



Body Imaging

Comparison of superb microvascular imaging to conventional color Doppler ultrasonography in depicting renal cortical microvasculature

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ABSTRACT

Purpose: The aim of the study was to compare Superb Microvascular Imaging (SMI) to conventional color Doppler ultrasonography (CDUS) and power Doppler ultrasonography (PDUS) in depicting kidney cortical microvasculature.

Methods: Using 3.5 MHz curve-linear array ultrasound transducer and manufacturer recommended color Doppler settings (Canon Medical Systems) for KIDNEY sonography, we performed kidney CDUS, PDUS, and SMI in 20 healthy adults (10 man and 10 women, mean age 27 years). Color Doppler signals in all color Doppler images were quantified by counting color pixel intensity, calculating area ratio of color to total region of interest (AR), and measuring distance of cortical end vessel to the kidney capsule. We used one-way analysis of variance (ANOVA) and post-hoc to test the difference in color pixel intensity, AR, and distance of cortical end vessel to the kidney capsule among SMI, CDUS, and PDUS and in all paired groups.

Results: The differences in color pixel intensity, AR, and distance of cortical end vessel to the kidney capsule were significant among CDUS, PDUS, and SMI, as well as in all paired groups ($P < 0.001$). Color pixel intensity and AR in SMI were significantly higher than CDUS and PDUS ($p < 0.001$). The distance of cortical end vessel to the kidney capsule in SMI was significantly less than in CDUS and PDUS ($p < 0.001$). Inter- and intra-observer reliability of quantifying color Doppler images was good (Intraclass correlation coefficient: 0.79–0.92).

Conclusion: Our results suggest that SMI seems more sensitive than CDUS and PDUS in depicting kidney cortical microvasculature.

1. Introduction

The renal circulation has unique anatomical and functional characteristics. The microvascular blood flow in the kidney is generally regulated according to the specific needs of the tissues as long as the arterial pressure is sufficient to sustain adequate tissue perfusion [1]. One important factor affecting kidney function is the status of blood supply to kidney glomerulus via the interlobular arteries or cortical radial arteries. These vessels are directed toward the cortical substance to form end-arteries through lateral branches as afferent arterioles to supply renal corpuscles, enter Bowman's capsule, and end in the glo-

merulus. The size of microvasculature in the kidney is very small ($< 200 \mu\text{m}$ in diameter) [1,2]. The hemodynamic status in kidney cortical microvasculature associates with kidney function [3,4]. Assessing cortical microvasculature blood flow representing kidney perfusion is challenge due to the small caliber of the vessels with slow flow. Conventional color Doppler ultrasonography (CDUS), based on the mean Doppler frequency shift induced by blood flow velocity, easily present the overall renal vascular structure, as well as the flow direction and velocity [5]. CDUS has been used as a standard of care in assessing kidney disease and renal transplantation [6–8]. However, CDUS is not sensitive in depicting small vessels or low velocity flow [9]. Power

Abbreviations: AR, area ratio of color to total region of interest; CDUS, conventional color Doppler ultrasonography; PDUS, power Doppler ultrasonography; SMI, Superb Microvascular Imaging

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Table 1
Ultrasound machine settings for color Doppler imaging.

Parameters	Frequency	Color gain	Mechanical index	Color scale (Max)
CDUS	2.5 MHz	35	1.0–1.4	24.1
PDUS	2.5 MHz	40	1.0–1.4	12.0
SMI	3.0 MHz	35	1.3–1.6	1.2

Note: CDUS, conventional color Doppler; PDUS, power Doppler imaging; Max, maximum; SMI, superb microvascular imaging.

Doppler ultrasonography (PDUS) is based on the total integrated energy of Doppler shifted echoes for depicting slower blood flow [10]. PDUS is reportedly sensitive to low-velocity and microvascular blood flow and is widely used among currently available non-invasive imaging techniques [8]. However, the main drawback of PDUS is high sensitivity to tissue motion [11]. Although contrast enhanced ultrasound, microbubbles can display microvessels in the cortex, contrast agent administration requires additional cost and expertise [12,13]. By employing advanced Doppler algorithms and filters to improve the depiction of blood flow while suppressing bulk tissue motion, a new Doppler technique was developed and named Superb Microvascular Imaging (SMI, Canon Medical Systems, California). Recently, a few studies on using SMI to display microvasculature in inflammatory soft tissue [14], in small lesions of hepatocellular carcinoma [15], and breast cancer [16] have been reported.

The aim of this study was to compare SMI with CDUS and PDUS in depicting microvasculature of the kidney cortex in healthy adults.

2. Material and methods

2.1. Participation

The Institutional Review Board at Rocky Vista University approved the study (IRB# 2018-0003) and all subjects provided written informed consent before kidney sonography.

Total 20 healthy adults volunteers (10 men and 10 women, age range 23–35 years, mean age 27 years) were recruited in the study in two days. All subjects had body mass index (BMI) < 30%, no history of kidney disease, hypertension, cardiovascular disease, or diabetes. Subjects emptied their bladder prior to the ultrasound examination. Subjects were positioned left lateral decubitus for imaging the right kidney and right lateral decubitus for imaging the left kidney, respectively.

2.2. Color Doppler ultrasonography of the kidneys

An Aplio i800 ultrasound scanner (Canon Medical Systems USA, Tustin, CA) equipped with a curved linear array transducer (PVI-475BX, 1.8–6.2 MHz) was used in the study. Manufacturer recommended grayscale and color Doppler settings for *KIDNEY* sonography (Table 1) were applied for acquiring grayscale, CDUS, PDUS, and SMI images of the kidneys in all subjects throughout the study. The scanning frequency affects the sensitivity of color Doppler imaging in optimizing small vessels and is inversely correlated with penetration depth in the tissue. In order to acquire consistent color Doppler data, scanning frequencies for SMI, CDFI, and PDUS in this study were selected based on

company-recommended presets for renal scanning using commercially available software. In this report, color Doppler refers to all three color-coded flow imaging modes (CDUS, PDUS, and SMI), while CDUS refers to conventional color Doppler ultrasonography. We began with grayscale imaging to assess size and echotexture of the kidneys. We then switched to the color Doppler modes to observe vasculature of the kidneys cortex using CDUS, PDUS, and SMI. Technical considerations in performing kidney cortical CDUS, PDUS, and SMI included: 1) Using a small color box in the cortical region to maintain high frame rate and resolution of the color Doppler exam; 2) Using manufacturer's color Doppler presets for renal study is more sensitive than those settings for abdominal exam; 3) A region of interest (ROI) encompassing the kidney cortex was zoomed in for improving the visualization of vasculature in color Doppler images. Each color Doppler mode was performed twice at the same ROI in each kidney. A single observer (JG) who had 30 years of experience in kidney sonography performed kidney color Doppler ultrasonography in all subjects. All static color Doppler images with Joint Photographic Experts Group (JPEG) format were transferred to a computer for off-line imaging processing.

2.3. Quantification of color Doppler microvasculature of the kidney cortex

Color Doppler imaging techniques can improve the visualization of blood flow in small vessels. Based on color Doppler settings and the detection of flow from Doppler frequency shifts, color-coded images representing mean blood flow velocity are overlaid on the grayscale (B-mode) image to form color Doppler images displayed on the ultrasound scanner monitor [6]. In a color Doppler image, the grayscale background is mapped with pixels with little variance in red (R), green (G), blue (B) components, whereas the Doppler signals are mapped with pixels with large difference in R, G, and B components. To quantify total color pixel in a ROI (total 8168 pixels) and measure the area ratio of color to total ROI (AR), we used an ultrasound image analysis software (GetColor-pixels, Chongqing Medical University, Chongqing, China) to separate color from gray background (Fig. 1a-c). Doppler signal pixels can be differentiated from grayscale background pixels by setting a threshold. If the value (maximum value of R/G/B – minimum value of R/G/B) is smaller than this threshold, the pixel is considered a background pixel; otherwise, it is considered a Doppler signal pixel. Using the same method in our previous work [6], we set a threshold of 50, which completely deleted the background grayscale pixels, allowing us to count the color pixels. All grayscale pixels in the background were deleted (zero pixel), which was confirmed using ImageJ (<https://imagej.nih.gov/ij/>) histogram analysis (Fig. 1a-c) [17]. We counted total color pixels in all color (R, G, and B) channels in the ROI because color-codes used for mapping Doppler signals differed among CDUS, PDUS and SMI images.

In addition, we measured the distance from the kidney cortex end vessel (the closest vessel to the kidney capsule) to the kidney capsule using RadiAnt DICOM Viewer (Medixant, Poznan, Poland), twice in each color Doppler image mode (Fig. 1a-c). The average of 8 measurements (2 measurements in a ROI × 2 in each kidney × 2 kidneys in each subject) in each color Doppler mode in each subject was used for analysis.

A single observer (JG or AT) performed quantification of kidney cortical color Doppler microvasculature two times in 10 subjects for testing intra-observer repeatability. Two operators (JG and AT)

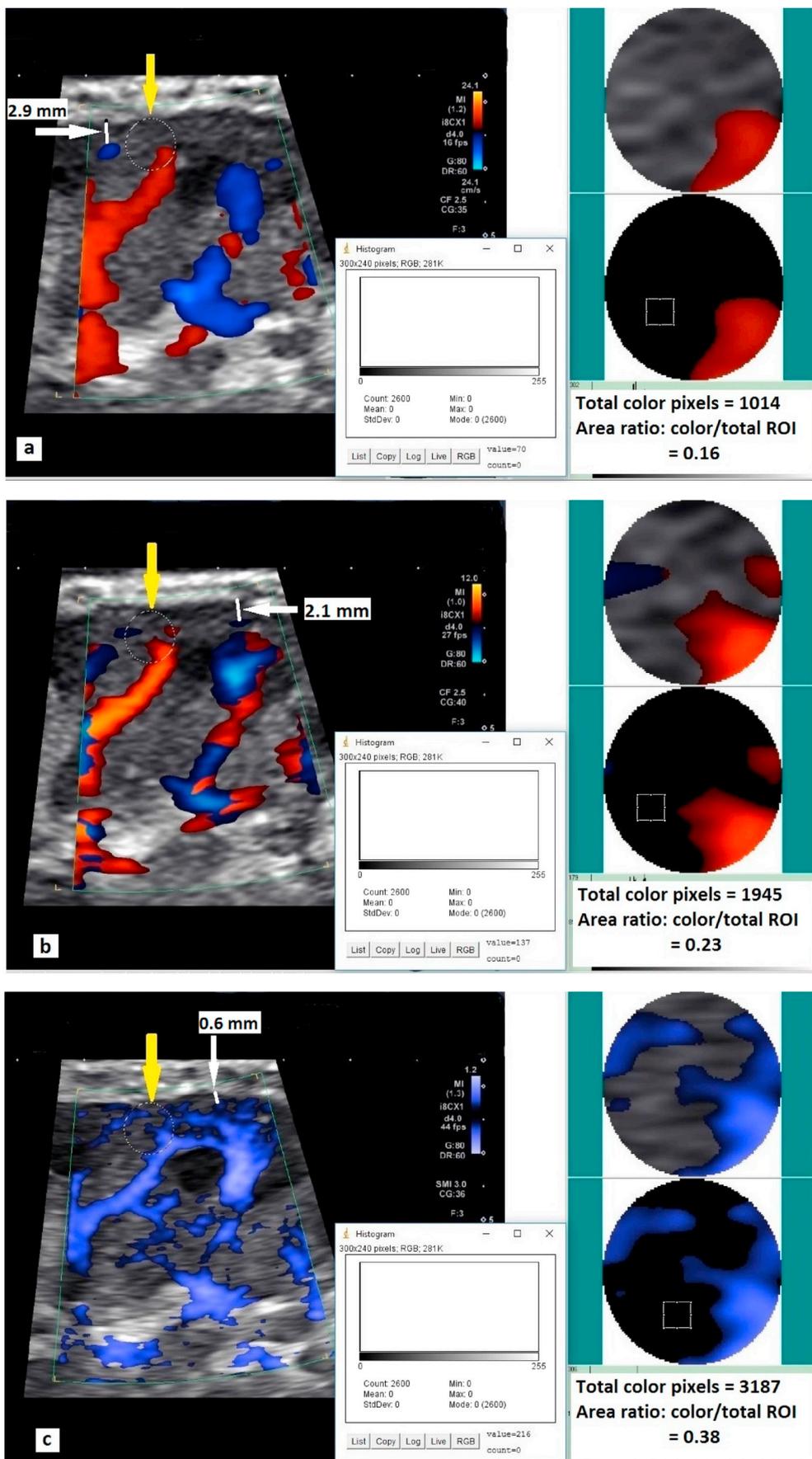


Fig. 1. a-c. Conventional color ultrasonography (CDUS, 1a), power Doppler ultrasonography (PDUS, 1b), and Superb Microvascular Imaging (SMI, 1c) of the left kidney cortex (zoomed image) were acquired from a 28-year-old healthy man. We first completely separate color pixels from the grayscale background (gray colored region in right upper rounded image) using off-line imaging processing software (GetColor-pixels). As a result, all grayscale pixels in the background (black colored region in right lower rounded image) are deleted, which is confirmed by zero pixel values in the background region using histogram analysis of ImageJ (histogram). Hence, only color pixels representing Doppler signals are counted for analysis. Total color pixels are counted 1014, 1945, and 3187 in CDUS, PDUS, and SMI, respectively. The area ratio of color to total region of interest (ROI, yellow arrow) measures 0.16, 0.23, and 0.38 in CDUS, PDUS, and SMI, respectively. The distance (white solid line pointed by a white arrow) of cortical end vessels to the kidney capsule measures 2.9 mm, 1.3 mm, and 0.6 mm in CDUS, PDUS, and SMI, respectively. Values of color pixel count and area ratio of color to total ROI are higher and the distance of cortical end vessel to the kidney capsule is less in SMI than in CDUS and PDUS. Our results suggest that SMI seems more sensitive than CDUS and PDUS in depicting cortical microvasculature of the kidney ($p < 0.001$). (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

Table 2
ANOVA of variables among CDUS, PDUS, and SMI images.

Parameters	CDUS	PDUS	SMI	ANOVA (p)
^a Vessel-capsule distance	4.5 ± 2.1	2.44 ± 1.0	1.06 ± 0.43	< 0.001
Total color pixel Intensity	942.21 ± 152.4	1850.7 ± 1249.3	2881.4 ± 1590.3	< 0.001
Area ratio: Color/Total ROI	0.11 ± 0.14	0.23 ± 0.15	0.36 ± 0.19	< 0.001

Note:
^a Vessels-capsule, the distance (mm) between end vessel in the cortex to the kidney capsule; ANOVA, one-way analysis of variance; CDUS, conventional color Doppler ultrasonography; PDUS, power Doppler ultrasonography; ROI, region of interest for counting color pixel intensity; SMI, superb microvascular imaging.

performed quantification of kidney cortical color Doppler microvasculature in same 10 subjects separately for testing inter-observer reproducibility.

2.4. Statistical analysis

All quantitative parameters including color pixel intensity, AR, and distance of cortical end vessels to kidney capsule are expressed by mean and standard deviation (SD). One-way analysis of variance (ANOVA) was used to test the difference in each of color pixel intensity, AR, and distance of cortical end vessels to kidney capsule among CDUS, PDUS, and SMI modes, which are shown with box-and-Whisker plots. We then used the Post-hoc Tukey honestly significant difference (HSD) test to examine the difference in color pixel intensity, AR, and distance of cortical end vessels to kidney capsule in all paired groups. Intra- and inter-observer reliability was analyzed using an intraclass correlation coefficient (ICC). A *p* value < 0.05 is considered statistically different. All statistical analyses were conducted by using SPSS software (SPSS Version 25.4, SPSS Inc., Chicago, IL).

3. Results

Values of color pixel intensity, AR, and distance of cortical end vessel to kidney capsule for CDUS, PDUS, and SMI are listed in Table 2. The difference in color pixel intensity, AR, and distance of cortical end vessel to kidney capsule was significant among CDUS, PDUS, and SMI (*p* < 0.001). Color pixel intensity and AR in SMI were higher than that in CDUS and PDUS (Fig. 2a and b). The distance of cortical end vessel to kidney capsule in SMI was less than that in CDUS and PDUS (Fig. 2c). Using Tukey's HSD test, the difference in color pixel intensity, AR, and distance of cortical end vessel to kidney capsule in all paired groups (between SMI and CDUS, between SMI and PDUS, and between CDUS and PDUS) were significant (*p* < 0.01, Table 3). ICC for intra- and inter-observer reliability was good to excellent (0.79–0.92) [18].

4. Discussion

The microcirculation of each organ is a precisely organized functional network. An intact microcirculation is vital for the function of every organ (kidney) in the human body for transportation of oxygen and nutrients as well as for the removal of toxins [1]. SMI uses advanced ultrasound algorithms to preserve the subtlest slow-flow components that are not able to be depicted using CDUS or PDUS techniques [19]. SMI was designed with a novel clutter suppression algorithm that separates flow signals from overlying tissue motion artifacts.

Conventional wall filters can remove clutter artifacts produced by voluntary and involuntary patient motion, which usually consist of low Doppler frequency shifts that overlap with small vessels and slow flow. As result, conventional wall filters designed to eliminate clutter artifacts remove small vessels and slow flow, as well [14]. To our knowledge, this is the first report on quantitatively comparing SMI to CDUS and PDUS in depicting cortical microvasculature in healthy adult kidneys.

We have demonstrated the higher sensitivity of SMI in depicting kidney cortical microvasculature compared with CDUS and PDUS using multiple quantitative measures. Total color pixels and AR were measured after separating color pixels from the grayscale background, which directly counted Doppler pixels and the ratio of the area of Doppler pixels (color-coded) to the area of the total ROI (Fig. 1). In addition, the distance of end vessels of the cortex to the kidney capsule represents the sensitivity of color Doppler image in depicting small vessels because vessel closer to the kidney capsule are smaller. In other words, the shorter distance of the cortical end vessel to the kidney capsule indicates the higher sensitivity of SMI in depicting smaller vessels in the cortex near the kidney capsule.

We have reported that color pixels intensity and AR are higher in SMI than that in CDUS and PDUS. The distance of cortical end vessel to kidney capsule is less in SMI than that in CDUS and PDUS. The results suggest that SMI is more sensitive than CDUS and PDUS in depicting the microvasculature in the kidney cortex. Our results are compelling with those reports that SMI has better spatial resolution and sensitivity than CDUS and PDUS in assessing tissue microvasculature [14–16]. Importantly, the repeatability and reproducibility in performing color Doppler images was good to excellent (ICC: 0.79–0.92).

Limitations of this study include the small sample size and the study was performed in healthy young (age range 23–35y) adult kidneys only. The feasibility and the difference in color Doppler techniques for depicting kidney cortical microvasculature in healthy adults in different age groups (young, middle age, and senior) and in patients with kidney disease and renal transplants need further evaluation. Although the color maps used in three color Doppler modes were not the same, we counted color pixels in all red, green, and blue channels. Hence, the total color pixels represent all color pixels displayed in the ROI regardless of the specific color. Finally, we did not have contrast enhanced ultrasound for comparison with conventional color Doppler modes in depicting microvasculature in kidney cortex.

5. Conclusion

Our results suggest that SMI seems more sensitive than CDUS and PDUS in depicting kidney cortical microvasculature in healthy adults.

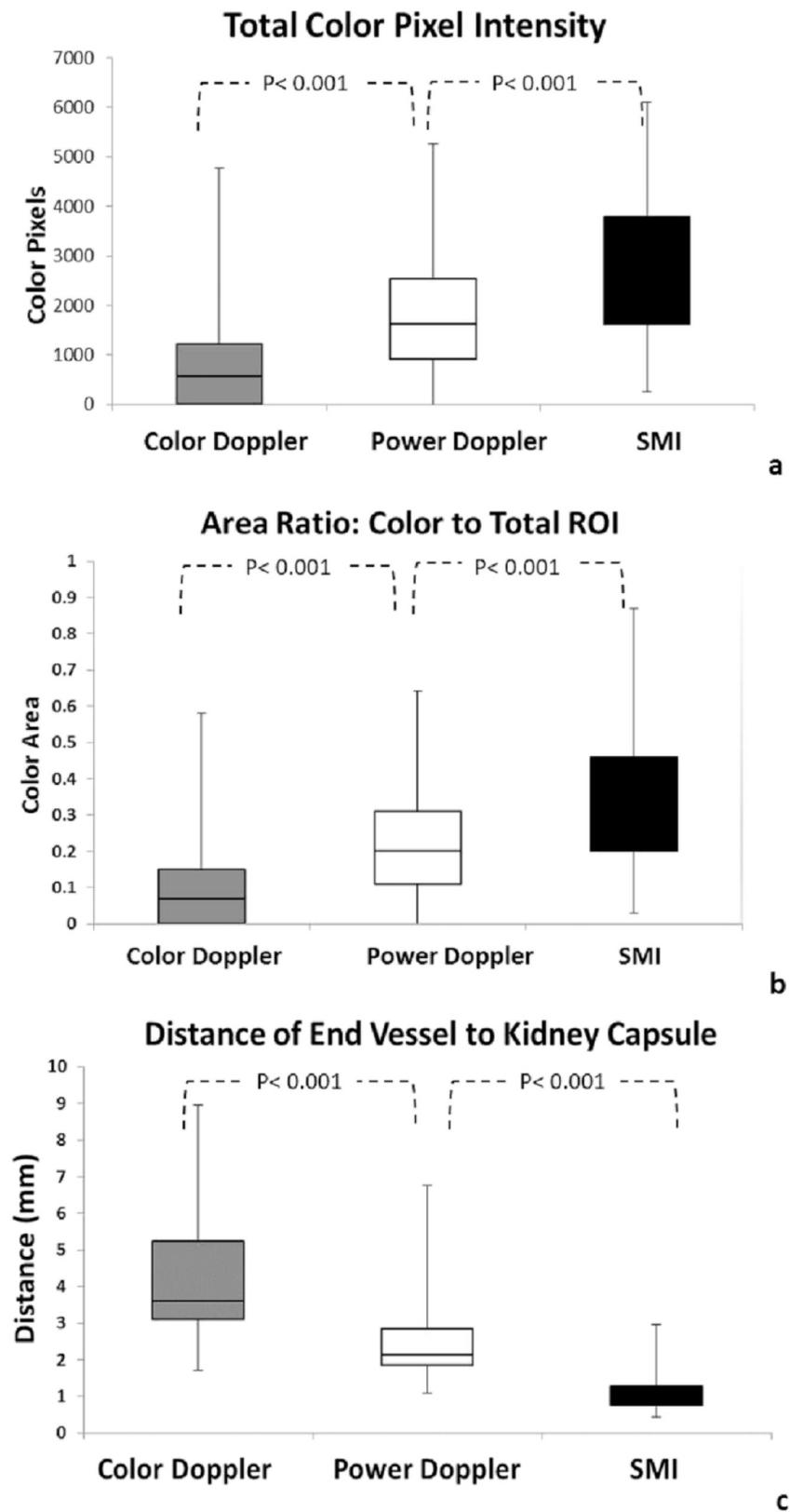


Fig. 2. a-c. Box-and-Whisker plots show significant differences ($p < 0.001$) in total color pixel intensity (2a), area ratio of color to total region of interest (ROI, 2b), and the distance of cortical end vessel to the kidney capsule (2c) among conventional color Doppler ultrasonography (CDUS), power Doppler ultrasonography (PDUS), and Superb Microvascular Imaging (SMI) (one-way ANOVA), as well as in all paired groups (post-hoc test) (all $p < 0.001$). Gray, white, and black colored box represent CDUS, PDUS, and SMI, respectively.

Table 3
Post-hoc Tukey HSD test of variables in paired groups (p value).

Parameters	CDUS vs PDUS	CDUS vs SMI	PDUS vs SMI
^a Vessel-capsule distance (mm)	< 0.001	< 0.001	< 0.001
Total color pixel Intensity	< 0.001	< 0.001	< 0.001
Area ratio: Color/Total ROI	< 0.001	< 0.001	< 0.001

Note:

^a Vessels-capsule, the distance (mm) between end vessel in the cortex to the kidney capsule; Tukey HSD test: Tukey's honestly significant difference test is used to examine the difference of a paired group (equal sample sizes per group) with 95% confidence interval. P value < 0.05 indicates a statistical significance in a paired groups. CDUS, conventional color Doppler ultrasonography; PDUS, power Doppler ultrasonography; ROI, region of interest for counting color pixel intensity; SMI, superb microvascular imaging.

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