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Original Article

Evaluation of CT perfusion parameters for assessment of split renal function in healthy donors

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ABSTRACT

Objectives: To assess feasibility of automatically calculated CT perfusion parameters using two different methods of drawing regions of interest (ROIs) to reflect split renal function in comparison with MAG3 renography.

Methods and materials: 51 potential kidney donors (24 males, 27 females) were prospectively evaluated by preoperative CT perfusion. Post processing was done twice; one with ROI around renal cortex only and the other around cortex and medulla. Perfusion parameters (perfusion, peak enhancement intensity PEI and blood volume BV) were compared between the two methods. Split values for each of these parameters were calculated and compared to split renal function measured by MAG3 renography using paired samples *t* test.

Results: Perfusion was significantly lower in method 2 than in method 1 while PEI and BV showed no significant difference between the two methods. Split values of CT parameters showed no significant difference from corresponding renography split function (p value > 0.1) except BV by method 1 and perfusion by method 2 which showed significant difference (*p* value < 0.05).

Conclusion: Certain CT perfusion parameters can reflect split renal function. Perfusion was more accurate in reflecting split renal function with ROI around the cortex while BV was more accurate with ROI around the whole parenchyma.

1. Introduction

Selective assessment of renal function is a fundamental part of donor evaluation to ensure that the donor has 2 well functioning kidneys with evenly divided renal function [1,2]. The evaluation of split renal function is commonly done by the gold standard renal scintigraphy with 99mTc mercapto-acetyl-triglycine (MAG3) which is somewhat, time consuming with additional radiation exposure [3,4].

Renal perfusion is an essential functional parameter for evaluating renal vascular damage in patients with renal artery stenosis, ureteral obstruction, chronic allograft rejection, and other renal diseases [5]. Several imaging modalities have been proposed for the noninvasive assessment of renal perfusion, including contrast enhanced CT,

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dynamic contrast-enhanced MRI and contrast-enhanced US. Contrast enhanced CT is a useful tool for the noninvasive assessment of renal perfusion as it is widely available with strict linear relationship between the measured renal tissue attenuation and the concentration of the contrast medium [6–8]. The measurement of renal perfusion has predominately been validated with an extended gamma variate model which requires a high rate of contrast medium injection (e.g., 15 mL/s) to produce a bolus injection time that is as short as possible. This high-rate injection is impossible to deliver with a peripheral catheter because of the small diameter of the peripheral vein; therefore, a central venous catheter is mandatory, which is invasive and cannot be used easily in routine clinical practice. Thus, a validation of the renal perfusion measurement after low-rate contrast medium injection is mandatory for applying MDCT in clinical practice [9].

Although isotopic renography is the method of choice for determining split renal function, it has several sources of errors as variations in depth of both kidneys [10]. Due to these limitations of isotopic renal renography as well as associated additional cost and radiation exposure, many authors challenged to find alternative methods for assessment of split renal function especially with computed tomography. In the early nineties, Dawson and Peters [11] introduced application of the Rutland-Patlak plot [12,13] with CT using a method which they denoted "dynamic CT" providing a model for calculation of single kidney function. Few years later, Frennby et al. [14,15] suggested a more feasible algorithm which included manual ROI drawing in all individual CT images in order to calculate the total attenuation value in each kidney which was assumed proportional to that kidney's relative function. Their results showed good agreement in comparison with ^{99m}Tc-DTPA renography. A similar algorithm was tried by El-Diasty et al. [16] and they calculated uncorrected CT clearance of the kidney by dividing the mean attenuation value (MAV) of each kidney by the MAV of the suprarenal aorta. They found a constant ratio of 1:5 between the uncorrected CT clearance and the isotopic clearance in all subjects.

Experimental studies found that time attenuation curves obtained from 64-multidetector CT were qualitatively and quantitatively similar to those obtained with electron-beam CT, and the results can be significantly improved by modification of image analysis methods [17,18]. Further studies are required on human kidneys concerning the best ROI drawing, the appropriate time window and the amount of contrast media and the rate of injection [19].

This study aimed to assess the feasibility of automatically calculated CT perfusion parameters to reflect split renal function in comparison with MAG3 renography, and to compare two different methods of drawing ROI into the renal parenchyma.

2. Materials and methods

2.1. Subjects

This prospective study was approved by the institutional committee of ethics. During a period of one year, 58 potential kidney donors were evaluated at our institution. Donor evaluation consisted of complete history and physical examinations, kidney and liver function tests, complete blood picture, coagulation profile, viral profile (including hepatitis B and C, and AIDS), urine examinations with both random and 24-h samples for proteinuria, creatinine excretion and clearance calculation, chest X-ray and abdominal ultrasonography. Based on this evaluation, seven subjects were excluded from the study; 4 had elevated serum creatinine, one with solitary kidney, one had renal fusion anomaly, and one had history of sever anaphylaxis to iodinated contrast media. Finally, 51 patients were included in this study (24 males, 27 females). Routinely, MAG3 scintigraphy was performed for all donors to assess split renal function.

2.2. CT scanning

CT scanning was preformed with a 64 rows CT scanner (Brilliance, Philips Medical Systems, Best, the Netherlands). First, unenhanced scan (120 kV, 180 mAs) of the whole urinary tract was obtained. This series was used to locate the renal hilum which was the level for the next perfusion study. *Perfusion scan*: The selected area at the renal hilum was scanned to obtain 8 parallel 5-mm-thick sections that cover 40 mm along *Z*-axis. The table position was fixed; CT perfusion was performed at 120 kV and 180 mAs with a field of view 35 cm, a matrix of 512 × 512 pixels and an acquisition time of 0.5 s per image. The acquisition started simultaneously (without delay) with IV bolus injection of 60 ml of iodixanol (320 mg iodine/ml) (visipaque) into an antecubital vein through 18-gauge peripheral IV line using a power injector at rate of 6 ml/s. This sequence lasts for 120 s at rate of one scan per 4.8 s providing total number of 200 images (25 images for each of the eight sections). *Arterial scan*: After the perfusion scan, second dose (60 ml) of the same contrast agent was injected IV. Start of the arterial scan was determined by an automatic bolus-tracking program. A region of interest was placed in the abdominal aorta just above the kidney. Scanning was started 5 s after a threshold of 150 H.U in the region of interest was reached. Volume scans were acquired from the level of the celiac axis to the common iliac bifurcation using the following scanning parameters: 120 kV, 200–240 mAs, 2.0 mm table speed, 0.75 s rotation speed, 64× 0.625 collimation, pitch 1.172 and image matrix of 512 × 512 pixels. Due to the parenchymal and venous opacification by the injected contrast in the perfusion scan, this arterial scan provided both vascular and nephrographic images simultaneously without the need to obtain another nephrographic phase. *Delayed scan*: Excretory phase scanning was then performed after 5 min using the same parameters used in the unenhanced scan.

MAG3 renography was done using "Philips bright view SPECT" scanner. After adequate hydration by taking 1500 ml of fluids in the two hours before examination, a bolus of 1.6–2 MBq/kg (3–5 mCi) of 99Tc MAG3 was given intravenously. The donor lies supine with his back facing the detector. Acquisition was one frame/second for one minute followed by one frame/20 s for 19 min. In case of diuretic renography, 0.5–1 ml/kg furosemide was injected

at 10 min after tracer injection. ROIs were taken for both kidneys with background ROIs for subtraction to calculate split uptake and to obtain renographic curves for each kidney. Renographic phases include the following: *Perfusion (vascular phase)* during the first minute of the study followed by *Uptake phase* lasts for 2.5–5 min and represents the ascending limb of the curve till the peak then followed by *Excretion or drainage phase* (descending limb of the curve).

2.3. Data analysis

The data acquired from perfusion scan were processed using (Brilliance Philips) workstation V3.01.5000. A total of 200 images are merged by the software into 8 axial images, each of them representing the dynamic scan at different anatomical levels. An input region of interest (ROI) was set over the abdominal aorta to obtain arterial time attenuation curve with calculation of peak arterial enhancement. Tissue ROIs were drawn in the kidney using two methods. In method 1 the ROI was drawn around the renal cortex only (Fig. 1) and in method 2 ROI was drawn around the renal cortex and medulla (Fig. 2). The CT perfusion software calculates the perfusion based on the maximum slope model as described by Miles [20], and the perfusion is calculated as the average slope of tissue enhancement divided by peak aortic enhancement. The following parameters were calculated: perfusion (measured in ml/100 ml/min), peak enhancement intensity (PEI) (measured in Hounsfield units), time to peak (TTP) (measured in sec), and blood volume (BV) (measured in ml/100 ml) Figs. 3 and 4. Split values of perfusion, PEI and BV were calculated and compared with split renal function obtained with MAG3 (Fig. 5). Also, the values of these parameters were compared between the two methods.

2.4. Statistical analysis

Values of perfusion, PEI and BV obtained by the two methods were compared by paired sample *T* test. Split values of these parameters were calculated and compared to the split renal function obtained by MAG3 renography using paired sample *T* test. *P* values less than 0.05 were considered statistically significant. The statistical analysis was performed using the Statistical Package for Social Sciences (SPSS for Windows Package 20.0 Chicago, IL).

3. Results

Results of perfusion parameters obtained by methods 1 and 2 are listed in Tables 1 and 2 respectively. Results of MAG3 split renal function are presented in Table 3. Perfusion and PEI in method 2 were significantly lower than those in method 1 ($p < 0.001$). BV showed no significant differences between the two methods ($p > 0.5$). For method 1, split values of perfusion and PEI showed no significant difference from renographic split renal function (p value = 0.4 and 0.1 respectively), while Split values of blood volume showed significant difference from renography split renal function (p value = 0.04). For method 2, split values of PEI and blood volume showed no significant difference from renography split renal function with p value = 0.8 and 0.3 respectively, while split values of perfusion showed significant difference with $p = 0.04$.

The average effective doses for un-enhanced, perfusion, arterial and delayed scans were 5.2, 12.6, 6.1 and 5.2 mSv respectively with the total average effective dose of about 29.1 mSv.

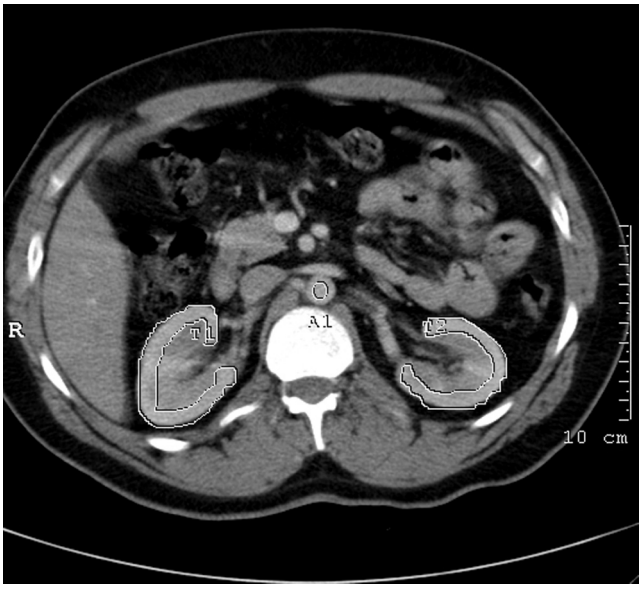

Fig. 1. Axial perfusion CT image shows ROIs around the renal cortex.

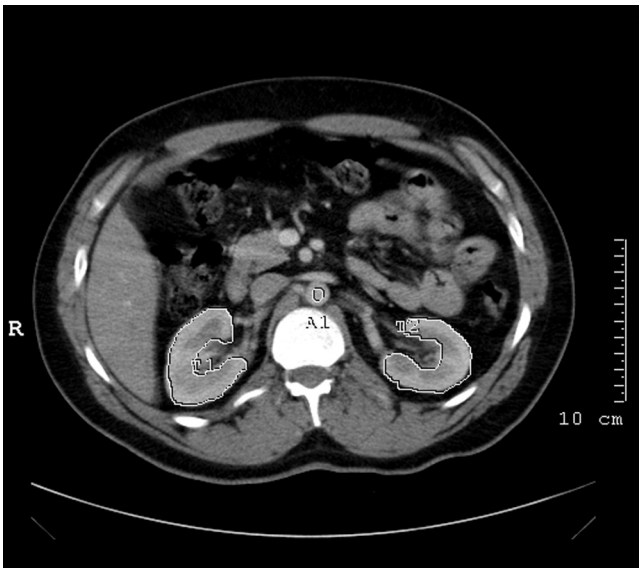

Fig. 2. Axial perfusion CT image shows ROIs around the renal cortex and medulla.

4. Discussion

Living donor renal transplantation is the best treatment option for patients with end stage renal disease, and it is a safe surgical procedure with excellent graft survival, donor's and recipient's outcome [21]. Hu et al. [22] stated that donor kidney function can predict donor's residual renal function and recipient's graft function after living-donor kidney transplantation. Precise measurement of the GFR traditionally requires radioisotopes, repeated blood sampling, and urine collection, which is troublesome and time consuming. The commonly used GFR estimation equations tend to underestimate GFR in the transplantation donor population which may exclude healthy potential donors. On the other hand, overestimation of GFR when using the urinary creatinine clearance may put donors at risk for development of chronic kidney disease in addition to the increased risk of allograft failure in the recipient [23,24].

Shokeir et al. [2] studied 300 potential kidney donors by ^{99m}technetium diethylenetetramine penta-acetic acid (DTPA) renography. A difference of 5.3% between two kidneys in estimated GFR was considered to be significant. They found 48% of the study group to have disparity in the function of both kidneys and the kidney of the lower function was donated in this entire group of donors. Therefore they use the renal isotopic scan as an integral part of routine donor assessment. In our study, 20% of donors showed difference in split function more than 5%, and this difference may be explained by smaller sample size in our study.

Hackstein and colleagues [25–28] have developed useful models applied to routine CT protocols. The key feature of their work was "two-point Patlak plot". The development of multislice CT systems, stimulated further interest in perfusion studies by advancing perfusion CT from single slice technique to a volume based examination. More recently, clinical use of CT perfusion imaging has been facilitated by the release of commercial software packages from a range of CT manufacturers. CT has the key advantage of linear relationship between the iodine concentration and the density changes in the tissue which makes processing straightforward and simpler compared to MRI where the contrast-signal relationship and the quantification are problematic [6].

In our study we used 64-channel MDCT in both anatomical evaluation and functional assessment of kidney donors using single protocol starting with non enhanced scan followed by perfusion scan, arterial and lastly delayed phase. In this protocol we obtained combined arterial and nephrographic phases as the parenchyma and renal veins, during arterial scan, were already enhanced from the contrast previously injected in the perfusion study. Other studies [29,30] investigated the use of split bolus techniques in assessing renal vascular anatomy and revealed good results comparable to standard three phase protocols. Namasivayam et al. [31] compared accuracy of depicting renal venous anatomy and variants at arterial and venous phases and concluded that arterial phase could be used alone for evaluating the renal venous anatomy with the same accuracy of dedicated venous phase.

We used 60 ml of contrast for the perfusion scan, and this amount is sufficient for most of perfusion studies not only in renal transplants but also in other clinical applications. In their study on renal masses, Chen et al. [32] used 30–40 ml contrast. A similar amount (30 ml) was used by Helck et al. [33] in their study on healthy donors. A dose of 0.8 ml/kg (48–80 ml contrast) was used by Zhong et al. [34] in their study on adult patients with Nutcracker syndrome.

The contrast injection rate in our study was 6 ml/s. Similar injection rates were used by other authors, and Chen et al. [32] used rate of 6.5 ml/s while Helck et al. [33] and Zhong et al. [34] used rate of 5 ml/s. Kandel et al.

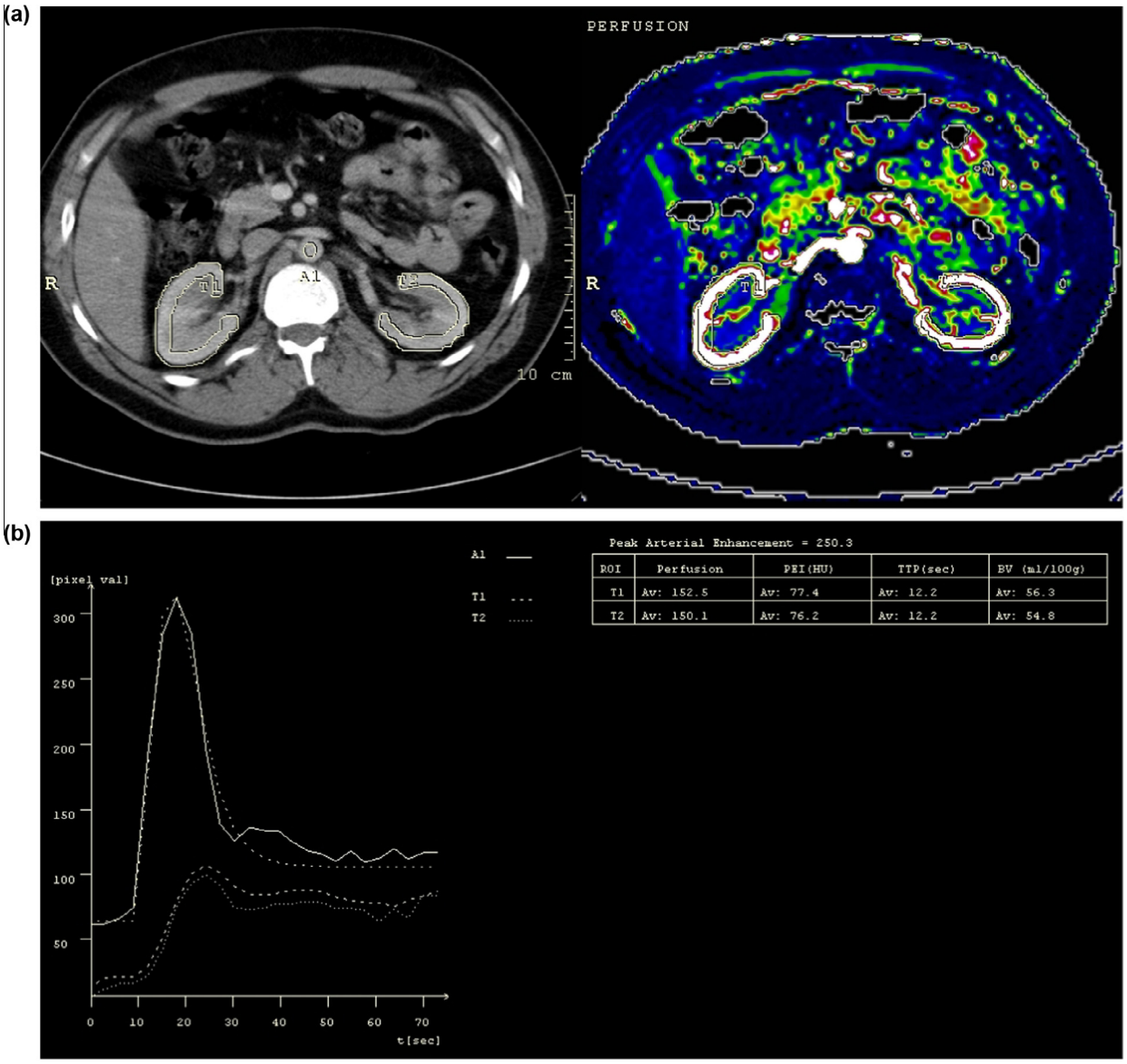

Fig. 3. Perfusion results by method 1 show (a) axial conventional image, color map image, (b) time attenuation curve and quantitative report.

[35] evaluated the effect of duration of contrast media injection on CT perfusion values in a swine model, and they found that perfusion values were not affected by the rate of injection and recommended that slower injection rate is sufficiently accurate for use in routine clinical practice.

For analysis of the perfusion study, we used the available software package in our workstation for post processing without the use of complicated mathematical models or equations. The target was to determine which of the perfusion parameters are more accurate in reflecting split renal function and to compare between ROI drawing in the renal cortex alone and in the whole renal parenchyma.

Perfusion and PEI were lower in method 2 than in method 1, and this may be explained by the fact that most of the renal blood flow goes to the cortex with subsequent accumulation of more contrast media in the renal cortex. We found wide range of normal values of CT perfusion parameters in healthy individuals. This recommends that in patients with unilateral renal disease, the perfusion values of the affected kidneys should not be compared to a reference range of different individuals. Instead, they should better be compared to the contra-lateral kidneys as a reference. The same recommendation was provided by Zhong et al. [34] in their study on patients with left nutcracker syndrome.

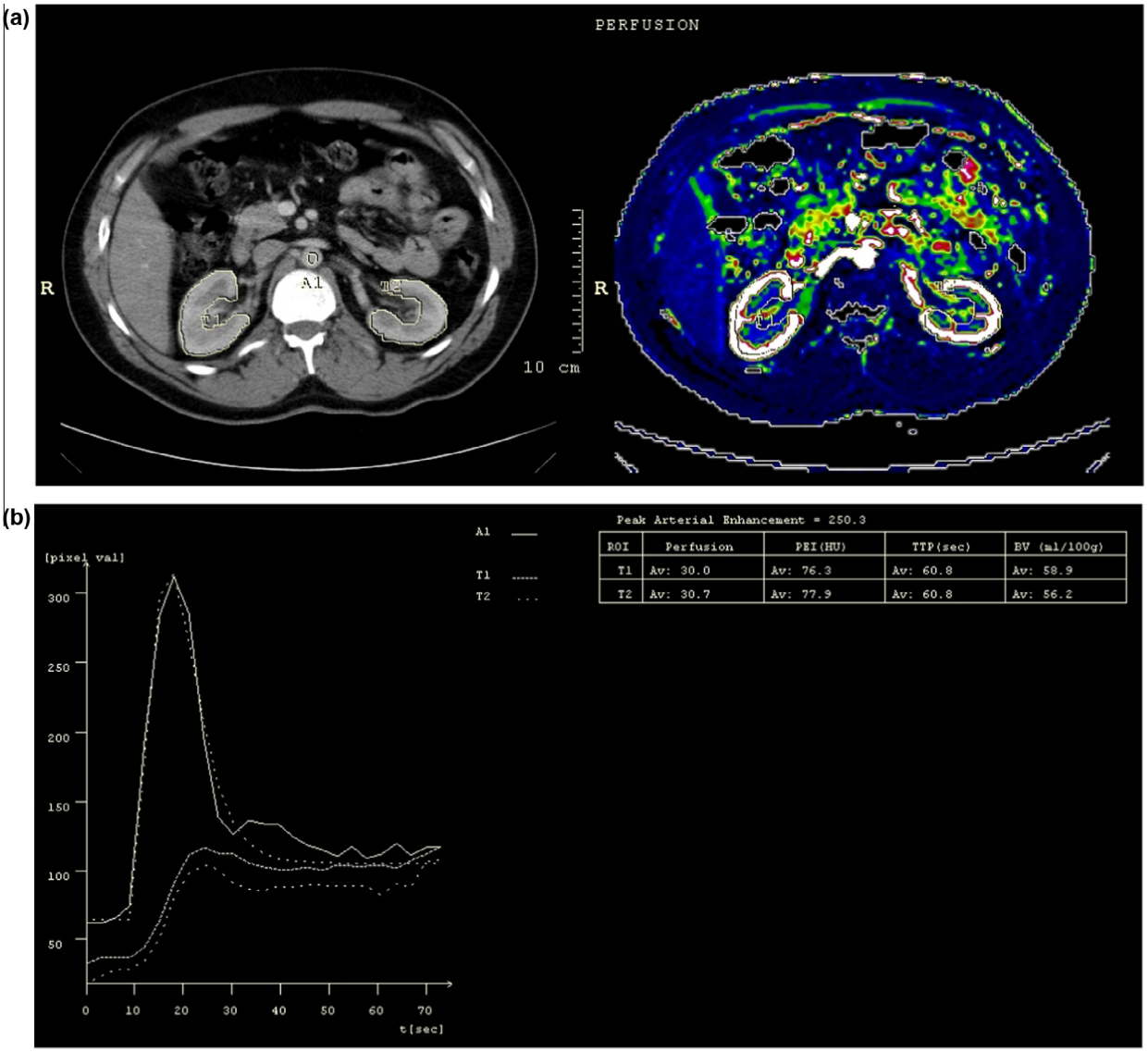

Fig. 4. Perfusion results by method 2 show (a) axial conventional image, color map image, (b) time attenuation curve and quantitative report.

We used MAG3 renography as a reference for split renal function, and split values of perfusion parameters were calculated and compared to MAG3 split renal function. For method 1, split values of perfusion and PEI showed no significant difference from renography split renal function, while split values of blood volume were significantly different. For method 2, split values of PEI and blood volume showed no significant difference from renography split renal function, while split values of perfusion were significantly different. This suggests that using multiple parameters increases the accuracy of CT perfusion in renal function assessment.

There are some limitations regarding the use of CT perfusion in our study, and the first is the relatively limited scan range during the perfusion scan (not exceed 40 mm along the *z*-axis). Recent technology advances that allow increase of the length of the scan during perfusion study either by increasing width or number of detectors used or by application of new toggling technique will overcome these disadvantages allowing for whole organ CT perfusion study [32–34,36].

The second limitation is the relatively high radiation dose. The effective dose from the perfusion scan was 12.6 mSv, reported radiation doses from perfusion scan in other studies were 9 mSv [33] and 10.1 ± 2.1 mSV [34], and these lower doses can be explained by lower scan parameters used in these studies. The total effective dose for our whole study was 29.1 mSv, and Chen et al. [32] reported total effective dose of 18.5 mSv; however, in their study they obtained only two phases: non enhanced scan and volumetric perfusion scan for the kidney. In addition to that, the CT urography working group of the European

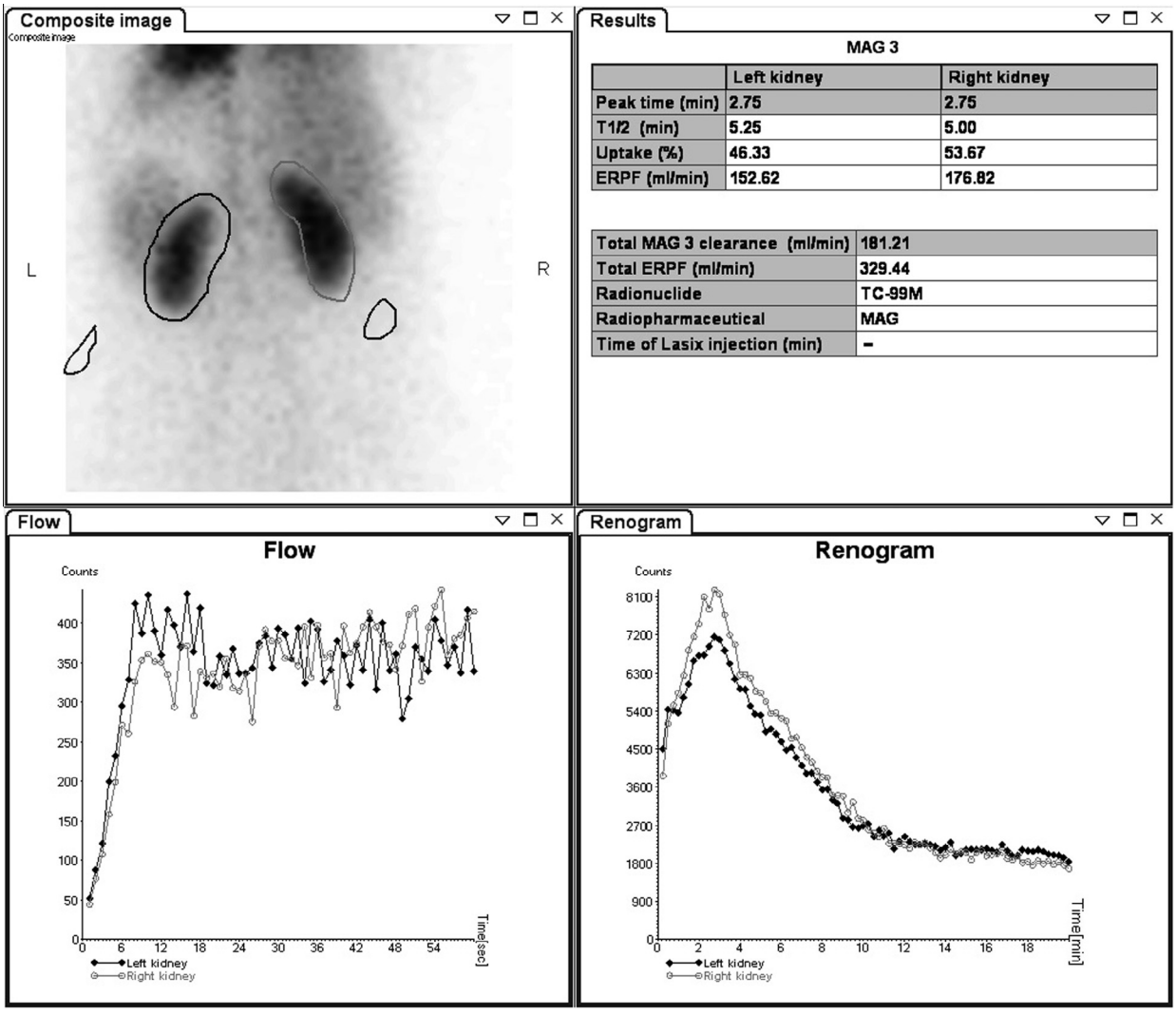

Fig. 5. MAG 3 renography shows perfusion image, flow curve, renographic curve and quantitative report.

Table 1
CT perfusion parameters by method 1.

	Minimum	Maximum	Mean	Std. deviation
Right perfusion (ml/100 ml/min)	29.50	198	122.4	46.46
Left perfusion (ml/100 ml/min)	33.80	195.4	122.7	47.29
Right PEI (HU)	44.10	104	73.69	13.84
Left PEI (HU)	41.70	101.60	73.50	13.89
Right BV (ml/100 g)	36.10	125.60	63.63	19.28
Left BV (ml/100 g)	30.50	116.50	63.60	17.60

Table 2
CT perfusion parameters by method 2.

	Minimum	Maximum	Mean	Std. deviation
Right perfusion (ml/100 ml/min)	25.40	186.40	103.87	44.28
Left perfusion (ml/100 ml/min)	19.70	168.6	89.6	45.1
Right PEI (HU)	43.60	99.40	70.52	13.01
Left PEI (HU)	42.80	91.70	68.24	12.39
Right BV (ml/100 g)	33.90	120.60	64.57	20.08
Left BV (ml/100 g)	30.40	116.10	63.14	19.05

Society of Urogenital Radiology ESUR reported in 2008 the effective dose from four phase CT urography to be between 25 and 35 mSv [37]. The radiation dose from MAG3 renography was 2.5 mSv.

In conclusion CT perfusion can be used for renal function assessment in integral MDCT protocol. CT perfusion parameters (perfusion and PEI by method 1; PEI and BV by method 2) can reflect split renal function with results comparable to MAG3 renography. Perfusion was more accurate in reflecting split renal function with ROI around the cortex while BV was more accurate with ROI around the whole parenchyma.

Table 3
MAG3 split renal function.

	Minimum	Maximum	Mean	Std. deviation
Right split function	45.20	57.30	50.90	2.70
Left split function	42.70	54.80	49.08	2.70

Conflict of interest

The authors declared that there is no conflict of interest.

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