# What is new in kidney biopsy in 2024: A narrative review

## Les nouveautés de la biopsie rénale en 2024: Revue narrative

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**Abstract**

**Introduction**: Kidney biopsy continues to be an essential diagnostic instrument for assessing both acute and chronic kidney disorders, although progress in alternative diagnostic methods.

**Aim**: This review offers a thorough analysis of the contemporary significance, methodologies, indications, contraindications, and consequences related to native kidney biopsy, as well as addressing the possible alternatives being studied as of now.

**Methods**: We incorporated research that examine human participants undergoing native kidney biopsy, employing diverse techniques like ultrasound, computed tomography-guided, percutaneous, or laparoscopic methods.

**Results**: Improvements in biopsy needle design and imaging methodologies have markedly enhanced the safety and precision of biopsies, while problems such as hemorrhage and infections continue to occur.

Furthermore, we examined prospective developments in kidney biopsy, namely the possible applications of artificial intelligence, non-invasive biomarkers, and genetic testing. Exome sequencing has demonstrated potential in elucidating genetic etiologies of idiopathic renal illnesses, while artificial intelligence technologies are commencing to improve diagnostic precision.

**Conclusion**: Although developing technology may eventually diminish the necessity for conventional biopsies, kidney biopsy now remains an essential part of a nephrologist's work, especially for unusual and intricate situations.

**Key words**: Kidney Biopsy; Percutaneous Renal Biopsy; Indications; Contraindications; Technique; Liquid biopsy; Exome Sequencing; Artificial Intelligence

**Résumé**

**Introduction**: La biopsie rénale se maintient comme un outil de diagnostic essentiel pour l'évaluation des affections rénales aiguës et chroniques, en parallèle de l'avancement des techniques de diagnostic alternatives.

**Objectif**: Cette revue propose une analyse actualisée et approfondie de l'importance, des méthodologies, des indications, des contre-indications et des conséquences associées à la biopsie du rein natif, tout en abordant les éventuelles alternatives actuellement à l'étude.

**Méthodes**: Nous avons intégré des recherches portant sur des sujets humains subissant une biopsie du rein natif, en utilisant diverses techniques telles que l'échographie, la tomodensitométrie guidée, la méthode percutanée, ou les méthodes laparoscopiques.

**Résultats**: Les améliorations dans la conception des aiguilles de biopsie et des méthodes d'imagerie ont considérablement optimisé la sécurité et la précision des biopsies, bien que des complications telles que l'hémorragie et les infections continuent de se produire. Nous avons également examiné les futurs développements dans le domaine de la biopsie rénale, notamment les applications potentielles de l'intelligence artificielle, des biomarqueurs non-invasifs et des tests génétiques. Le séquençage d'exome s'est révélé prometteur pour élucider les étiologies génétiques des maladies rénales idiopathiques, tandis que les méthodes d'intelligence artificielle commencent à améliorer la précision diagnostique.

**Conclusion**: Bien que les technologies émergentes puissent à terme réduire le besoin de biopsies conventionnelles, la biopsie rénale demeure à ce jour un élément fondamental du travail des néphrologues, en particulier pour les cas complexes et atypiques.

**Mots clés**: Biopsie rénale; Biopsie rénale percutanée; Technique de biopsie rénale; Biopsie liquide; Séquençage d'exome.

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## Introduction

Kidney biopsy has emerged as a favored technique for acquiring essential information that can be utilized alongside serological, urine, and genetic assessments to diagnosis various acute and chronic kidney illnesses (1).
In 1951, Iversen and Brun originally presented the percutaneous renal biopsy (PRB), utilizing intravenous pyelography for localization and employing a hepatic aspiration needle to biopsy the right kidney, positioning the patients in a seated position. The method achieved success in merely 53% of tries, while 60% of samples provided insufficient tissue for diagnosis. Notwithstanding these constraints, their expertise stimulated interest in the PRB and resulted in heightened biopsy endeavors worldwide. Nonetheless, the success rate persisted at an unacceptably low level. In 1954, Kark and Muehrcke introduced a modified approach that transformed the renal biopsy domain. By positioning the patient in the prone orientation and employing a Franklin-modified Vim-Silverman needle instead of an aspiration needle, a success rate of 96% was attained without significant problems (1). Since that time, the renal biopsy method has generally remained consistent, although the incorporation of real-time ultrasound (US) or computed tomography (CT), together with enhancements in biopsy needle design, has yielded substantial advancements (2). These advancements helped increase the accuracy and safety of kidney biopsy. Despite that, kidney biopsy persists as a procedure burdened with potential dangers, including hemorrhage and infection, while its indications and contraindications are continually refined in light of growing clinical evidence.
The objective of this review is to examine the current relevance and utility of the kidney biopsy, while addressing recent updates and developments in its technique, indications, contraindications, and possible complications. This review seeks to give a full overview of the procedure's position in modern clinical practice and identify any developing trends or changes in its implementation.

## Methods

We reviewed publications on native kidney biopsy in human patients that addressed one or more elements, including technique, indications, contraindications, complications, or future prospects. The studies concern either adult or pediatric patients having native kidney biopsy, utilizing procedures such as US or CT, percutaneous, or laparoscopic approaches. Multiple study designs, such as case reports, systematic reviews, and meta-analyses, were incorporated. These criteria provided a thorough overview of contemporary procedures and perspectives pertaining to native kidney biopsy. However, we omitted papers not involving human subjects. We examined the subsequent electronic databases: PubMed, Cochrane Library, Web of Science, Scopus, and Google Scholar. Only articles and studies published in English and French were selected. The search phrases included a blend of controlled vocabulary and free text, with the keywords being: (Kidney OR Renal OR Percutaneous renal biopsy) AND (Technique OR Indications OR Contraindications OR Complications OR Perspectives). The search was similarly conducted in French utilizing the following keywords: (Biopsie rénale OU Ponction biopsie rénale) ET (Technique OU indications OU Contre-indications OU Complications OU Futur). The selected papers were analyzed through a narrative synthesis to synthesize and integrate findings pertaining to kidney biopsy. This entailed classifying the literature into principal themes: technique, indications, contraindications, complications, and prospectives.

## Technique

The optimal biopsy is entirely safe, devoid of problems, and yields sufficient tissue for diagnosis, prognosis, and therapy guidance. Consequently, the equilibrium between these two criteria should dictate a successful kidney biopsy (3).

**Equipment**
The utilization of semi-automatic, spring-loaded biopsy instruments has become the normal practice as they successfully acquired a higher quantity of glomeruli per biopsy specimen for light microscopy than hand-operated biopsy needles, without an escalation in bleeding issues (4).
The selection of needle size is contingent upon the desire of the investigator conducting the biopsy (4). The sizes range from 14G to 22-gauge (5). The most utilized are the 16- gauge and 18-gauge (6). A 2023 review comparing 16- to 18-gauge needles indicated that the 16- gauge needle requires fewer passes, since its larger size allows for the acquisition of a substantial number of glomeruli with minimal attempts. This thereby reduces the duration of the procedure and may improve patient comfort and adherence. Nonetheless, the review indicated a marginal increase in overall problems associated with the 16-gauge needles, despite major and mild complications being statistically comparable between the two needle gauges. The analysis underscores that the selection of a 16- or 18-gauge needle must be personalized, taking into account each patient's specific clinical situation and risk assessment (6).
The 2010 American College of Radiology guidelines provided evidence corroborating this viewpoint (7). However, the most recent amended guidelines do not specify a particular gauge; rather, they indicate that the clinician should be cognizant of the different biopsy needle sizes and kinds
To guarantee accuracy and safety throughout the process, kidney biopsies can be carried out utilizing a variety of imaging modalities. Among the primary methods are the following:

- Blind kidney Biopsy: In this conventional approach, the biopsy site is located and marked using US prior to the procedure. The actual biopsy is then carried out without the use of real-time imaging, depending instead on the initial localization. Despite being simple and affordable, this approach might not be as used.
- Real Time US-guided kidney biopsy: Employing

continuous US imaging during the procedure, this method is typically the preferred way. It enables real-time view of the kidney, the needle, and surrounding tissues. Because of its accessibility and efficiency, this technique is frequently employed.

Over the years, studies have been conducted comparing these two imaging techniques, which found that they do differ in tissue adequacy and complication rates (8-10). The research agrees on the superiority of real time US-guided biopsies, although their findings vary. This could be due to the different methodologies, patient groups, and clinical situations. Maya et al. (2007) found that real-time US guidance increased kidney tissue yield and decreased hemorrhagic complications, making it the preferable method (8). Pokhrel et al. (2018) concluded that US-guided biopsy had equivalent tissue adequacy and bleeding risks to blind biopsy with fewer needle passes (9). As for Pongsittisak et al. (2019), they found that real-time US-guided biopsies yielded tissue samples with more glomeruli and similar complication rates to the blind method, but the authors recommended the real-time method still (10).

CT-guided kidney Biopsy: Because CT guidance provides better resolution and tissue contrast than other imaging modalities, it is mainly used for renal biopsies including masses. This makes it possible to locate lesions precisely and clearly identify surrounding essential structures, which is very helpful in complex cases. Additionally, CT is useful in some situations where other methods might not work as well, such as in patients who are obese or have anatomical abnormalities. However, when compared to real-time US- guided biopsy, CT guidance may not always lead to increased accuracy or lower complication rates, despite its precise imaging capabilities. Because of this, it is typically only used in situations where ultrasonography is insufficient or not accessible (4, 11-14).

Although there are practical difficulties with each modality, the choice of imaging guidance is ultimately determined by the anatomy of the patient, the probable pathology, and the available resources and knowledge rather than being rigidly governed by absolute contraindications.

**Personnel**

Various specialists, including nephrologists and radiologists, may do a kidney biopsy. Radiologists prefer smaller gauge needles, specifically 18 gauge, in accordance with prior recommendations predicated on the assumption that a lower gauge equates to enhanced safety. available and choose the right size according to the clinical context (15). Nephrologists favor the utilization of bigger 14- or 16-gauge needles, as they enhance diagnostic precision and facilitate the extraction of a greater quantity of glomeruli compared to smaller needles. Provided that Radiologists persist in preferring smaller needles, the biopsy is more suited for a Nephrologist's expertise (3).

**Position**

Kidney biopsy is generally conducted in the prone posture. A pillow is positioned under the abdomen at the umbilical level to align the lumbar spine and support the kidneys (2, 4). However, we note that a recent study published in 2019 comparing individuals who underwent kidney biopsy in prone vs sitting positions indicated that the sitting position yields a comparable number of retrieved glomeruli, with less side effects and greater comfort than the prone position (16).

**Performance**

Skin sterilization is performed with povidone-iodine or chlorhexidine solution. A sterile fenestrated drape is positioned over the site to preserve a sterile environment. Lidocaine is used to anesthetize the skin and the puncture canal (2, 4). While a multitude of imaging techniques can be employed for performing this procedure, as described previously, we will use the US-guided technique as an example to illustrate the procedure. Under US guidance, the needle is directed to the renal capsule, followed by the infiltration of local anesthetic into the perirenal tissues, and subsequently along the needle's trajectory upon removal. A stab incision is performed into the dermis to facilitate the insertion of the biopsy needle (2). As the needle nears the capsule, the patient is directed to inhale until the kidney is positioned such that the lower pole, where the probability of encountering a major blood vessel is comparatively minimal (4), is directly beneath the biopsy needle, and then to cease breathing. The biopsy needle tip is positioned against the renal capsule, and the trigger mechanism is activated, deploying the needle into the kidney. The needle is promptly retracted, the patient is instructed to resume respiration, and the needle's contents are analyzed. A subsequent insertion of the needle is typically required to acquire more tissue. If inadequate tissue is acquired, more needle passes are performed. Renal tissue is partitioned into three specimens, designated for light microscopy, electron microscopy, and immunohistochemical analysis (2). After acquiring adequate kidney tissue, the physician applies pressure to the patient's back for 10–15 minutes to control bleeding. The skin incision is thereafter dressed, and the patient is transferred directly to bed for observation (2, 11).

## Indications

**Indications vary among doctors and vary even geographically. The main indications are the following.**

**Nephrotic Syndrome**: A biopsy is generally warranted in adults, excluding those with nephrotic syndrome and a positive anti-PLA2R antibody test. The diagnosis of membranous nephropathy requires no additional confirmation (2, 4, 17). In prepubertal children, it is warranted solely if clinical manifestations deviate from those typical of minimal change illness, which is generally the etiology of nephrotic syndrome in this population. The primary indications for kidney biopsy in children include insufficient response to glucocorticoids, steroid dependency, a recurrent course, or an onset age beyond 12 years (2, 18, 19).

**Acute Kidney Injury**: In cases of acute kidney injury, a kidney biopsy is warranted if acute kidney injury

due to diminished kidney perfusion, obstruction, or hemodynamic factors has been excluded, if the injury persists despite addressing the underlying cause, or if additional indicators necessitate a biopsy, such as the emergence of proteinuria or hematuria (2, 20).

**Chronic Kidney Disease**: for diagnostic purposes when the cause is unidentified (2, 20).

**Systemic Disease with Renal involvement**: A kidney biopsy yields critical information and can assist in diagnostic determinations for individuals with systemic diseases exhibiting urine abnormalities and/or renal dysfunction (2, 4, 11).

**Proteinuria**: Proteinuria beyond 1g/day is a definitive indication for a biopsy. Nevertheless, even mild proteinuria may warrant a biopsy in the following circumstances: when accompanied by hematuria, indicative of systemic illness, and/or associated with renal failure characterized by increased serum creatinine levels (2, 4, 20).

**Hematuria**: Hematuria in the context of nephritic syndrome necessitates a kidney biopsy to confirm the diagnosis and guide subsequent treatment. Renal biopsy. Conversely, isolated hematuria without proteinuria or renal impairment is often not indicative, as a diagnosis of IgA Nephropathy, for example, would not alter the treatment approach. Nonetheless, it serves as an indication in Japan following recent guidelines (11, 20).

**Familial Renal Disease**: A biopsy of one sick individual may provide a diagnosis and reduce the need for further study of family members (2).

## Contraindications

The majority of contraindications for percutaneous kidney biopsy are relative rather than absolute, with the principal issue being a coagulation condition that must be rectified before the procedure (2, 4, 20). Because hematological results directly affect bleeding risk, they are essential in determining the safety of a renal biopsy. Particularly linked to an increased risk of serious consequences are decreased hemoglobin levels and an increased activated partial thromboplastin time (aPTT) (22). One study indicated that the requirement for blood transfusions was strongly connected with baseline hemoglobin levels below 100 g/L (23). While according to a survey completed by nephrologists in Australia, the cut-off was 90 g/L (24), and a study in Canada identified a lower value of 70 g/L (25). As for aPTT, according to French guidelines, an aPTT ratio of 1.2 is a fair cutoff point to use when making decisions (14). However, there is presently no official evidence that pinpoints the precise cut-off value. Platelet counts are equally significant. Major bleeding is significantly more likely to occur in patients whose pre-biopsy platelet counts are less than 150,000 cells/mm³ (26). Some studies consider a lower threshold of < 120,000 cells/mm³ (27, 28). While among Australian nephrologists, the most often used platelet cut-off was 100,000 cells/mm³ (24).

It's interesting to note that there is ongoing debate on the predictive value of prolonged bleeding time. Although a longer bleeding duration may potentially raise the risk, prior research has not conclusively linked bleeding duration to bleeding issues following a biopsy (29). The inability of the patient to cooperate may also be considered as a contraindication; yet, sedation frequently presents a viable option (2). In addition, solitary kidney is seen as a contraindication; nonetheless, some contend that open biopsy may reduce the dangers (2). Despite the progress achieved, doing a biopsy on a solitary kidney constitutes a significant decision that necessitates thorough deliberation (21). Uncontrolled blood pressure above 140/90 mmHg is a relative contraindication (4), although it is uncommon for hypertension to be so severe as to prohibit a biopsy (21). Additional relative contraindications encompass pyelonephritis, hydronephrosis, severe anemia, substantial renal tumors, and cysts (2, 20). Anatomically abnormal kidneys may contraindicate percutaneous kidney biopsy; yet, developments in imaging techniques facilitate alternate methods. For example, conducting an open biopsy enhances the visualization of the kidney's architecture (4, 21).

Absolute contraindications specific to each imaging modality used for renal biopsy have not been conclusively found by any investigations. However, in certain clinical situations, the choice of modality is guided by relative contraindications and practical limits. For example, because too much adipose tissue makes it difficult to get a good acoustic window and makes it difficult to see the kidneys clearly, US-guided renal biopsies are typically not done on obese patients. The general contraindications for CT imaging also apply to CT-guided kidney biopsy. Severe renal insufficiency is a major example because of the possible nephrotoxic effects of the contrast material used, which can be used to improve lesion localization and vascular structure identification during CT-guided. Additionally, contrast agent allergies or the necessity for some groups, such as pregnant women, to avoid radiation exposure, are also considered major contraindications to this particular technique (30, 31).

## Complications

The most common and severe complication of kidney biopsy is bleeding, which can range in severity. However, with minimally invasive techniques largely replacing the need for surgical interventions, the management of these complications has undergone significant evolution. Even though severe bleeding complications are uncommon, they can occasionally call for treatments like blood transfusions or, in the worst situations, nephrectomy, which now only happens 0.01–0.2% of the time (4, 29). A key component of post-biopsy bleeding management is superselective renal artery embolization, which provides a minimally invasive and efficient way to halt bleeding while maintaining renal function. This method is especially useful for treating complications that can result from renal biopsy, such as renal hemorrhage, arteriovenous fistulas, and pseudoaneurysms (32–34). Superselective embolization stops bleeding and minimizes damage to healthy renal parenchyma by

using segmental catheterization to target specific injured vessels, ensuring optimal preservation of renal function (35). By eliminating the need for surgical hemostasis and making embolization the go-to treatment for bleeding complications following a biopsy, this method has revolutionized the treatment of severe renal hemorrhage (36).

Other bleeding-related complications can be encountered post-biopsy, such as bleeding into the urinary tract, which may induce obstructive symptoms but is normally not considered a severe problem (4). Hematuria is also prevalent; microscopic hematuria occurs in virtually all individuals receiving percutaneous kidney biopsy and is classified as a minor complication or not a complication at all (4, 23). Macroscopic hematuria, apparent to the naked eye, is a minor problem (4, 23, 29). Additionally, perinephric hematoma, which can leak into the retroperitoneal area, is another bleeding-related concern (4, 23, 29).

Less frequent consequences include discomfort, infection, harm to surrounding organs, and the creation of an arteriovenous fistula (4, 23, 37). It should be noted that biopsy risks may vary depending on the imaging technique utilized. As mentioned before, studies have shown that blind biopsy has higher bleeding risks. Real-time US guidance reduces hemorrhagic complications, making it safer than the former technique (8, 10). And, when chosen properly for the patient and clinical setting, both CT-guided and US-guided techniques are safe and effective, with no discernible differences in the risks of complications (12, 15).

**Table 1**. summarizing kidney biopsy complications.

| *Complication* | *Explanation* | *Type* |
|---|---|---|
| *Bleeding related* | Bleeding requiring transfusion | Major |
| | Bleeding requiring nephrectomy | |
| | Bleeding leading to death | |
| | *Macroscopic Hematuria* | *Minor* |
| | *Microscopic Hematuria* | |
| | *Perinephric Hematoma* | |
| *Others* | *Infection* | |
| | *Injury of adjacent organs* | |
| | *Arteriovenous Fistulae* | |
| | *Pain* | |

### Prospectives

Advancements in non-invasive diagnostic techniques, genetic testing, and artificial intelligence (AI) are shaping the future of kidney biopsy. Despite its limitations, including invasiveness and unsuitability for continuous monitoring, kidney biopsy is a crucial instrument for identifying and managing intricate or uncommon renal pathologies, among others. The advancement of 'liquid biopsy' alternatives is a primary objective, as non-invasive biomarkers exhibit potential to enhance traditional biopsies by elucidating disease causes and providing novel therapy options. Although these methods may precede kidney biopsy in certain instances, such as Anti-PLA2R dosage in the context of MN following the most recent KDIGO guidelines (17), in the future, it might replace kidney biopsy in regard to more pathologies. Regardless, it will probably remain necessary for diagnosing uncommon or complex disorders (38).

Exome sequencing (ES) has emerged as a viable method for detecting unexplained kidney diseases (UKD). ES has demonstrated efficacy in identifying genetic variations associated with pathologies such as collagenopathies and tubulopathies, elucidating 32.6% of UKD cases in a particular research. Nonetheless, although it can diminish the necessity for biopsy in specific hereditary renal disorders, ES cannot entirely replace biopsy, particularly when genetic testing does not yield a complete diagnosis. ES is anticipated to augment, rather than supplant, biopsy in several situations (39).

Moreover, innovations in AI and digital pathology are revolutionizing the future of renal biopsy. AI demonstrates potential in enhancing diagnostic precision through the analysis of whole-slide images, identification of illness patterns, and outcome prediction. AI-driven technologies may mitigate the deficiency of renal pathologists and standardize diagnosis via methodologies such as 3D pathology. Nonetheless, obstacles such as the requirement for extensive datasets and the resolution of the "black box" issue concerning AI interpretability persist. Ultimately, AI is expected to hopefully complement rather than substitute kidney biopsy, equipping nephrologists with a more powerful diagnostic instrument in the forthcoming years (40).

In conclusion, although various forthcoming breakthroughs may enhance the accuracy and efficiency of kidney biopsy in nephrology, we cannot assert with certainty that we can move past kidney biopsy as of now, nor in the near future. Currently, kidney biopsy is an essential diagnostic technique, and is expected to maintain its significant role in patient management.

## Conclusion

This review highlights the prevailing practices, obstacles, and progress associated with kidney biopsy. Although the future of kidney biopsy is ambiguous, the findings from this research indicate that its significance is not decreasing. The integration of developing technologies, including artificial intelligence, biomarkers, and genetic testing, holds tremendous promise for improving the accuracy and efficiency of kidney biopsy. While it remains uncertain if kidney biopsy will be entirely replaced by non-invasive alternatives, forthcoming advancements suggest a promising future for this vital diagnostic procedure. As the discipline progresses, continuous research and technical innovations will probably guarantee that kidney biopsy remains an essential instrument in nephrology.

**Declarations**

**Patient and Public Involvement Statement** No patients or members of the public were involved in the design, conduct, reporting, or dissemination of this review. The study focused on synthesizing existing literature on kidney biopsy advancements and did not require direct patient involvement.

**Competing interests** The authors declare that they have no competing interests.
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