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ULTRASOUND

Diagnostic efficacy and safety of ultrasound-guided kidney transplant biopsy using cortex-only view: a retrospective single-center study

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Abstract

Purpose Cortical biopsy is the cornerstone to reveal a cause of unexplained dysfunction of the kidney transplant. Nevertheless, only a few studies have reported the biopsy technique with its performance. We described a novel technique of ultrasound (US)-guided kidney transplant biopsy using cortex-only view and analyzed its diagnostic efficacy and safety.

Materials and methods Between January 2014 and December 2016, a consecutive series of 188 patients who underwent US-guided kidney transplant biopsy using cortex-only view by an experienced radiologist were evaluated (mean age, 46.1 ± 12.5 years; range, 21–79 years). Biopsy time, biopsy distance, biopsy core number, and glomerular number per patient were recorded. Successful biopsy (e.g., adequate, 10 or more glomeruli; marginal, 7–9 glomeruli) and complication rates were investigated, using Banff criteria and Clavien-Dindo classification, respectively.

Results Mean biopsy time, distance, and core number were 20.6 ± 6.7 min (range, 10–44 min), 3.2 ± 0.7 cm (range, 2.1–5.4 cm), and 1.9 ± 0.3 (range, 1.0–3.0), respectively. Mean glomerular number per patient was 20.4 ± 10.0 (range, 0–54). Adequate and marginal biopsy rates were 87.2% (164/188) and 95.2% (179/188), respectively. There was no major complication requiring treatment (no patient with Clavien-Dindo grade 2 or greater complication), while there were self-limiting minor complications in 5 patients (overall complication rate, 2.7%).

Conclusion US-guided biopsy using cortex-only view is feasible and safe in sampling cortical tissues of kidney transplant.

Key Points

- *Ultrasound (US)-guided kidney transplant biopsy using cortex-only view is feasible and safe.*
- *Adequate and marginal biopsy rates were 87.2% and 95.2%, respectively.*
- *No major complication requiring treatment occurred after biopsy.*

Keywords Kidney · Biopsy · Transplant · Allograft · Ultrasonography

Abbreviations

BMI Body mass index
US Ultrasound

Introduction

Early diagnosis of a cause of renal allograft dysfunction is of great importance for optimal management and graft survival [1]. Currently, biopsy of cortical tissues is essential because it can reveal a cause of unexplained renal dysfunction of the kidney transplant [2], while clinical or imaging investigations cannot reliably predict renal allograft rejection [3–5]. Percutaneous core biopsy under ultrasound (US) guidance is currently universal to obtain cortical tissues of a kidney transplant [6]. However, the reported rates of successful US-guided biopsy for the kidney transplant are quite broad (approximately, 55–85%) [7]. Nevertheless, there are not many studies describing US-guided biopsy techniques in detail [7–9], in which only the cortical tangential approach or its variant is introduced.

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However, the best approach for biopsy may differ from patient to patient due to a certain degree of the anatomical variance (e.g., location and shape of a kidney transplant). In addition, the presence of medium-to-large intrarenal or perirenal vessels or abnormal perirenal fluid in the possible biopsy pathway also may affect the needle approach to avoid complications. Therefore, a knowledge of various biopsy techniques enables biopsy operators to choose the most optimal way for effective and safe tissue sampling.

The purpose of this study was to describe a novel technique of US-guided kidney transplant biopsy using cortex-only view and retrospectively analyze its diagnostic efficacy and safety for patients of single tertiary institution.

Materials and methods

Study patients

This study was approved by the Institutional Review Board of our Institution. The acquisition of informed consents was waived for this retrospective study. This study was performed according to the Principles of the Declaration of Istanbul as outlined in the Declaration of Istanbul on Organ Trafficking and Transplant Tourism. Between January 2014 and December 2016, a consecutive series of 207 patients who underwent US-guided biopsies of the kidney transplants were retrospectively searched by means of the electronic chart review. Among them, 19 patients were excluded for following reasons: (a) no biopsy under the cortex-only view technique ($n = 14$) and (b) renal mass biopsy in the kidney transplant ($n = 5$). For the 14 patients who did not undergo a biopsy through the cortex-only view, the ultrasound examination prior to the biopsy suggested that the biopsy through the cortex-only view is not suitable because of small cortical volume and/or abundant medium-to-large-sized intrarenal vessels under the cortex-only view. For these patients, cortical tangential approach was alternatively utilized for the biopsy [8], which yielded adequate biopsy without major complication for all the cases.

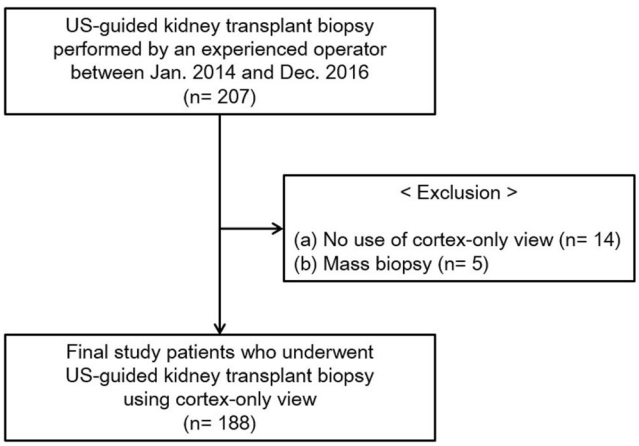

Fig. 1 Flowchart of study patients

Thus, a total of 188 patients who underwent cortical biopsies using the cortex-only view technique were finally included in this study (Fig. 1). The number of final study patients was higher than the sample size calculated with the alpha of 0.05, power of 0.80, non-inferiority margin of 0.1, and previously reported adequate biopsy rate of 0.87 from a previous report [8]. During the study period, of the 188 patients, 175 patients underwent biopsies once, and 10 and three patients underwent biopsy twice and three times, respectively. For the 13 patients with a history of multiple biopsies, only the data of the first biopsy were analyzed.

Renal biopsy

All suspected kidney rejection episodes such as elevation in serum creatinine or persistent proteinuria with/without hematuria were the biopsy indication by the decision of clinicians. For the patients taking the antiplatelet or anticoagulant agents, the medications were discontinued for 7 days before the biopsy.

An experienced genitourinary radiologist (S.Y.P.) who had more than 5 years of experience in the renal cortical biopsy performed the cortical biopsies in kidney transplants using the cortex-only view technique. US (Aixplorer, SuperSonic Imagine) with a convex probe of frequencies ranging 3.5–5.0 MHz was used for the image guidance. We used one of the 18-gauge semi-automatic biopsy guns (M.I. Biopsy Instrument, M.I. Technologies, or Mission Disposable Core Biopsy Instrument, Bard). With the patient in the supine position, 1% lidocaine of 10 ml was percutaneously injected using a 22-gauge spinal needle from the skin to renal surface under US guidance. None of the patients received general sedation.

Renal tissues were sampled in the lateral cortex of the kidney transplant. On gray and color Doppler US images, a cortical region with less vascularity and no visible hypoechoic renal medulla was considered to be the optimal biopsy site (Fig. 2). We termed this US imaging technique as the "cortex-only view" because US images of the cortex-only view at the optimal biopsy site depict only the renal cortex without low echoic medullary regions. This approach allowed longitudinal visualization of the planned needle trajectory. The expected tract was always in the cortex prior to the device deployment. Neither the inferior epigastric artery nor any abnormal fluid collection was in the possible biopsy pathway. The biopsy site was not limited to any particular region in the kidney, as it would be with the cortical tangential approach [8].

We manually inserted an 18-gauge semi-automatic biopsy needle without the use of attached guide device within the optimal site of a kidney transplant. Then, in order to determine whether or not the biopsy needle was located in the expected site, we sweep the US probe medially and laterally to avoid

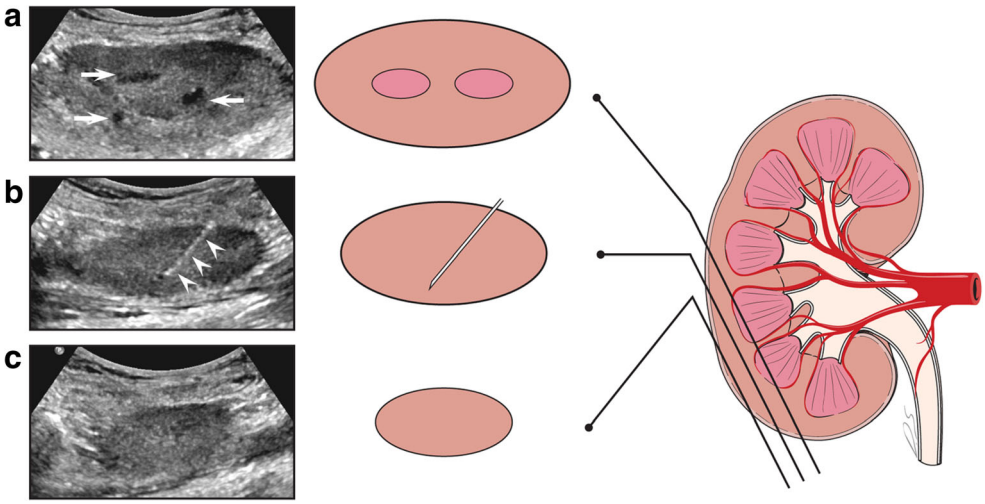

Fig. 2 Illustrations of US-guided kidney transplant biopsy using cortex-only view. **a** US image shows hypoechoic renal medullary regions (arrows) surrounded by renal cortex at the medial part of a kidney transplant. **b** US image shows the optimal site for biopsy, where a biopsy needle (arrowheads) is seen in the cortical region without hypoechoic renal medulla. **c** US image shows the most lateral part of a kidney transplant, where cortical volume is relatively small to obtain long cortical samples without injuring posterior renal capsule

incorrect needle position via partial volume artifact. The slot portion of an inner needle was manually deployed, and then the spring-loaded outer sheath was finally deployed for the side cutting. We tried not to puncture the renal capsule of far side because bleeding to the posterior aspect of a kidney may not be controlled by manual compression. The breath-hold was not mandatory. In most patients, at least two cores were routinely obtained [10]. However, the sample size of the two cores was smaller than expected; additional cores were obtained [8]. Conversely, when it was expected that a risk of bleeding is high and the sample size of first core is 1 cm or greater [11], no additional biopsy was performed, based on the decision of the biopsy operator. Immediate evaluation of the biopsied specimens using a light microscope to assess glomerular number was not performed in the biopsy room.

After the biopsy, manual compression of 3–5 min was done. After the manual compression, immediate gray and color Doppler US were performed to evaluate any biopsy-related complications such as active bleeding, and images were captured and stored. No other procedure except manual compression was performed to prevent bleeding. All the patients were closely monitored during 4–6 h after the biopsy in order to identify the procedure-related complications, and discharged. [12].

Data analysis

Clinical, radiological, and pathological data were evaluated. In terms of clinical data, age, gender, body mass index (BMI), and serum creatinine level of the patient were investigated. Type of transplanted kidney (e.g., deceased donor kidney or living donor kidney) and location of the kidney transplant were assessed. Recent use of antiplatelet or anticoagulant agents before the biopsy was also investigated. In terms of radiological data, size and cortical thickness of the kidney transplant, and distance, core number, and time of the biopsy were analyzed. The longest diameter of a kidney transplant measured on US was considered as the kidney size of a patient. On US images obtained before the biopsy, the cortical thickness was measured at upper, mid, and lower polar regions before biopsy, and averaged (i.e., mean cortical thickness of a patient). Biopsy distance was defined as the needle length from the skin to renal surface on US image. Biopsy time was the interval of image acquisition between first and last US images. In terms of pathological data, total glomerular number and histologic diagnosis using the biopsy specimens were recorded on the basis of the pathologic reports. According to Banff 97 criteria, the adequate biopsy was defined as the presence of 10 or more glomeruli in the biopsied specimens, and marginal biopsy was defined as the presence of 7 or more glomeruli [10].

Biopsy-related complications were investigated by reviewing radiologic reports and electronic medical charts which were recorded since the biopsy. The events occurring within 30 days after the biopsy were considered as biopsy-related complications [13]. Major complication was defined by Clavien-Dindo classification 2 or greater requiring transfusion, intervention, or surgical treatment [14]. Fisher's exact test was applied to analyze the relationship between the use of antiplatelet or anticoagulant agents and complication. Mann-Whitney test was used to assess whether or not BMI, kidney size, cortical thickness, biopsy distance, or core number is associated with the occurrence of the complication.

Results

Clinical characteristics

The mean age of patients was 46.7 ± 11.9 years (range, 19–79 years). The gender of patients was men of 133 and women of 55. The mean BMI was 22.9 ± 3.5 kg/m^2 (range, 16.1–33.1 kg/m^2). The mean serum creatinine before the biopsy

was 3.21 ± 2.82 mg/dl (range, 0.6–16.9 mg/dl). The type of donor kidneys consisted of living donor kidneys for 133 and deceased donor kidneys for 55. The kidney transplants were located in right iliac fossa for 174 and in left iliac fossa for 14. In 19 patients, antiplatelet or anticoagulant agents had been administered for 17 and 2 patients, respectively, which medications were discontinued for 7 days before the biopsy.

Radiologic and biopsy characteristics

The mean size of kidney transplants was 11.2 ± 1.1 cm (Table 1). The mean cortical thickness of the kidney was 0.9 ± 0.1 cm. The mean distance of biopsy needle from the skin to renal surface was 3.2 ± 0.7 cm. In terms of the biopsy core number, majority of patients (92.0%, 173/188) underwent sampling of two cores. Four patients underwent sampling of three cores because two cores were considered to be insufficient for the pathologic examination. In 11 patients, only one core was sampled because active bleeding along the biopsy tract after the first sampling was identified by immediate US examination and one core sample was considered to be sufficient by a biopsy operator. Thus, the mean core number of a biopsy was 1.9 ± 0.3. The mean biopsy time was 20.6 ± 6.7 min per patient.

Biopsy efficacy

In this study, total glomerular number per biopsy was 20.4 ± 10.0 and glomerular number per core was 10.1 ± 5.0 (Fig. 3). The adequate biopsy rate was 87.2% (164/188) and marginal biopsy rate was 95.2% (179/188). The majority of histologic diagnosis was acute or chronic rejection (59.6%, 112/188), acute tubular necrosis (16.0%, 30/188), and glomerulonephritis (10.6%, 20/188) (Table 2). For two of the 188 patients (1.1%), histologic diagnosis was not made because total glomerular number per biopsy was 0 and 1, respectively.

Complications

There were no major complications requiring treatment (no patients with Clavien-Dindo grade 2 or greater complication), while there were self-limiting minor complications in five patients (overall complication rate, 2.7%). Three patients had a small amount of perirenal hematoma and two had intrarenal arteriovenous fistula without symptoms. All the minor complications of 5 patients were detected on US examination conducted immediately after the biopsy. Those patients discharged with no medical or interventional treatment as scheduled. Recent use of antiplatelet or anticoagulant agents ($p = 0.417$), BMI ($p = 0.138$), kidney size ($p = 0.786$), cortical thickness ($p = 0.465$), biopsy distance ($p = 0.917$), or core number ($p = 0.301$) were not significant different between the patients with complication and ones without complication.

Table 1 Radiologic and biopsy characteristics

Parameter	Value
Kidney size (cm)	11.2 ± 1.1 (range, 8.0–13.7)
Cortical thickness (cm)	0.9 ± 0.1 (range, 0.6–1.5)
Biopsy distance (cm)	3.2 ± 0.7 (range, 2.1–5.4)
Biopsy core number (*n*)	1.9 ± 0.3 (range, 1.0–3.0)
Biopsy time (min)	20.6 ± 6.7 (range, 10.0–44.0)

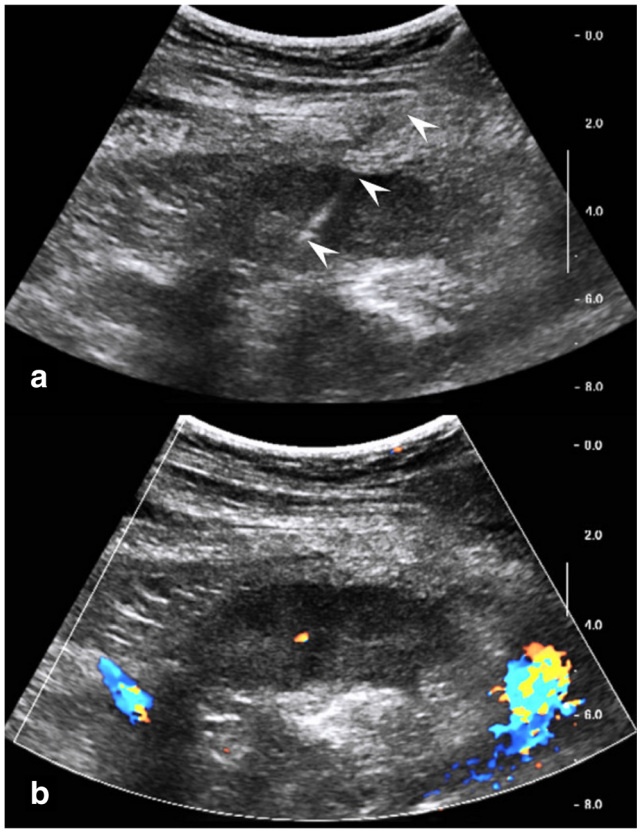

Fig. 3 US images of a 39-year-old male patient who underwent US-guided biopsy of the kidney transplant using cortex-only view. (**a**) US image of cortex-only view shows a hyperechoic biopsy needle within the lateral cortex (arrowheads), where hypoechoic medullary regions are not seen. Biopsy distance was 3.6 cm and two cores were sampled. Biopsy time was 18 min. (**b**) On color Doppler image acquired immediately after the biopsy, no major complication was identified. In pathologic examination, total glomerular number was 31 and acute rejection was diagnosed

Discussion

Literature review [8, 9, 12, 13, 15–22] indicates that the overall success rate of biopsy for a kidney transplant is 53–99% although the biopsy schemes and criteria of successful biopsy were heterogeneous (Table 3). When the criterion of adequate biopsy was total glomerular number of 10 or greater, the

Table 2 Biopsy efficacy and pathologic results

Parameter	Value
Glomerular number (*n*)	
Total glomerular number per biopsy	20.4 ± 10.0 (range, 0–54)
Glomerular number per core	10.1 ± 5.0 (range, 0–27)
Successful biopsy (%)	
Adequate biopsy rate	87.2 (164/188)
Marginal biopsy rate	95.2 (179/188)
Pathologic results (*n*)	
Acute rejection	80
Chronic rejection	32
Acute tubular necrosis	30
Glomerulonephritis	20
Diabetic nephropathy	8
Drug toxicity	5
Infection	5
Nonspecific*	7
Normal	1

Data of total glomerular number per biopsy and glomerular number per core are mean ± standard deviation (range)

*Nonspecific category consisted of five showing nonspecific inflammations and two with total glomerular number per biopsy of 0 or 1 leading to inaccurate pathologic diagnosis

adequate biopsy rates ranged from 56 to 87%. In addition, major complication rate was generally less than 5% in the previous studies. In this study, US-guided biopsy using the cortex-only view allowed the adequate biopsy rate of 87.2% and marginal biopsy rate of 95.2% without major complications requiring treatment. In addition, most of the biopsy specimens (98.9%, 186/188) were adequate to reveal a pathologic cause of renal dysfunction. Moreover, the biopsy did not require much time (mean biopsy time, 20.6 ± 6.7 min). Thus, the present biopsy method seems to be a useful and safe approach to reveal the cause of renal dysfunction in patients who underwent kidney transplantation.

The location, longitudinal axis, and corticomedullary configuration of kidney transplants are not identical for each patient, and the anatomical variance can affect the biopsy approach. Therefore, in order to perform sufficient and safe renal cortical sampling, biopsy operators need to know various biopsy approaches. Because sampling medullary tissues may be associated with increased post-biopsy bleeding [23], placement of a biopsy needle within the cortical regions without passing the medulla is helpful for safe procedure. The cortex-only view can visualize the region of lateral cortex with only small interlobular vessels outside the corticomedullary junction.

Under the cortical tangential view, a biopsy needle obliquely passes from medial to lateral direction for

Table 3 Summary of previously published percutaneous biopsy of kidney transplant (since 2000)

Author	Year	Case number	Gauge	Core number	Glomerular number	Glomerular criterion (*n*)	Success rate (%)	Major complication (%)
Nicholson et al	2000	34	18	NA	8.5 ± 5.8	7	52.9	0
Preda et al	2003	345	14	NA	NA	NA	94.8	2.9
Furness et al	2003	2127	NA	NA	NA	NA	NA	0.4
Schwarz et al	2005	448	16	NA	NA	7	76.0	0.4
		1222	18	NA	NA	7	53.0	0.2
Patel et al†	2010	290	18	1.2 ± 0.4	21.7 ± 10.1	10	87	0.7
Patel et al*†	2011	339	NA	NA	NA	7	90.6	NA
		1063	NA	NA	NA	7	96.0	NA
Laute et al**	2013	282	16	NA	9 (0–39)	10	70	0
Torres-R. et al	2014	219	16	2.3 ± 0.5	11.6 ± 5.9	10 7	56.2 83.6	0
Redfield et al	2016	3738	NA	NA	NA	NA	NA	0.4
Morgan et al†	2016	2514	NA	NA	NA	NA	99.5	1.9
Tsai et al	2016	269	NA	NA	NA	NA	NA	1.1
Boban et al†	2017	259	NA	1.2 ± 0.4	NA	10	82.7	0
Ours		188	18	1.9 ± 0.3	20.4 ± 10.0	10	87.2	0

*Biopsy data were separately analyzed in this study, according to the presence or absence of a quality assessment program on radiologist performance

**Data of glomerular number are median (range) in this study. Otherwise, the data of core number and glomerular number were mean ± standard deviation

† Biopsy was performed by using cortical tangential approach or its variant (i.e., tangential extraperitoneal retrorenal approach in a study of Boban et al). The other studies described only certain regions of the transplanted kidney biopsied or did not provide details on biopsy approaches

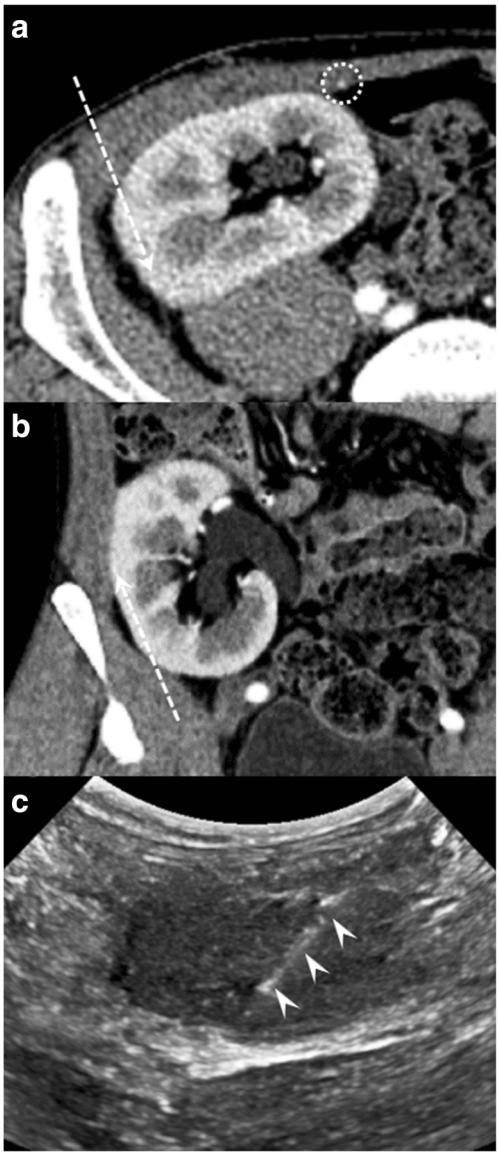

Fig. 4 Computed tomography (CT) and US images of a 23-year-old male patient who underwent US-guided biopsy of the kidney transplant using cortex-only view. **a**, **b** On axial and coronal CT images, the possible needle path using cortex-only view (dotted arrow) is located at the lateral aspect of right inferior epigastric artery (dotted circle) without overlap. **c** US image shows a hyperechoic biopsy needle within the lateral cortex (arrowheads)

sampling lateral renal cortex [8]. However, medially and superficially located inferior epigastric artery or fluid collection sometimes interferes with the needle pathway to the optimal cortical region. As shown in Figs. 2 and 4, under the cortex-only view, the needle pathway is anatomically parallel to the course of the interior epigastric artery on the outer side. In addition, our method does not require advanced hardware or software for biopsy. Thus, the cortex-only view can be applied simply and safely by using conventional ultrasound system and biopsy kit in practice.

The core size of biopsy needle for renal cortical sampling usually ranged from 14 to 18 gauge [6]. Technically, the application of a larger needle core (e.g., 14 or 16 gauge) may increase the yield of tissue sampling [15, 24], while large biopsy needle may be associated with higher risks of renal and vascular damages and, subsequently, major complications [25]. In this study, the use of an 18-gauge biopsy needle provided acceptable biopsy yield (i.e., mean glomerular number per biopsy, 20.4 ± 10.0) by two cores sampling (i.e., mean biopsy core number, 1.9 ± 0.3), as minimizing biopsy-related complications (i.e., overall complication rate of 2.7% and no major complication). Previous studies also suggested that the use of an 18-gauge needle can achieve adequate tissue sampling with low complication rate [26, 27]. Technically, sufficient tissue sampling with a biopsy device of smaller gauge and fewer cores is ideal.

The risk of biopsy-related complication may be higher for stable allografts than for inflamed or rejected ones [16]. Furthermore, in the dysfunctioning kidneys, biopsy operators often need to perform biopsy at the relatively thin cortex [28]. Thus, accurate targeting within the cortical region is of great importance for achieving successful biopsy and reducing the number of biopsy cores and complications. In this study, there was no major complication in the biopsy for the kidneys with various ranges of cortical thickness (range, 0.6–1.5 cm). From this point of view, the cortex-only view may allow effective and safe cortical sampling because biopsy needle is technically located within the renal cortex on US images.

In this study, the mean biopsy distance was 3.2 ± 0.7 cm (range, 2.1–5.4 cm), which implies that the majority of kidney transplant biopsies needs a short biopsy needle of 10 cm or less. Our data may help select the optimal length of a biopsy gun for the kidney transplant. However, BMI of our study patients was relatively low (mean ± standard deviation, 22.9 ± 3.5 kg/m^2), which might be associated with the short biopsy distance and low complication rate. Thus, the feasibility and complication of the present biopsy technique should be tested for population of high BMI or western countries.

This study has several limitations. First, all the biopsies were performed by a single experienced radiologist. Thus, our data require external validation performed by radiologists with various experience levels. Second, we did not compare cortex-only view with other biopsy methods such as the cortical tangential view. Because of the preference of a biopsy operator, most of the biopsies were performed with the cortex-only view during the study period. However, from the literature review and our data, which are summarized in Table 3, it seems that the cortex-only view can achieve biopsy performance that is acceptable, as well as comparable to those of other methods, without major complications. Nevertheless, because the number of study patients was still smaller than the sample size for the non-inferiority margin of 0.05 based on the previous study data [8], further studies with large population are required. Third, the number of arteries in the

specimens was not included in determining the biopsy success because it was not always described for every patient in our pathologic reports. However, only for two patients, pathologic diagnosis was not made by using biopsy samples. Most of the biopsy specimens in this study (98.9%, 186/188) were adequate to reveal a pathologic cause of renal dysfunction.

In conclusion, US-guided biopsy using cortex-only view is feasible and safe in sampling cortical tissues of kidney transplant. Awareness of the present technique may increase the options for operators to conduct effective and safe biopsy. Accordingly, the presented technique can be used together with the previously reported techniques, providing a radiologist with the possibility to make a clinical decision whether one of the techniques is preferable. However, because this is a retrospective single-center study, current data require further external validation.

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Compliance with ethical standards

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Statistics and biometry No complex statistical methods were necessary for this paper.

Informed consent Written informed consent was waived by the Institutional Review Board.

Ethical approval Institutional Review Board approval was obtained.

Methodology
- Retrospective
- Cross sectional study
- Performed at one institution

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