

## Comments and extensions to EFSUMB guidelines on renal interventional ultrasound (INVUS)

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### Abstract

A substantial evidence base for interventional ultrasound approaches to renal diagnostic sampling and therapeutic access exists. This review comments on the evidence-based recommendations regarding ultrasound-guided renal access which have been published recently within the framework of Guidelines on Interventional Ultrasound (INVUS) of the European Federation of Societies for Ultrasound in Medicine and Biology (EFSUMB) from a clinical practice point of view. Specific aspects of tissue handling and workup, procedural approach and patient interaction are discussed. Indications, contraindications, risk factors and methods to reduce these risks are considered.

**Keywords:** guideline, abscess, cysts, ablation, drainage

### Introduction

Recently the EFSUMB guidelines on interventional ultrasound (INVUS) have been published including information relevant to renal ultrasound [1-9]. The mentioned guidelines are in a series of guidelines [10-15] and comments on guidelines [16-24] published over the last decade. A PubMed search revealed 1560 publications relevant to the topic of renal intervention as of the end of 2015. In addition to the published guidelines, we aim to extend beyond the evidence, with respect to issues incompletely covered by the guidelines, and to provide guidance to clinicians

from personal experience. As interventional access to the kidney by ultrasound is relevant and used in various conditions including relief of excess fluid in urinary tract obstruction or to obtain histological information, this information should enhance technical knowledge and overall safety. As already indicated in the guidelines, alternative imaging options should be considered frequently, requiring a multi-disciplinary decision. An important contributor to overall success is the experience of individual investigators [25].

Indications and contraindications for ultrasound guided interventions are discussed in the EFSUMB guidelines [7,26] for diffuse renal diseases in general, kidney transplant and focal renal lesions. Here we describe background knowledge in more detail.

### Description of the intervention including technical issues, specimen preparation, biopsy and cytology for optimal results.

When employing the EFSUMB guidelines, several procedural aspects deserve to be highlighted and are dis-

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cussed below. As most of these items are based on personal experience and not formally covered by evidence, they should simply support individual decision making.

#### ***Issues related to histological workup***

Handling of the tissue sample should be carefully planned, considering the intended result. To allow for light microscopy, immunohistochemical and electron microscopy analyses, additional biopsy cores might be required.

The quality and appropriateness of the sample should be verified immediately following the procedure, both visually and by submerging the sample into 0.9 % saline solution, which helps to differentiate adipose from renal tissue. Experienced investigators will easily distinguish renal tissue from non-renal material. On site review of the sample for adequacy and discussion with a nephropathologist of the workup required improves the diagnostic process.

If renal parenchymal disease is suspected, frozen instantaneous sectioning should be avoided. Rather, prearranging a rapid histological evaluation with a nephropathologist allows a shared initial assessment for sample adequacy and sample apportionment. Such specimens should be provided non-denatured in saline solution within 4-5 hr.

#### ***Handling issues related to the intervention***

For native kidney biopsies, when the patient is positioned prone, a mid-abdominal support will be placed. After localising the INVUS target in the positioned patient, the puncture site will be marked, body hair carefully removed, the skin cleaned and skin anesthesia performed. The skin incision should be along the skin folds and allow easy passage of the needle. Through the incision, deep anesthesia is applied in volumes of local anesthetic proportional to the target depth. For renal biopsies 8-10 ml anesthetic will usually be sufficient. As air impairs ultrasound identification of the targets, care should be taken to remove it completely from the syringe. During the biopsy, patient cooperation is extremely important due to kidney movement with respiration. Consequently, caution as to the depth of sedation is necessary. Venous access should be placed and a saline infusion immediately available. A nurse responsible for monitoring tasks throughout the procedure is mandatory. In case of a patient with reduced capability for cooperation, a short anesthetic might be considered to allow an inspiratory ventilation hold whilst performing the biopsy.

Patient positioning must be adapted to provide optimal access for the procedure in a comfortable posture, while allowing the necessary monitoring by assisting personal. As the prone position is favorable for renal biopsies, older or handicapped patients might not tolerate the required posture or intervention time. Thus a test

inspiration maneuver demonstrating sufficient duration, should be executed before performing the biopsy.

The advantages of a reusable device include its weight, which reduces the repulsion force experience, its dependability, and the calibrated mode of action. On the contrary, the weight poses difficulties in extended procedures on delicate structures, the feather constant of the spring-load system wears and requires recalibration, careful sterilization is required, and loads exceeding the structural limits imposed during handling of the device might interfere with its accuracy. Single-use devices are usually light-weight, and their functionality has been proven. Each user has to individually familiarize him- or herself with the repulsion, as handling certainly improves with experience. Fewer complications have been observed with spring-loaded vs. tru-cut needles [27].

Needle length has to be chosen according to the depth of the target region, between 15 and 20 cm which allows for a small segment of the needle to remain in the needle guide. Either direct measurement or formulas should be applied [28] to predetermine the required needle length. Patients should be warned of potentially frightening noises upon release of the spring-loaded device before employment, to reduce the risk of movement.

Sample size and quality in diffuse renoparenchymal disease has been thoroughly studied. Overall, 14-gauge needles did not improve histological assessment, yet tended to create more complications. Smaller sized needles (16-18 gauge) are sufficient with lower complication rates, while further size reduction compromises histological assessment [29-32].

#### ***Access routes – Native kidneys***

Native kidneys are approached from behind in a prone position. In inspiration, the lower pole of the left kidney (see bleeding complications) is the preferred target. The presence of both kidneys should be confirmed and morphological abnormalities requiring special decision making detected. Morphological abnormalities which might not allow a representative tissue collection include kidneys which are malrotated and/or display scars or cysts in the lower pole. Furthermore, biopsies might be complicated by ribs, iliac bone or the absence of perirenal fat tissue in extremely slim patients (see bleeding complications and BMI). In the latter, bowel or large vessels (aorta, caval vein) might be in critical proximity. The kidney should be targeted orthograde.

Measuring the distance from the surface to the target region allows appropriate selection of the needle length. The outer scale on the biopsy gun should be used as a guide. Formulas to calculate the optimal depth of the needle insertion are available and reduce bleeding complications [28].

The final positioning of the needle should avoid bending and consecutively high shear forces between needle and outer cannula. The needle should be advanced half way to the kidney, and while the patient maintains inspiration, be then advanced forward to its final position in front of the kidney. Immediately, the biopsy needle should be released and thereafter the needle withdrawn from the kidney (fig 1).



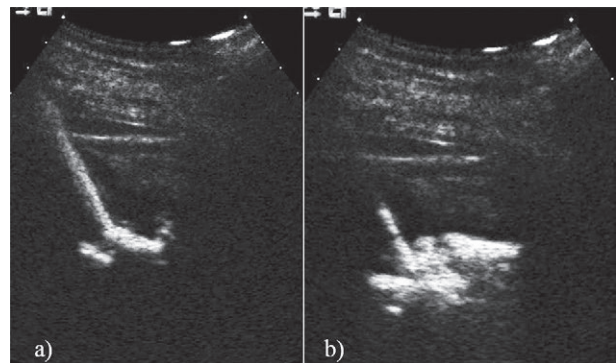
**Fig 1.** Percutaneous biopsy of a small isoechoic renal lesion (< 12 mm).

If inspiration cannot be maintained, or if the patient continues breathing, the needle must be quickly retracted to a safe position, minimising kidney contact. Otherwise severe laceration injuries can result. This risk is thought to be reduced by performing the procedure during inspiration, as the kidney moves away from the needle when the patient starts breathing. Contrast enhanced ultrasound is helpful in some patients to identify focal lesions and guide the biopsy [33,34]. Abscess drainage can be guided using extravascular and intracavitary application of contrast enhanced ultrasound avoiding radiation exposure [4,5,35-37] (fig 2).

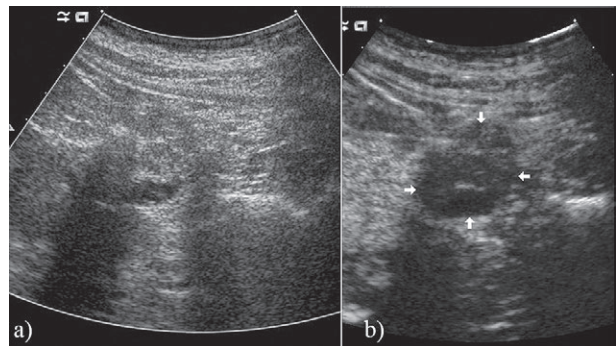
CEUS is established to guide radiofrequency ablation. The result with complete (fig 3) or incomplete necrosis can be displayed using CEUS directly after ablation or in the follow up [4,5,24].

#### **Access routes – Transplanted kidneys**

The approach to a transplanted kidney is ventral in a prone patient. The preferred target location is the upper pole, being remote from large vessels and the ureter. Normally, respiration-related movement is limited or absent, yet must be compensated for if present. Access to this pole is sometimes difficult with cranial implantation sites such as the aorta in pediatric transplantation or the common iliac artery, as it might be obstructed by interfering bowel. Sometimes, an enema might resolve access difficulties. Careful exclusion of interfering vessels is required, especially in median positions where the inferior epigastric artery should be positively identified and avoided. Contrast enhanced ultrasound is helpful in some patients to identify focal lesions and guide the biopsy [38].



**Fig 2.** Percutaneous abscess drainage with extravascular and intracavitary application of contrast enhanced ultrasound. The puncture (a) and exclusion of communication (b) are shown.



**Fig 3.** Evaluation of percutaneous radiofrequency thermoablation (RFA) of renal cell carcinoma using B-mode (a) and contrast enhanced ultrasound (b). The total necrosis is shown in (b). No recurrence occurred over the next five years.

### **Biopsy for parenchymal assessment in renal impairment**

#### *Patient selection:*

- Suspected reno-parenchymal disease, particularly glomerular disease.
- Assessment of renal transplants.

#### *Contraindications:*

- As discussed in the EFSUMB guidelines [7,26]
- Pre- and post-glomerular renal failure (exclusion of pre-renal functional deterioration is complicated and sometimes impossible in renal transplant recipients)
- Severe renovascular disease requiring immediate intervention

#### *Indications:*

Renal biopsies should only be performed if information affecting significant therapeutic consequences can be deduced, which outweighs the potential complications in acute and chronic kidney disease. A nephrologist should be closely involved in the planning of the biopsy and the necessary analyses. Execution of the

biopsy by a nephrologist is not inferior to a radiologist [39].

**Specific symptoms, conditions or kidney diseases requiring renal biopsy:**

Acute renal failure without other recognized causes, particularly in the presence of signs of nephritic glomerular involvement, defines an urgent absolute indication for renal biopsy. Acute renal failure of other causes can often only be unambiguously differentiated from simple prerenal conditions or acute tubular necrosis by renal biopsy. However if signs of nephritis, proteinuria or severe inflammatory involvement are present, renal biopsy should be considered even in the ICU environment.

Beyond this, further indications include: nephrotic range proteinuria, nephritic syndrome, suspected renal involvement in systemic disease (e.g. lupus erythematosus, vasculitis), evaluation of therapeutic response, otherwise unexplained functional loss after renal or other types of transplantation, or suspected drug toxicity due to critical drugs such as calcineurin inhibitors.

In pregnancy, severe acute renal failure and life threatening nephrotic syndrome before the 32<sup>nd</sup> week of gestation, especially if fetal conditions preclude safe delivery, requires a renal biopsy. Complication rates increase with

gestational age and thus biopsy should be postponed until delivery if feasible.

Currently no clear evidence supports the routine use of protocol biopsies following renal transplantation, though protocol biopsies appear to be safe [40].

**Contraindications for biopsies of focal lesions and/or parenchymal disease.**

Contraindications to biopsy of focal lesions have not been validated by clinical studies; they are based predominantly on limited evidence, clinical experience, and legal requirements. Absolute and relative contraindications are shown in Table I.

**INVUS for nephrostomy insertion; drainage of the collecting system without fluoroscopy**

Percutaneous nephrostomy is performed successfully in 95-98% of patients with a dilated renal collecting system. It is used to resolve hydronephrosis especially in cases with compromised retrograde transureteral accessibility in obstructive (retroperitoneal fibrosis, tumor or stone disease) or fistulating diseases, and even for diagnostic antegrade pyeloureterography. Bilateral nephrostomies limit quality of life to the extent that unilateral

Table I. Contraindications for biopsies of focal lesions and/or parenchymal disease.

Absolute contraindications	Relative contraindications
Absent informed consent for the procedure planned except in life threatening conditions.	Preoperative biopsy of resectable tumors with a high probability of malignancy especially urothelial cell carcinoma [41,42] though biopsy of renal carcinomas does not increase rate of metastases nor is bleeding frequently observed [43].
Lack of cooperation.	Renal masses exceeding 4 cm [44].
No diagnostic or therapeutical benefit.	Target lesion assumed to have high bleeding risk.
Poor needle guidance.	High risk access route (blood vessels, bowel).
Bleeding disorders.	Close proximity to major vessels.
A. Severe plasmatic disorder [29,45,46]	
B. Effective oral anticoagulation	
C. Inherited or acquired disorders	
D. Evaluation should not be based on bleeding time	
E. Prolonged PTT indicates higher risk	
Severe thrombocytopenia.	Adrenal masses with suspected pheochromocytoma.
Drugs (low-dose aspirin does increase the risk for mild, yet not severe complications [45,47].	Suspected hydatid cyst.
Metabolic disorders (storage diseases such as cystinosis, uremia: CKD $\geq$ 4: danger of HD requirement, increased bleeding risk if serum creatinine $>$ 196 $\mu$ mol/l) [31,48,49].	Anomalies of kidney shape and position.
Uncontrolled arterial hypertension ( $>$ 160 mmHg systolic blood pressure, $>$ 120 mmHg mean arterial blood pressure) [31,49,50].	Biopsy of solitary native kidneys with acceptable risk possible [51,52].
Ureteric obstruction with insufficient drainage.	
Acute pyelonephritis.	
Suspected vascular malformation/tumor.	
Small kidneys $<$ 9 cm.	
Isolated hematuria.	

access is usually preferred. Non fluoroscopy-based approaches are the procedure of choice for pregnant women. Contra-indications are similar to other INVUS of the kidney, yet given the prospect to avoid renal replacement therapy, benefit-risk evaluations might differ.

Macroscopic hematuria is frequent, yet significant bleeding is limited to 1-2%, leaving a bleeding-associated mortality of 0.2%. Injury to adjacent organs is infrequent. Septic dissemination of a preexisting pyelonephric infection might occur, whilst de novo contamination during puncturing is recognised. Displacement and obstruction of nephrostomy tubing may develop.

In preparation, the patient is fasted to allow for intubation if required. Intravenous access is placed and blood tests similar to other renal INVUS procedures are applied. The target region is confirmed to be dilated.

Available catheters range from straight short-term polyurethane to pigtail long-term silicone catheters. The patient is approached laterally whilst prone and bent forward, following local anesthesia. The guide wire needle is passed through the posterior inferior calyx at an angle of approximately 30° to the orthograde plane which should provide easy access to the central pelvis. After dilatation, the catheter is advanced over the guide wire, which is finally removed. Correct position can be confirmed by adding a small amount of contrast media.

Ultrasound guided and contrast enhanced intracavitary approaches have been described for the kidneys and other organs [35,53,54] (fig 4). The first case report was described on the EFSUMB website [www.efsumb.org] and a prospective study has been published [55].

### Specific considerations for biopsies

#### Role of cytology

There is only a limited role for fine needle aspirates in renal tumor analysis, as diagnostic certainty is limited; discrimination between benign and malignant lesions is incorrect in up to 60 % of cases [56].

#### Local anesthesia and intravenous sedation

Local anesthesia reduces patient discomfort, pain and uncontrolled movements.

Intravenous sedation is discouraged since it might limit the patient's ability to cooperate with respiratory movements and compromise successful intervention.

#### Infection

Standard sterile precautions should be applied. The US probe preferably should be cleaned from gel residue and disinfected to the manufacturer's recommendations, as ethanol-based solutions might not be applicable to a given US probe. A sterile probe cover is recommended, yet needs to contain an acoustic coupling medium, preferably sterile gel. The device for puncture guidance should be either sterile single use or thoroughly autoclavable. Antiseptic skin cleaning, a sterile interventional field and instrument table, sterile clothing for the interventionalist, combined with barrier precautions (mask, cap and sterile gloves) has been proposed. Antibiotic prophylaxis is not recommended for renal interventions [57,58].

#### Blood pressure lowering

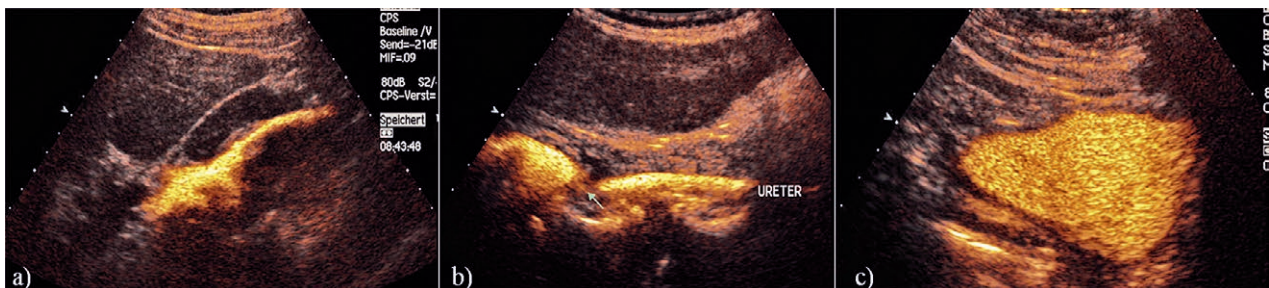
Limited evidence without controlled data suggests calcium channel blockers, clonidine or hydralazine for peri-procedural blood pressure reduction. Caution should be used as vasodilatation could enhance bleeding [29,50,59,60].

#### Counselling of complications

Carefully assessment of risk and appropriate pre-interventional counseling is recommended. The following complications should be discussed with the patient as is appropriate for the clinical scenario.

##### Organ loss

The risk of death or overall organ loss, including emergency nephrectomy, is low and lower for INVUS in transplanted as compared to native kidneys [39,48,61-66]. The risk increases with subcapsular/perirenal hematoma [62].



**Fig 4.** Percutaneous nephrostomy using contrast enhanced ultrasound. The puncture site (a), cause of stenosis (b, arrow) and contrast filled urinary bladder (c) are shown.

**Hemorrhage**

Post-interventional hemorrhage is a serious concern in renal biopsies. Retroperitoneal hematoma should be treated conservatively in most cases. Severe involvement of adjacent organs might require surgical intervention such as compression of the liver with local ischemic damage. Severe bleeding episodes seldom occur in the absence of aspirin [47] and single operators do not further reduce the risk [67].

**AV-fistula**

AV-fistula frequently occurs after biopsy, particularly in renal grafts, with a high rate of spontaneous closure [52,68]. Three dimensional imaging might improve identification of the feeder morphology [69]. Interventional embolization and coiling of the feeder vessel or the aneurysm itself are rarely required. Malignant conversion with total or partial organ loss, is rare [25,66,70-81].

**Infectious complications**

If aseptic procedures are followed thoroughly, with special emphasis in immunocompromised patients, infectious complications are rare. Yet severe infections including urosepsis, perirenal abscess formation and skin infiltration might be observed.

**Rare complications**

Further rare complications include hydronephrosis, bladder tamponade, renal functional impairment, pneumothorax and other tissue lesions [41,42,48,82-84].

**Needle tract seeding of malignant tumors**

The risk of renal cell carcinoma seeding after fine needle puncture or nephrostomy is described only in case reports. While data indicate a clinically significance risk for liver tumor biopsies, it is almost negligible in renal cancers [85,86].

**Management of complications****Prevention**

Risk assessment and patient selection for INVUS:

1. A rigorous assessment should be undertaken with respect to the expected overall benefit, the procedural risk, the timeline and potential alternative approaches
2. When interpreting the risk for a patient, the conditions specified in the section on bleeding complications above need to be considered, as platelet count or INR may be insufficient. Notably, the clinical bleeding history should also be considered in decision making [87].
3. The risk of interrupting antiplatelet or conventional anticoagulant therapy needs to be stratified according to the clinical condition. NOACs, which are also not reflected by the global function tests, need to be considered.

**Bleeding risk modification and risk reduction techniques**

Bleeding risk factor modification and risk reduction techniques should be undertaken as per current anticoagulation guidelines. The risk of bleeding should be weighed against the risk of changing the anticoagulation treatment. Conditions without an increased bleeding risk include monoclonal gammopathies [88], diabetes mellitus [89], pediatric kidneys in most reports [90-93] and outpatients [94,95]. For advanced guidance, bleeding risk predictors are summarized in Table II.

Table II. Prediction of increased bleeding risk after percutaneous renal biopsies.

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1. Disturbed cellular or plasmatic hemostasis
    - a. Platelet count and INR [50,96]
    - b. Platelet dysfunction such as in uremia or storage disease [97,98]
  2. Arterial hypertension [49,50]
  3. Type of renal affection
    - a. Systemic infectious and storage diseases including hepatitis C infection, HIV, amyloidosis and cystinosis [50,96]
    - b. Renal diseases including thin basement membrane syndrome, vasculitis, rapidly progressive glomerulonephritis or acute interstitial nephritis [89]
    - c. Acute renal failure [31] though this is not confirmed in smaller studies
    - d. Severe, chronic renal functional impairment [31,89]
  4. Number of needle passes [31]
  5. Female gender [31,72,99]
  6. Glucocorticoid therapy [31]
  7. Age [31]
  8. Low resource settings [100]
  9. Right kidneys [72]
  10. Lower BMI [72]
  11. Lower blood pressure in renal transplantation [72]
  12. High blood pressure, systolic >170 mmHg [63]
  13. Renal grafts tend to demonstrate more hematuria [101], yet less overall hemorrhage [25,29,48, 63,81,102-104]
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**Follow-up strategies to reduce complications**

**Post biopsy strategies to reduce complications**

1. Post-intervention, thorough compression of the biopsy area is performed before placing the patient on a sandbag for native, or a sandbag on the kidney for transplanted kidneys, for at least 4 hrs (nevertheless there is no evidence to do so).
2. Surveillance should be adapted to the patient’s risk profile according to ASA criteria. Intermediate or ICU facilities should be available on demand.
3. Day care might be appropriate for selected low risk patients, if no periprocedural bleeding occurs [89].

**Follow up**

- Post-intervention US scanning is recommended to identify fluid collections, hematoma or persistent needle track flow (“patent track”) by color duplex. Immediate hematoma formation after percutaneous renal biopsy predicts clinically significant bleeding complications [104, 105].
- If clinical deterioration suggests persistent bleeding, repeat US supplemented by CEUS should be applied [106].
- Given most bleeding complications in native kidneys and renal transplants occur within the first 8 hrs after INVUS, bed rest should be mandated during this period [47,48,62,99,107-109].

- Bleeding complications are unlikely, if the following applies:
  - Absence of hematoma 1 h after biopsy at US [104] and significant bleeding causing clinical signs is absent after 18 hrs [50].
  - A hematoma is present but <2cm [84] and no hematocrit changes occur within the first 6 hrs [110,111].
- The patient should be educated on what action to take and how to access supportive care in an emergency.
- Extended postprocedural monitoring has not been proven beneficial.

We developed a procedural guideline for outpatient biopsies based on the guidelines and above comments. Patients qualify as having a low risk for renal biopsy-related complications and conversion into a high risk condition if the following conditions apply (Table III).

**Conclusion**

Renal INVUS for diagnostic and therapeutic purposes play a valuable role in nephrology supported by a broad evidence base. Aspects of the procedure technique are amenable to optimization, particularly handling of histological tissue, patent preparation, approach and pre-procedural risk identification. Bleeding risk modification and post-interventional strategies minimise patient harm

Table III. Patients with low risk renal biopsies and controlling low-high risk converting conditions.

Low risk for renal biopsy	Low-high risk converting conditions
Cooperative.	Biopsy of a right kidney
Absence of inborn or acquired plasma or cellular bleeding disorders, aspirin is discontinued.	Duplex mode unavailable during the procedure.
Absence of storage disease and uremia (CKD ≥4) (diabetes mellitus and monoclonal gammopathies do not per se manifest a high risk).	Use of calcium channel blockers, clonidine or hydralazine for blood pressure control.
Serum creatinine <196 umol/l or acute renal injury.	Not calculating optimal depth of insertion (body weight [kgX10]/body height [cm]) – 0.5 = depth [cm]) for native kidneys prior to biopsy.
Blood pressure < 100 mmHg diastolic and < 160/170 mmHg systolic and mean between 60 – 120 mmHg.	Requirement of ≥ 3 needle passes.
Absence of ureteral obstruction or dilated renal pelvis.	Hematoma on ultrasound evaluation within the first hour post biopsy (especially > 2 cm).
Absence of acute pyelonephritis.	Decreasing hematocrit 6 hours post biopsy.
Absence of suspicion for vascular malformation/tumor.	
Kidney length > 9 cm.	
Absence of isolated hematuria.	
No high risk access route.	
Biopsy site not in close proximity to major vessels.	
Absence of anomalies of kidney shape and position.	
BMI ≥ 18 kg/m <sup>2</sup> .	

when combined with EFSUMB guideline recommendations. Further clinical studies are still required to optimize several aspects of renal INVUS. For further illustrating images we refer to the textbook [112,113] and the EFSUMB website (www.efsumb.org).

**Conflict of interest:** none

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