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Rapid Estimation of Split Renal Function in Kidney Donors using software developed
for Computed Tomographic Renal Volumetry

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Rapid Estimation of Split Renal Function in Kidney Donors using software developed for Computed Tomographic Renal Volumetry

Abstract

Purpose: To evaluate the speed and precision of split renal volume (SRV) measurement (SRV), which is the ratio of unilateral renal volume to bilateral renal volume, using a newly developed software for computed tomographic (CT) volumetry and to investigate the usefulness of SRV for the estimation of split renal function (SRF) in kidney donors.

Method: Both dynamic CT and renal scintigraphy in 28 adult potential living renal donors were the subjects of this study. We calculated SRV using the newly developed volumetric software built into a PACS viewer (n-SRV), and compared it with SRV calculated using a conventional workstation, ZIOSOFT (z-SRV). The correlation with split renal function (SRF) using ^{99m}Tc -DMSA scintigraphy was also investigated.

Results: The time required for volumetry of bilateral kidneys with the newly developed software (16.7 ± 3.9 sec) was significantly shorter than that of the workstation (102.6 ± 38.9 sec, $p < 0.0001$). The results of n-SRV ($49.7 \pm 4.0\%$) were highly consistent with those of z-SRV ($49.9 \pm 3.6\%$), with a mean discrepancy of $0.12 \pm 0.84\%$. The SRF also agreed well with the n-SRV, with a mean discrepancy of $0.25 \pm 1.65\%$. The dominant

side determined by SRF and n-SRV showed agreement in 26 of 28 cases (92.9%).

Conclusion: The newly developed software for CT volumetry was more rapid than the conventional workstation volumetry and just as accurate, and was suggested to be useful for the estimation of SRF and thus the dominant side in kidney donors.

Keywords

CT volumetry, split renal function, kidney donor

Introduction

Renal transplantation is well recognized as a better modality than hemodialysis for improving the quality of life (QOL) in patients with end-stage renal disease. The enhancement in the QOL afforded by renal transplantation can be maintained as long as the renal allograft functions well. Living-donor kidney transplantation allows an individual to donate a healthy kidney to someone whose kidneys have failed. In clinical renal transplantation, allografts from living-related donors have superior graft function and survival compared with cadaver allografts (1, 2).

Preoperative radiological evaluation of kidney donors is used to select the kidney that is to be harvested in each patient. Traditionally, renal angiography and excretory urography have been used to evaluate the anatomy of renal arteries and renal function, respectively, in potential kidney donors. However, several studies have shown that helical computed tomography (CT) angiography can replace renal angiography and excretory urography in the evaluation of potential kidney donors (3-9). Hence, helical CT angiography has become an accepted method for the evaluation of living donors before they undergo laparoscopic nephrectomy. Renal scintigraphy has been necessary, however, to obtain a measure of the function of the donor's kidneys and thus ensure that both are functioning well. If there is asymmetry in the renal function, it is important to

ensure that the better functioning kidney remains with the donor and that the donating kidney is adequate.

Several previous reports have compared split renal function (SRF) estimated by CT data sets with SRF estimated by renal scintigraphy (10-16). According to these reports, there is a significant relationship between SRFs estimated by the two methods ($r=0.43-0.97$). In studies of pre-transplant donor kidney function, it was concluded that scintigraphy can be replaced by CT in the assessment for SRF with a favorable relationship between these modalities (11, 12). In most studies, however, the contours of the kidneys are drawn manually to measure the volume of each kidney. This method is time-consuming in daily practice and may cause inter-observer variation. In this study we used a newly developed software that estimates the kidney volume within several seconds, and evaluated the relationship between renal function and the renal volume thus estimated. Furthermore, we also evaluated a method for assessment of SRF by CT data using the degree of renal enhancement and renal volume, as presented in previous reports (10-15).

Materials and Methods

The development of the renal volumetry software examined in this study was

supported by FUJIFILM Corporation. The study adapted the requirements of our institutional review board for a retrospective observation study and no informed consent was obtained.

We used ^{99m}Tc -DMSA scintigraphy as a function test for SRF. Twenty-eight consecutive adult potential living renal donors for renal transplantation (7 men and 21 women with a mean age of 56 years), who underwent both dynamic CT and renal scintigraphy with ^{99m}Tc -DMSA from July, 2004 to January, 2007 were included in this study. The median interval between CT and ^{99m}Tc -DMSA scintigraphy was 1 month, ranging from 0 to 12 months. We confirmed that there was no change in subjects' renal function during these intervals by reviewing all of their laboratory tests.

CT examinations were performed with 4- or 64-slice multi-detector row CT (MDCT) scanners (Aquilion multi [4DAS] or Aquilion 64, Toshiba Medical Systems, Tokyo, Japan). The settings used for the Aquilion multi-machine were 120kVp, 400mA, 0.5s/rot, 1mm \times 4, and helical pitch=5, and for the Aquilion 64 machine, 120kVp, 350mA, 0.5s/rot, 0.5mm \times 64, and helical pitch=41. The CT protocol consisted of an unenhanced scan, followed by two enhanced scans in the arterial and renal parenchymal phases after injection of contrast medium. According to the standard protocol at our institution, the arterial scan was started when bolus-triggering scans showed an aortic

attenuation of 150 HU on the Aquilion multi or 200 HU on the Aquilion 64 machine.

The scan for the renal parenchymal phase was started about 90 seconds after starting the injection.

For ^{99m}Tc -DMSA scintigraphy, an intravenous bolus injection of 100MBq of ^{99m}Tc -DMSA was administered to each patient. The patients assumed a supine position on a bed beneath which a gamma camera (GCA9300A/DI, Toshiba Medical Systems, Tokyo, Japan) was located. The gamma camera was equipped with a low-energy, high-resolution, parallel-hole collimator. Posterior planar images were obtained at precisely 2 hours after injection for a preset time of 5 minutes on a 512 by 512 matrix. Acquisition was performed using energy windows of 140keV ($\pm 10\%$). Before and after the injection, a syringe containing ^{99m}Tc -DMSA was held 30cm from the collimator surface and 10 seconds were counted off in order to calibrate the device for renal uptake measurements. The absolute individual renal parenchymal uptake of ^{99m}Tc -DMSA per injected dose was quantified by computer (GMS5500, Toshiba Medical Systems, Tokyo, Japan) analysis. For quantification, both the physical decay of ^{99m}Tc from the time of injection to planar image data acquisition and the tissue attenuation of gamma rays from ^{99m}Tc -DMSA in the kidney were corrected mathematically. The renal depth (cm) was estimated from an equation using body weight (kg) and height (cm). The relative right

renal uptake (%) was also calculated from the formula: relative right renal uptake (%) = (the absolute right renal uptake) \times 100 / (the absolute right renal uptake + the absolute left renal uptake). The relative right renal uptake represents the SRF of the right kidney.

The volume of each kidney was calculated using the trial software, which was developed in cooperation with FUJIFILM Corporation. The software can be launched on a PACS viewer/workstation (Synapse, FUJIFILM Corporation, Tokyo, Japan). CT images of the renal parenchymal phase with slice thickness of 5mm were used. With this software, the renal contour was drawn and the renal volume was measured automatically by applying a single click on the renal parenchyma (Fig.1). Information concerning the density and topography around the point clicked, and the morphology of the kidney was utilized. With this software, the pelvicalyceal systems, fat and vessels in the renal sinus, and renal cysts were excluded automatically. Manual correction of the contouring could be done easily, if necessary. The time taken to calculate the renal volume of each kidney was measured.

Volumetry for both kidneys of all subjects was also done by an experienced technician using a commercially available workstation (ZIOSOFT, ZIOSOFT Inc., Tokyo, Japan). With ZIOSOFT, three-dimensional (3D) reconstruction images of the bilateral kidneys were created using CT images of the renal parenchymal phase with a

slice thickness of 5mm, removing adjacent structures such as intestines and vessels manually. Pelvicalyceal systems, fat in the renal sinus, and renal cysts were excluded semi-automatically by threshold setting. After creating 3D reconstruction images of the bilateral kidneys, the volume of each side of kidney was obtained. The time required for creating 3D images of bilateral kidneys and subsequently performing volumetry using ZIOSOFT was measured for each subject, too.

The split renal volume (SRV) of the right kidney was calculated as follows: $SRV (\%) = (\text{right renal volume} \times 100) / (\text{right renal volume} + \text{left renal volume})$.

The Hounsfield units (HU) for each kidney on the unenhanced (U) and renal parenchymal phase (PP) were also measured. A circular ROI about 1 centimeter in diameter was drawn manually on the upper, middle, and lower poles of each kidney.

The mean contrast enhancement of each kidney was calculated as follows: $[(HU_{\text{upper ROI PP}} - HU_{\text{upper ROI U}}) + (HU_{\text{middle ROI PP}} - HU_{\text{middle ROI U}}) + (HU_{\text{lower ROI PP}} - HU_{\text{lower ROI U}})] /$

3. The modified enhancing renal volume ($\text{cm}^3 \cdot \text{HU}$) was defined as the product of the volume and the mean contrast enhancement for each kidney. The relative modified enhancing volume (modified SRV) of the right kidney was thus derived.

Five major issues were investigated in this study:

1. Feasibility of the software:

(1) Percentage of successful volumetries.

(2) Percentage of volumetries that needed manual contour correction.

(3) Time required for volumetry using the newly developed software.

2. Comparison between the newly developed software and ZIOSOFT

(1) The times required for volumetry of bilateral kidneys (volumetric data are given separately for each side) in each subject by the newly developed software and ZIOSOFT were compared.

(2) The volumes for each kidney obtained by the newly developed software and ZIOSOFT were compared.

(3) Agreement in SRVs calculated by the new software (n-SRV) and ZIOSOFT (z-SRV) was assessed.

3. Correlation and agreement between n-SRV and SRF measured with ^{99m}Tc -DMSA scintigraphy.

4. Correlation and agreement between modified SRV and SRF measured with ^{99m}Tc -DMSA scintigraphy.

5. Determination of the dominant kidney: The dominant side was determined when there was more than 10% difference in the n-SRV or SRF. Here, the cutoff was set at 10% as in our institute; i.e., if the split renal function for right and left kidneys differed

by more than 10%, it was considered to be significant. The results from each method were compared to measure the agreement between the two approaches.

Statistical Analysis

Variables were given in means \pm standardized deviation (range). Paired t-tests were used for the assessment of the relationship between quantitative data sets. Pearson's correlation coefficient was used to determine the correlation between quantitative data sets. Bland-Altman plots (graphical representations illustrating repeatability of observations) were used to show the relationship between the results of the two methods (17). Microsoft Excel for Windows was used for the estimation of paired t-tests. Bland-Altman plots were made by means of the MedCalc 7.4.4.0 statistical software package.

Results

The n-SRV, z-SRV, modified SRV and SRF of the right kidney in each case are shown in Table 1.

1. Feasibility of the software

The volumes of all kidneys (56 kidneys in 28 cases) were successfully measured utilizing the newly developed software. Manual correction was needed 6

times in 4 kidneys (7.1%) after the single-click automatic contouring. The time required to measure volume of a kidney with the newly developed software was 8.4 ± 2.8 (5.6-22.4) sec. In one kidney, manual correction was needed 3 times to remove the veins and fat in the renal sinus, and this volumetry took the longest time (22.4 sec).

2. Comparison between the newly developed software and ZIOSOFT

The time required to calculate bilateral kidney volumes using the newly developed software was 16.7 ± 3.9 (11.5-28.4) sec, and that using ZIOSOFT was 102.6 ± 38.9 (55-196) sec. Hence, the time required for volumetry using the newly developed software was significantly shorter than that using ZIOSOFT ($P < 0.0001$).

The renal volume calculated with the newly developed software (137.6 ± 26.6 (84.6-190.4) cm^3) was significantly smaller than that with ZIOSOFT (152.7 ± 30.0 (97.7-214.2) cm^3 , $p < 0.0001$). However, these calculations showed good linear correlation with statistical significance ($r = 0.95$, $p < 0.0001$) (Fig 2).

The n-SRV of the right kidney was 49.7 ± 4.0 (44.8-67.1) % while the z-SRV of the right kidney was 49.9 ± 3.6 (46.1-65.2) %. The n-SRV was consistent with z-SRV, having a mean discrepancy of $0.12 \pm 0.84\%$ and a maximum difference of 1.9 % (Fig 3).

3. Comparison between n-SRV and SRF measured with ^{99m}Tc -DMSA scintigraphy

The SRF of the right kidney was 49.5 ± 4.6 (43.4-69.3) %. There was a good linear correlation between the n-SRV and SRF, with statistical significance ($r=0.93$, $p<0.0001$) (Fig 4). The Bland-Altman plot showed that the mean difference between n-SRV and SRF was 0.25 ± 1.65 , the maximum difference was 3.6, and there was no bias with change in magnitude (Fig 5).

4. Comparison between modified SRV and SRF measured with ^{99m}Tc -DMSA

The modified SRV of the right kidney was 50.2 ± 4.0 (44.6-67.1) %. There was a good linear correlation between the modified SRV and the SRF with statistical significance ($r=0.90$, $p<0.0001$) (Fig 6). The Bland-Altman plot showed that the mean difference between the modified SRV and SRF was 0.74 ± 1.93 , the maximum difference was 5.3, and there was no bias with change in magnitude (Fig 7).

5. Determination of the dominant kidney.

In one case (case 12 in Table 1) the right-side kidney was determined to be dominant by both SRF and n-SRV. In 25 cases, the difference between the right and left kidney on both SRF and n-SRV was less than 10%. Therefore, there was agreement between the SRF and n-SRV as to which kidney was dominant in 26 of 28 cases (92.9%, Table 2). Both kidneys were therefore assessed to be equivalent in volume and function

in those cases. There was a discrepancy between SRF and n-SRV in two cases (cases 13 and 14 in Table 1), but the differences were very small. In one case, the left side was dominant in n-SRV, but on SRF there was no dominance; the difference between SRF and n-SRV of the right kidney was 2.4%. In the other case, the right kidney was established as the dominant kidney on SRF, but the two kidneys were equivalent in volume on n-SRV; in this case the difference between SRF and n-SRV of the right kidney was 0.7%.

Discussion

The present study showed that renal volumetries with the newly developed software were successful in all subjects. The calculation time was reduced significantly compared to that of the conventional method using ZIOSOFT. The difference between n-SRV and z-SRV was as small as $0.12 \pm 0.84\%$. Therefore, as far as the ratio of the volume of each kidney is concerned, our findings strongly suggested that n-SRV can replace z-SRV.

The n-SRV showed a significant correlation with SRF ($r=0.93$), as expected. There was also good agreement between the dominant side determined by n-SRV and that by SRF.

The previous reports on estimation of SRF using CT data sets revealed a significant

correlation between the SRF estimated by CT and that by scintigraphy data ($r=0.43-0.97$) (10-15). This is in accordance with our result ($r=0.93$). In the previous reports, the degree of renal enhancement was taken into consideration for the estimation of SRF (10-15). According to Frennby et al., the glomerular filtration rate (GFR) of a kidney was assumed to be proportional to the amount of contrast medium that had accumulated in that kidney a few minutes after bolus injection, and directly proportional to the attenuation capacity of the contrast medium (CM) in that kidney, with the attenuation capacity calculated by subtracting the number of HUs of all the voxels of the kidney before CM injection from that after CM injection. (18). Several studies have been based on this theory (10-12, 14). The number of voxels of a kidney is proportional to the kidney volume; therefore, the attenuation capacity of the CM is assumed to be represented by the product of the volume and the mean contrast enhancement, which is referred to as the modified enhancing renal volume in our study. In our study, we could not prove that the correlation of modified SRV and SRF was better than that of n-SRV and SRF, where n-SRV is the simple ratio of renal volumes and modified SRV is the renal volume ratio taking the degree of renal enhancement into consideration. This may be explained by the fact that there was no statistically significant difference in the degree of enhancement between the two (right and left) kidneys in our study; hence, the

difference in the volume may be mostly related to the renal function. According to Summerlin et al., the split renal volume, calculated solely by measuring the volume of the renal parenchyma in renal donors without adjusting for contrast accumulation, was the best correlation with radionuclide renography data (16). Therefore, this simple method of measuring SRV seems to be applicable in populations in which no bilateral difference in renal function is expected, such as potential donors for living renal transplantation. This method of estimation of SRF from routine CT data sets may replace renal scintigraphy with no additional exposure to radiation.

In the current study, the newly developed software enabled us to measure the renal volume in a short time with little effort. The measuring process includes clicking on the renal parenchyma for subsequent automatic contouring and calculation of the volume, which can be done in 10 seconds. Manual corrections can be made until satisfactory contouring is obtained. This method can reduce the inter-observer variation that might be caused by manual contouring. In our experience, no special training was required to use this software, if an operator can recognize renal features and its contours. In addition, this software can be installed and launched on the PACS viewer/workstation (Synapse, FUJIFILM Corporation, Tokyo, Japan). Volumetry of the kidneys can be performed regardless of time constraints and is feasible in routine clinical practice.

One of the limitations of our study is the fact that we assessed the accuracy of ratio of volumes of two kidneys in each patient but did not assess the accuracy of the absolute volumes in this study. In fact, we have investigated the accuracy of the volumetry using a renal phantom, and these results will be published elsewhere. In brief, that study showed that the actual renal volume can be calculated more accurately by adding a linear correlation correction. However, regarding the ratio of two kidneys in the same patient, there is little possibility that the correction of renal volume using the correlation line would change our findings. Another limitation is that the software requires good renal enhancement for automatic renal volumetry. If the enhancement of the renal parenchyma is weak, as is often the case in patients with impaired renal function, the software may not recognize the appropriate renal contour for the measurement. Manual correction would be required for these patients. Lastly, the number of patients in this study is small, at only 28. No patients with poor renal function were included. Further studies with more patients with impaired renal function are required to confirm rapid n-SRV measurement as the substitute for SRF.

Conclusions

The newly developed software enabled us to measure the renal volume in a

short time with little effort compared to the conventional MDCT volumetry method.

Since the SRV derived from the simple volumetry correlates well with SRF, MDCT with the software is useful in providing sufficient information concerning the dominant kidney, renal artery anatomy, and calculi or mass lesions in the kidneys of donors. The simple volumetric method with MDCT has the potential to replace renal scintigraphy for the assessment of SRF as a preoperative imaging examination for living-donor transplantation.

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Figure legends

Figure 1: CT images on the workstation showing measurement of the left renal volume using the newly developed software. The renal contour is drawn, and pelvicalyceal systems, fat and vessels in the renal sinus are excluded automatically. The “+” mark shows the point that was clicked.

Figure 2: Correlation between the renal volume calculated with the newly developed software and that with ZIOSOFT (n=56)

Figure 3: Bland-Altman plot of split renal volume of the right kidney calculated with the newly developed software (n-SRV) and that with ZIOSOFT (z-SRV)

Figure 4: Correlation between split renal function (SRF) and split renal volume of the right kidney (n=28) calculated with the newly developed software (n-SRV)

Figure 5: Bland-Altman plot of split renal function (SRF) and split renal volume of the right kidney calculated with the newly developed software (n-SRV)

Figure 6: Correlation between split renal function (SRF) and modified SRV of the right kidney (n=28)

Figure 7: Bland-Altman plot of split renal function (SRF) and modified SRV of the right kidney

Table 1: Subjects' age, sex, n-SRV, z-SRV, modified SRV and SRF of the right kidney

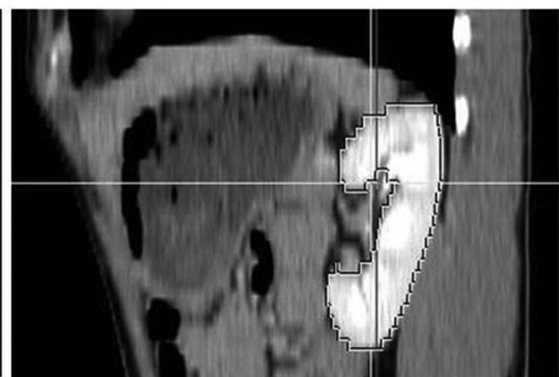
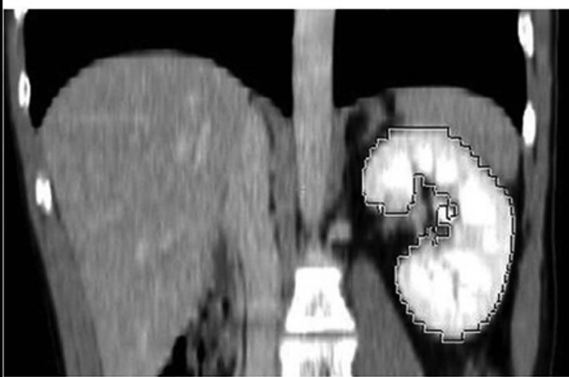
Case No.	Age	Sex	n-SRV*	z-SRV†	modified SRV	SRF‡
1	32	M	48.4	48.5	48.7	46.9
2	53	F	48.8	49.0	48.2	48.7
3	52	F	46.8	48.0	46.9	46.2
4	64	F	53.8	54.0	54.5	51.2
5	58	F	47.5	46.9	47.1	48.0
6	42	F	47.7	48.4	48.7	48.4
7	54	F	46.4	46.7	47.0	45.5
8	29	M	50.9	50.8	52.6	47.3
9	62	F	52.8	53.2	52.4	52.8
10	63	F	52.6	52.9	53.6	51.8
11	54	F	49.7	50.1	50.8	50.7
12	32	F	67.1	65.2	67.1	69.3
13	62	F	45.8	47.6	47.0	43.4
14	50	F	44.8	46.1	44.6	45.5
15	75	F	47.4	47.4	47.4	46.4
16	61	F	49.0	48.8	49.3	51.4
17	56	F	50.1	49.6	50.9	52.1
18	66	F	50.4	51.7	51.3	47.2
19	62	F	49.3	48.8	51.0	48.1
20	66	M	50.6	51.6	51.3	51.9
21	49	M	47.8	47.8	48.4	48.2
22	60	F	51.0	50.6	50.9	50.1
23	60	M	48.6	49.4	50.0	47.9
24	60	M	48.1	48.3	48.3	50.9
25	59	M	47.5	46.6	46.7	45.2
26	37	F	49.2	49.3	49.4	49.5
27	68	F	51.0	49.3	51.9	51.5
28	73	F	49.8	49.9	50.7	49.8

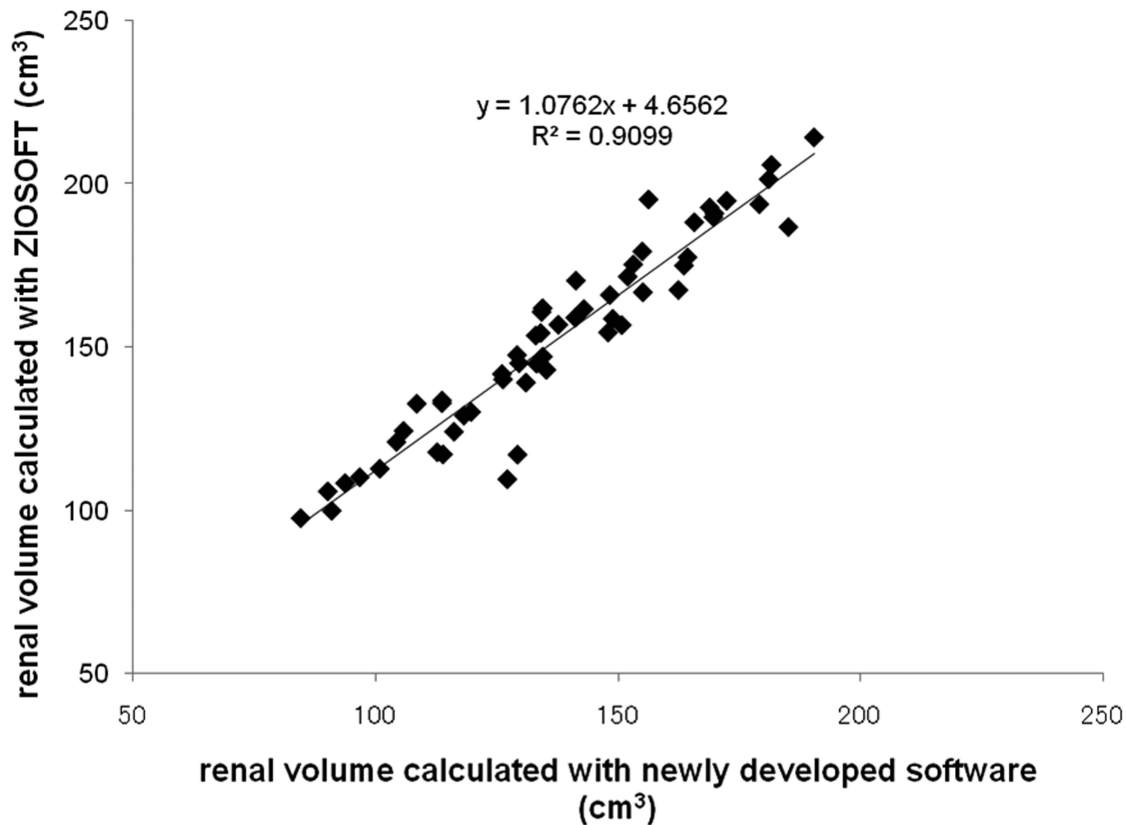
*n-SRV; split renal volume calculated with newly developed software, †z-SRV; split renal volume calculated with ZIOSOFT, ‡SRF; split renal function

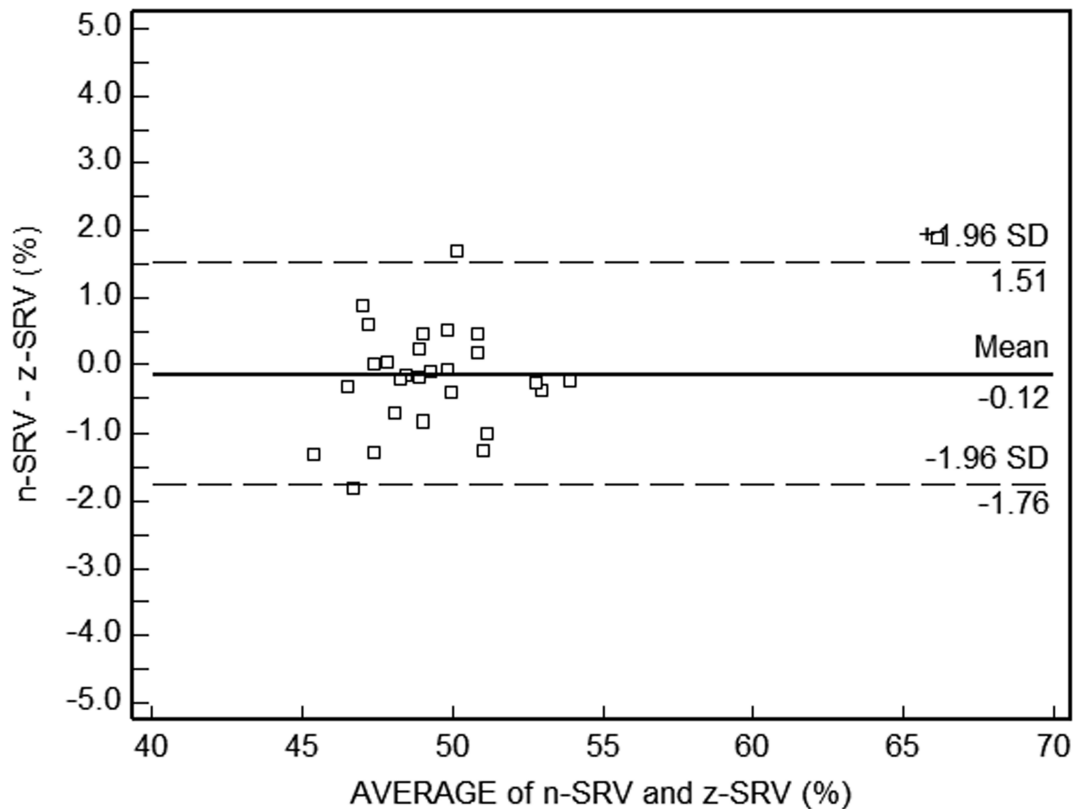
Table 2: The dominant kidney as determined by SRF and n-SRV

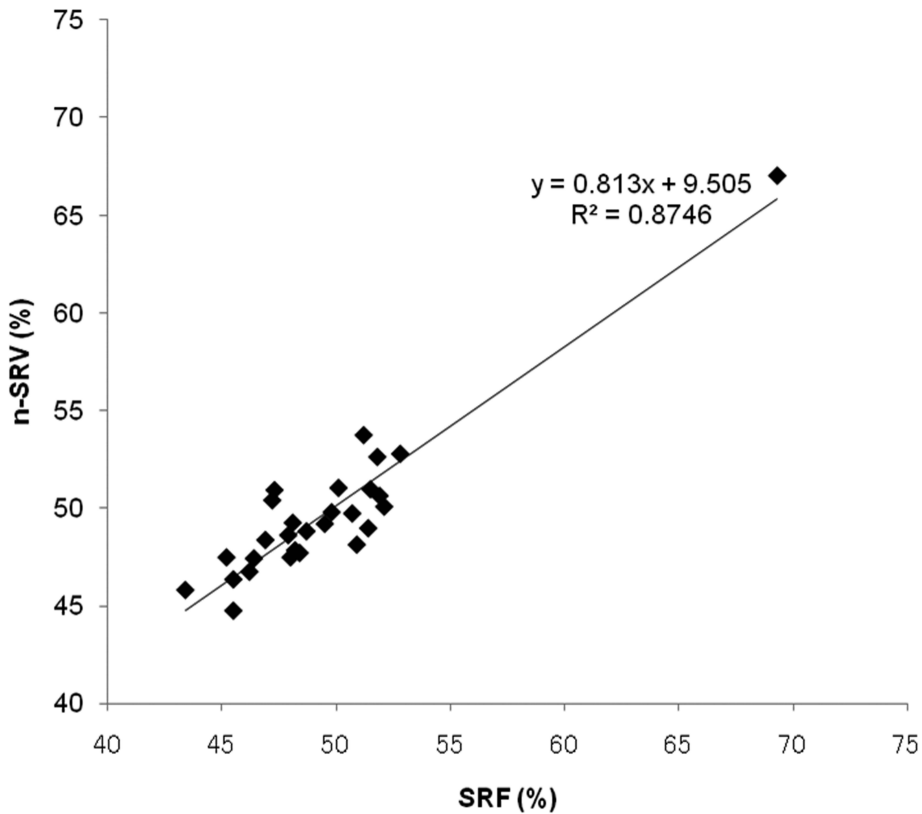
		n-SRV [†]		
		Right > Left	Right = Left	Right < Left
SRF*	Right > Left	1	0	0
	Right = Left	0	25	1
	Right < Left	0	1	0

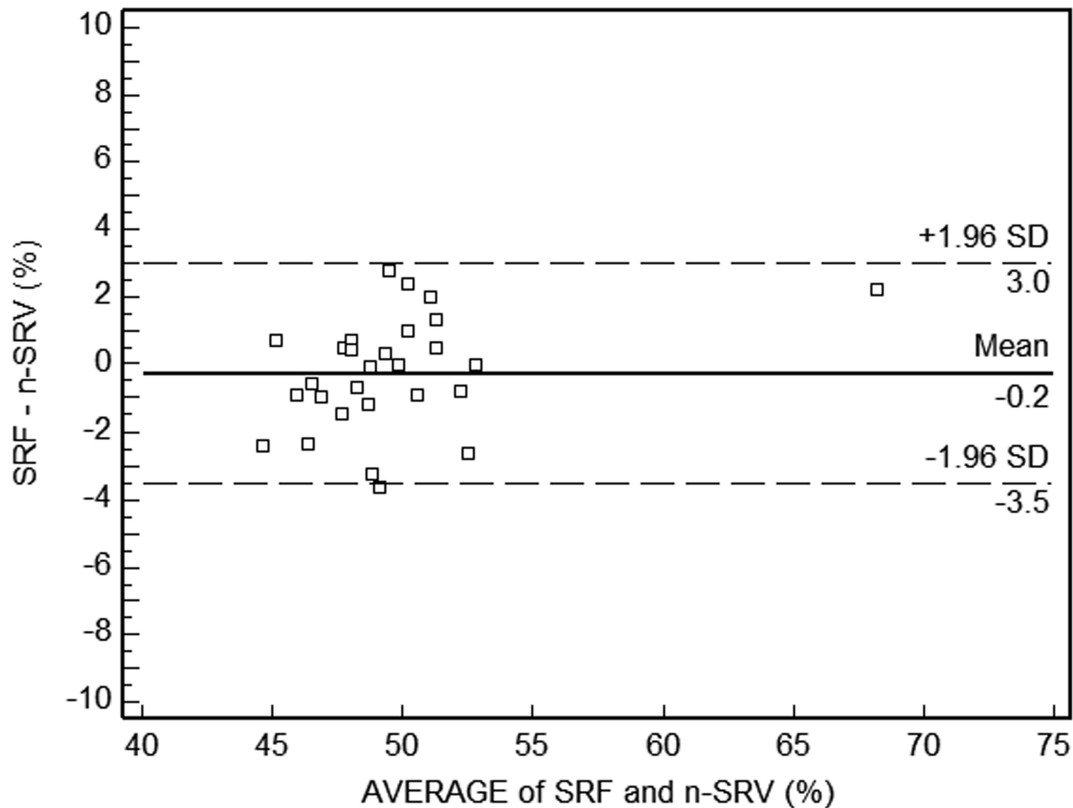
SRF*=Split renal function, n-SRV[†]=Split renal volume calculated with newly developed software

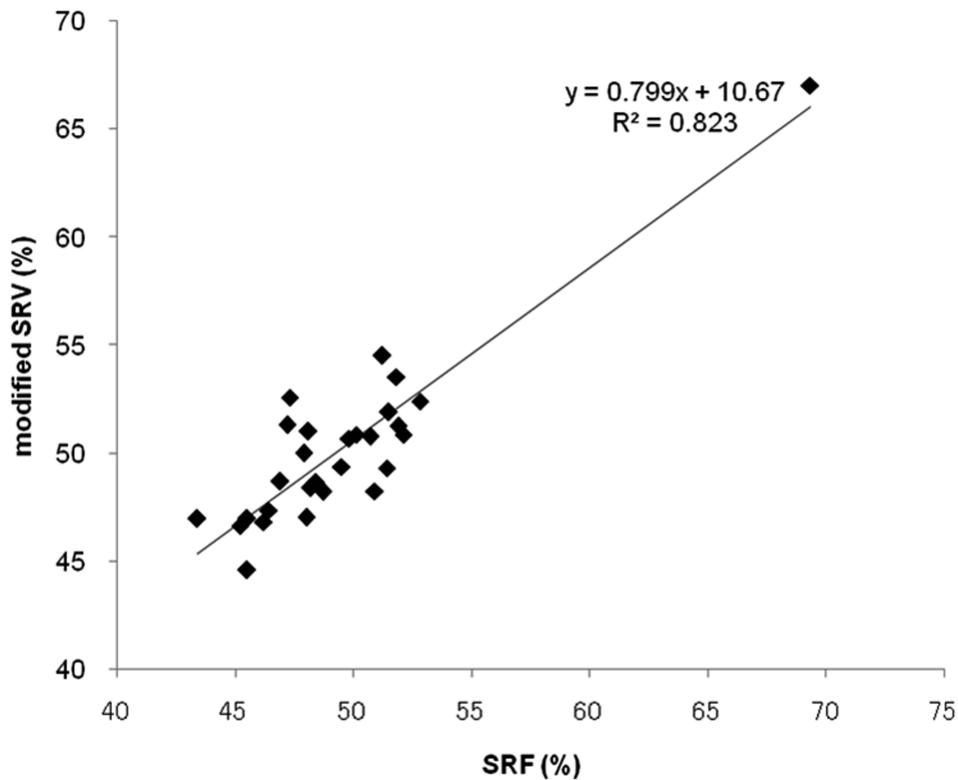












SRF - modified SRV(%)

