# Ultrasound-guided renal biopsy

Renal medicine was revolutionized in the 1950s and 60s by the introduction of percutaneous renal biopsy into clinical practice. Before this, although clinical syndromes of renal disease were described, diagnoses remained elusive and there was little understanding of the pathogenesis of even common kidney diseases (D'Agati and Mengel, 2013). Since the 1980s, percutaneous biopsy has been performed under ultrasound guidance using spring-loaded biopsy needles. In experienced hands, this procedure is associated with a low risk of serious haemorrhage and so has become a routine part of clinical practice around the world. In 2015, in Scotland (where there is a comprehensive registry to record all kidney biopsy procedures) 726 native kidney biopsies were performed in 699 patients: a rate of 130 biopsies per million patients per year (Metcalfe, 2015).

Those physicians involved in the care of patients who might undergo renal biopsy should have a general understanding of its indications and contraindications as well as a working knowledge about the practicalities of the technique and the important aspects of peri-procedural patient care. Most importantly, they should be aware of the potential for bleeding complications particularly, as patients may present with delayed haemorrhage to general practice or the general medical or surgical take.

This article cover these topics and provides 'top tips' for the trainee physician. It focuses on non-targeted ultrasound-guided biopsy of the renal cortex in native or transplanted kidneys. Biopsy of a renal mass in cases of suspected cancer is beyond the scope of this review.

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## Indications and contraindications for renal biopsy

### Indications

The decision to perform a renal biopsy should always be made by a senior nephrologist or transplant surgeon. Biopsy is requested in cases of suspected 'intrinsic' renal disease in order to establish a diagnosis, to guide therapy, to inform prognosis or to assess the response to existing therapy. Thus, indications in native kidneys include suspected primary glomerular disease (e.g. glomerulonephritis), interstitial nephritis and in situations where biopsy may help to establish the diagnosis of a systemic disease (e.g. anti-neutrophil cytoplasmic antibody-associated vasculitis). In the case of transplanted kidneys, any cause of allograft dysfunction that is not readily explained by pre-renal or post-renal causes will usually prompt a biopsy. The aim of biopsy is to discriminate between the many causes of allograft dysfunction including transplant rejection, immunosuppressive drug toxicity (e.g. calcineurin inhibitors), viral infections (e.g. polyoma virus nephropathy) and recurrent glomerular disease (e.g. immunoglobulin A nephropathy).

Most biopsies are performed in response to a clinical scenario such as the development of impaired and unexplained renal dysfunction, unexplained persistent haematuria, significant proteinuria or allograft dysfunction. Typical indications for renal biopsy are listed in *Table 1* (see also Dhaun et al, 2014). In some centres, 'surveillance' biopsies are carried out in transplanted kidneys with normal graft function, in order to detect early subclinical rejection.

**Table 1. Common indications for biopsy of native and transplanted kidneys (alphabetical order)**

| | |
|---|---|
| Native | Assessment of response to therapy (e.g. following immunosuppression for glomerulonephritis) |
| | Haematuria of likely renal origin with additional evidence of glomerular disease (e.g. significant proteinuria) * |
| | Nephrotic syndrome |
| | Proteinuria >1g per day (unless likely diabetic nephropathy) |
| | Suspicion of 'intrinsic' renal disease: renal impairment or active urinary sediment (e.g. glomerulonephritis or tubulointerstitial nephritis with urine dipstick abnormalities) |
| | Suspected multisystem disease (e.g. anti-neutrophil cytoplasmic antibody vasculitis, cryoglobulinaemia, systemic lupus erythematosus) |
| Transplant | Assessment of therapy response (e.g. following treatment of rejection) |
| | 'Protocol' biopsy in patients at high risk of rejection |
| | Unexplained allograft dysfunction |

** Persistent haematuria in the absence of other features of chronic kidney disease – particularly visible or symptomatic haematuria – would usually be referred for a urological work-up in the first instance.*

### Contraindications

Typical contraindications to renal biopsy are listed in *Table 2*. Individuals and centres vary in their approach to these. Ideally, any modifiable risk factor for bleeding should be corrected before biopsy (e.g. antiplatelet agents should be withheld for 7 days before the procedure). In some patients, there is a fine balance to be struck between the risk of peri-procedural bleeding and thrombosis (e.g. renal biopsy in a patient with antiphospholipid syndrome who has been prescribed lifelong anticoagulation) and a thoughtful dialogue between nephrologist, radiologist and haematologist may be required.

There is no consensus on best practice regarding aspirin therapy. Whereas some centres routinely suspend aspirin therapy for 7 days before and 2 days following a renal biopsy, others continue aspirin. Comparison between centres suggests that stopping aspirin does not reduce the risk of major bleeding complications (Mackinnon et al, 2008). Other antiplatelet agents (e.g. clopidogrel) are almost always withheld before biopsy, ideally for at least a week.

In practice, anticoagulation and antiplatelet agents (including aspirin) are usually discontinued. Therefore it is important to liaise early with nephrologists about any patient in whom a renal biopsy may be required so that the procedure is not delayed if these agents are not stopped in a timely fashion.

**Table 2. Typical contraindications for biopsy of native or transplanted kidneys**

| |
|---|
| Anticoagulant therapy or coagulopathy (unless supported by clotting factor transfusion) |
| Antiplatelet therapy within 7 days (relative contraindication – see main text) |
| Hypertension >160/90 mmHg |
| Morbid obesity |
| Other bleeding diathesis (including uraemia) |
| Platelet count <50×$10^9$/litre (unless supported by platelet transfusion) |
| Single functioning native kidney (relative contraindication) |
| Small, scarred kidneys (typically <9 cm in bipolar length) (relative contraindication) |
| Uncooperative patient (e.g. delirium) |

## Technique of renal biopsy

### Patient preparation

Patients should be appropriately counselled about the potential advantages of having a renal biopsy and the risks involved. This should include a discussion of the potential for serious haemorrhagic complications, including the risk of delayed bleeding, as well as the possibility of a non-diagnostic biopsy.

Blood tests are typically obtained in the 24–48 hours before the biopsy. These often include a full blood count, urea and electrolytes, coagulation profile and a 'group and save'. An assessment of serum creatinine levels (usually alongside an estimation of glomerular filtration rate) will show any renal dysfunction to be stable or progressive. On occasion renal function may be significantly improved than it was when the biopsy was requested and so the procedure may no longer be necessary. Significantly deranged renal function is a risk factor for bleeding. A gross derangement in clotting should be corrected before biopsy (aiming for a platelet count >50x$10^9$/litre and an international normalized ratio <1.5, seeking haematological advice if required). In case of any post-biopsy haemorrhage red cells should be available for immediate transfusion.

Blood pressure is checked before the biopsy and regularly in the hours following. Hypertension increases bleeding risk and a blood pressure >160/90 mmHg is generally a contraindication to the procedure. If blood pressure is too high then it is usually safest to defer the procedure until the blood pressure is well-controlled. Alternatively, antihypertensives (and/or anxiolytics if appropriate monitoring is available) may be administered before the biopsy in order to reduce blood pressure into a safe range. However, in this case further treatment may be required post-biopsy if blood pressure rebounds significantly. It is advisable for the patient to have an intravenous cannula in place because of the risk of peri-procedural vasovagal events and bleeding. This should be sited away from potential sites of dialysis fistula formation (e.g. preferring the dorsum of the hands).

Some centres administer desmopressin acetate as a subcutaneous injection an hour or so before the biopsy for its pro-thrombotic effect, either routinely or in high-risk cases. A double-blind randomized controlled trial found that desmopressin acetate reduced the risk of minor bleeding complications in subjects with relatively normal renal function (Manno et al, 2011). However, there remain no sufficiently-powered trials to provide evidence of the effect of desmopressin acetate on the incidence of major bleeding complications and any benefit must be offset against the potential thrombotic risk (Mannucci and Lusher, 1989).

### The biopsy procedure

A renal biopsy is typically performed by either an appropriately trained nephrologist or radiologist (*Figure 1*). As it is carried out under local anaesthesia, with or without mild sedation, patients are ideally fasted for at least for 4 hours. An initial ultrasound scan is performed with the patient supine. For biopsy of a native kidney the patient

**Figure 1. The typical patient set-up for renal biopsy with the operator identifying the optimal site and needle track for biopsy of the left kidney.**

## TOP TIPS

- Multidisciplinary dialogue may be necessary in planning kidney biopsies in complex patients at high risk of bleeding, e.g. in the presence of the antiphospholipid syndrome.
- Desmopressin therapy may be used to reduce the risk of bleeding following a biopsy.
- Although rare, patients may present with potentially life-threatening bleeding for up to 2 weeks following a kidney biopsy.
- Bleeding risk is particularly high in patients with dialysis-dependent renal failure.
- Any patient in whom a biopsy may be required should be discussed at an early stage with the nephrology team.

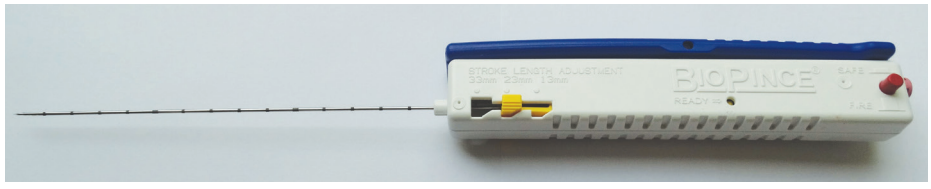


Figure 2. The spring-loaded biopsy needle.

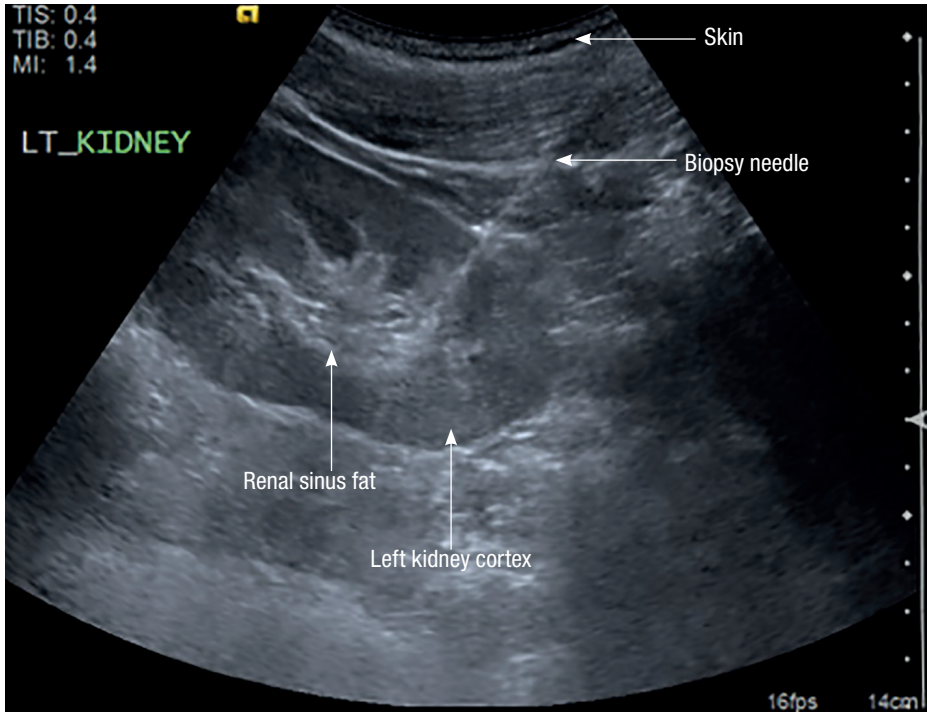


Figure 3. Ultrasound image showing the deployed biopsy needle within the cortex.

is then positioned prone, the kidneys re-scanned and a suitable site for entry of the biopsy needle marked. Under aseptic conditions and continuous ultrasound guidance local anaesthetic is infiltrated into the subcutaneous tissues and down onto the renal capsule. A spring-loaded biopsy needle (*Figure 2*) is then inserted down onto the surface of the kidney (needle gauge is usually 14–16G for transplant kidneys and 16–18G for native kidneys). The patient is asked to hold his or her breath in order to maintain the kidney in a fixed position and the needle is deployed (*Figure 3*). This is repeated until two or three cores of renal cortex are obtained. A repeat ultrasound scan is performed following completion of the procedure to look for immediate bleeding.

### Specimen analysis and biopsy utility

The cores of renal cortex which have been taken are usually processed in three ways. Formalin-fixed tissue is used to provide morphological information about the glomeruli, tubulointerstitium and vasculature (e.g. showing the presence and type of any infiltrating inflammatory cells). Fresh tissue is used for immunofluorescence, i.e. probed with antibodies to immunoglobulins, complement components and other informative targets. Finally, tissue is analysed with electron microscopy in order to examine the ultrastructure of glomerular cells. In many cases, all three components are required in order to arrive at a complete diagnosis. For example, in minimal change nephropathy (a common cause of nephrotic syndrome), light microscopy and immunofluorescence are usually completely normal but electron microscopy will reveal effacement of podocyte foot processes. In addition to their core clinical utility, renal biopsies may be used in epidemiological and mechanistic research into the pathogenesis of renal disease (Dhaun et al, 2014).

The histological information that is gleaned from a biopsy provides only a 'snapshot' of any disease process as it is taken at one time in the natural history of the disease and from an anatomically-restricted area of the kidney (which may be relevant if sample size is small and a focal glomerular disease is present). On occasion, therefore, it can only be interpreted in the context of the referring clinician's pre-biopsy clinical suspicion.

### Post-procedural care

Patients are typically nursed supine for 4 hours after the biopsy and then for 2 hours sitting up. Pulse rate and blood pressure are checked regularly and the urine is inspected for visible haematuria. In the absence of haemodynamic instability, and once the patient has passed urine without visible haematuria, he/she can be safely discharged from hospital. It is not usually necessary to repeat blood tests immediately following the procedure.

Patients are advised to avoid heavy lifting or strenuous exercise in the 2 weeks following a renal biopsy, in order to reduce the risk of surges in blood pressure that might provoke haemorrhage from the biopsy site. Some centres also routinely advise against sexual intercourse during this period. All patients are counselled again about the risk of delayed haemorrhage, which can be life-threatening. They should be advised that for up to 2 weeks after the biopsy they should remain vigilant for sudden or severe loin pain, visible haematuria or symptoms suggestive of internal bleeding (e.g. light-headedness, clamminess, shortness of breath). Should any of these symptoms occur, they should seek urgent medical assistance and inform the health-care team that they have had a recent renal biopsy.

## Complications and their management

### Minor complications

Minor complications are relatively common. Mild pain may be experienced at the biopsy site but is usually controlled by simple oral analgesia. Visible haematuria occurs in 2–4% of those undergoing the procedure (Corapi et al, 2012; Tondel et al, 2012). Patients should be reassured that this does not usually herald a serious complication, and usually resolves with conservative management. Perinephric haematomas are evident in up to 1 in 5 patients when routine post-procedural ultrasound scanning is performed (Corapi et al, 2012). However, as these almost always resolve spontaneously, no clinical benefit is obtained by such routine ultrasound scanning.

### Major complications

Bleeding is the main major complication following renal biopsy and occurs in 1–2% of patients. This risk is higher in patients in whom the biopsy is performed for an urgent indication, in older patients, in those with poor renal function (particularly when estimated glomerular filtration rate is <30 ml/min/1.73m$^2$) and in the presence of uncontrolled hypertension (Corapi et al, 2012; Tondel et al, 2012). In the authors' centre the bleeding risk is particularly high in patients who are dialysis-dependent at the time of biopsy. Major haemorrhage is usually retroperitoneal and thus presents with syncope or hypovolaemic shock but a paucity of other clinical signs. Initial management comprises attentive fluid resuscitation, including red cell transfusion, and correction of any coagulopathy. Urgent angiography may be able to identify the bleeding point, which can often be embolized using a percutaneous, radiologically-guided approach. If this fails then nephrectomy may be required.

### Other complications

Other potential complications are urinary (clot) retention (0.3%), the formation of an intra-renal arteriovenous fistula and perforation of an intra-abdominal viscus (very rare).

## Conclusions

Biopsy of native and transplanted kidneys is routine in current clinical practice. Physicians may encounter patients who are due to undergo or have recently undergone a renal biopsy procedure in different environments (hospital wards, general practice, the emergency department). Therefore, a working knowledge of the procedure and its potential complications is essential for all doctors. A kidney biopsy is requested to confirm a suspected diagnosis and therefore a comprehensive clinical assessment (history, examination, 'nephritic screen') is essential. However, any patient in whom a biopsy may be required should be discussed at an early stage with the nephrology team so that delays are minimized. **BJHM**

*Conflict of interest: none.*


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### KEY POINTS

- Renal biopsy is essential for the diagnosis and management of many kidney diseases.
- Renal biopsies are performed in routine clinical practice (>100 procedures per million population per year).
- The decision to biopsy a kidney is always taken by a senior nephrologist or transplant surgeon; biopsies are performed by an experienced nephrologist or radiologist.
- Biopsies are performed percutaneously under ultrasound guidance using spring-loaded biopsy devices.
- In experienced hands, renal biopsy is a generally safe and well-tolerated procedure.
- There is a low risk of haemorrhage, which if not recognized promptly could be life-threatening.


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