Approach to Renal Biopsy

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Contents

Abstract

The percutaneous kidney biopsy has transformed both the fields of nephrology and pathology. Prior to its introduction in the 1950s, analysis of kidney tissue was available only from deceased autopsy specimens. Advances in technology, technique, and imaging have led to both an improvement in tissue yield in addition to lower morbidity from complications. The kidney biopsy is currently the diagnostic gold standard for nearly all kidney diseases. Although a thorough history and physical in addition to basic serum and urine studies can aid the clinician, the biopsy is oftentimes the next necessary

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H. Trachtman et al. (eds.), *Glomerulonephritis*,
https://doi.org/10.1007/978-3-319-49379-4_1

step to confirm a specific diagnosis. Direct sampling of kidney tissue also adds significant prognostic value and can guide management strategies for a variety of disease states. This chapter will outline the history of the kidney biopsy, review tissue adequacy and staining, provide an overview of techniques for native and transplant kidneys along with the associated complications, and discuss future directions and possibilities with this procedure.

Keywords

Kidney biopsy · Renal biopsy · Medical history · Nephrology · Nephropathology · Renal pathology · Bleeding complications · Proteomics

Historical Perspective

The earliest reports of diseased human kidneys were gross findings on postmortem examination, which date back to the mid-nineteenth century, and the first reports of open kidney biopsies are from the 1890s. Physicians in this era were performing "nephropexy" to surgically fix mobile kidneys in patients who suffered from Bright's disease (now an obsolete term referring to nonspecific glomerulonephritis). In 1901, surgeons in New York performed renal decapsulation in a 43-year-old female with chronic Bright's disease followed by kidney tissue sampling which revealed advanced chronic interstitial nephritis (Edebohls 1904). Interestingly, these surgeries were meant to cure the patients of their kidney disease, as decapsulation of the swollen organs was hypothesized to relieve the inflammation and promote healing.

The next several decades saw similar publications where renal sampling was performed via the open approach. An interesting surgical approach to hypertension in the 1940s was splanchnicectomy and sympathectomy, which were performed to mechanically vasodilate the splanchnic capillary beds to allow for a decrease in blood pressure. As this was an open procedure that exposed the kidneys, open renal tissue sampling was often performed secondarily. Many of the fathers of renal pathology (e.g., Robert Heptinstall from Great Britain) examined tissue from open biopsies and published the first reports on renal vascular histologic changes associated with hypertension (Heptinstall 1953).

The percutaneous kidney biopsy was first described in 1951 by Iversen and Brun in Copenhagen, Denmark (Iversen and Brun 1951). The initial technique utilized an aspiration liver biopsy needle in conjunction with intravenous pyelography imaging. The patient was positioned in the sitting position and a 1.9 mm serrated needle was used to cut the tissue, followed by applied suction to the needle to secure the sample. Minor complications of gross hematuria and pain were noted, but no major complications developed. However, tissue yield was only adequate for diagnosis in 50% of cases.

The technique was modified in 1952 by Kark and Muehrcke at Presbyterian Hospital in Chicago (Kark and Muehrcke 1954). Their technique improved sampling by placing the patient in the prone position and avoided suction aspiration of the tissue. In their published description, a 4 in. sandbag was placed under the prone patient's lower abdomen to displace the kidney more posteriorly. The procedures were performed using anatomic landmarks and palpation of the kidney with respiration. A 20 gauge exploring needle was inserted, and the patient inhaled and exhaled deeply. If the needle tip was in the kidney, the hub of the needle would swing up and down in an arc during inspiration/expiration as the kidney was pushed by the diaphragm. Once the depth and location were confirmed, the physicians would anesthetize and insert a modified Vim-Silverman needle. Rather than aspiration of tissue described by Iversen and Brun, the modified needle used a cutting edge and longitudinal groove which retained a 1–2 cm core of tissue when the needle was withdrawn. In their own words, the tissue was "punched and bitten from the kidney." Their publication demonstrated adequate tissue for diagnosis in 96% (48/50) of biopsies. Complications included gross hematuria in 8%, pain in

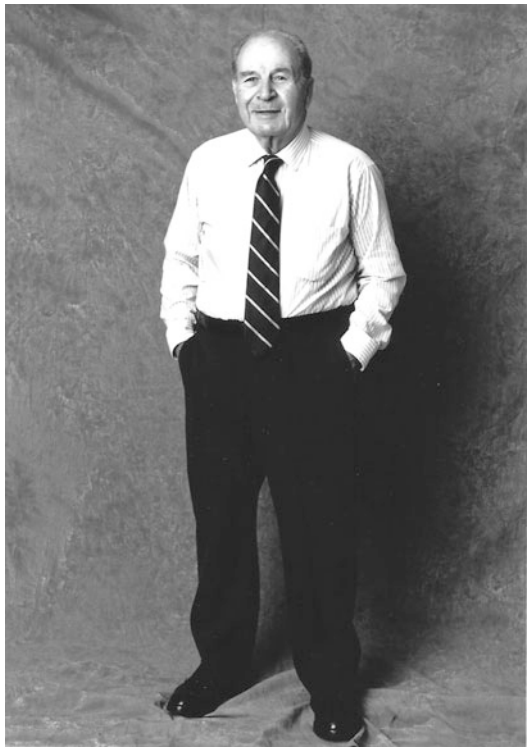

Fig. 1 Dr. Robert Kark, the pioneer of the percutaneous kidney biopsy in Chicago, Illinois. (Image courtesy of Dr. Stephen Korbet and Dr. Roger Rodby at Rush Presbyterian Hospital, Chicago, Illinois)

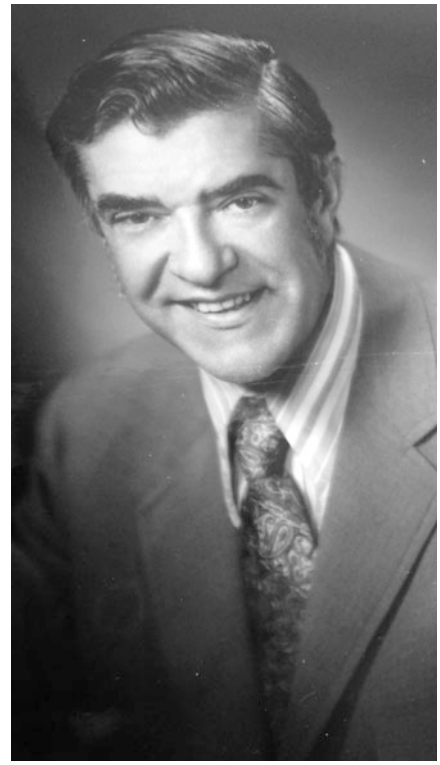

Fig. 2 Dr. Robert Muehrcke, who worked with Dr. Kark (Figure 1) in Chicago, Illinois. (Image courtesy of Dr. Stephen Korbet and Dr. Roger Rodby at Rush Presbyterian Hospital, Chicago, Illinois)

10%, and one patient (2%) required a transfusion. Remarkably, the clinical diagnosis changed based on the histologic findings in half (25/50) of the patients. The physician pairing of Drs. Kark and Muehrcke were joined by Dr. Conrad Pirani, a pathologist at the University of Illinois in Chicago. Pirani applied systematic semiquantitative scores of activity and chronicity in his evaluation of their renal tissue that are still utilized today (Figs. 1, 2, and 3).

Around this same time, pioneers were pushing the boundaries of pathology by coupling fluorescent probes to antibody to detect immunoglobulin in frozen sections. Drs. Robert McCluskey and Gloria Gallo at New York University first published the application of immunofluorescence in human kidney biopsy samples in 1966 (D'Agati et al. 2013, McCluskey et al. 1966). Similarly, electron microscopy (which had been developed in the 1930s) was being utilized to examine kidney biopsy specimens. In addition to showing fine resolution of glomerular structures such as the podocyte foot processes and fenestrated endothelium, a host of new diseases were discovered. Diffuse foot process effacement was identified as the hallmark finding of minimal change disease. "Zebra" inclusion bodies of lipid storage diseases such as Fabry's disease were reported. To this day, nephropathology is one of the few subspecialties in pathology where electron microscopy remains a standard of care (Figs. 4, 5, and 6).

Newer technology pertaining to the kidney biopsy over the past 60 years has mostly included advances in the use of real-time ultrasound or CT guidance and the quality of automated biopsy needles. The spring-loaded biopsy gun was developed in 1982, with a modified Tru-Cut needle.

Fig. 3 Franklin modified Vim Silverman needle. The upper needle is the outer trocar. Once the tip of this needle is in the renal capsule, the lower needle is punched into the kidney. When retrieved, the end splits to allow the operator to retrieve the tissue core

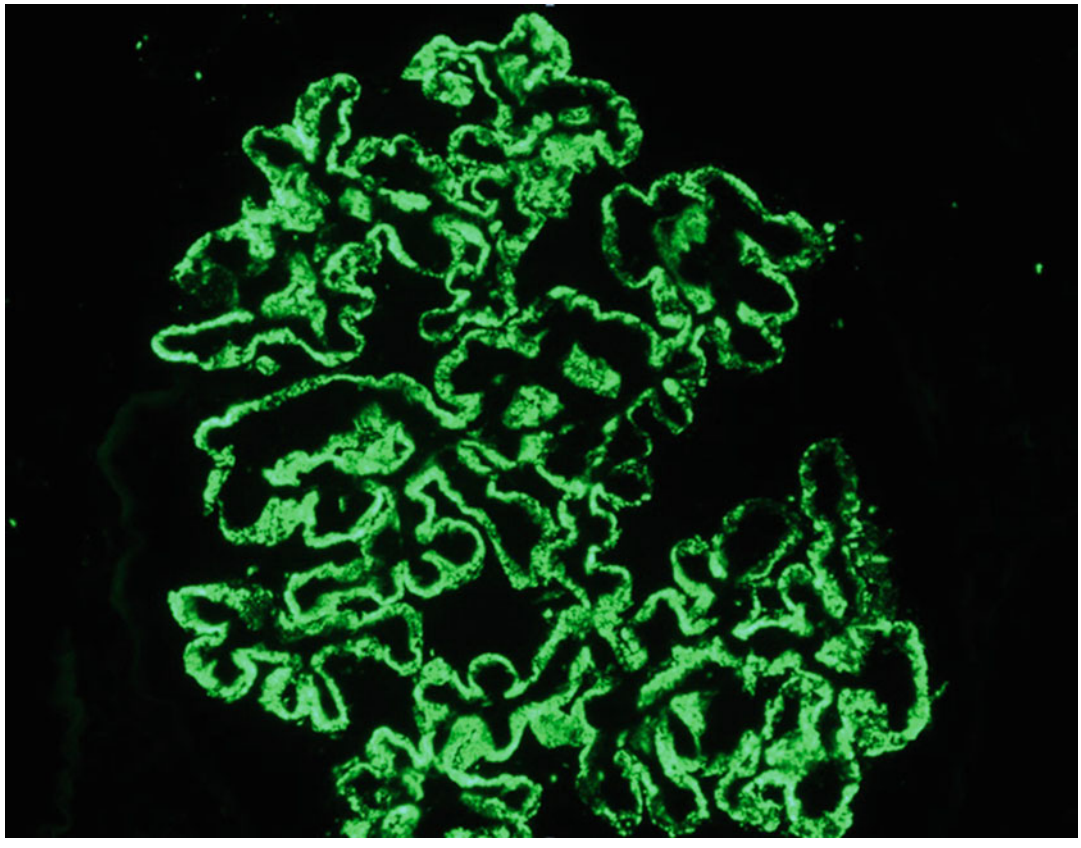

Fig. 4 Image of the IgG immunofluorescence, showing the granular capillary loop staining in a case of membranous nephropathy

When the tip of this biopsy needle is in place, the spring is released. The inner trocar is thrust forward first, followed quickly by a forward thrust of the outer cutting cannula. This delayed movement traps the tissue in the notch of the trocar when the cutting sheath is advanced (Fig. 7).

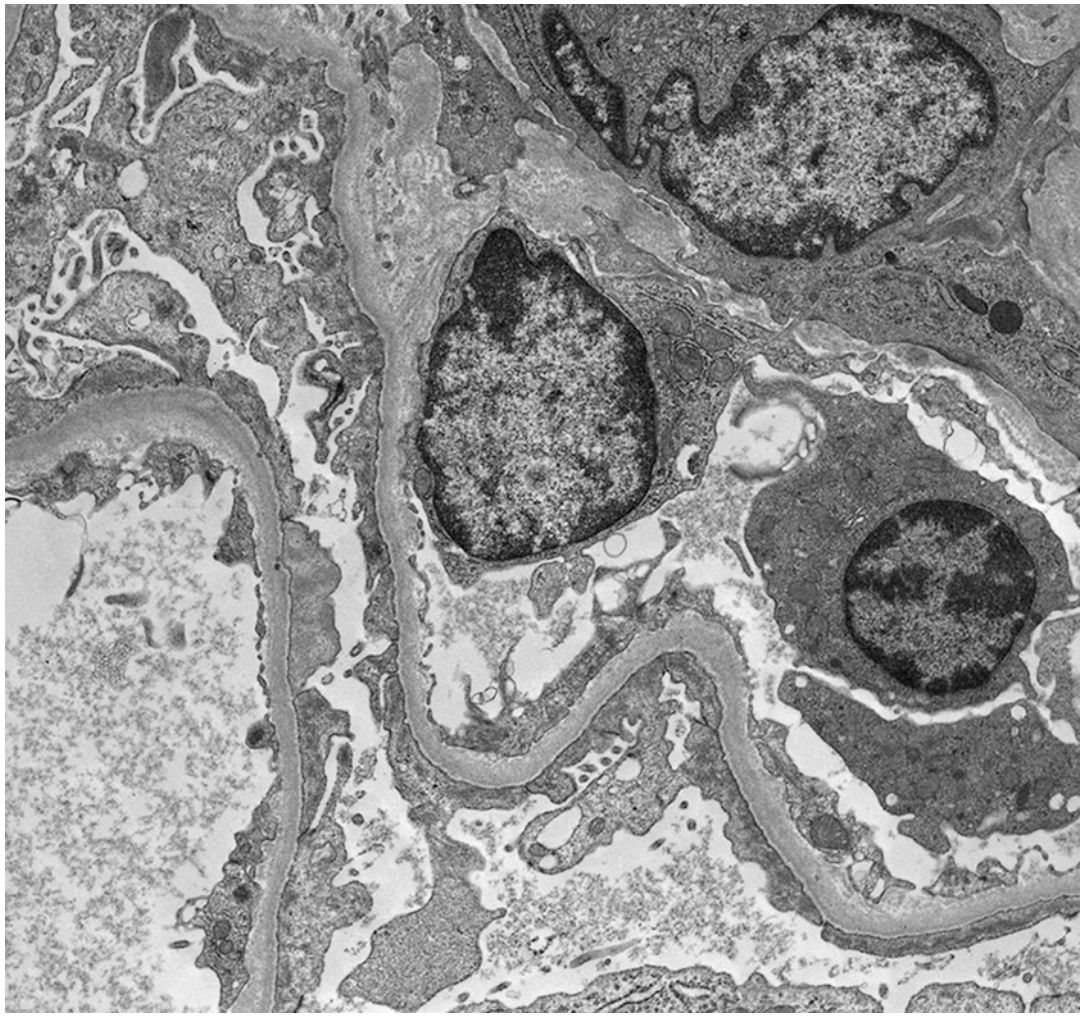

Fig. 5 Image of the diffuse foot process effacement seen in minimal change disease (×7000)

Another advance in the field during this time included alternative approaches to the kidney itself. This includes a transvenous approach, which was modified in the 1990s from transjugular liver biopsy technicians (Lindgren 1982). With this procedure, the kidney is accessed via the venous system into a medullary interlobular vessel. The needle is passed through the vein into kidney cortex for sampling. Theoretically, this approach has the benefit of minimizing bleeding into the renal capsule, as any bleeding would drain directly into the vein whose wall was breached. Glomerular yield can also be a concern with this approach, as this technique accesses the kidney from the inside out, with most glomeruli in the outer cortex of the organ. Open or laparoscopic surgical biopsies can still be performed in certain circumstances (e.g., severe bleeding diatheses) or if a patient is already undergoing an open surgical procedure. The yield of surgical biopsies is excellent as there is direct visualization of the kidney with sampling, but these procedures carry the additional morbidity and mortality of general anesthesia.

Despite these alternative approaches, the percutaneous renal biopsy remains the standard of

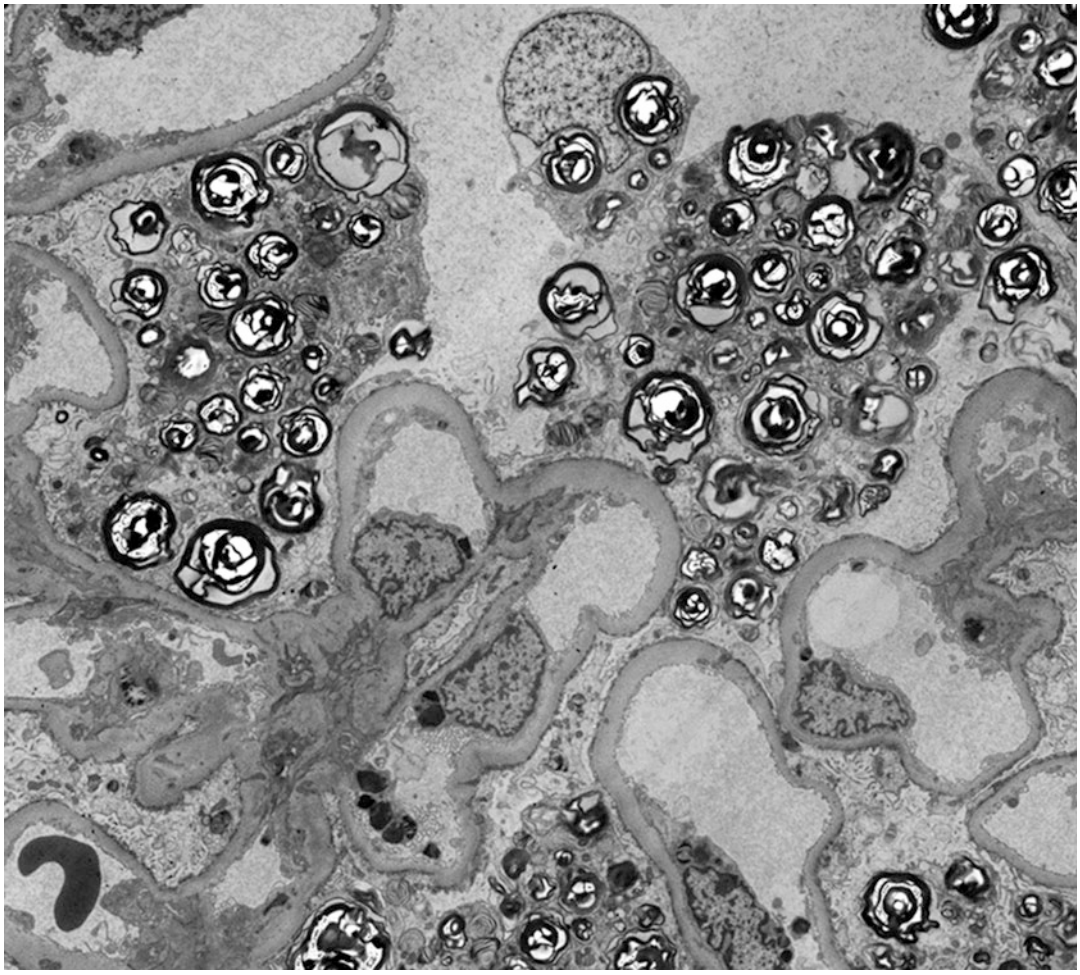

Fig. 6 Image of the "zebra body" inclusions seen in Fabry's disease (×2000)

care. The modifications of real time imaging and spring-loaded biopsy guns have established the procedure as a safe and effective method of obtaining kidney parenchyma.

Tissue Adequacy

The earliest case series from Iversen and Brun reported adequate tissue for diagnosis in less than half of their patients. The uses of spring-loaded automated biopsy guns and imaging advances have certainly improved tissue sampling, but there is still no absolute quantifiable metric to gauge adequacy. Oftentimes, sampling 10 glomeruli will not be diagnostic if there is a very focal lesion. Other times, even one glomerulus can provide the clinician enough information to make a diagnosis.

In modern practice, the number of cores required for an adequate sample depends on the length of the needle. Needles that take shorter cores may require three or more samples to ensure adequate sampling, whereas longer devices may take cores that are several centimeters long, and one pass may be all that is required. Kidney tissue can be viewed under a light or dissecting microscope directly as a wet mount to ensure that the core is kidney tissue rather than skeletal muscle, adipose tissue, or nonrenal organs. Immediate

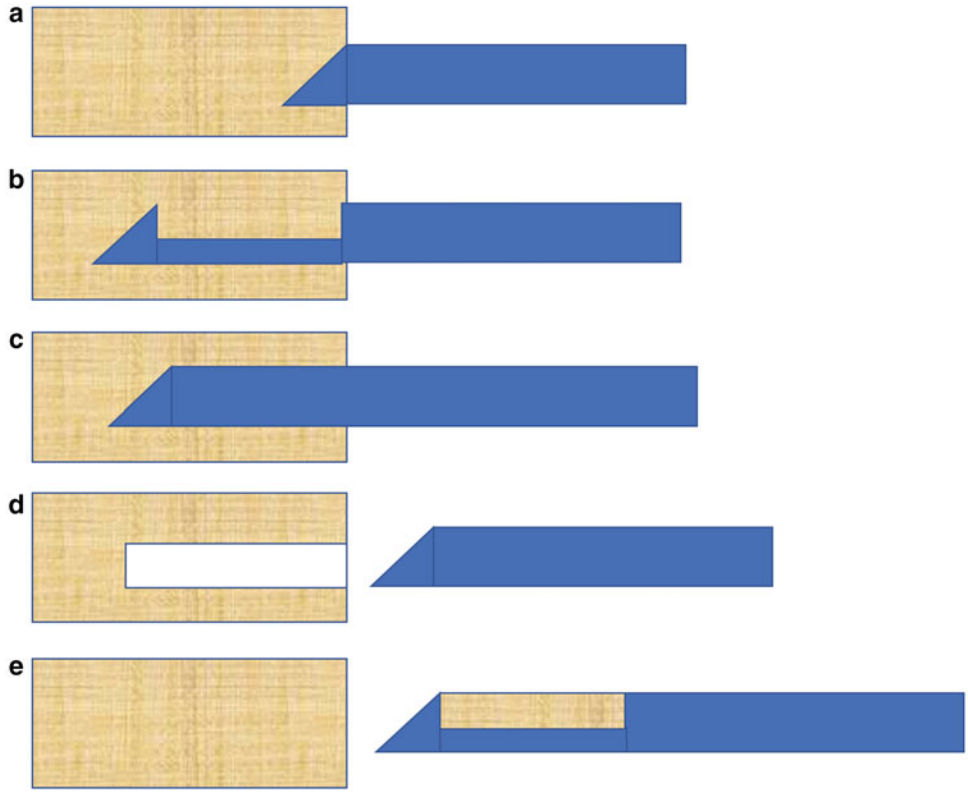

Fig. 7 Schematic of the cutting action of the spring-loaded biopsy gun. (**a**) Needle (in blue) introduced into kidney (brown). (**b**) When the gun is fired, the inner trocar is advanced, followed quickly by (**c**). (**c**) Outer cutting cannula is advanced. (**d**) Closed needle is retracted. (**e**) Tissue wedge obtained when outer cannula is retracted

direct visualization with a well-trained eye can also ascertain how much of the sample is cortex, medulla, or a mixture of both.

There is no absolute number of glomeruli that makes an individual biopsy diagnostic. The greater the number of glomeruli in the sample, the lower the likelihood of missing a focal lesion (e.g., segmental scar in FSGS, crescent in ANCA-related disease). For example, biopsy of a patient with nephrotic syndrome secondary to FSGS has a 35% chance of missing a segmental scar on light microscopy if only 10 glomeruli are sampled, and segmental scars are present in 10% of glomeruli. However, if 20 glomeruli are sampled, the statistical likelihood of missing a segmental lesion drops to 12% (Corwin et al. 1988). Based on these statistical analyses, it is ideal to have a sample taken that has at least 10 or more glomeruli for evaluation. Biopsies with smaller numbers of glomeruli can and should still be interpreted, but awareness of the possibility of a sampling error should be noted (Fig. 8).

Tissue Staining

Once a biopsy sample is deemed adequate by the proceduralist, the tissue is fixed and stained. Complete evaluation of kidney tissue obtained by renal biopsy typically entails three components:

- Light microscopy (LM)
- Immunofluoresence (IF)
- Electron microscopy (EM)

The standard approach is to remove the ends of cores for EM and place them in a suitable fixative such as formalin or glutaraldehyde. If the sample

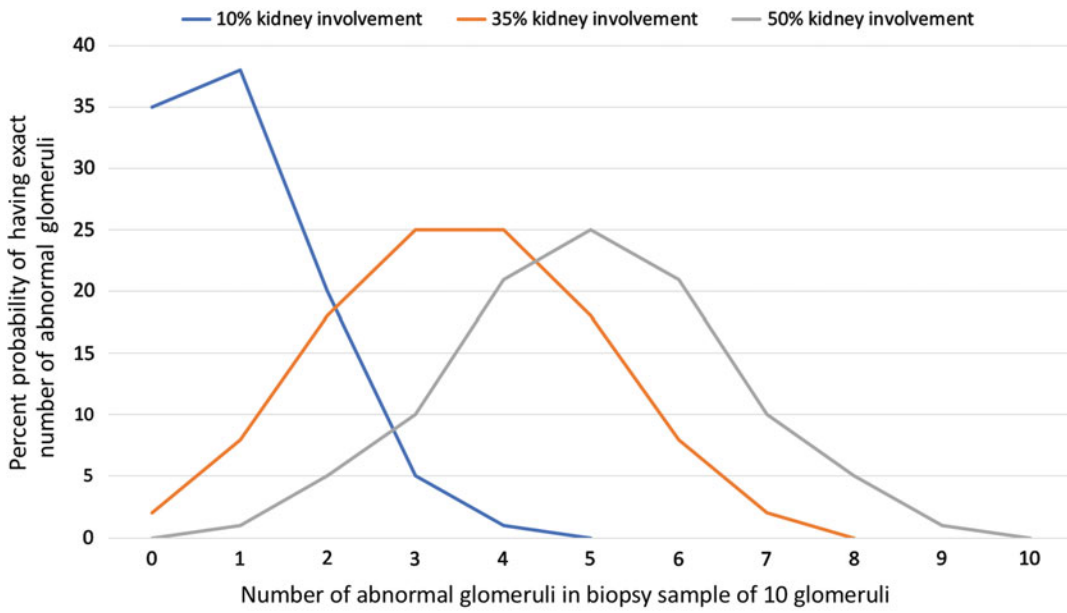

Fig. 8 The graph represents a binomial distribution of the number of abnormal glomeruli, which would be found in biopsy samples obtained from kidneys with an actual percentage of abnormal glomeruli of 10%, 35%, and 50% (represented by the blue, red, and green lines, respectively). As you can see, if a focal lesion is only affecting 10% of the glomeruli, there is a 35% chance of missing the lesion if only 10 glomeruli are sampled. (Data adapted from Corwin et al. 1988)

is mostly kidney cortex, the remaining core can then be divided for IF and LM, and additional passes may need to be made if adequacy is a concern. LM tissue is most commonly fixed with formalin, although various laboratories may use other solutions. IF is best performed on unfixed sections, so the sample reserved for IF should be set aside for separate transport to the laboratory (Walker et al. 2004). In situations where tissue might be limited, the clinician can make a decision to reserve larger cores for different purposes. This decision would be guided by determining which stain will provide the greatest clinical relevance for that individual scenario.

When examining tissue under the microscope, the pathologist and clinician should evaluate the four discrete compartments of the kidney (Fig. 9).

1. Glomeruli
2. Tubules
3. Interstitium
4. Vessels

Further details of kidney histopathologic interpretation and classification of glomerular diseases will be reviewed in future chapters.

Indications for Kidney Biopsy and Patient Preparation

The indications for kidney biopsy vary greatly from patient to patient. When a thorough history, physical, and ancillary blood and urine testing do not bring the clinician to a specific diagnosis, a kidney biopsy usually offers the highest diagnostic sensitivity. Other times, a kidney biopsy may be performed to ascertain the degree of activity versus chronicity to determine if the disease might be reversible. For example, a patient with systemic lupus erythematosus and a serum creatinine of 4.0 mg/dL may not be treated with aggressive immunosuppression for lupus nephritis if the biopsy revealed chronic fibrotic changes. The indications for kidney biopsy include, but are not limited to:

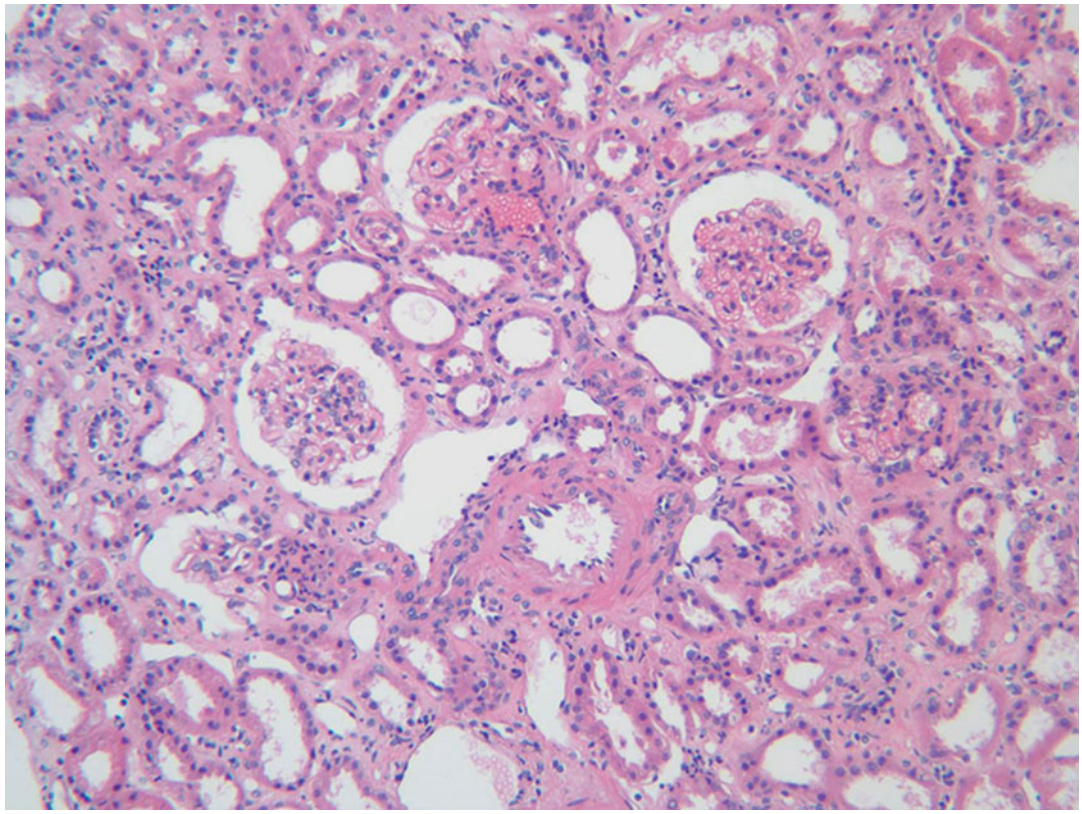

Fig. 9 Hematoxylin and Eosin stain demonstrating the four compartments of the kidney that are evaluated histologically

1. Unexplained decrease in glomerular filtration rate
2. Nephrotic or nephritic syndrome
3. Unexplained proteinuria
4. Isolated glomerular hematuria

The procedure is typically under performed under ultrasonographic or CT guidance by a nephrologist or interventional radiologists. Institutions or individuals may have differing prebiopsy protocols. However, most providers agree that the patient should have the following labs prior to the procedure:

1. Complete blood count
2. Prothrombin time/international normalized ratio
3. Activated partial thromboplastin time
4. Type and Screen

For nonemergent biopsies, antiplatelet or antithrombotic agents and nonsteroidal anti-inflammatory drugs should be discontinued at least 1 week in advance of a scheduled biopsy. For hospitalized inpatients that require heparin, this medication should be held approximately 6–12 h in advance to allow the aPTT to normalize. Blood pressure control should be optimized and informed consent and documentation of allergies should be performed in advance of an elective procedure.

Contraindications to Kidney Biopsy

The relative and absolute contraindications for percutaneous kidney biopsies have changed with the improved safety of the procedure. In general, the majority of clinicians and position papers agree that the following are absolute contraindications to kidney biopsy:

1. An uncooperative patient
2. Severe uncontrolled hypertension
3. Refractory bleeding diathesis

Relative contraindications include but are not limited to:

1. Hydronephrosis
2. Active skin infection over biopsy site
3. Anatomic abnormalities of the kidney (e.g., multiple bilateral cysts)
4. Solitary kidney

In many of these circumstances, kidney biopsy may be readdressed once the active issue (e.g., infection, hydronephrosis) is resolved. Anatomic abnormalities in one kidney may necessitate the contralateral kidney to be biopsied. Biopsy of patients with a solitary kidney will be discussed as a special consideration later in this chapter, but can now be considered by an experienced operator due to the improved safety reported using real time imaging. For situations in which there is an uncorrectable bleeding diathesis, non-percutaneous techniques (open or transjugular renal biopsy) may be acceptable alternatives.

Complications of Kidney Biopsy

Complications of kidney biopsy include bleeding, infection, puncture of another organ, and arteriovenous fistula formation. Puncture of liver, spleen, pancreas, and small bowel has all been reported but are very rare with real time imaging. Arteriovenous fistula formation may occur in patients if the walls of smaller veins and arteries are damaged. These typically are clinically silent and resolve spontaneously. In rare circumstances where fistulas form and become symptomatic, they can be addressed with arterial embolization. Bleeding complications can occur around the kidney (perinephric) or within the kidney and cause bleeding into the collecting system. This can lead to pain, a prolonged hospitalization, urinary obstruction, or a need for transfusion. As it is the most common and clinically relevant complication that can occur after kidney biopsy, it will be discussed in more detail.

The kidneys receive 20% of the cardiac output. With such a vascular organ, it might be expected that puncturing this would potentially lead to life-threatening blood loss. Fortunately, the majority of bleeding after kidney biopsy is restricted to the capsule and is self-limited. Prospective studies from the 1970s showed that CT imaging after kidney biopsy revealed evidence of perinephric hematoma in 14/20 patients, although only 1 had clinically evident bleeding. The remaining 13 patients that demonstrated bleeding on CT imaging had no change in hematocrit, blood pressure, or heart rate (Rosenbaum et al. 1978).

Minor bleeding complications such as microscopic or gross hematuria occur in the majority of patients and will resolve spontaneously. Major complications are usually defined as need for further treatment or intervention. This includes transfusion of blood products, coil embolization for persistent bleeding, or surgical repair. The overall incidence of transfusion requirements varies between studies, but a meta-analysis showed an overall transfusion rate of 0.9%, with a 0.6% rate of angiographic intervention. Death was reported on two cases out of a total of 8,971 procedures, for an overall incidence rate of 0.02% (Chung et al. 2014). Some single center studies show transfusion rates as high as 5–9%, but these include higher-risk populations (Korbet et al. 2014).

The change in hemoglobin concentration is evaluated postbiopsy to monitor for bleeding. One series reported an average drop in hemoglobin concentration of 0.9 g/dL in patients without clinically evident bleeding (Whittier et al. 2004). As a result of these findings, patients undergoing kidney biopsy can be expected to have a small decrease in hemoglobin concentration. However, a more severe drop of >2 g/dL is more suggestive (but not an absolute indicator) of clinically significant bleeding (Table 1).

Selecting the Needle Gauge

The modern spring-loaded devices use 14-, 16-, or 18-gauge needles, with an outer diameter of 2.11, 1.65, and 1.27 mm, respectively. The majority of renal biopsies are performed using 14- and

Table 1 Complication rate of native kidney biopsy

Complication	Reported frequency (%)	Number needed to harm
Gross hematuria	3	33
Perirenal infection	0.2	50
Arteriovenous fistula	0.4	250
Transfusion requirement	1	100
Intervention required to stop bleeding	0.6	166
Nephrectomy	0.01	1000
Death	0.02	500

16-gauge needles, with 18-gauge needles reserved for children or very small individuals. There is no significant difference in adequacy when comparing 14- and 16-gauge needles, but some studies have noted a lower yield with the smaller 18-gauge needles (Hogan et al. 2016). Some studies have shown a higher rate of transfusion with the use of 14-gauge needles although the risk was still quite low at 2.1%. Other studies have demonstrated no differences in complication rates or transfusion requirements based on needle size (Corapi et al. 2012). Based on a balance of yield and bleeding risk, most institutions use 16-gauge automated needles as the standard of care, with larger or smaller gauges available for unique circumstances (Fig. 10).

Fig. 10 Examples of the modern spring loaded automated cutting needles used for kidney biopsy. The length of needle can vary from 15 to 25 cm, and the gauge from 14 to 18. The Inrad device (bottom) also allows the operator to select the length of core to be taken (13 mm, 23 mm, or 33 mm)

Technique for Native Kidney Biopsy

Various institutions have differing protocols for performing kidney biopsies. In general, the patient should have peripheral intravenous access placed beforehand. The patient is then placed prone, and a pillow or towel can be placed under their abdomen if this does not cause significant discomfort. Some institutions will use ultrasound guidance to localize the kidney only, and then perform the biopsy with a "blind" approach. However, most institutions use real-time ultrasonography to visualize the entire procedure, as this leads not only to a lower rate of major complications, but also increases diagnostic yield. Once an appropriate path to the kidney has been identified, the skin is prepped and draped, and local anesthesia (usually 1% buffered lidocaine) can be injected to numb the skin and the tract of the biopsy needle. If the kidney is particularly deep, then a spinal needle may be necessary to apply anesthesia to the appropriate depth. A scalpel may be used to create a small skin incision to facilitate passage of the larger biopsy needle bore. Variations in kidney position with inspiration and expiration should be noted, and the patient should be instructed if and when to hold their breath in or out. If real time ultrasonography is available, then the biopsy needle will be guided directly into the lower pole via direct visualization, and the biopsy gun is deployed to take the core. Either kidney can be accessed for

sampling depending on the patient's position, anatomy, and surrounding tissue structures.

If the "blind" approach is being taken, the kidney is localized with ultrasonography prior to the procedure. The depth of the kidney is measured along with the angle of the ultrasound probe relative to the skin. Visualization of the kidney with inspiration/expiration is particularly important if the procedure is performed with this method. After skin prep and anesthesia is applied, anesthesia to the capsule is performed with a smaller gauge needle, and the operator will inject anesthesia down to the depth of the kidney measured during imaging. Oftentimes, the kidney can be felt with the finder needle, and tactile resistance can be noted as the needle tip enters through the capsule. Similar to the original description by Kark and Muehrcke, placing the needle to the level of the kidney and asking the patient to inhale and exhale deeply should cause the hub of the needle to smoothly swing cranially during inspiration and caudally during exhalation. Once the operator is comfortable with their positioning, the anesthetizing needle is withdrawn, a skin incision is made, and the blind approach is replicated with the biopsy needle.

Regardless of which approach is performed, once the spring loaded mechanism of the biopsy gun is deployed, the needle is withdrawn and the tissue in the chamber is mounted onto a slide for direct analysis. If necessary, more cores are taken until the clinician is satisfied with tissue adequacy. Once the procedure is complete, a local adhesive is placed over the skin incision, and the patient is turned supine which applies pressure over the biopsy site. Most protocols advise that the patient lie on their back over the next 4–6 h with frequent monitoring of vital signs during this time period.

There are few studies comparing the "blind" approach versus real time ultrasound imaging during kidney biopsy. One study evaluated post-biopsy complications by comparing these two techniques while also comparing the primary operators (nephrologists vs. interventional radiologists). No difference in complications was noted regarding the two techniques (Maya et al. 2007). Other studies have shown a higher complication rate and lower yield when using the blind approach. As a result, most institutions have moved away from using ultrasonography for localization only and have embraced the real time imaging approach.

Technique for Transplant Kidney Biopsy

Transplant renal biopsy is generally performed to evaluate for renal allograft dysfunction. Acute or chronic rejection, recurrence of primary disease, and other etiologies can only be definitively diagnosed with direct histologic examination of the tissue. Some institutions also perform protocol transplant biopsies at scheduled intervals to diagnose subclinical allograft dysfunction, but this is not a universal standard. The biopsy technique for transplanted kidneys is very similar to the native organ, but the approach is modified for the graft's new position.

In the early 1990s, it was routine to perform blind biopsies of the graft using ultrasound localization, or even with localization based solely on physical palpation and anatomic landmarks. Today, real time ultrasound guidance is nearly universal at all transplant centers. The preprocedural steps of optimizing coagulopathy and blood pressure are the same as described above for native biopsies. However, as the transplanted kidney lies in the iliac fossa overlying the iliopsoas muscle, it occupies the extraperitoneal space. Depending on the thickness of the subcutaneous tissue, the kidney is very superficial, and either the upper or lower pole can be accessed depending on the position it was transplanted. On rare occasions, the kidney transplant may be placed intraperitoneally; real time imaging will confirm this location so the procedure can be modified accordingly with special attention to avoiding surrounding bowel.

Kidney Biopsy Procedure in Unique Circumstances

Special considerations need to be given to specific populations that require percutaneous kidney biopsy. We will discuss:

- Pregnancy
- Solitary Kidneys
- Mechanical Ventilation

Pregnancy

There are many issues that arise when considering percutaneous kidney biopsy in a pregnant patient. The physical space occupied by the gravid uterus has an impact on the organ location and may also detract from the patients ability to lie in the prone position. Additionally, the risks of the procedure apply not only to the mother but also her fetus. Due to these concerns, most practitioners are wary of performing a kidney biopsy during pregnancy. Unless the diagnosis will alter management before delivery, the biopsy should be deferred until the postpartum period. However, a histologic diagnosis during pregnancy often needs to be emergently confirmed. These include scenarios such as evaluating for preeclampsis versus de novo glomerular disease or determining treatment options for lupus nephritis, which may be limited due to their teratogenic nature.

Data on complications after kidney biopsy in pregnancy are sparse. A meta-analysis showed that the risk of complications was highest in a "grey area" of pregnancy between 23 and 28 weeks gestation. The total complication rate remained relatively low at 1.3%. Interestingly, the results of the kidney biopsy altered therapeutic management in about two-thirds of patients (Packham et al. 1987). This information can be extremely useful in counseling regarding continuation or termination of pregnancy and maternal-fetal morbidity. Needless to say, if percutaneous kidney biopsy is deemed to be necessary in pregnancy, real time imaging is recommended if possible.

Solitary Kidneys

As outlined above, a solitary kidney is considered a relative contraindication for kidney biopsy. The rationale is not because of a higher incidence of complication, but rather that the consequence of an adverse event (e.g., nephrectomy) will be much more deleterious in these individuals. Prior to the 1990s, a solitary kidney was considered an absolute contraindication to percutaneous biopsy. However, an improved safety profile arrived with the acceptance of real-time ultrasound guidance and in automated biopsy guns. As a result, some institutions began performing biopsy of solitary kidneys with small but encouraging results (Mendelssohn et al. 1995). In the event that biopsy of a solitary kidney is performed, the procedure should be performed by an experienced operator under real time imaging guidance, and an extended observation to monitor for bleeding should be the standard of care.

Mechanical Ventilation

The intensive care is fraught with acute kidney injury from sepsis, ischemia, and toxins. However, severe systemic diseases such as ANCA associated vasculitis and thrombotic microangiopathy are also frequently encountered in this setting. A percutaneous kidney biopsy can still be obtained cautiously in this critically ill population. Particularly, patients on mechanical ventilation pose unique positional problems for the percutaneous approach. This can be overcome if the intubated patient can be prone positioned for the short period of time needed to perform the biopsy. Real time imaging can often reveal a satisfactory approach in the lateral decubitus position if proning is not possible. The movement of the kidney with the ventilator can be predicted if the patient is maintained on assist control ventilation. This allows the proceduralist to specifically time when the cutting edge is deployed into the kidney. One paper evaluated renal biopsy in ICU settings, with 57% of the patients on mechanical ventilation. A total of 98% of patients had sufficient yield, with 21 mean glomeruli per biopsy. Bleeding complications were higher in this study, with 22% having bleeding severe enough to warrant transfusion. However, baseline levels of hemoglobin were lower, and the biopsy may not necessarily have caused the transfusion requirement in all of these

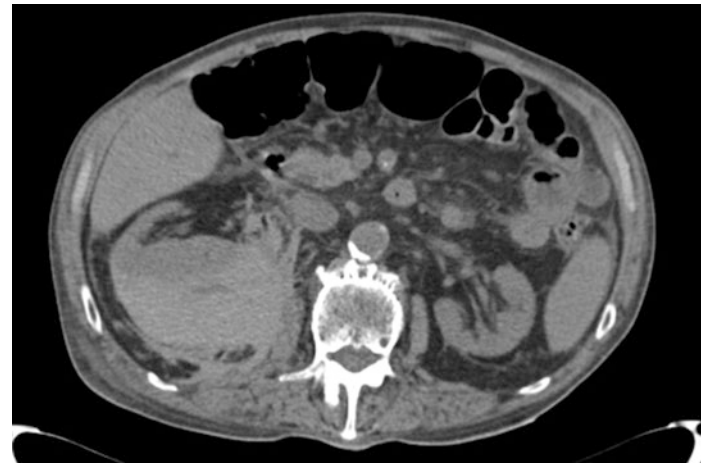

Fig. 11 Computed tomography of the abdomen without contrast reveals a large right retroperitoneal hematoma following kidney biopsy

patients. Despite the increased bleeding risk, 21% of these patients had biopsy findings that modified their treatment (Augusto et al. 2012). With most intensive care units now adopting point of care ultrasound technology, mechanical ventilation should not be a significant barrier to pursuing a kidney biopsy when indicated.

Addressing Postbiopsy Complications

Despite the relative safety of percutaneous kidney biopsy, prompt recognition of postprocedural complications and knowledge of available institutional resources is of utmost importance. The majority of complications occur within the first 24 h after the procedure. Suspicion for bleeding can be obvious (severe pain, hypotension) or subclinical (drop in Hb concentration of 2 g/dL). Immediate assessment of the patient's hemodynamic stability to rule out life-threatening hemorrhage is the first step followed by imaging to evaluate for perinephric bleeding. Ultrasound scanning can be performed relatively quickly and can identify up to 70% of hematomas, but is not as sensitive as CT imaging. There is no universal consensus on the routine use of any postprocedure imaging, and these scans are typically reserved for when there is suspicion for bleeding.

In the event that perinephric bleeding is substantial and is accompanied by a corresponding drop in hemoglobin, transfer to an intensive care setting for close monitoring is warranted. Transfusions and serial blood counts can be given, and stabilization of the hemoglobin suggests that the bleeding is contained. Continued bleeding warrants evaluation for arterial embolization of the vascular supply (typically performed by interventional radiologists) or surgical evaluation (typically performed by transplant surgeons or urologists) (Fig. 11).

Future Directions for Kidney Biopsy

The future era of information derived from the kidney biopsy is moving towards precision and personalized medicine. Molecular information has led to targeted chemotherapy in the field of oncology, as it moves beyond diagnosis by also predicting response to treatment. The fields of nephrology and nephropathology are moving beyond light microscopy and immunofluorescence into areas like proteomics (study of individual proteins), which has already transformed our understanding of diseases that were formerly lumped into the bucket of "renal amyloid." Using glomerular laser-capture microdissection and subsequent mass spectrometry on the samples has allowed us to identify the protein precursors of amyloid such as transthyretin, apolipoprotein A1, or beta-2 microglobulin.

Similarly, extraction of tissue from biopsy samples can provide insight into the molecular mechanisms that lead to their pathogenesis. This

has already been performed in diabetic nephropathy using gene microarray to determine overexpressed genes in diabetic nephropathy compared to healthy individuals (Baelde et al. 2004). Another exciting endeavor that will aid our understanding of diseases is the Precision Medicine Project, which was launched by the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK). Using human kidney biopsy specimens from participants, the initiative aims to create a kidney tissue atlas using single cell RNA sequencing to define and identify cells, pathways, and targets for specific diseases. The future of kidney biopsy interpretation looks bright and will incorporate morphology, immunopathology, serology, genetics, and molecular information. Using these new technologies, the information from the kidney biopsy will provide the clinical information needed to optimize disease-specific treatment on an individualized basis.

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