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REAL TIME ULTRASOUND GUIDED PEDIATRIC PERCUTANEOUS RENAL BIOPSY: THE TRADITIONAL METHOD VERSUS ANGLED TANGENTIAL APPROACH

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Aim: **The aim of the present study was to compare the success and complication rates of pediatric renal biopsy procedures between the angled tangential approach and the traditional approach.**
Methods: **From 2004 to 2009 we prospectively enrolled pediatric patients who had undergone real time ultrasound guided renal biopsy with angled tangential approach. For comparison, we retrospectively reviewed pediatric patients who had undergone traditional renal biopsy between 2002 and 2004. Adequacy of renal tissue histopathological samples and the complication rates were compared between groups.**
Results: **One hundred twenty-eight patients underwent traditional renal biopsy (Group A) while 166 patients underwent biopsy performed with angled tangential approach (Group B). The rate of inadequate material was higher in Group A compared to Group B (6.3% vs. 0.6%, p = 0.006). In four cases (three in Group A and one in Group B) renal biopsies revealed normal renal tissue. While a major complication (hemoperitoneum requiring transfusion) occurred in one case in Group A, no major complications were seen in Group B.**
Conclusion: **Compared with the traditional technique, the angled tangential approach resulted in a higher adequate material rate and lower complication rate. These findings indicate that angled tangential approach could be considered for pediatric percutaneous renal biopsies.**

Key-words: Kidney, biopsy – Ultrasound (US, guidance).

Percutaneous renal biopsy (PRB) is a routine method for diagnosing parenchymal diseases since it was first carried out in 1951 in parallel to the development of imaging tools (1-4). Renal biopsies, which performed under the guidance of direct urinary system and intravenous pyelography graphies previously were replaced by real time biopsies under the guidance of ultrasonography (US). Indications for PRB in children include persistent proteinuria and/or hematuria of unknown origin, differentiation of nephrotic syndrome and/or nephritic syndrome, rapidly progressive glomerulonephritis, and acute or chronic renal failure when the cause and extent of the disease are unknown. In patients with systemic disorders such as systemic lupus erythematosus or Henoch-Schönlein purpura, examination of renal tissue may be necessary to document the histological type and magnitude of the renal injury which is necessary in planning management of the disease (3, 4).

PRB is a safe and practical procedure that provides important information to the pediatric nephrologist in establishing the diagnosis, evaluating the acuteness and severity of the disease, monitoring disease progression, and assessing the response to therapy (1-4). Its efficiency increased with routine practice and with the experience obtained. Although the rate of complications decreased considerably, it still has major and minor complications that have to be taken into consideration, being an invasive procedure.

In this study, we aimed to compare the success and complication rates of pediatric renal biopsy procedures between the angled tangential approach and the traditional approach.

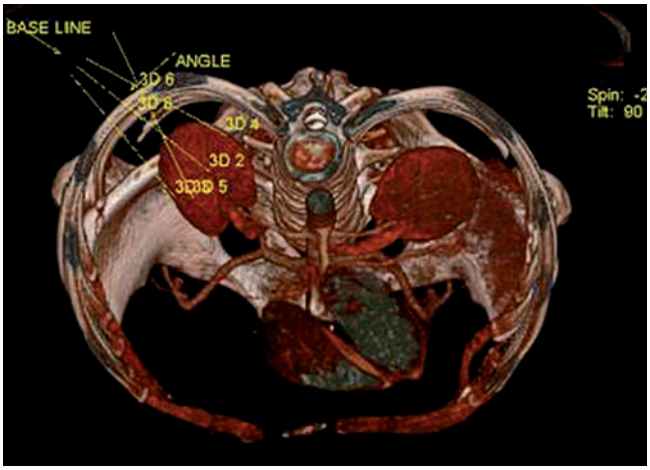

Fig. 1. — Corticomedullar position of biopsy needle for obtaining material to angled tangential approach on VRT (Volume Rendering Technique) image.

Material and methods

Study design

We retrospectively reviewed pediatric patients who had undergone traditional renal biopsy between March 2002 and May 2004 (Group A). For comparison, we prospectively enrolled consecutive pediatric patients who had undergone real time ultrasound guided renal biopsy with angled tangential approach from June 2004 to May 2009 (Group B). Ethical Committee approval was obtained.

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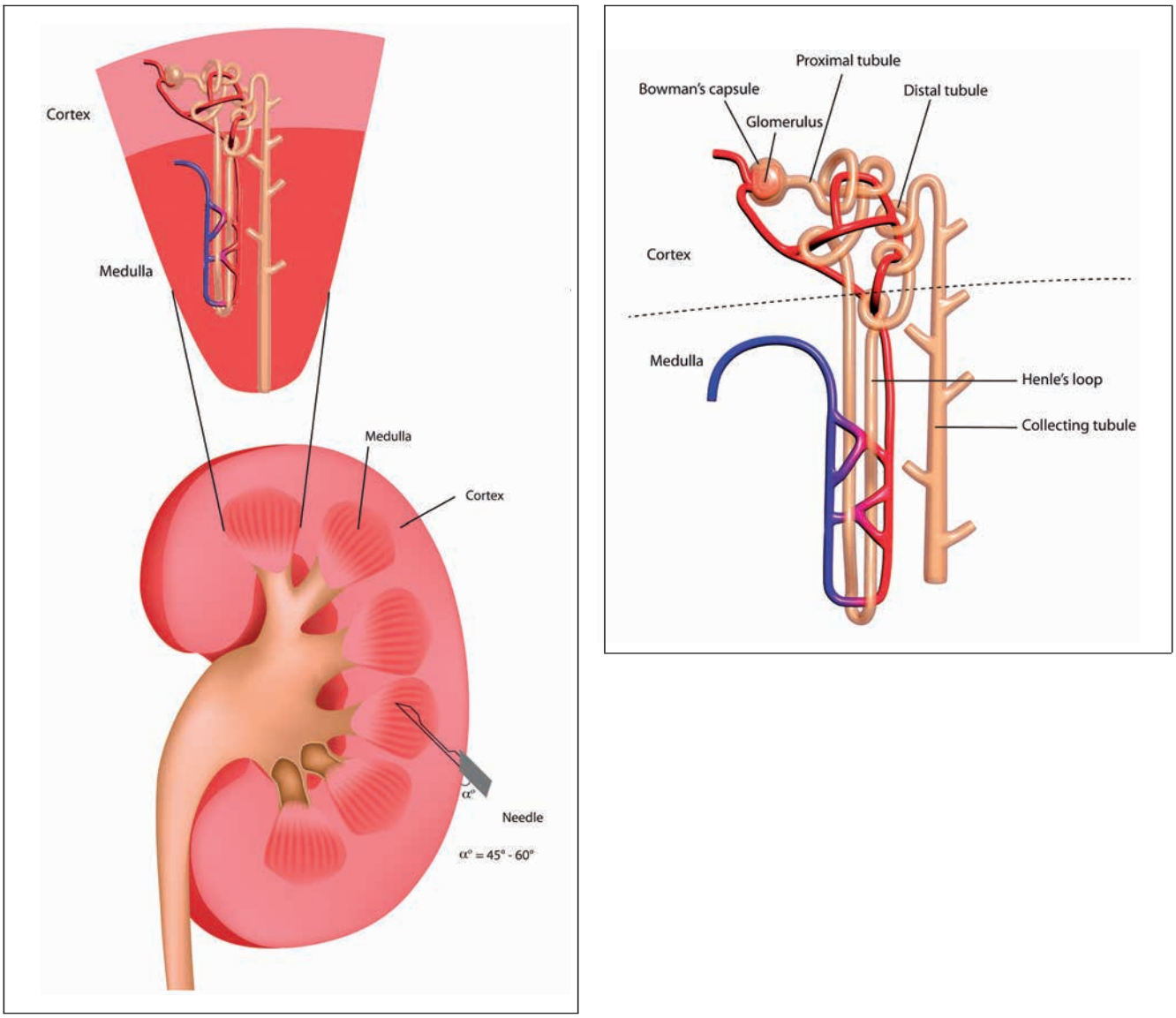

Fig. 2. — Biopsy needle route with angle between 45-60 degrees with reference to the renal capsule or base line of the convex probe.

The study protocol conformed to the Helsinki declaration; all patients (parents) were fully informed and signed consent forms. After obtaining informed consent, subjects were screened with systemic arterial blood pressure, complete blood count, coagulation parameters, and urine analysis. Cases with hypertension underwent the procedure after being rendered normotensive. Cases with impaired coagulation parameters underwent the procedure after parameters were corrected. In addition, cases with active urinary system infection underwent biopsy after their infection was controlled. Nephrotic syndrome refractory to steroids, nephritic syndrome, hematurea and proteinurea, acute or chronic renal failure whose cause is unknown and were considered to be indicated for biopsy were included in our study. Biopsy indication was determined by pediatric nephrology clinic in all cases.

Percutaneous renal biopsy procedure

All procedures were performed by two experienced interventional radiologists who had performed at least 400 renal biopsies prior to this study. The biopsies were performed under sedation with midazolam (0.03 mg/kg, IV), ketamine (1 mg/kg, IV) and locally administrated prilocaine (4 ml, 2%) combination due to the rapid effect, effective sedation and strong analgesia (5). All ultrasound examinations were performed in all biopsies with a high-resolution Toshiba Nemio 20 ultrasound scanner (Toshiba Medical Systems Co, Ltd, Tokyo, Japan) equipped with a 3.5 to 5 MHz convex probe. Renal biopsies were performed utilizing an 18-gauge, 15 mm biopsy needle with a spring-loaded biopsy gun (Pro-Mag, Manan Medical Product, Northbrook, IL). At least two core biopsy materials were obtained in both patient groups in prone position from the left kidney. The main characteristic of Group A was that the sampling of the renal cortex was obtained randomly at the lower pole. In Group A, local anaesthetic was introduced to infiltrate the skin, subcutaneous and perinephric tissues, primarily. A small stab wound was cutted with scalpel to simplify passage of the biopsy needle access. Then the biopsy needle was inserted towards to the lower pole of the left kidney. When the first

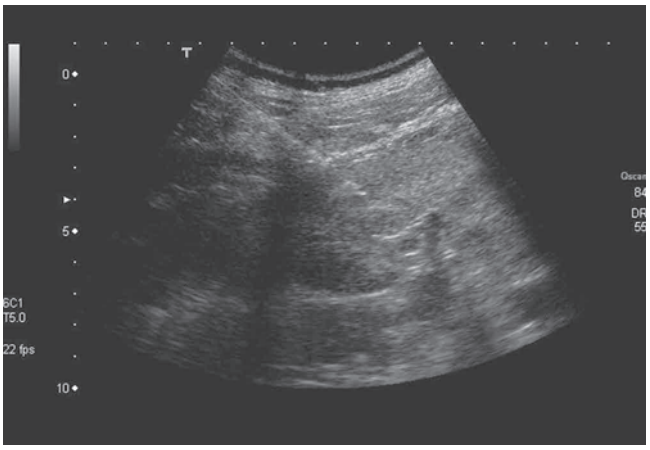

Fig. 3. — Needle pathway.

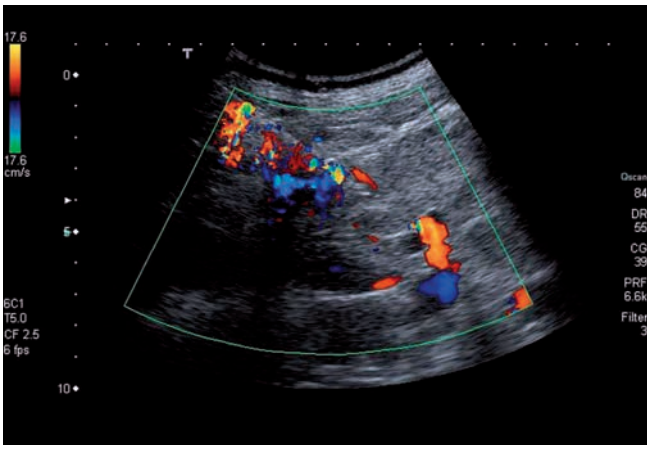

Fig. 4. — Color Doppler mode imaging to avoid major vascular structures on the needle pathway.

radiologist holding the probe for real-time US guidance, the other radiologist advanced the needle to be eligible for tru-cut renal biopsy. The main characteristic of Group B is that the biopsy needle route with angle between 45-60 degrees with reference to the renal capsule or base line of the convex probe as much as possible with the tip of the needle directed away from the renal hilum for receiving into the corticomedullary region (Fig. 1, 2). This tract passed from the 'Brödel's line' (a relatively avascular line between the anterior and posterior segmental branches of the renal artery) which is located posterior to the lateral convex border of the kidney (Fig. 3) (6). We also used color Doppler mode imaging to avoid major vascular structures on the needle pathway. The central echogenic hilum was avoided (Fig. 4).

Postprocedural follow-up

In both groups, patients were instructed to remain in bed with a sandbag at back for 24 h following the biopsy. Vital signs were measured at half hour intervals for the first two hours and hourly for a day thereafter. Each urine sample voided was examined for gross hematuria for a day. Follow-up hemoglobin measurements were performed 2–4 and 6–12 h after biopsy. Doppler US examination of the punctured kidney has been performed in all patients on the next day and the patients were discharged after 24 h if there was no complication. Patients who developed macroscopic hematuria were followed up until the bleeding stopped. Patients with perirenal hematomas were discharged but ultrasonography has been repeated at a two-week interval in outpatient clinics until hematomas resolved.

Table I. — Clinical diagnosis prior to biopsy.

	Group A (n)	Group B (n)	Total, n (%)
Nephrotic syndrome	60	75	135 (45.9%)
Nephritic syndrome	25	39	64 (21.7%)
Hematuria and/or proteinurea	25	24	49 (16.6%)
ARF/CRF whose cause is unknown	14	23	37 (12.6%)
Macroscopic hematurea	3	5	8 (2.7%)
Congenital nephrotic syndrome	1	0	1 (0.3%)
Total	128	166	294

Outcome analysis

All biopsy specimens were studied by light microscopy and immunofluorescence microscopy at the Pathology Department of our hospital. Biopsy samples were subjected to preliminary evaluation under light microscope and in regions containing glomeruli; tissue was separated for immunofluorescence examination and frozen with liquid nitrogen. Biopsy material containing at least ten glomeruli has been considered as adequate for proper diagnosis. Complications have been classified as "major" and "minor". Major complications are those which require a clinical intervention or invasive procedure, whether transfusions of blood components, the formation of an obstruction of the urinary tract with subsequent acute renal insufficiency, septicemia, or the death. Minor complications are those which do not require a clinical intervention beyond simple observation, such as transient macrohematuria, mild lumbar pain at the biopsy location, or a small perirenal hematoma (< 5 cm) that will resorb spontaneously without the need for any intervention (1, 2, 7).

Statistical analysis

Data were analyzed using the Statistical Package for Social Sciences 16.0 for Windows (SPSS Inc., Chicago, IL). Groups were compared using Fisher's exact test in terms of the adequacy of biopsy material and complications. The results for all items were expressed as mean ± SD, assessed within a 95% reliance and at a level of $p < 0.05$ significance.

Results

Group A (traditional biopsy group) contained 128 patients (64 male, 64 female; mean age 8.5 ± 3.8 years), and Group B (angled tangential approach group) contained 166 patients (82 male, 84 female; mean age 8.1 ± 3.0 years).

Among cases indicated for biopsy, clinical presumptive diagnosis were as follows: 135 (45.9%) nephrotic syndrome, 64 (21.8%) nephritic syndrome 49 (16.7%) hematurea and/or proteinurea, 37 (12.6%) renal failure (acute and chronic) with unknown reason, eight (2.7%) macroscopic hematuria, one congenital nephrotic syndrome (Table I). Accord-

Table II. — Histopathological diagnosis groups after biopsy.

	Group A n (%)	Group B n (%)	Total n (%)
Focal segmental glomerulosclerosis	23 (18%)	38 (22.9%)	61 (20.7%)
Minimal change disease	24 (18.8%)	29 (17.5%)	53 (18%)
Henoch Schönlein nephritis	21 (16.4%)	32 (19.3%)	53 (18%)
Membrano-proliferative glomerulonephritis	14 (10.9%)	13 (7.8%)	27 (9.2%)
Acute post infectious nephropathy	13 (10.2%)	15 (9%)	28 (9.5%)
Amyloidosis	6 (4.7%)	9 (5.4%)	15 (5.1%)
Congenital nephrotic syndrome	6 (4.7%)	9 (5.4%)	15 (5.1%)
Hemolytic uremic syndrome	5 (3.9%)	9 (5.4%)	14 (4.8%)
Chronic nephropathy	5 (3.9%)	6 (3.6%)	11 (3.7%)
Hereditary nephropathy	2 (1.6%)	2 (1.2%)	4 (1.4%)
Inadequate material	8 (6.3%)	1 (0.6%)	9 (3.1%)
Normal	1 (0.8%)	3 (1.8%)	4 (1.4%)
TOTAL	128 (100%)	166 (100%)	294 (100%)

ing to the histopathological results, 61 (20.7%) cases were diagnosed with focal segmental glomerulosclerosis, 53 (18%) with minimal change disease; 53 (18%) with Henoch Schönlein nephritis, 27 (9.2%) with membrano-proliferative glomerulonephritis, 28 (9.5%) with acute post infectious nephropathy, 15 (5.1%) with amyloidosis; 15 (5.1%) with congenital nephrotic syndrome, 14 (4.8%) with hemolytic uremic syndrome, 11 (3.7%) with chronic nephropathy, and four (1.4%) with hereditary nephropathy (Table II).

Consequently, nine cases (eight cases in Group A, one case in Group B) were not established any diagnosis due to inadequate material (3.1%). Inadequate material rates difference between groups was found to be statistically significant ($p = 0.006$). In four cases (three cases in Group A, one case in Group B) renal biopsies revealed normal renal tissue.

While a major complication (hemoperitoneum requiring transfusion) occurred in one case in Group A, no major complications were seen in Group B. The most frequently occurring minor complication was macroscopic hematuria, which occurred at the rate of 20.3% in Group A and 9.6% in Group B. Hematoma was detected in four cases in Group A and in three cases in Group B.

Discussion

Renal biopsy has become a fundamental diagnostic tool for the diagnostic assessment of many renal diseases in nephrology. US-guidence of renal biopsy is preferred by many practitioners due to providing much benefit such as represents a real-time imaging, low cost and without exposing ionising radiation for patients (1, 2). Percutaneous kidney biopsy is still a risky procedure although it is carried out under the guidance of ultrasonography. The success rate of the procedure is still not 100%. This may be attributed to the fact that kidney is a mobile organ and that the tissue obtained may not contain enough glomeruli to make a diagnosis (1-4, 7). Pathologists usually need more tissue to be sampled to make interpretations that are more reliable. In order to meet the demand of pathologists, thicker needles giving more tissue samples are in routine use. In cases with inadequate tissue samples repeat of the biopsy procedure is needed. However, repeat biopsy with a thick core biopsy needle increases the risk of complication while increasing diagnostic quality (3, 4).

In May 2004, a consensus meeting between radiology, pathology and pediatric nefrology clinicians was performed in our hospital to find a better approach to decrease the rate of nondiagnostic biopsies. From this date on to May 2009, pediatric percutaneous renal biopsy was standardized for passing through Broödel's line, which comprised the angled tangential approach. Patel et al described and performed this technique for US-guided renal transplant biopsies (1). In the present study, biopsy material was obtained randomly from the renal parenchyma in Group A, while posterolateral area, which is from lower pole of renal parenchyma, was used in Group B. The speciality feature of the defined tangential approach is that the biopsy needle route with angle between 45-60 degrees with reference to the renal capsule or base line of convex probe as much as possible with the tip of the needle directed away from the renal hilum for recieving into the corticomedullary region. The preferred site of the renal biopsy is the inferior pole of the left kidney because the renal pelvis and large caliber vessels are relatively far from this level (7-9). The superiority of angled tangential approach technique defined in this study over tangential technique defined by Patel et al. is that it increases rates of adequacy, and accuracy of the examination of the biopsy material in diseases involving only distal tubule and loop of Henle, rather than proximal nephron. In the study by Patel et al adequacy of the biopsy material was quite improved in glomerular diseases. However, in some specific diseases (PAN, RTA etc.) which involve components of distal nephron (distal tubuli, and loop of Henle) theoretically decrease the rates of accuracy, and adequacy. Since it is possible to obtain biopsy material from both proximal and distal components of nephron, procedural sensitivity and specificity will increase in all disease states independent of the diseased location of the nephron.

In the literature, nephrotic syndrome is the most common indication for renal biopsy both in children and in adult patients, accounting for approximately 42-47% of patients (10, 11). In the present study, the most frequent indication for PRB was also nephrotic syndrome (45.9%) which was followed by nephritic syndrome (21.7%) and urinary abnormalities, for example hematuria and/or proteinuria (16.6%). The most frequent histopathological group of diseases found in studies in the

literature is primary glomerulonephritis in both children and adult patients (12, 13). IgA nephropathy is the most frequent glomerulopathy in adults whereas MPGN and FSGS are the most common in children (11-13). In the present study, the most frequent histopathological finding was focal segmental glomerulosclerosis (20.7%). The second most frequent group of histopathology was minimal change disease, which was shown in 53 patients. The most striking feature in the present study is that amyloidosis was found in 15 patients which makes 5.1% of all study group and which does not exceed 0.5-3% in the literature (11, 12).

Biopsy is a dynamic procedure requiring caution. Experience and patient compliance are required in order to decrease complications while obtaining adequate tissue for sampling. In the traditional approach, sometimes only the collector system and tubular structures were seen, without any glomeruli, which are nondiagnostic. Histopathologically adequate tissue sampling was reported to be at the rate of 96% in literature, while in the present study the corresponding rate was 93.7% for the traditional approach group and 99.4% for the the angled tangential approach group (p = 0.006) (14).

Major complications are reported in 5-10% of the percutaneous renal biopsies in the literature (8). While microscopic hematuria is expected in all cases, macroscopic hematuria develops in 6.4-34.1% of the cases in the literature. Interobserver variability and experiences may in part explain this phenomenon. Walker *et al.* found that; under than 1% of those with macroscopic hematuria require blood transfusion (15). Arteriovenous fistula occurs at the rate of 0.5% and may be present months later with hematuria, hypertension or heart failure. Mortality is reported at the rate of 0.1% (4). The complication rate associated with the performance of percutaneous renal biopsy has significantly decreased in recent years as a result of the technological advances applied to the procedure. The use of automatic biopsy needles with guidence of US to localize the biopsy site and to visualize the needle trace for the execution of a safe procedure (1-3,7,8). In the present study, total of minor complications occurred in 42 cases (14.3%) and major complication in 1 case (0.3%). There was statistically significant difference between groups in terms of complication rates, which were 20.3% (n = 26) for Group A and 9.6% (n = 16) for Group B (p=0.007). In Group A, the minor complication rate (including perirenal hematoma and macroscopic hematuria) was 20.3% (n = 26) which was higher compared to the angled tangential approach was reduced to 9.6% (n = 16). In Group B, the rate of microscopic hematuria was 10%. To decrease the risk of hemorrhagic complications, we used color Doppler US guiding. using 18G needles might be an explanation. for the low incidence of perirenal hematoma.

In the present study, adequate material obtained revealed a significant difference between the two groups. Simple differences in practice approach for US guided renal biopsies may give rise to statistically significant difference in efficiency and safety for in pediatric patients. Each complication and repetition occurring in invasive procedures means delay in treatment for the patient and source of hopelessness and tiredness due to loss of labor and time for the physician. In this study, it was thought that risk benefit ratio should be constantly controlled in order to reduce these adverse occurrences to minimum and to enhance efficiency.

The present study has several limitations. First, only the rates of inadequate material and complications were counted to compare two renal biopsy procedures. It would be better if the mean number of glomeruli per core, the length of biopsy specimen, the puncture times are also analyzed and compared. Second, the design of the study (prospective case series and comparison to retrospective controls) was not a randomized, double-blind, placebo-controlled trial. Moreover, bias is to be anticipated for a combination of two different periods for retrospective data groups. However, we hope that this study will pioneer not only further studies on this method but also development of alternative options.

Conclusion

Compared with the traditional technique, angled tangential approach resulted in a higher adequate material rate and lower complication rate. These findings indicate that angled tangential approach may be considered for pediatric percutaneous renal biopsies.

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