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Three-dimensional ultrasound volume assessment of pediatric kidneys: comparison with conventional two-dimensional ultrasound

삼차원 초음파를 이용한 소아 신장 부피 측정: 기존 이차원 초음파와의 비교

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서울대학교 대학원
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이 논문을 전호용 석사학위논문으로 제출함

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전호용의 의학석사 학위논문을 인준함

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ABSTRACT

Objective: To evaluate the accuracy of pediatric renal volume assessment using the freehand three-dimensional (3D) ultrasound (US) technique and to validate the reliability of this technique.

Materials and methods: From December 2014 to March 2015, 17 children (7 boys and 10 girls; mean age, 8.71 years; range 1 to 17 years) who underwent both 3D ultrasonography and abdominal CT examinations within one week were included in our study. Freehand 3D renal US scanning was performed using the magnetic tracking system in a total of 31 normal kidneys. The 31 3D US datasets were measured twice per kidney by two different radiologists. Conventional two-dimensional (2D) renal volume was calculated by using the ellipsoid formula. For evaluation of accuracy, the reference renal volume (in milliliters) determined with CT was compared with those measured at 2D US and at 3D US datasets. Reliability of

3D US volume measurement was estimated by evaluating the intra-operator, interobserver and intraobserver agreements. Regarding the intra-operator agreement, the renal volume measurements of two 3D US scans of each kidney (available in 18 kidneys) by the same operator were compared. The interobserver agreement was assessed by comparing the measurements by the two observers for each kidney and the intraobserver agreement was evaluated using the two measurements per kidney by the same observer.

Results: The 3D US volume assessment showed the smaller standard deviation of the difference and better correlation with the standard reference (CT volume assessment) than that of 2D US technique. The intra-operator agreement in 3D US acquisition (ICC = 0.993), interobserver agreement between two radiologists (ICC = 0.997) and intraobserver agreement between two datasets of two radiologists (ICC = 0.997, ICC = 0.998) were all excellent.

Conclusion: Pediatric renal volume assessment using the freehand 3D US volume acquisition technique correlated better with CT volume assessment than the 2D volume assessment and showed excellent reliability in both US acquisition and measurement.

Keywords: Pediatric US, 3D US volume assessment, Pediatric kidney, Feasibility, Reliability

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LIST OF ABBREVIATIONS

US = Ultrasound

2D = Two−dimensional

3D = Three−dimensional

CT = Computed tomography

ICC = Intraclass coefficients

INTRODUCTION

Many renal disorders can cause changes in the kidney size and may affect the growth of the kidney in children (1, 2). Therefore, the exact measurement of the renal size is one essential requisite for the clinical decision making, not only initially but also during follow-up (1-5). Ultrasonography (US) is widely used as the basic imaging modality for evaluating kidneys in children. Among several ultrasonographic measurement methods, the longitudinal renal length is being used as an easily measured and useful surrogate of the renal size and its value is well-established by comparing with other methods such as excretory urography and established nomograms (6-8). However, this measurement does not represent the actual renal volume and it is reportedly an inaccurate indicator for the amount of renal parenchyma than is the renal volume (9).

Another ultrasonographic measurement method is two-dimensional (2D) renal volume assessment. This approach requires calculation based on the three orthogonal axes of the kidney and applying these measurements to the ellipsoid formula (10, 11). Even though 2D renal volume measurement reflects the renal volume than the longitudinal renal length measurement, this 2D volume assessment also shows limitations in accuracy and reliability (12, 13). The inaccuracy occurs because the formula does not take into account the variability in the shape of kidneys. In previous studies, the accuracy of 2D US volume assessment showed average 24% underestimation compared to MR volume assessment (11-13). Other studies reported large intra- and interobserver variation, and high observer error (12, 14-18).

Three-dimensional (3D) US techniques can also be applied for measuring renal volumes. Many studies in organ volume assessment using 3D US techniques have shown superior standardization and lower inter- and intra-observer variations (19-29). In addition, recent preliminary studies have shown high accuracy and reduction of interobserver variations and errors in renal volume assessment (30). Applying in the pediatric groups, consideration of special situation that may affect the accuracy of US evaluation, such as uncontrollable crying or breathing, might be required. To our knowledge, yet, no report has been published to date about the comparison between 3D US and 2D US volume assessment of pediatric kidneys to demonstrate the accuracy and feasibility. Thus, the aim of this study was to evaluate the accuracy of 3D US in the assessment of pediatric renal volume and to validate the reliability of this technique.

MATERIALS AND METHODS

Patients

From December 2014 to March 2015, 17 children (7 boys and 10 girls; age range 1 to 17 years; mean age, 8.71; median age, 8 years) who underwent both 3D ultrasonography and abdominal CT examinations within one week were included in our study. The underlying diseases they have are as follows: hematologic malignancy (n = 4), follow up after liver transplantation (n = 3), follow up after nephrectomy (n = 1), solid tumor in other organs (n = 2), acute appendicitis (n = 3), and others (n = 4). Infants were sedated for abdominal CT; no sedation was administrated for 3D US. Our Institutional Review Board approved this study and waived the requirement for informed consent.

US techniques and renal volume measurement by US

Among 17 patients, 2 patients had only one kidney; 1 had undergone left nephrectomy due to immature teratoma and 1 had congenital right renal agenesis. Another patient had a large renal abscess due to underlying immune-compromised state which led to failure of 3D US acquisition. Therefore, a total of 31 kidneys were evaluated with 3D US in 17 patients. All US examinations were performed with one US machine (LOGIQ E9; GE Healthcare, Chalfont St. Giles, UK) equipped with the position sensing system by one experienced operator (Y.H.C.). The renal volume measurement was performed in the prone position.

For conventional 2D renal volume measurement, the short and long-axis views of the kidney were acquired. The renal volume was calculated by using the ellipsoid formula: volume (ml) = craniocaudal length (cm) on the long-axis scan × width on the short-axis scan (cm) × (anteroposterior diameter on the short-axis scan (cm) + anteroposterior diameter on the long-axis scan (cm)) /2 × $\pi/6$ (31). These measurements were acquired once for each patient by the US operator (Y.H.C.) while performing the ultrasonography.

After the 2D US renal volume assessment, 3D renal US scanning was performed by the same operator, using the magnetic tracking system (Ascension Technology Corporation, Burlington, USA). The magnetic tracking is achieved by placing an electromagnetic transmitter near the area of scanning and attaching an electromagnetic sensor to the transducer (28, 32). The operator obtained the 3D US volume data by sweeping the probe from caudal to cranial following the kidney with the patients lying in the prone position. These processes took average 20 seconds. Among 31 kidneys, 3D US data was obtained once in 13 kidneys, while the other 18 kidneys were investigated two times.

The 31 3D US datasets were measured twice per kidney by two different radiologists A and B (A = Y.H.C. and B = H.J.) who were blinded to both 2D US and CT results. The 3D renal volume measurement was performed by manually drawing the renal contours on serial slices with an interslice spacing of about 5 mm on the software integrated in the US machine (Fig. 1). Each measurement was performed one day interval to be free from adaption and to be blinded to the previous results. Review of suitability of the results was performed immediately after each volume measurement, by scrolling up and down on the measured data. The 2^{nd} 3D US data which are available in 18 kidneys were additionally measured by one observer (H.J) in order to evaluate the correlation between two sequential 3D volume data acquisitions (intra-operator agreement). The average time for the 3D volume measurement per kidney was 2.2 minutes (range, 1-6 minutes).

CT techniques and volume assessment by CT

Abdominal CT was performed with the multi-detector CT scanner (SOMATOM Definition, Siemens Healthcare, Forchheim, Germany). All CT scans were performed at the single portal phase of contrast enhancement with or without breath-holding. The scanning parameters were 80-120 kVp, 90-120 mAs, rotation time 0.28 seconds, pitch of 2, 3 mm slice interval, and

128 × 0.6 mm detector collimation. For renal volume measurement on CT, the region of interest was drawn manually around the kidneys by one radiologist (H.J.). In manual segmentation, renal pelvis was excluded. The volume at each slice was calculated by multiplying the ROI area (cm^2) by the slice interval (2–3mm). Each slice volume was summated to calculate the total volume of each kidney.

Statistical analysis

For evaluation of validity, the reference renal volume (in milliliters) determined with CT was compared with those measured at 2D US and at 3D US datasets which include two datasets of each two radiologists. The mean difference and 95% limits of agreement (mean difference ± 1.96 standard deviation of the difference) between CT and 2D US (CT – 2D US) or CT and 3D US (CT – 3D US) were calculated. To evaluate the inter-method correlation between CT – 2D US or CT – 3D US, Pearson’ s correlation coefficient and intraclass correlation coefficients (ICC) using a two-way mixed-effects model with an absolute agreement definition were calculated. The ICCs of CT – 2D US and CT – 3D US were compared using F-test proposed by Alsawalmeh and Feldt (33). Bland-Altman analysis was also used to evaluate the agreement by calculating the bias (mean difference) and limits of agreement (1.96 standard deviations of the difference) (34).

Reliability of 3D US volume measurement was estimated by evaluating the intra-operator, interobserver and intraobserver agreements. Regarding the intra-operator agreement, the renal volume measurements of two 3D US scans of each kidney (available in 18 kidneys) by the same operator (Y.H.C.) were used. The interobserver agreement was assessed by comparing the measurements by the two observers for each kidney and the intraobserver agreement was evaluated using the two measurements per kidney by the same observer (Fig. 2). The ICC with 95% confidence interval and the Bland-Altman method were applied to confirm the reliability.

These analyses were carried out using SAS version 9.3 (SAS institute, Cary, NC) and IBP SPSS Statistics version 20

(IBM, Armonk, NY). A P value less than 0.05 was considered to indicate a statistical significance (35).

RESULTS

Thirty one kidneys in 17 patients were evaluated. All included kidneys were normal in appearance and there were no known history of renal disease. Baseline results of CT, 2D US, and 3D US measurements are provided in Table 1.

Validity of 3D US assessment

CT − 2D US and CT − 3D US showed similar mean differences. CT − 3D US showed narrower limits of agreement and higher Pearson's correlation coefficient values than CT − 2D US (Table 2). Both inter−method agreement of CT − 2D US and CT − 3D US resulted as excellent, but inter−method agreement of CT − 3D US was significantly higher than that of CT − 2D US (Table 3). On Bland−Altman plots, the mean and standard deviation of bias of CT − 2D US were higher and wider than those of CT − 3D US (5.8 ± 15.1 ml vs. 5.5 ± 11.0 ml) (Fig. 3). However, there was significant difference between CT and

3D US volumes which were measured by radiologist A (Y.H.C.).

Reliability of 3D US assessment

Among 18 kidneys which were obtained twice by the same radiologist, intra-operator agreement in 3D US acquisition was excellent (ICC = 0.993, 95% CI: 0.980, 0.997, P < 0.001). Bland-Altman plot showed no systematic errors between two acquisitions (mean bias, −0.5 ± 10.9) (Fig. 4). In the 3D US measurement, data from 31 kidneys showed all excellent results in interobserver and intraobserver agreements. Interobserver agreement between two radiologists showed that ICC was 0.997 (95% CI: 0.993, 0.999, P < 0.001) and negative systematic errors were noted on Bland-Altman plot (mean bias, −3.2 ± 11.5) (Fig. 5). Intraobserver agreement between two datasets of two radiologists showed that ICCs were 0.997 (95% CI: 0.992, 0.998, P < 0.001) and 0.998 (95% CI: 0.996, 0.999, P < 0.001). In addition, Bland-Altman plot showed no systematic errors in two datasets (Fig. 6).

DISCUSSION

There have been several US techniques to acquire 3D US volume data (21, 36). Many previous reports have used the 3D US technique using the mechanically swept 3D probe (36, 37). In our study, we applied the free-hand scanning technique using the magnetic tracking system to obtain the 3D US data. This freehand technique has some advantages over the mechanically-swept 3D ultrasound. First, the freehand technique can cover the larger volume and it can even image large internal organs such as liver. Second, the freehand technique can freely change the imaging plane while obtaining 3D data. In our study, renal ultrasonography could have a limited sonic window due to overlapped ribs or adjacent lung. However, we changed scan directions and angles easily while scanning and improved the sonic window for better visualization of kidneys. This might result into superiority in accuracy of 3D US assessment over 2D US assessment for normal kidneys in our study.

Our study showed that the accuracy of 3D US volume assessment showed similar to the result of 2D US assessment, but showed smaller standard deviation and better correlation with the standard reference (CT volume data), compared with 2D US assessment. According to the results obtained from F-test, 3D US correlated better with CT results than 2D US. Besides the higher accuracy of 3D US volume assessment, the reliability of 3D US technique was also excellent. The repeatability of image acquisition, the repeatability of volume measurement, and the reproducibility of volume measurement were all excellent, higher ICC value than 0.95.

As we could expect, 2D US volume assessment is less accurate because it is based on the ellipsoid formula and non-ellipsoid contour of renal parenchyma is omitted in 2D US assessment (9, 12, 15). However, most of irregular renal contour can be achieved by manual segmentation in 3D US. Furthermore, scanning obliquely from the orthogonal planes can lead to impairment in accuracy and precision. Furthermore, inadequate depiction of the kidney can result into poor accuracy and repeatability (10). This inadequacy usually occurs because of obesity or overlying bowel gas or ribs, and inadequate demarcation of the renal borders due to surrounding tissue, renal scaring, or a lack of perirenal fat. This inadequacy can also be expected in 3D US assessment, because it contains 2D US acquisition process. However, 3D US image acquisitions using the freehand technique are less constraint from the axis of the kidney. We could minimize this inadequacy by changing scan directions and angles during scanning and acquiring data in the axis that had least omission in visualization of the kidney. Furthermore, excellence in reliability may enhance precise comparison and improve standardization during US follow-up or comparison with other imaging modalities.

While several previous studies about 3D US renal volume assessment used MR data for comparison (36-38), we used voxel-count method applied to CT images as the standard of reference to compare accuracy between 2D and 3D US assessments. Volume assessment with CT has been shown to be an objective method in previous studies both in in vitro and in vivo (39-42). In the previous studies, volumes obtained from CT assessment showed no substantial deviation from the true renal volume and the results of that in vitro study additionally suggest high accuracy of the technique.

In this study, systematic errors were noted in measurements between two different radiologists. The results of radiologist A were mean 3% smaller than those of radiologist B. This tendency of underestimation in radiologist A was consistently observed in both two measurement sessions. We presumed that the radiologist A tended to draw the renal contours slightly more tightly. Regardless of these systematic errors between two radiologists, correlation with CT volume measurement and reliability were excellent.

There are some limitations in our study. First, our study was performed in patients who had normal kidneys with no history of renal disease. Previous studies showed more obvious inaccuracy in the patients with hydronephrosis or acute renal disease due to its variability in the shape of the kidney (43). Further study in patients with renal disease would be required to validate accuracy and reliability of 3D US assessment. Second, some artifacts that are present at 2D US have been shown to be amplified on 3D US image by the reconstruction algorithm throughout all planes. Furthermore, some specific artifacts can be derived from data acquisition, reconstruction, or volume rendering of 3D US. Especially in the pediatric patient group, uncontrollable situations such as crying or breathing are often encountered during the examination. These may affect misregistration of electromagnetic positioning devices (38, 44). However, these artifacts did not seem to affect the final results of volume measurement as shown in our study.

In conclusion, pediatric renal volume assessment using the freehand 3D US volume acquisition technique better correlated with CT volume assessment than the 2D volume assessment did and showed excellent reliability in both US acquisition and measurement.

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Table 1 CT, 2D US, and 3D US volume measurement data

		Min (ml)	Max (ml)	Mean (ml)	SD (ml)
CT		33.63	247.54	106.47	57.62
US 2D		31.23	226.48	100.67	49.16
US 3D	A−1	30.10	244.45	99.74	53.05
	A−2	31.39	253.13	99.58	54.37
	B−1	34.99	242.17	102.20	53.41
	B−2	35.52	241.00	103.45	54.76

SD standard deviation, *A−1* 1st dataset of radiologist A (Y.H.C.), *A−2* 2nd dataset of radiologist A (Y.H.C.), *B−1* 1st dataset of radiologist B (H.J.), *B−2* 2nd dataset of radiologist B (H.J.)

Table 2 Difference and correlation between CT – 2D US and CT – 3D US

		CT – 2D US	CT – 3D US			
			A−1	A−2	B−1	B−2
Mean difference (ml)		5.80 (5.73%)	6.73 (6.32%)	6.89 (6.47%)	4.27 (4.02%)	3.02 (2.84%)
Limits of agreement (ml)	Lower	−0.32 (−0.32%)	1.59 (1.49%)	2.22 (2.09%)	−0.60 (−0.06%)	−1.02 (−0.96%)
	Upper	11.91 (11.77%)	11.86 (11.14%)	11.55 (10.85%)	9.14 (8.58%)	7.05 (6.62%)
P−value		0.062	0.012	0.005	0.083	0.136
Pearson correlation coefficient (*r*)		0.972	0.977	0.980	0.979	0.985

A−1 1st dataset of radiologist A (Y.H.C.), *A−2* 2nd dataset of radiologist A (Y.H.C.), *B−1* 1st dataset of radiologist B (H.J.), *B−2* 2nd dataset of radiologist B (H.J.)

Table 3 Inter−method agreement between CT − 2D US and CT − 3D US

	CT − 2D US	CT − 3D US			
		A−1	A−2	B−1	B−2
ICC	0.955	0.987	0.989	0.988	0.992
95% CI	(0.903, 0.979)	(0.970, 0.994)	(0.976, 0.995)	(0.973, 0.995)	(0.982, 0.996)
P−value	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001
Difference in *P*−value (F−test) by comparing with CT − 2D US	−	0.004	0.001	0.002	< 0.001

A−1 1st dataset of radiologist A (Y.H.C.), *A−2* 2nd dataset of radiologist A (Y.H.C.), *B−1* 1st dataset of radiologist B (H.J.), *B−2* 2nd dataset of radiologist B (H.J.)

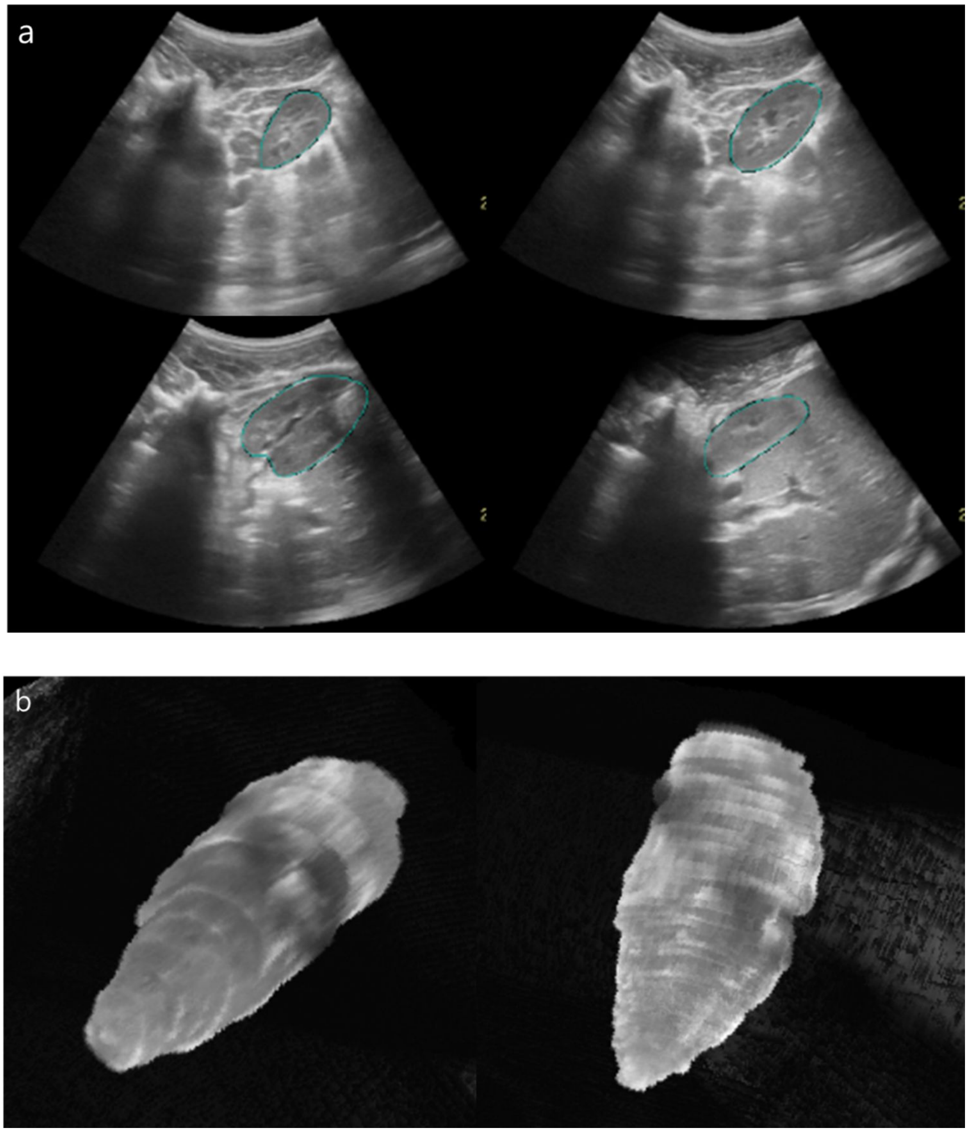


Figure 1. Images obtained at 3D US measurement

(a) Images show delineation of the outer contour of kidney in serial stages. Outlined areas mean the consecutively included area. (b) Rendered 3D bow view obtained through summation of interslice images. White elliptic structure signifies the space included for volume measurement.

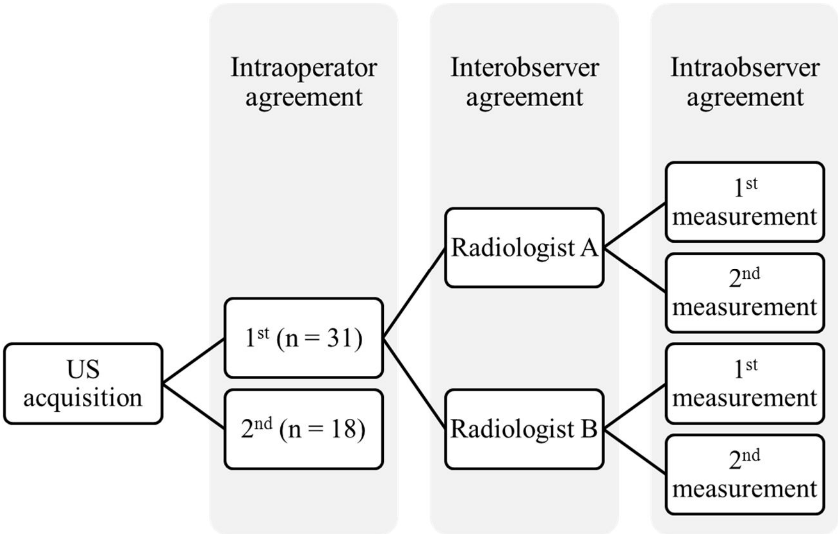
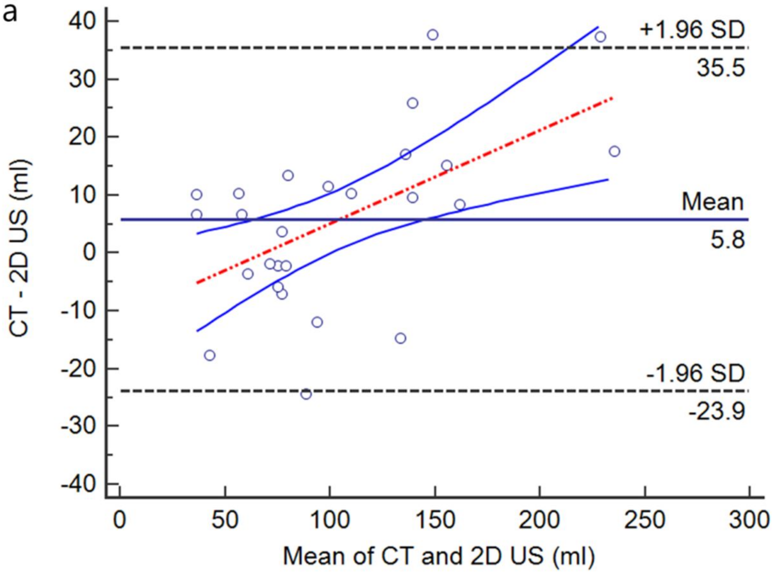


Figure 2. Schematic explanation of study for reliability

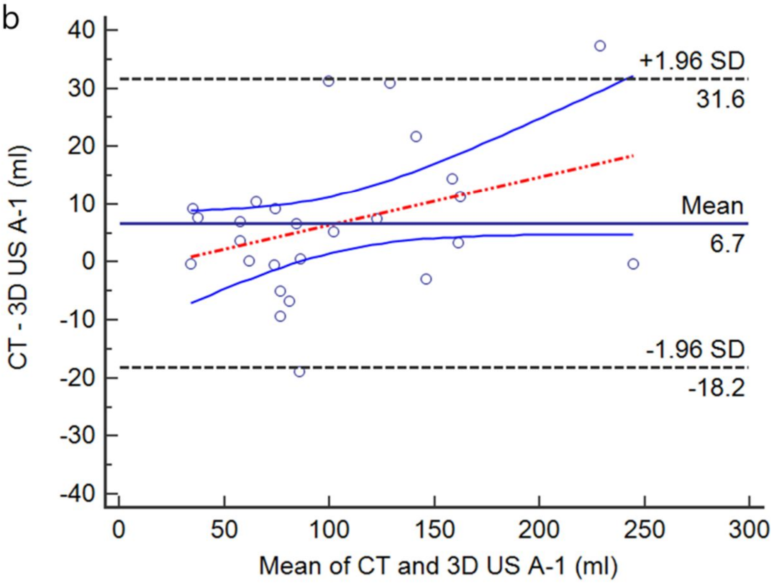
Intra-operator agreement was evaluated in two different acquisitions. Interobserver agreement was evaluated in two different radiologists. Intraobserver agreements were evaluated in two measurements of each radiologist.

a



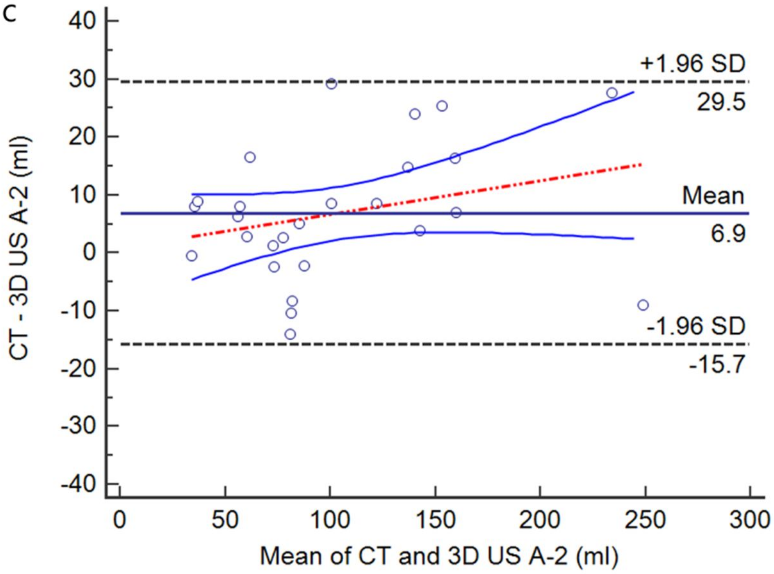
+1.96 SD
35.5
Mean
5.8
-1.96 SD
-23.9
CT - 2D US (ml)
Mean of CT and 2D US (ml)
40
30
20
10
0
-10
-20
-30
-40
0
50
100
150
200
250
300

b



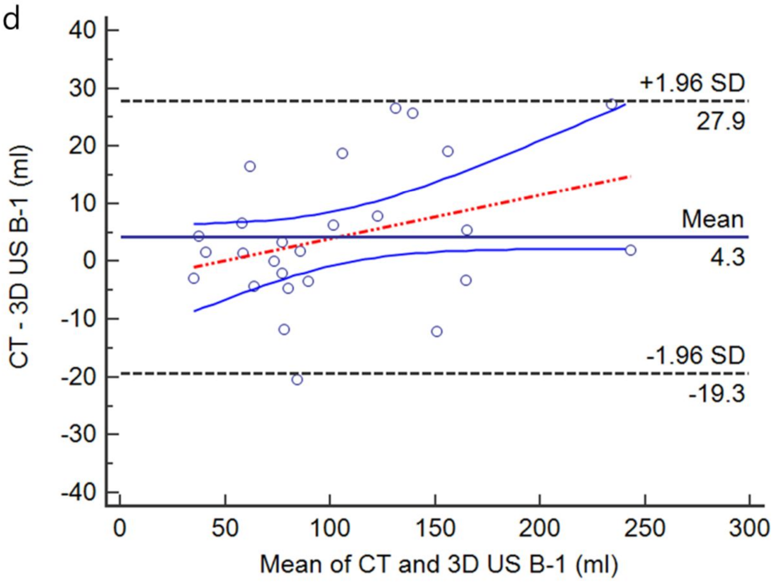
+1.96 SD
31.6
Mean
6.7
-1.96 SD
-18.2
CT - 3D US A-1 (ml)
Mean of CT and 3D US A-1 (ml)
40
30
20
10
0
-10
-20
-30
-40
0
50
100
150
200
250
300

c



40
30
20
10
0
-10
-20
-30
-40
+1.96 SD
29.5
Mean
6.9
-1.96 SD
-15.7
CT - 3D US A-2 (ml)
0
50
100
150
200
250
300
Mean of CT and 3D US A-2 (ml)

d



40
30
20
10
0
-10
-20
-30
-40
+1.96 SD
27.9
Mean
4.3
-1.96 SD
-19.3
CT - 3D US B-1 (ml)
0
50
100
150
200
250
300
Mean of CT and 3D US B-1 (ml)

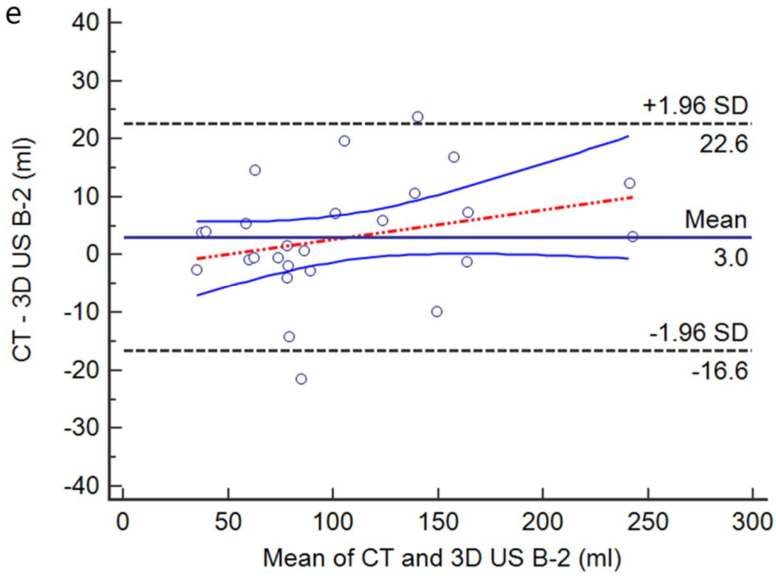


Figure 3. Bland−Altman plots represent differences between US volume assessment and CT volume assessment

(a) Differences between CT and 2D US. (b−e) Differences between CT and each of four 3D US datasets. (b) Differences between CT and 3D US, 1st measurement of radiologist A (Y.H.C.). (c) Differences between CT and 3D US, 2nd measurement of radiologist A. (d) Differences between CT and 3D US, 1st measurement of radiologist B (H.J.). (e) Differences between CT and 3D US, 2nd measurement of radiologist B. *Red dashed line* regression line of differences, *blue solid lines* 95% CI of regression line of differences, *black dashed lines* 95% CI of mean differences (± 1.96 standard deviation)

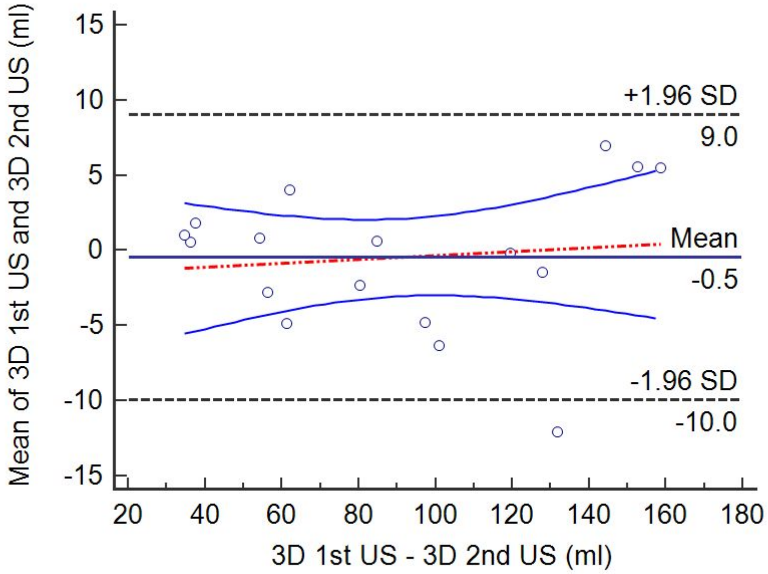


Figure 4. Bland−Altman plot represents differences between two sets of 3D US acquisition

Red dashed line regression line of differences, *blue solid lines* 95% CI of regression line of differences, *black dashed lines* 95% CI of mean differences (± 1.96 standard deviation)

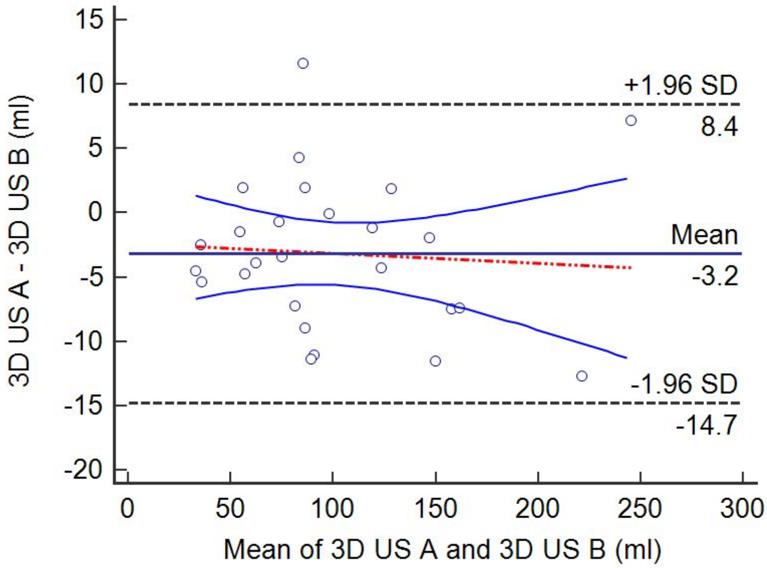


Figure 5. Bland−Altman plot represents differences between two radiologists of 3D US measurement

Red dashed line regression line of differences, *blue solid lines* 95% CI of regression line of differences, *black dashed lines* 95% CI of mean differences (± 1.96 standard deviation)

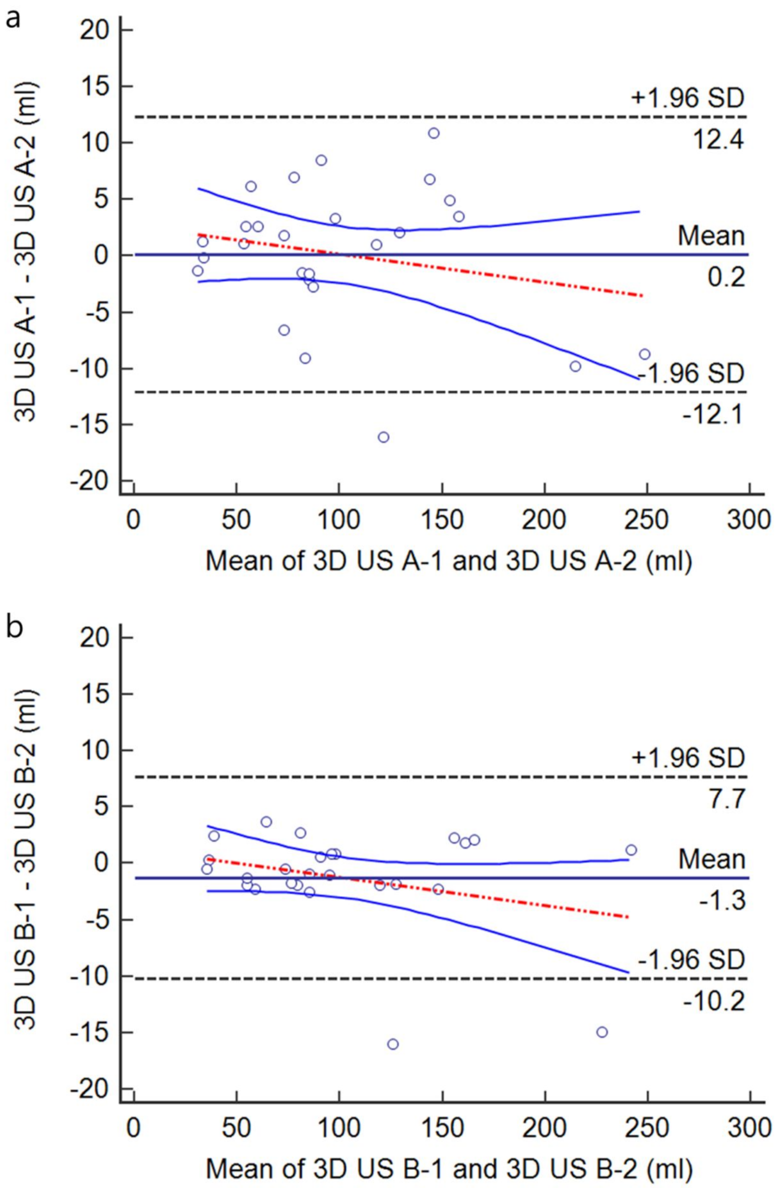


Figure 6. Bland–Altman plot represents differences between two sets of 3D US measurement in each radiologist

(a) Differences between two measurements of radiologist A (Y.H.C.). (b)

Differences between two measurements of radiologist B (H.J.). *Red dashed line* regression line of differences, *blue solid lines* 95% CI of regression line of differences, *black dashed lines* 95% CI of mean differences (± 1.96 standard deviation)

국문초록

목적: 삼차원 초음파 방법을 이용한 소아 신장 부피 분석의 정확도를 확인하고 이 방법의 재현성을 검증한다.

대상 및 방법: 2014년 12월부터 2015년 3월 동안 일주일 간격으로 삼차원 초음파와 복부 전산화 단층 촬영을 시행한 17명의 소아(7명의 남아와 10명의 여아; 중간 나이 8.71세; 범위 1세부터 17세)를 연구에 포함하였다. 프리핸드 삼차원 신장 초음파 스캔은 자기장 추적 장치를 이용하였고 총 31개의 정상 신장에서 시행하였다. 두 명의 다른 영상의학과 의사가 31개의 삼차원 데이터를 두 차례씩 측정하였다. 기존의 이차원 신장 부피는 타원 계산식을 이용하여 계산하였다. 정확도의 분석을 위해 전산화 단층 촬영에서 얻은 신장 부피(밀리리터 단위)를 기준으로 이차원, 삼차원 초음파 데이터를 비교하였다. 삼차원 초음파 측정의 재현성은 검사자내, 측정자간, 측정자내 동의 정도를 분석하였다. 검사자간 동의 정도 분석을 위해 한 명의 검사자가 시행한 각 신장의 두 삼차원 초음파 스캔을 비교하였다. 측정자간 분석은 두 측정자가 측정한 측정 데이터를 비교하였고, 측정자내 분석은 한 측정자가 측정한 두 번의 측정 데이터를

비교하였다.

결과: 삼차원 초음파 부피 분석은 이차원 초음파 방법에 비해 표준 참조치인 전산화 단층 촬영과의 표준 편차 범위가 작았고 더 밀접한 연관성을 보였다. 삼차원 초음파의 검사자내 동의 정도는 ICC 값 0.993, 측정자간 동의 정도는 ICC 값 0.997, 그리고 측정자내 동의 정도는 두 검사자에서 각각 ICC 값이 0.997, 0.998로 모두 우수하였다.

결론: 프리핸드 삼차원 초음파를 이용한 소아 신장 부피 분석은 이차원 부피 분석과 비교하여 CT 결과에 보다 밀접한 연관성 보였고 초음파 촬영 및 측정 과정 모두에서 우수한 신뢰도를 보였다.

주요어 : 소아 초음파, 삼차원 초음파, 소아 신장, 재현성, 신뢰도

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