; discussion 370-362.
50. Nielsen MB, Torp-Pedersen S. Sonographically guided transrectal or transvaginal one-step catheter placement in deep pelvic and perirectal abscesses. AJR Am J Roentgenol 2004;183:1035-1036.

51. Lorentzen T, Nolsoe C, Skjoldbye B. Ultrasound-guided drainage of deep pelvic abscesses: experience with 33 cases. Ultrasound Med Biol 2011;37:723-728.
52. Karstrup S, Solvig J, Nolsoe CP, Nilsson P, Khattar S, Loren I, Nilsson A, et al. Acute puerperal breast abscesses: US-guided drainage. Radiology 1993;188:807-809.
53. Lorentzen T, Nolsoe CP, Adamsen S. Percutaneous radiologic gastrostomy with a simplified gastropexy technique under ultrasonographic and fluoroscopic guidance: experience in 154 patients. Acta Radiol 2007;48:13-19.
54. Nolsoe C, Nielsen L, Karstrup S, Lauritsen K. Ultrasonically guided subclavian vein catheterization. Acta Radiol 1989;30:108-109.
55. VanSonnenberg E, McMullen W, Solbiati L. Tumor Ablation: Principal and Practice. 1st Ed. Editors New York: Springer Science Business Media, 2005.
56. Chen MS, Li JQ, Zheng Y, Guo RP, Liang HH, Zhang YQ, Lin XJ, et al. A prospective randomized trial comparing percutaneous local ablative therapy and partial hepatectomy for small hepatocellular carcinoma. Ann Surg 2006;243:321-328.
57. Lu MD, Kuang M, Liang LJ, Xie XY, Peng BG, Liu GJ, Li DM, et al. [Surgical resection versus percutaneous thermal ablation for early-stage hepatocellular carcinoma: a randomized clinical trial]. Zhonghua Yi Xue Za Zhi 2006;86:801-805.
58. Goldberg SN, Gazelle GS, Mueller PR. Thermal ablation therapy for focal malignancy: a unified approach to underlying principles, techniques, and diagnostic imaging guidance. AJR Am J Roentgenol 2000;174:323-331.
59. Solbiati L, Livraghi T, Goldberg SN, Ierace T, Meloni F, Dellanoce M, Cova L, et al. Percutaneous radio-frequency ablation of hepatic metastases from colorectal cancer: long-term results in 117 patients. Radiology 2001;221:159-166.
60. Livraghi T, Solbiati L, Meloni F, Ierace T, Goldberg SN, Gazelle GS. Percutaneous radiofrequency ablation of liver metastases in potential candidates for resection: the "test-of-time approach". Cancer 2003;97:3027-3035.
61. Sorensen SM, Mortensen FV, Nielsen DT. Radiofrequency ablation of colorectal liver metastases: long-term survival. Acta Radiol 2007;48:253-258.
62. Elias D, De Baere T, Smayra T, Ouellet JF, Roche A, Lasser P. Percutaneous radiofrequency thermoablation as an alternative to surgery for treatment of liver tumour recurrence after hepatectomy. Br J Surg 2002;89:752-756.
63. Gillams AR, Lees WR. Radio-frequency ablation of colorectal liver metastases in 167 patients. Eur Radiol 2004;14:2261-2267.
64. Ewertsen C, Grossjohann HS, Nielsen MB. Image fusion involving ultrasound. Ultraschall Med 2006;27:128-129.
65. Ewertsen C, Grossjohann HS, Nielsen KR, Torp-Pedersen S, Nielsen MB. Biopsy guided by real-time sonography fused with MRI: a phantom study. AJR Am J Roentgenol 2008;190:1671-1674.
66. Seitz K, Judmaier G. [The extended repertoire of sonography: contrast enhancement, radio frequency ablation and puncture]. Ultraschall Med 2007;28:158-160.
67. Skjoldbye B, Bachmann Nielsen M. Contrast enhanced ultrasonography and US-guided interventions. Ultraschall Med 2006;27:4-7.
68. Stang A, Keles H, von Seydewitz C, Hentschke S, Malzfeldt E, Teichmann W, Braumann D. Percutanous and intraoperative ultrasound-guided radiofrequency ablation of hepatic tumours. Ultraschall Med 2007;28:181-188.