REPRODUCUBILITY OF THE PAEDIATRIC RADIONUCLIDE RENOGRAM

Anita Brink
MBChB (UP) DCH(SA) FCNP(SA)

A thesis presented in part fulfilment of the requirements for the degree of
MASTER OF MEDICINE

UNIVERSITY OF CAPE TOWN

Supervisor: Professor MD Mann

Declaration

I declare that this dissertation is my own work. It has not been previously submitted for any degree or examination at this or any other University.

Anita Brink 28 January 2010

Index

Acknowledgements

I would like to thank the following people:

1. Professor Mike Mann for his support and tremendous help with this project.
2. Dr Wynchank for his keen eyes.
3. Anneli Hardy for the statistical advice.
4. Dr Martin Šámal for providing us with the experimental software.

Dedication

I dedicate this project to my loving husband Janus, Michelle, Ariana and my two dads.

Literature Review

Introduction

The differential renal function (DRF) of kidneys calculated from ^{99m}Tc-mercaptoacetyltriglycine (^{99m}Tc- MAG3) renograms plays a central role in the management of various diseases of the kidneys and urinary tract in paediatric medicine and urology.

In evaluating the hydronephrotic kidney it is essential to differentiate between the obstructed and non-obstructed renal system. The definition of obstruction of the kidney has changed over the years and currently the definition used to make clinical decisions is a restriction to urine flow that gives rise to symptoms, or threatens renal function or, particularly in the foetus and infant, limits the ultimate functioning potential of the developing kidney (1, 2, 3). Therefore a change in DRF is used to guide treatment in unilateral hydronephrosis while in bilateral hydronephrosis a change in DRF is interpreted in conjunction with a reliable method to measure global renal function. This is usually the glomerular filtration rate (GFR) (4, 5, 6). In cases with a poorly functioning kidney the decision to do pyeloplasty or nephrectomy also depends on the differential renal function (7).

Similarly a renogram followed by an indirect cystogram is important in the evaluation of children with vesico-ureteric reflux (VUR) (8). In addition to providing information on the reflux, DRF can be measured and larger cortical defects detected. When surgery is planned, the choice between repair and nephrectomy may be influenced by the DRF (9).

Because ^{99m}Tc dimercaptosuccinic acid (DMSA) studies can detect very small cortical defects it is considered the gold standard for evaluating children with urinary tract infection and hypertension. However, Ritchie et al (9) showed that the DRF calculated on a ^{99m}Tc-DMSA scan and a ^{99m}Tc-MAG3 renogram are very similar, unless it is a very poorly functioning kidney. The mean DRF of the left kidney using ^{99m} Tc-DMSA was 50.5% (range 5.0-93.5%) and using ^{99m}Tc-MAG3 was 49.8% (range 6.2%-90.7%). The mean difference between the two methods never exceeded 4.3%. They concluded that if a MAG3 renogram is used to assess drainage or reflux in a child with urinary tract infection (UTI) a ^{99m}Tc-DMSA scan is unnecessary if the DRF is within normal limits on the ^{99m}Tc-MAG3 study (9). Patzer et al (10) has shown that hypertension is linked to the more pronounced cortical scar. These scars can be picked up on MAG3 renography (11).

Renography is not part of the initial surgical work-up of boys with posterior urethral valves (PUVs). After successful treatment of PUVs long-term urological care is needed. Renography is done some weeks after surgery to estimate a baseline DRF. Renal deterioration secondary to bladder dysfunction requires follow-up care as about one third of patients will develop renal failure in their lifetime. Because both kidneys can be unequally affected DRF estimation is combined with a measured GFR to give absolute single kidney function on the repeated scans (6).

MAG3 renography is also used in children with dysplastic kidneys, such as multicystic kidneys where an absence of renal uptake on the side of the ultrasound abnormality confirms the diagnosis. If there is a peripheral ring of MAG3 uptake the diagnosis of multicystic kidney is incorrect and the patient will be treated as a patient with severe hydronephrosis (6).

In children with duplex kidneys isotope studies are mandatory to determine the renal function of the affected moiety. The surgical approach to complicated duplex systems is largely determined by the function of the affected moiety (6).

Methods used to process the renograms

The guidelines for standard and diuretic renography published by the European Association of Nuclear Medicine (EANM) recommend that only the Integral and Rutland Patlak plot methods are used to process renograms. The guidelines also state that there is a point where the global renal function is so impaired that no method can be recommended for the assessment of DRF. They do not define this "point" (12, 13).

In the Integral method recommended by the guidelines, the parameter determined is the area under the background-corrected renogram. This represents the cumulative uptake during a selected time interval (12). The terminology used in the literature for this method is not always consistent as some authors refer to it as the area under the curve method (14, 15).

In everyday practice the biggest difficulties in obtaining reproducible estimates of DRF stem from identifying the margins of a poorly functioning kidney and drawing appropriate background regions of interest (ROI). There are two groups of patients in which we frequently experience problems in processing. The first group is children with massive hydronephrosis where the kidney extends into the flank and part of the standard perirenal or C shaped background region of interest lies outside the body outline. The intra-renal activity is also not uniform. The large pelvis is photopaenic on the one to two minute image used to calculate DRF and background activity may be over-subtracted. The second group is children with poor renal function. The uptake by the kidney may be so poor that the kidney outline merges into the background and reproducible ROIs cannot be drawn. The difficulties are probably the greatest in small babies with a low GFR (12, 13, 16).

The reproducibility of measurements of differential renal function on renograms is critical for decision making but there is very little data on how reproducible studies are. The effects of age, global renal function, asymmetry in renal function and method used on the reproducibility of the DRF calculated for a patient are unknown (12).

Reproducibility in normal adults

Piepsz et al (17) evaluated reproducibility of renal study results in 13 healthy adult volunteers. They had ^{99m}Tc MAG3 renograms on two occasions one week apart. The studies were processed using different algorithms. The article did not state if they were processed by one or more observers. All the studies were processed using a rectangular perirenal background ROI. The difference between the first and second measurement was calculated for each patient.

The values for DRF were very reproducible, for all methods, with a mean difference between the first and second measurement of 0.3% (17).

The standard deviation (SD) of the differences represented the precision of the technique. The study found that the SDs differed depending on the algorithm used to process the renogram. The Integral method gave an SD of 1.7% and the Rutland Patlak plot method, using 4 points between one and two minutes, gave a slightly greater SD of 2.8% (17).

Reproducibility in patients with asymmetrical renal function

The reproducibility of ^{99m}Tc-MAG3 renograms in a wide population was investigated by Lezaic et al (18) who included 50 adult and 50 paediatric cases in their study. These patients were referred to their department for clinical reasons. They included a wide range of DRF from symmetrical to solitary kidneys. The differential renal function for each study was calculated twice on separate occasions by three different observers. They processed the renograms using only the Integral method with perirenal background ROIs. The average intra-observer repeatability range for the 50 adult patients was 2.61% and the inter-observer repeatability was 4.20% (18). The term repeatability was defined as = "$\sqrt{2}$ x 1.96 x within subject SD (s_ω)" or 2.77s_ω (19).

These authors also subdivided their paediatric patients into different groups and looked at the reproducibility of differential renal function at different levels of asymmetry in renal function. They established two groups of DRF, one group (n = 23) with symmetrical renal function (45%-55%) and a second group (n = 42) with asymmetrical renal function (30%-70%). The two groups were not independent as the 23 patients with DRF in the normal range 45%-55% were included in the larger group. Thus the group termed asymmetrical function, 30%-70%, included patients with symmetrical renal function. They excluded patients that were extreme outliers for asymmetry in differential renal function. The difference between the SDs for the two groups was not statistically significant. The SD was 2.23% for the group with symmetrical renal function and 2.16% for the bigger group that included patients with asymmetrical renal function (18).

Piepsz et al (17) looked at the accuracy of ^{99m}Tc - MAG3 renograms in 18 patients, all older than 2 years, who had both a ^{99m}Tc - MAG3 renogram and a ^{99m}Tc-DMSA scan within 15 days. The DRF obtained using the ^{99m}Tc–DMSA renal scan was used as the reference value. The indications for the scans were renal infection with or without vesico-ureteric reflux. Because the ^{99m}Tc–DMSA scan was used as the reference value, children with

hydronephrosis were excluded. ^{99m}Tc–DMSA scans overestimate the function of the hydronephrotic kidney and could therefore not be used as a comparison with ^{99m}Tc - MAG3 in children with hydronephrosis (20). Piepsz et al (17) also excluded children with renal failure and acute pyelonephritis. Five of the 18 patients had asymmetrical renal function. The asymmetry ranged from 21%-70% for the right kidney and the SDs were 2.2% for the Integral method using a rectangular background region and 2.8% for the Rutland Patlak plot method (17).

Reproducibility in immature kidneys

It is known that neonates have immature renal function and that clearance of MAG3 increases as the tubular function matures. When global renal function is measured by determining the GFR using inulin, the GFR of an infant is less than that of an adult, even when corrected for body surface area (21).

The 50 paediatric cases evaluated by Lezaic et al (18) were divided into two subgroups, 25 children younger than 6 months and 25 older than 6 months. They found a slightly better inter-observer reproducibility in children older than six months. The SD was 1.48% for the group under six months and 1.34% for the group greater than 6 months (18).

Ozcan et al (14) reprocessed 394 ^{99m}Tc - MAG3 renograms in 101 children with a prenatal diagnosis of unilateral hydronephrosis and at least three studies per patient, using the Integral method (referred to as area under the curve in their article) and the Rutland Patlak plot method. The studies were reprocessed by a single observer once per method.

The mean difference between the DRF obtained by the two methods (Rutland Patlak plot DRF minus Integral method DRF) was -0.8% for all 394 renograms. For each imaging study the 95% limits of agreement were calculated. For all 394 studies they were -7.0% to 8.6%. For the initial study, the median patient age was 3.5 months and the 95% limits of agreement were -12.5% to 8.7%. The mean difference between the two methods was -1.9%. For the last study on each patient, done at a median age of 47.1 months, the mean difference and 95% limits of agreement were smaller, 0% and -5.2% to 5.2% respectively (14).

The SD of the mean difference between of the two methods was 3.9% for all the studies. When dividing the patients into discrete age groups they found that the SD for the group 0-2.9 months was 7.1 %, for the group 3.0-5.9 months 4.7% and for the 6.0-8.9 months group 3.5 %. There was no statistically significant difference when separating the patients into age groups (ANOVA, P = 0.072). This could be due to the differences in numbers between the groups analysed. The group under 3 months included 41 patients and the group older than one year 212 patients but there was a definite trend of decreasing agreement in the younger children, with the poorest agreement in the youngest group. The authors attributed this trend to the fact that renal function is immature in the neonate and young baby (14).

Reproducibility in cases with abnormal global renal function

In patients with poor renal function the measurement of DRF can be problematic. In these patients there is poor renal extraction of the radiopharmaceutical from the blood so a large proportion of the tracer remains in the blood and extracellular fluid. This results in a poor target to background ratio (16).

A study by Lythgoe et al (22) looked at the accuracy of DRF in 35 children with solitary kidneys and 20 children with two kidneys. Eighteen of the patients with solitary kidneys were boys with PUVs, eight with a GFR > 50 ml/min/1.73m^2 and ten with a GFR of less than 50 ml/min/1.73m^2. Seventeen of the patients had a multicystic kidney and were scanned before age one year. They assumed, based on age, that the multicystic kidney group all had abnormal renal function. They do not indicate if the GFR values given in the PUV group were measured or estimated. Three observers then processed these studies as if there were two kidneys. They used 24 different methods. The variances were not equal so they analysed it by looking at the paired differences between the three operators for mean and SD. The largest differences were found with the solitary kidney group with poor GFR and the smallest differences were seen in the group with two kidneys and normal GFRs (22).

We know that there is a level of decreased global renal function at which we cannot separate the renal and background activity accurately, but could not find any literature on this level (12, 16). We also failed to find any papers on differences in the reproducibility of different algorithms at impaired levels of renal function.

Accuracy of the ^{99m}Tc -MAG3 renogram

It is more difficult to establish the accuracy of estimates of DRF. One of the methods used has been to compare a ^{99m}Tc -MAG3 renogram and ^{99m}Tc –DMSA scan within a relatively short time period, usually within four weeks (17, 22). Another method used is to analyse patients with solitary kidneys as if they have two kidneys. The reasoning is that we know the DRF for this kidney should be 100 % and a different value is directly due to processing artefacts (22).

In the group of 18 patients used by Piepsz (17) they calculated the difference between the DRF of the ^{99m}Tc –DMSA and ^{99m}Tc -MAG3 renogram, taking into account the negative or positive sign for this difference. The mean of the differences would represent a systematic bias, but they found no statistically significant bias. The SD of the difference represents the accuracy. The Integral and Rutland Patlak methods gave comparable good results with SDs < 3 % .

Lythgoe (22) investigated the accuracy of 24 different methods, 12 methods using background correction, in two ways using both children with solitary kidneys and children who had a ^{99m}Tc -MAG3 renogram and ^{99m}Tc –DMSA close to each other. For the solitary kidney group the background subtracted methods gave lower means and SDs than the non-background methods. In this group the values of one observer was compared to the expected

value of 0. The mean inter-method difference DRF from the 12 methods using background subtraction ranged from 0.1%-6.1% with SDs of 2.8%-9.2% (22).

The patients who had both a ^{99m}Tc -MAG3 renogram and ^{99m}Tc –DMSA, had normal GFRs, two kidneys and a range of DRF of 12%-88% with a mean DRF of 51%, Lythgoe (22) found the DRF values from the left kidney obtained by three observers for each of the 24 methods were not significantly different. The differences between the 24 methods used to calculate DRF on the MAG3 renogram and DMSA studies were compared using the observations of a single observer. For the methods using background correction the mean paired difference between the DRF of ^{99m}Tc-DMSA and ^{99m}Tc -MAG3 ranged from 0.0%-1.0% with a range of SD values from 3.7% -4.3%.(22)

Lythgoe (22) found the methods that model the kidney such as Rutland Patlak plot and deconvolution with background correction had the greatest accuracy and the lowest variance. The difference between the single and two kidney groups was attributed to the difficulty operators have when dealing with poorly functioning or solitary kidneys. (22).

Conclusion

The differences reported between the Integral and Rutland Patlak plot methods are small, about 1%. The reproducibility of both methods is good, between 1.7% and 2.2% for the integral method and about 2.8% for the Rutland Patlak plot. The studies also suggest that the reproducibility is decreased in very young children, and in patients with poor renal function. The interactions between age, GFR, level of asymmetry and method used to process on the reproducibility of the renogram in the individual patient have not been investigated.

We were unable to find any reports of studies to which determined if there is consistency between results from different manufacturers, using the same method to estimate the DRF.

Method

Introduction

Since 12th December 2000, MAG3 renograms performed on children in our department have been stored in an electronic storage system in the original Picker format. The renograms done from 12th December 2000 to the end of November 2008 were therefore available for reprocessing in this study.

All the patients were referred to our department as part of their diagnostic workup. The common indications for the studies were hydronephrosis detected on antenatal ultrasound, vesico-ureteric reflux evaluation and the investigation of dysplastic kidneys. The vast majority of the children had a normal estimated GFR (eGFR) or measured GFR (mGFR). The Schwartz method (21) is used to calculate eGFR at this hospital, while the two sample method with ^{51}CrEDTA as tracer is used to measure mGFR (20). The Schwartz nomogram is not accurate in children with liver disease or insulin dependant diabetes mellitus, but there were no children with these diseases in our series (29).

Before starting the study ethics approval was obtained from the Research Ethics Committee, Health Sciences Faculty, University of Cape Town.

Imaging protocol

The MAG3 dose was calculated according to the relevant EANM guidelines (3) at the time of study; the "adult" 70MBq MAG3 dose for a surface area of 1.73m^2 was scaled to the child's surface area (25). The minimum dose was 15 MBq.

All the studies were acquired with the child supine on the same Philips Axis Dual Head camera (previously known as Picker and then Marconi) using a LEHR collimator. Posterior images were recorded in a 128 x 128 matrix at 1 second per frame for the first two minutes. Thereafter the images were recorded at 15 seconds per frame for 40 minutes. These were the default Philips settings and allowed the data to be recast into 10 second frames using Philips algorithms. When indicated furosemide was administered 20 minutes after the injection of MAG3.

The original processing at the time the data was acquired and reported was done by an experienced nuclear physician using the version of the Philips Integral method running on the Odyssey software at that time. From December 2000 to 3rd of April 2003 the Odyssey FX software was used and since then Odyssey LX 9,4.

Tight renal ROIs and C-shaped renal background ROIs were drawn on a summed image of the 60-120 second frames. Care was taken to ensure that the renal regions included the whole kidney and did not cut the kidney and that the background regions did not extend outside the

body outline. If regions of interest could not be drawn meeting these criteria, the DRF was not included in the report.

Patients

To ensure that the study population was not dominated by "typical" cases who have a normal GFR and normal symmetrical or moderate asymmetry of DRF, we defined groups to cover as wide a spectrum of DRF and GFR as possible and set a limit on the maximum number of patients in each group.

The predefined groups were: **Table 1**.

GFR	**DRF**	**Maximum number**
> 80ml/min/1.73m^2	45-55%	30
	40-44%	10
	35-39%	10
	30-34%	10
	25-29%	10
	20-24%	10
	15-19%	10
	10-14%	10
	1-9%	10
	Solitary left kidney	15
	Solitary right kidney	15
60-79ml/min/1.73m^2	45-55%	10
	35-44%	10
	25-34%	10
	1-24%	10
	Solitary left kidney	10
	Solitary right kidney	10
40-59ml/min/1.73m^2	45-55%	10
	35-44%	10
	25-34%	10
	1-24%	10
	Solitary left kidney	10
	Solitary right kidney	10
≤ 39ml/min/1.73m^2	45-55%	10
	35-44%	10
	25-34%	10
	1-24%	10
	Solitary left kidney	10
	Solitary right kidney	10

The original reports were then reviewed in the order in which the MAG3 renograms had been done. In children with ectopic kidneys the areas used for background subtraction differ from standard renograms, there is also a difference in renal depth. We did not include children with ectopic kidneys or renal transplant patients as the processing differs significantly from the standard renal processing. The remaining patients were allocated to a group on the basis of the DRF in the original report and the measured or estimated GFR recorded within two months of the date of the renogram after checking that there were no movement artefacts in

the first five minutes of the renogram and that there was no reason to suspect that there was a change in global renal function between the date of the renogram and the GFR estimation or measurement.

To ensure that we did not introduce a bias associated with some patients included more than others we only used one study per patient. If the DRF of a renogram and the associated GFR placed the patient in a group which was already full, a subsequent renogram of that patient was included in the study if it fell into a group which was not full.

From the beginning of December 2000 until the end of November 2008 1415 ^{99m}Tc-MAG3 renograms were performed in our department and a total of 177 patients were selected for this study.

Five of the patients met the inclusion criteria but could not be analysed by one or more of the methods. The first patient had a large cystic mass in the right kidney displacing the cortical tissue anteriorly. In the second both kidneys were large and the background ROIs extended outside the body outline. The third patient had a very large hydronephrotic right kidney and the background ROI on that side extended outside the body outline. The fourth patient had a creatinine of 249 μmol/l and an estimated GFR of 28ml/min/1.73 m^2. The target to background ratio was too poor for reproducible regions to be drawn. The fifth patient had a cystic structure overlying the lower pole of the left kidney. This structure accumulated activity as the study progressed. It could not be processed using the experimental Rutland Patlak plot software (see following paragraph) and was therefore excluded from the study.

Processing

All the studies were processed five times per method by the author. Four different methods were used. The Integral method provided on the Philips Odyssey LX software package, the Philips Europak Rutland Patlak plot, and two experimental programs written in Matlab by Dr Šámal. The one was the Integral method and the other the Rutland-Patlak plot method.

Philips Integral method (PI)
Philips Rutland Patlak plot method (PRP)
Experimental Integral method (SI)
Experimental Rutland Patlak plot method (SRP)

The calculation for DRF was performed on the data recorded 60-120 seconds after injection of MAG3 with the PI method. The SI method used the fixed time interval of 60-150 seconds. The time interval for the SRP was chosen by the user and it was a variable time interval for each study, but the end of the time interval did not exceed three minutes. New regions of interest were drawn each time the study was processed. Tight renal ROIs were drawn on the summed 1 – 2 minute image, great care being taken to ensure the renal ROIs did not cut the kidney. In patients who only had one kidney, the renal ROI was drawn around the kidney and another "renal" ROI of a similar size and shape drawn in the expected position of the missing kidney. The Philips software was set to generate C- shaped peri-renal background ROIs 3 pixels wide and separated from the renal ROI by 1 pixel. These background ROIs could be adjusted if necessary. For example the width of a background ROI could be reduced if it

encroached on the body outline. The experimental software automatically generated a circumferential perirenal background ROI 1 pixel wide with a 1 pixel gap between the manually drawn renal ROIs. A cardiac ROI within the cardiac outline was used for the Rutland Patlak plots. In two studies the heart was not in the field of view and the blood pool ROI was drawn over the spleen.

The values for DRF below 0 or above 100 were replaced by 0 or 100 respectively by the SI method. The values above a 100 were not replaced by 100 with the SRP method

Statistical analysis

The results were entered into a Microsoft Office 2003 Excel software package spreadsheet. The data was analysed using Statistica 8.0 (26) and Microsoft Office 2003 Excel.

For each patient and each method the mean DRF for the left kidney and the variance of five measurements were calculated. The mean DRF for all the methods was calculated for each patient.

The method specific mean DRF for a particular patient was plotted against the mean DRF for all the methods (All Mean). This was done to see if there was any deviation in the line of identity for the methods.

Comparison of the three methods with each other was done using Bland-Altman plots. We compared the methods with each other as we do not have a "gold standard".

Analysis of precision

For each method we calculated the standard deviation from the mean for the 5 estimates (SDp). We then calculated the mean standard deviation (mean SDp) and the standard deviation of the SDp (SD of SDp) for each method.

To establish if DRF, age, GFR, asymmetry and side of the affected kidney had an influence on the standard deviation we plotted the SDp against the aforementioned factors for each method.

We know that younger children have lower GFRs. To determine if there is a relationship with high SD, method and low GFR for age. We used the normal values published by Piepsz and divided the children into groups of normal and abnormal GFR for age (27). As the data did not have a normal distribution a Spearman rank correlation coefficient was calculated for age and GFR for age in different subsets.

Analysis of Factors

For the three methods taken together we wanted to investigate the impact of covariates (in this case GFR and age) on the differentiation between the DRF measurements from the different methods. Two possible techniques to consider for multiple measurements on the same unit are repeated measures ANOVA and multilevel linear modelling or linear mixed modelling. Both these techniques are sensitive to outliers and assume that the dependent variables display normality of the residuals (28).

However, cases have been selected in such a way that "typical" cases with normal GFR and normal symmetrical or moderate asymmetry of DRF do not dominate the sample and thus that cases with extreme values were included proportionally by design. Consequently, the dependent variables (DRF measurements) do not display distributions that follow a bell shaped curve and are not normally distributed. Instead these dependent variables display 3 peaks due to the clustering of values at both the ends (-0, 100+) as well as in the middle. As a result, the techniques suggested are not appropriate to differentiate between the different methods while controlling for covariates.

Analysis of accuracy

We used children with solitary kidneys to determine to accuracy of the methods. A solitary kidney should have a differential renal function of 100% and any deviation from this value would because of an error in calculating differential renal function.

Analysis stemming from observations

On closer inspection of the patients with the highest SDp we saw that most were young and most had a low GFR. We performed Chi-squared tests separating the patients into groups on the basis of SD and GFR, and SD and age using four months as a cut-off.

Results

Patient selection

172 patients were included in the study. They fell into the following groups

Table 2. Included patients

GFR	DRF	Maximum number	Final number included
>80ml/min/1.73m^2	45-55%	30	30
	40-44%	10	10
	35-39%	10	10
	30-34%	10	10
	25-29%	10	8
	20-24%	10	8
	15-19%	10	6
	10-14%	10	7
	1-9%	10	9
	Solitary left kidney	15	11
	Solitary right kidney	15	7
60-79ml/min/1.73m^2	45-55%	10	4
	35-44%	10	7
	25-34%	10	3
	1-24%	10	7
	Solitary left kidney	10	5
	Solitary right kidney	10	3
40-59ml/min/1.73m^2	45-55%	10	4
	35-44%	10	1
	25-34%	10	4
	1-24%	10	3
	Solitary left kidney	10	2
	Solitary right kidney	10	3
≤ 39ml/min/1.73m^2	45-55%	10	1
	35-44%	10	1
	25-34%	10	0
	1-24%	10	1
	Solitary left kidney	10	2
	Solitary right kidney	10	5

Table 3.**The remaining 1244 studies were not included for one of the following reasons**:

Reason for exclusion of study	Number
No differential renal function given in the original report	11
Patient used already	189
No recent GFR or creatinine available	745
Transplant renograms	121
Ectopic kidneys	20
Poor technical quality	7
Movement artifacts	4
Group full	141
Could not be processed	5
Study lost	1

Of the eleven children who did not have DRF in the original reports three children had massive hydronephrosis and the kidney extended to the body margin. Background regions could not be drawn within the body outline. The remaining eight patients had very poor target to background ratio and one or both kidneys could not be differentiated from the background.

Seven studies could not be used due to poor technical quality. One was not acquired for the standard time period. Three studies had poor patient positioning. One was acquired on the wrong camera head. In one the camera was started after the MAG3 injection. In another there was a camera fault and the study stopped 3 minutes after the beginning.

The Indications for the Renograms, and the Ages and GFRs of the 172 patients

All the studies were performed as part of the children's routine investigations. Ninety children with hydronephrosis were investigated. In 28 cases the children were evaluated for VUR and the renogram was performed as a precursor to indirect cystography. The other indications included dysplastic kidneys, posterior urethral valves, Takayasu's arteritis and neuropathic bladder. In one case no record of the indication could be found. The indications for the studies on the patients in each group are listed in the appendix, table A28-A31.

There was a wide spread in age and GFR in the patients studied. The information is summarised below.

Table 4: Ages and GFR of the patients

	Age (in months)	GFR (ml/min/1.73m^2)
Mean	52.2	95.4
Median	33.7	91.0
Minimum	0	19
Maximum	195	230
Lower quartile	7.1	68.0
Upper quartile	87.9	117.0
Standard Deviation	52.4	35.9

In 21 children we used the measured GFR and in 151 we estimated the GFR using the Schwartz method.

The GFR values were corrected for surface area. Some of the "low" GFRs in children younger than two years were within normal limits for age and were not due to an impairment of renal function. When the surface area corrected GFRs were compared with the normal range for GFR published by Piepsz (27), 21 of the 172 patients had a GFR below the 10th centile; of them two were less than six months old, two were between six months and two years and 17 older than two years.

The raw data and demographics of all the patients are in the appendix in Table A.5-A.32.

The Philips Europak Rutland Patlak method

Soon after starting to process each renogram five times with each method, it became obvious that the PRP method sometimes gave discrepant results. With this method, it was not uncommon for four of the 5 estimates of DRF on a particular patient to be similar and one very different. We were unable to identify reasons for this in patients selected for this study and in those seen in the department for diagnostic studies at that time. To obtain an estimate of the magnitude of the problem we decided to analyse as a subset the results of the 30 children in this study with symmetrical DRF and normal GFR.

The mean value and standard deviation for the left kidney were calculated for the first thirty patients, for each method. The standard deviation was 1.05 for the PI method, 1.31 for the PRP method, 0.52 for the SI method and 0.63 for the SRP method.

Four patients, patients 3, 16, 20, 30, had standard deviations of 3.97, 4.12, 3.49 and 5.22 respectively for the 5 results using the PRP method.

We could not identify a cause and therefore dropped this method from the study.

The relevant details of the patients are listed in the appendix in tables A.33 to A.36.

The results of each group using the remaining three methods of processing are summarized in tables A.37 to A.61 in appendix.

Evaluation of the Raw Data

On inspection of the raw data, there was one extreme outlier with the PI method. This child, patient 130, had a mean DRF of 139% using the PI method but the SI and SRP methods both gave mean values of 100% and standard deviations of 0. The 5 results of the PI method ranged from 111% to 180% for the left kidney. The child has a small solitary left kidney. At the time of the study he was 66 months old and had an eGFR of 20 ml/min/1.73m^2. The target to background ratio was very poor and the outlines of the left kidney were not clearly defined. The PI method values are clearly incorrect and therefore we excluded this patient from the rest of the analysis, leaving 171 patients in the study.

The Mean DRF of the left kidney

Table 5: **The Mean, SD, and ranges for the three methods (n= 171)**

	PI	SI	SRP
Mean	55.2	52.4	52.6
SD	31.3	30.1	30.3
Minimum	-8.6	0	-0.6
Maximum	113.2	100	101.6
No <0%	8	0	2
No > 100%	17	0	4

The mean DRFs for the left kidney were similar for the SI and SRP methods. The mean using the PI method was higher. Two-way ANOVA analysis showed that the DRFs of the left kidney were significantly different for the three methods (F = 36456.7, df 2 and 340. The treatment and residual mean squares were 243166.2 and 6.67 respectively. P = 0.001).

The large SD of the DRF was expected because we collected a stratified sample to ensure the data set covered the full range of possible DRFs.

The minimum and maximum DRFs were less than 0% and greater than 100% respectively with the PI and SRP methods. They were 0% and 100% with the SI method.

Comparison of the estimates of DRF of the left kidney of individual patients

The DRFs of each patient obtained by each method were plotted against each other, with the line of identity. (Figures 1 to 3)

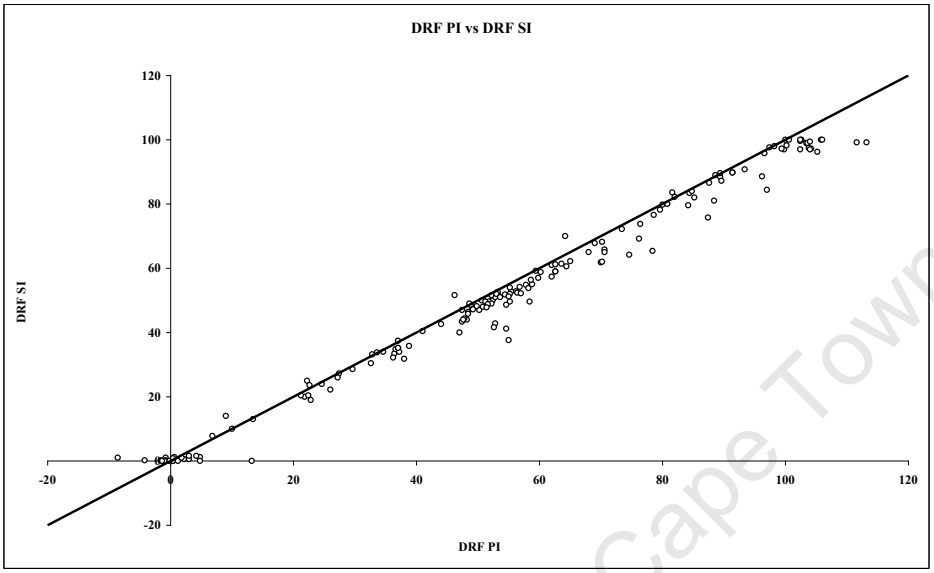

Figure 1: The line of identity and the XY scatter plot of the mean values of the DRF determined by the SI method against the mean values for the PI method.

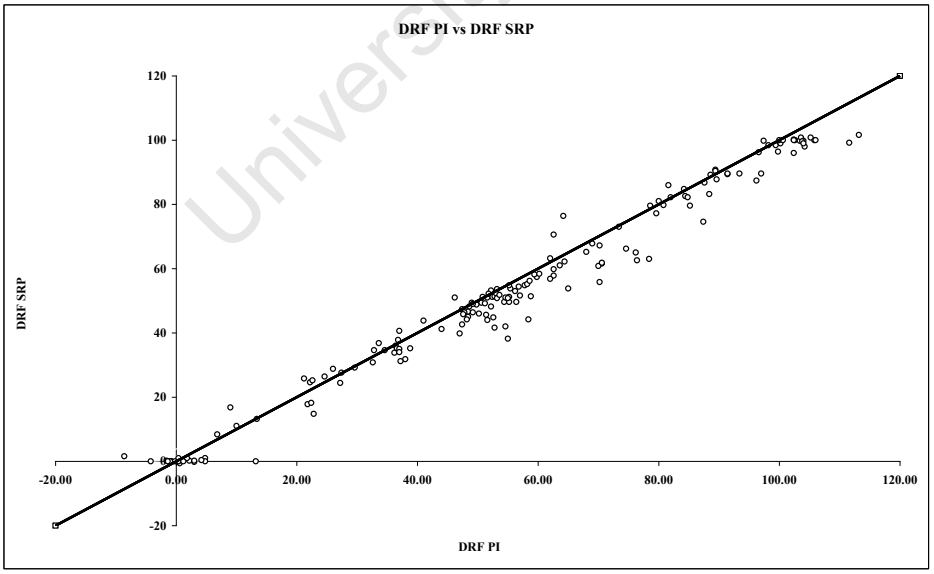

Figure 2: The line of identity and the XY scatter plot for the mean values of the DRF determined by the SRP method against the mean values for the PI method.

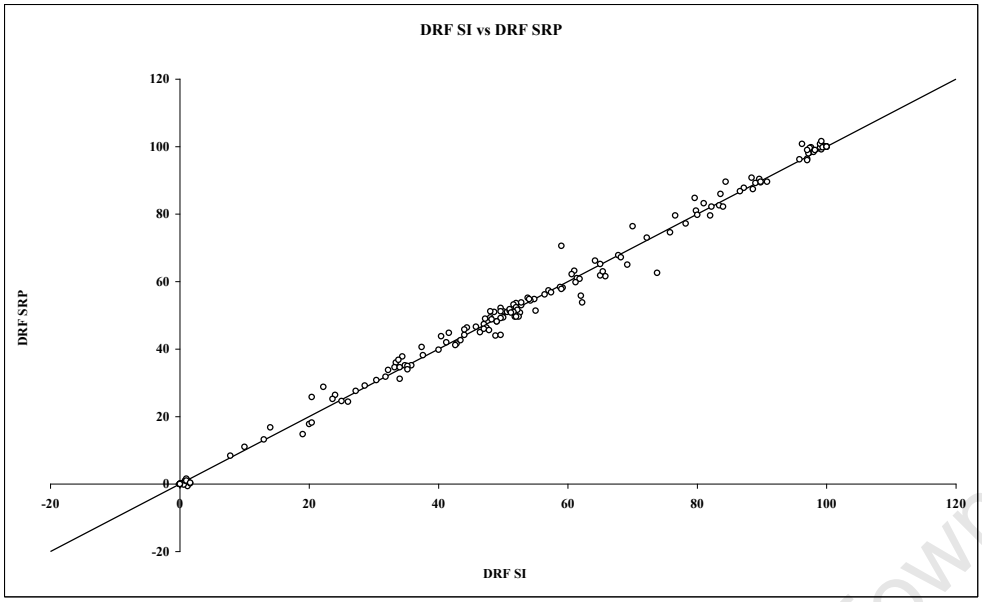

Figure 3: The line of identity and the XY scatter plot for the mean values of the DRF determined by the SI method against the mean value for the SRP method.

There was a very close correlation between the DRF estimates using the 3 methods; PI and SI r=0.993, PI and SRP r=0.990, and SI and SRP r=0.997, n=171.

Bland Altman Plots of the DRF of left kidney from the Philips Integral, Experimental Integral and Experimental Rutland Patlak plot methods

The Bland-Altman plots (Figures 4-6) comparing the three methods with each other show that there is very good agreement between the SI method and SRP method for all ranges of DRF (Figure 6). The agreement between the PI method and the other two methods is not as close, with the PI method systematically giving higher values for the left kidney than the SI (Figure 5) and SRP methods (Figure 4).

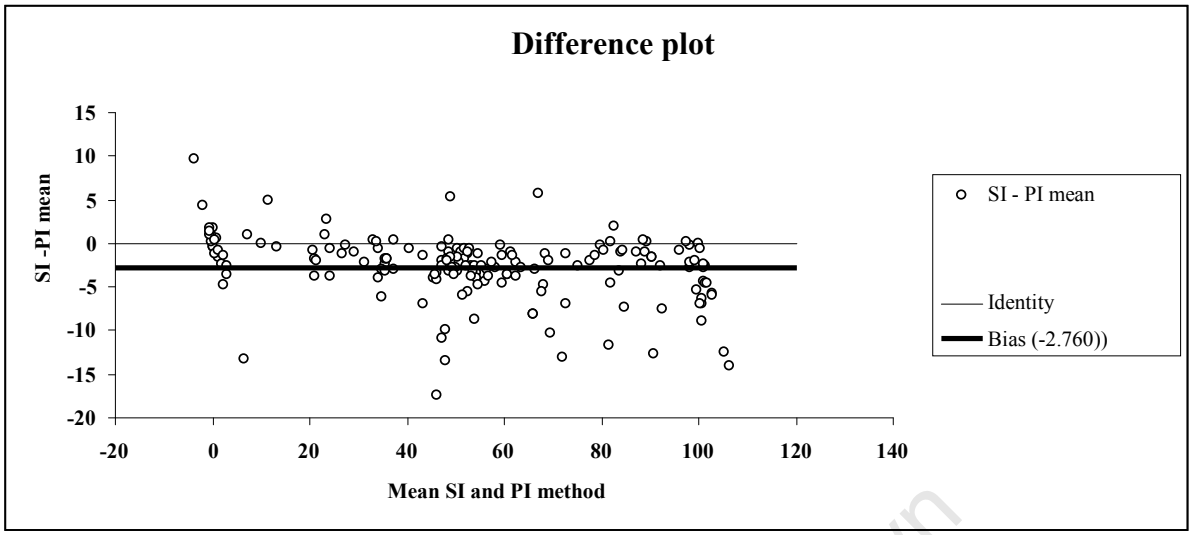

Figure 4: The Bland-Altman plot for the PI method and SI method

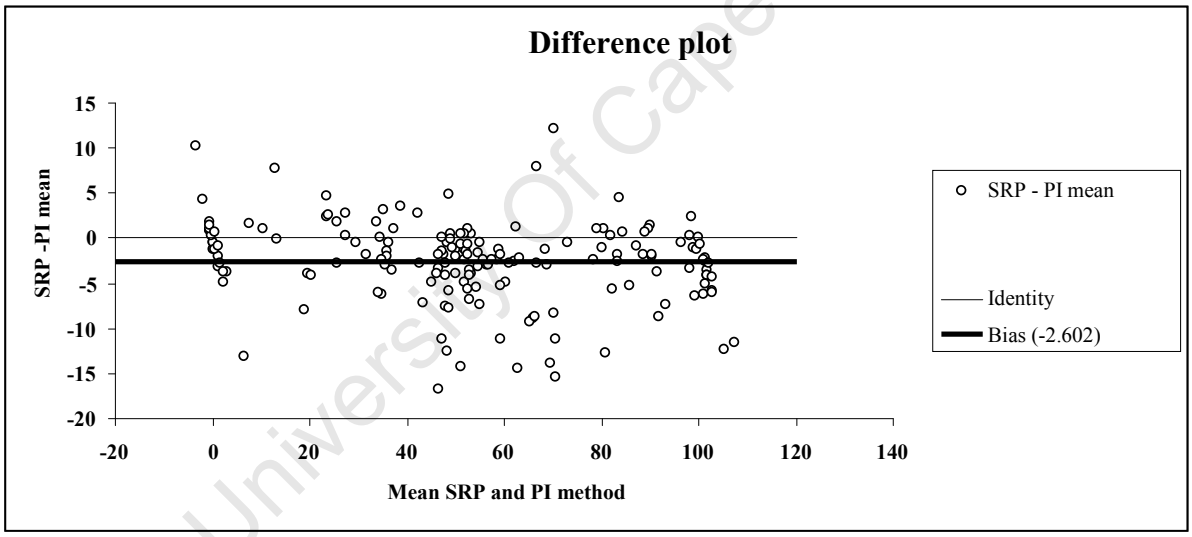

Figure 5: The Bland-Altman plot for the PI method and the SRP method

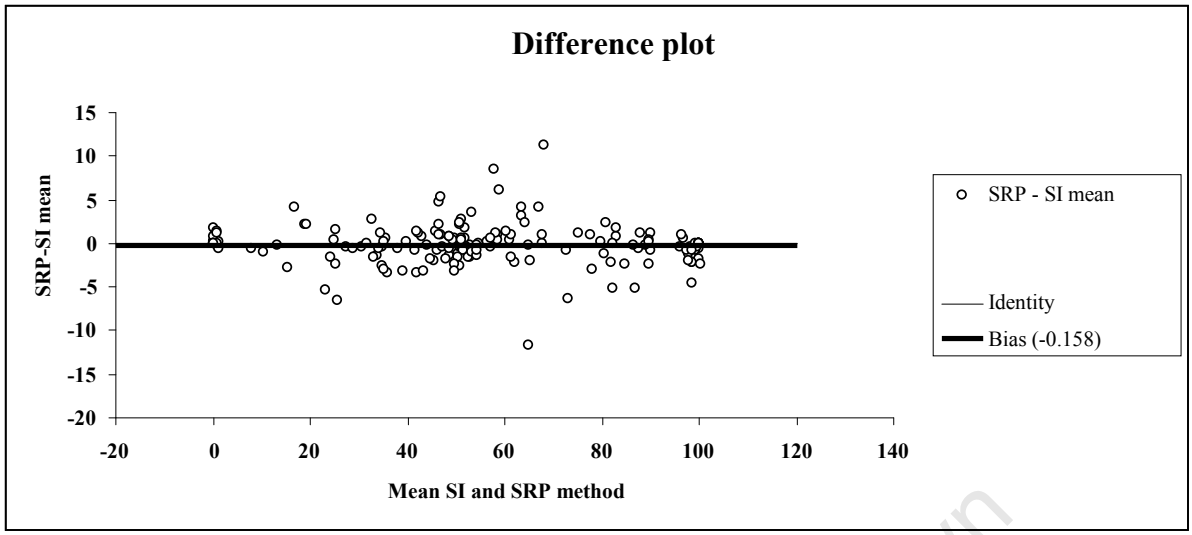

Figure 6: The Bland-Altman plot for the SI method SRP plot method

Bland Altman Plots of the standard deviation of the five estimates of DRF of the left kidney using the Philips Integral, Experimental Integral and Experimental Rutland Patlak plot

We are using the standard deviation of the DRF for each method as an index of variability.

The plots of the difference between the standard deviation of the left kidney DRF from each method and the mean of the standard deviations of the three methods are shown in Figures 7, 8 and 9. They illustrate that for all three methods the standard deviation increases as the mean standard deviation increases. This is most marked using the PI method.

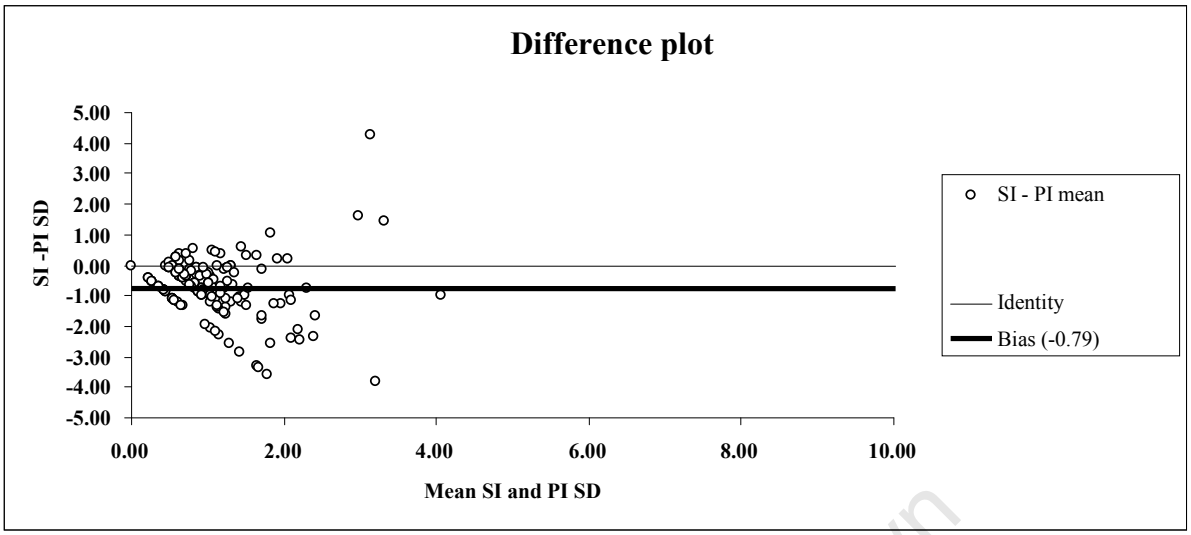

Figure 7: Differences between the standard deviation for SI method and the standard deviation of the PI method plotted against the mean standard deviation of the SI and PI methods.

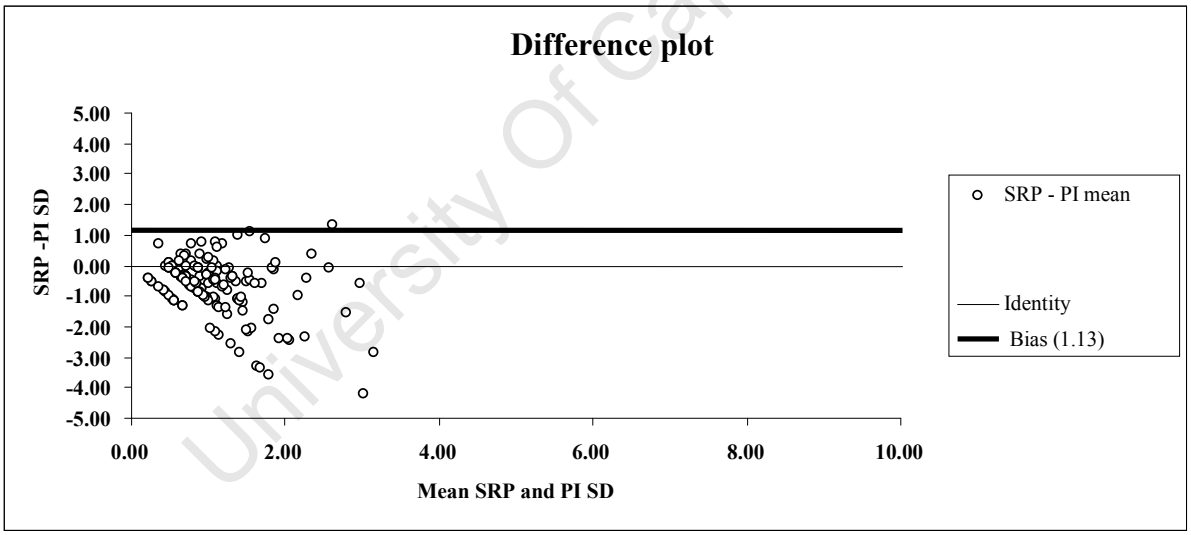

Figure 8: Differences between the standard deviation of SRP method and the standard deviation of the PI method plotted against the mean standard deviation of the SRP and PI methods.

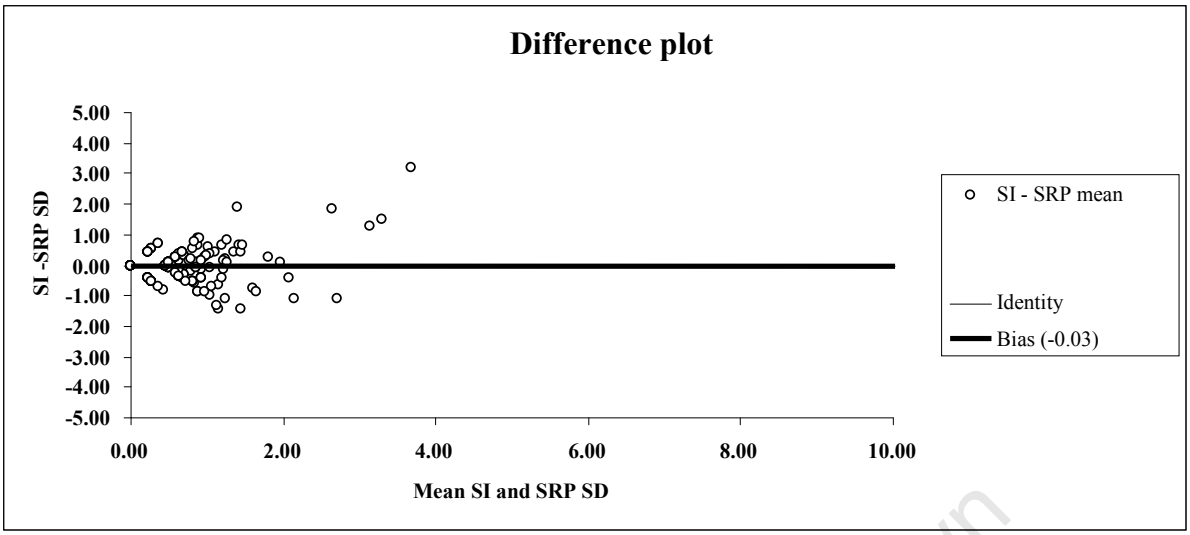

Figure 9: Differences between the standard deviation of SI method and the standard deviation of the SRP method plotted against the mean standard deviation of the SI and SRP methods,

Table 6: Mean, SD and ranges of the standard deviation of the five estimates of DRF of the left kidney for the three methods (n=171)

	PI Standard Deviation	SI Standard Deviation	SRP Standard Deviation
Mean	1.68	0.71	0.75
SD	2.39	0.73	0.58
Minimum	0	0	0
Maximum	9.1	5.3	3.3

A two way ANOVA analysis showed that the SDs of the DRFs of the left kidney were significantly different for the three methods (F = 66.66, df 2 and 340. The treatment and residual mean squares were 34.59 and 0.52 respectively. P = 0.001)

The mean standard deviation for the SI method and the SRP method were very similar. The mean standard deviation for the PI method was significantly higher.

The standard deviation of the standard deviation, used to determine variability is also low for the SI method and the SRP plot. It is bigger for the PI method. The ninety-fifth centile for the PI method is 3.39, 1.84 for the SI method and 1.96 for the SRP method. The maximum standard deviation was 3.3% for the SRP, 5.3% for the SI method and 9.1 % for the PI method.

The Standard Deviation and DRF of the left kidney for each of the three methods

The XY plots of the standard deviation of the individual methods and the mean DRF of all three methods of analysis are shown in the Figures 10-12.The SD remained similar across the spectrum of mean DRF for all three methods and was low in the vast majority of cases.

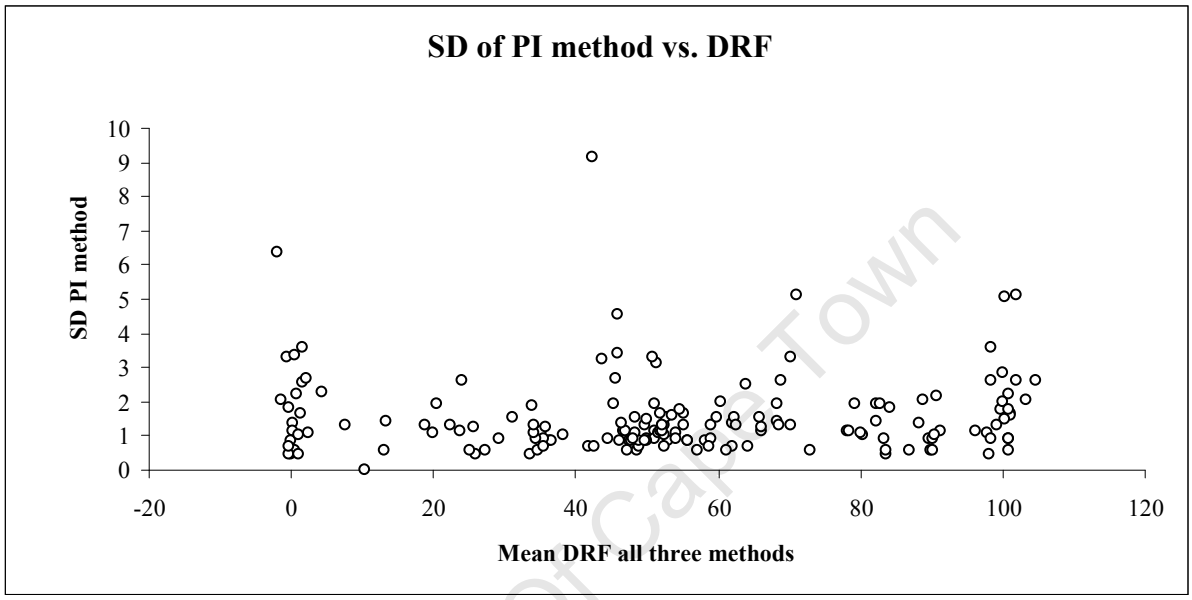

Figure 10: The standard deviation of the PI method plotted against the mean DRF of all three methods.

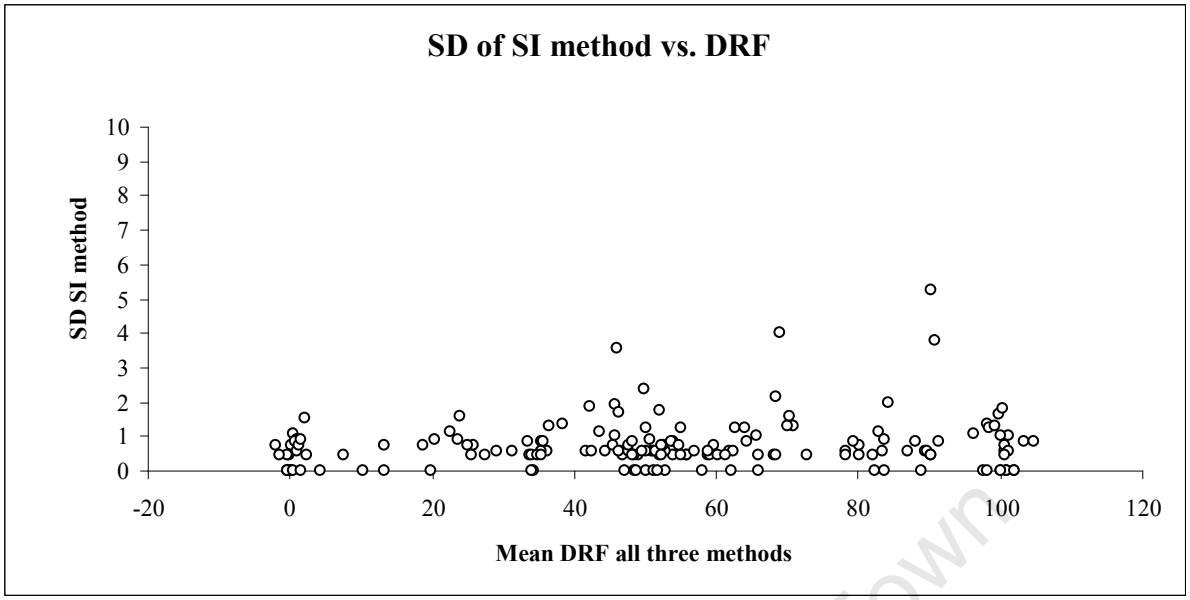

Figure 11: The standard deviation of the SI method plotted against the mean DRF of all three methods.

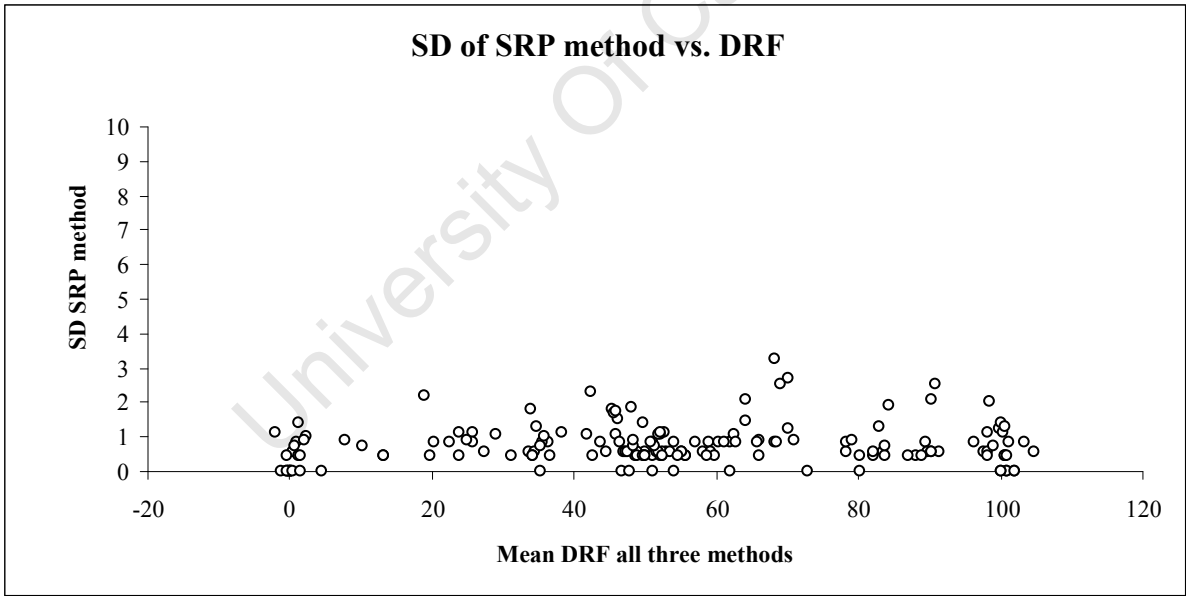

Figure 12: The standard deviation of the SRP method plotted against the mean DRF of all three methods.

There is no clear trend between the standard deviation of the methods plotted against the mean DRF of all three methods.

Standard Deviation and Age for individual methods

The XY plots of the standard deviation obtained with each method versus age in months are shown in Figures 13-15.

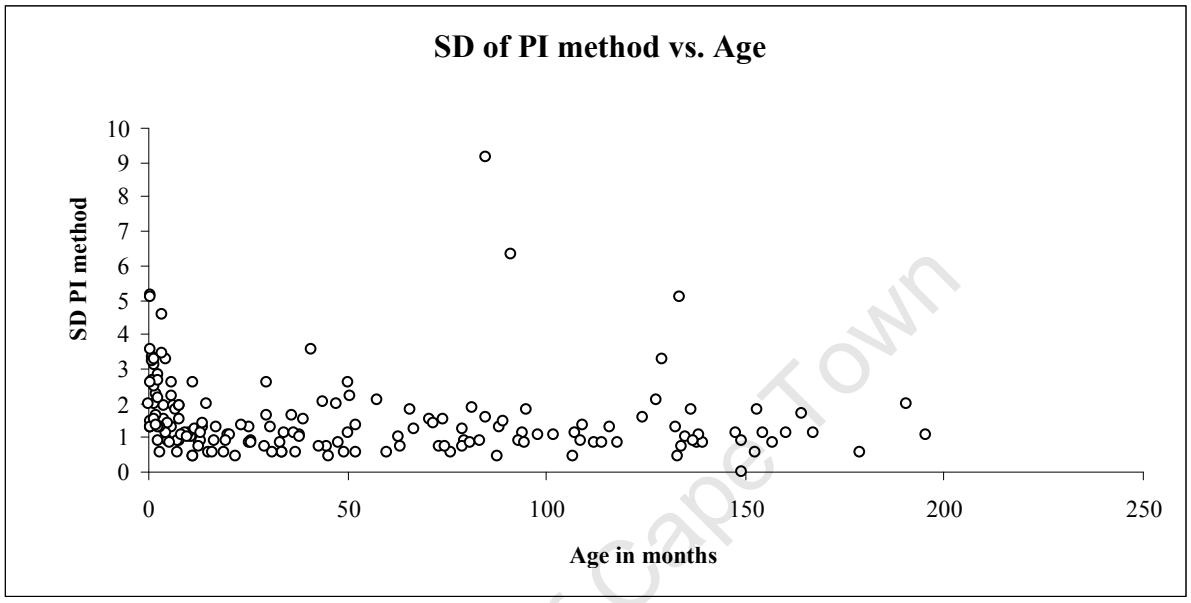

Figure 13: The standard deviation of the PI method plotted against the age of the patients.

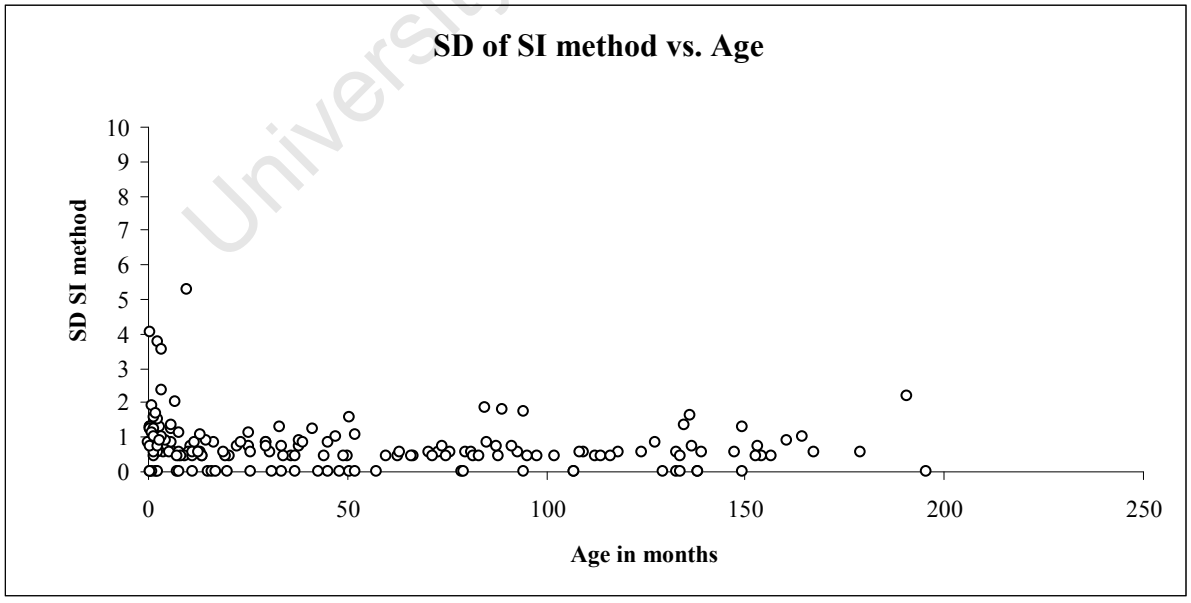

Figure 14: The standard deviation of the SI method plotted against the age of the patients.

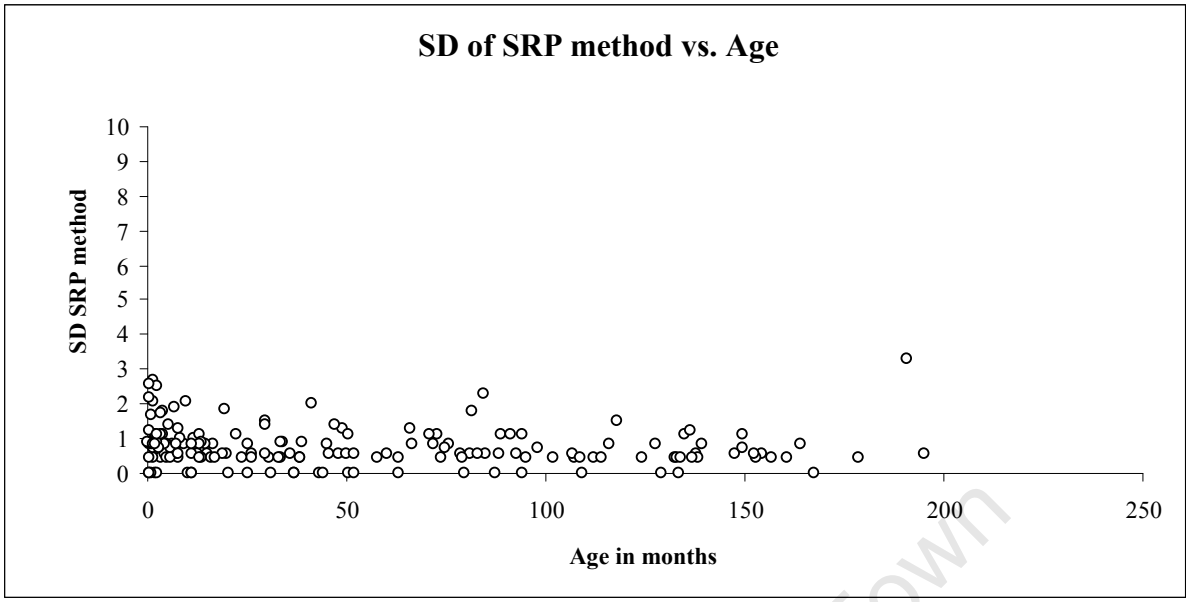

Figure 15: The standard deviation of the SRP method plotted against the age of the patients.

The SDs in children younger than six months tended to be larger than the older children when using the PI method and SI method. However with the PI method some of the older children also had a higher SD. There was no distinct pattern between age and standard deviation for the SRP plot method.

The Spearman Rank correlation coefficient was calculated for each of the three methods against age. The subdivision of children into groups of greater than and less than 6 months and 12 months respectively was based on the subdivisions in the literature and on visual inspection of the XY scatter plots shown in figures 13-15. When all children were included in the calculation there was a correlation between the SD of each method and age (Table 7). However when children were subdivided on the basis of age there was a correlation between the SD of the PI method and age for children younger than 6 months and 12 months but not for those who were older than 6 months or 12 months. There was no correlation between the SD and age subdivisions for the SI and the SRP methods.

Table 7. Spearman Rank correlation coefficients for the each of the three methods against age.

	PI		SI		SRP		n
	ρ	P	ρ	P	ρ	P	
All	-0.331	= 0.00001	-0.264	< 0.0005	-0.211	< 0.01	171
>6months	-0.009	> 0.05	-0.033	> 0.05	-0.114	> 0.05	131
≤6 months	-0.319	< 0.05	0.014	> 0.05	-0.084	> 0.05	40
>12months	0.073	> 0.05	-0.014	> 0.05	-0.048	> 0.05	113
≤12 months	-0.521	< 0.00005	-0.245	> 0.05	-0.150	> 0.05	58

Standard Deviation and GFR for individual methods

The XY plots of the SD vs. the GFR obtained with each method are shown in Figures 16-18.

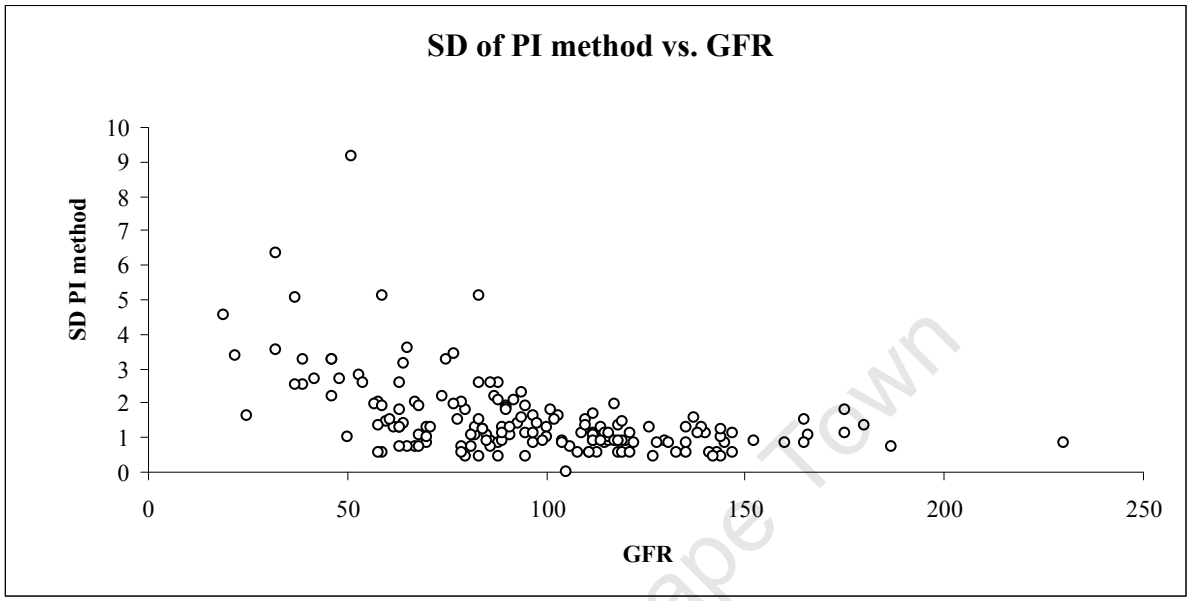

Figure 16: The Standard Deviation of the PI method plotted against the GFR (ml/min/1.73m^2) of the patients.

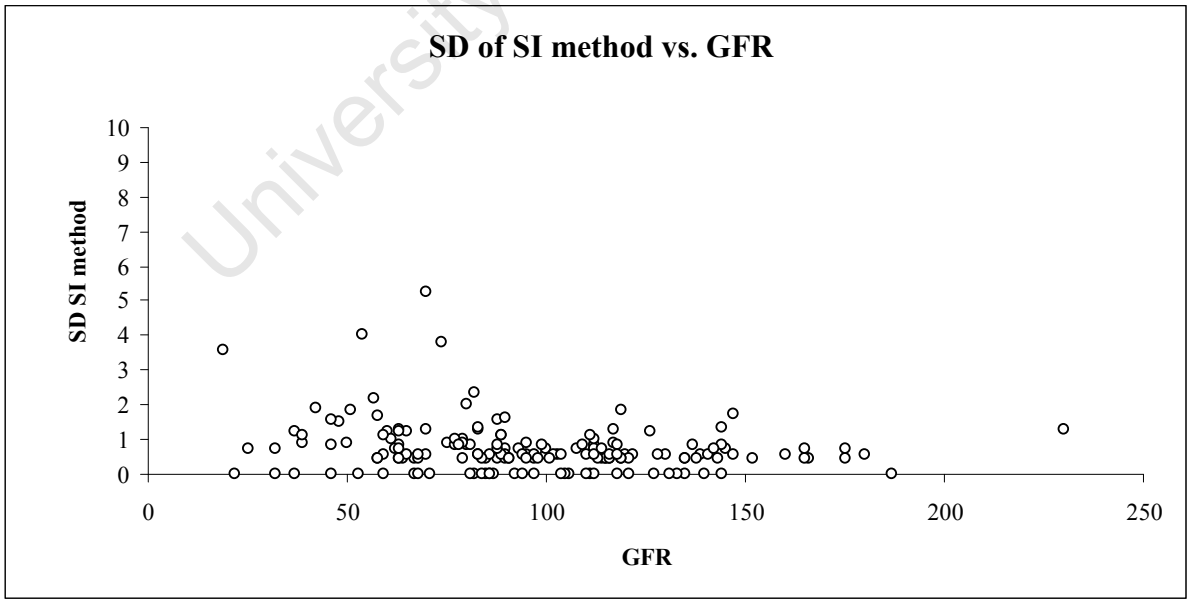

Figure 17: The Standard Deviation of the SI method plotted against the GFR (ml/min/1.73m^2) of the patients.

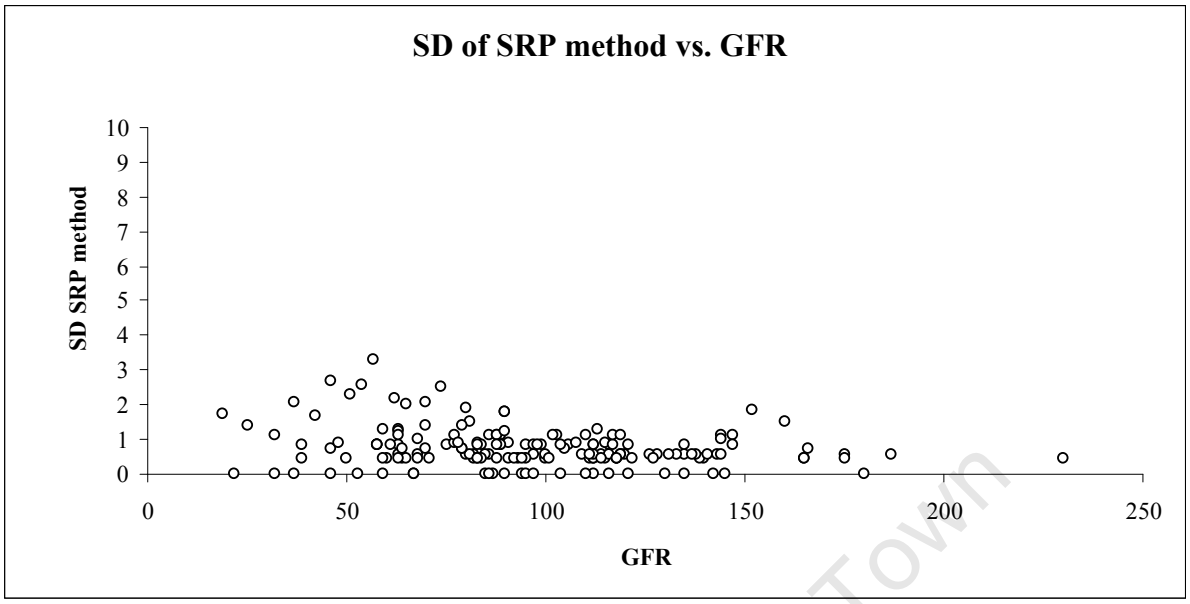

Figure 18: The Standard Deviation of the SRP method plotted against the GFR (ml/min/1.73m^2) of the patients.

There was a clear trend between GFR and SD for the PI method, the patients with higher SD all having a GFR below 80 ml/min/1.73m^2. The small number of patients who had a SD above two when analysed by the SI and SRP plot method all had a GFR below 80 ml/min 1.73m^2.

Table 8. The Spearman rank correlation coefficient was calculated for each of the three methods for GFR in different age groups

	PI		SI		SRP		n
	ρ	P	ρ	P	ρ	P	
All	-0.504	< 0,000001	-0.223	< 0.005	-0.210	< 0.01	171
>6months	-0.325	< 0.001	-0.072	>0.05	-0.149	>0.05	131
≤6 months	-0.540	< 0.001	-0.127	>0.05	-0.027	>0.05	40
>12months	-0.327	< 0.0005	-0.057	>0.05	-0.120	>0.05	113
≤12 months	-0.549	< 0.00001	-0.207	>0.05	-0.117	>0.05	58

When all children were included there was a correlation between SD for each method and GFR. When they were divided on the basis of age there was a correlation between GFR and SD in all the age groups when processed by the PI method, but not with the other two methods.

For the PI method there was a correlation with the SD and the ratio of the GFR to the 10th centile for a child of that age, ρ = -0.445, P < 0.00001. There was no correlation for the SI and SRP methods (ρ = -0.078, P = >0.05 and ρ = -0.119, P > 0.05 respectively)

The asymmetry in DRF, side of the kidney with the highest uptake and the SD

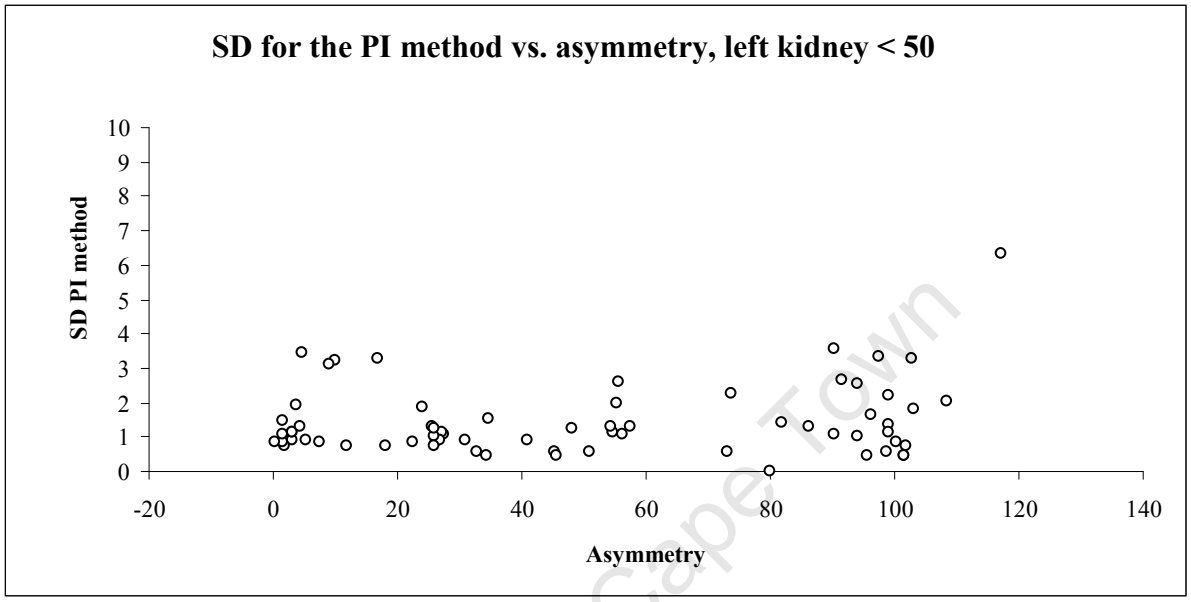

Figure 19: For patients in whom the DRF of the left kidney was less than 50, the standard deviation of the PI method was plotted against the asymmetry in renal function. Asymmetry was the difference between the DRF's of the left and right kidney.

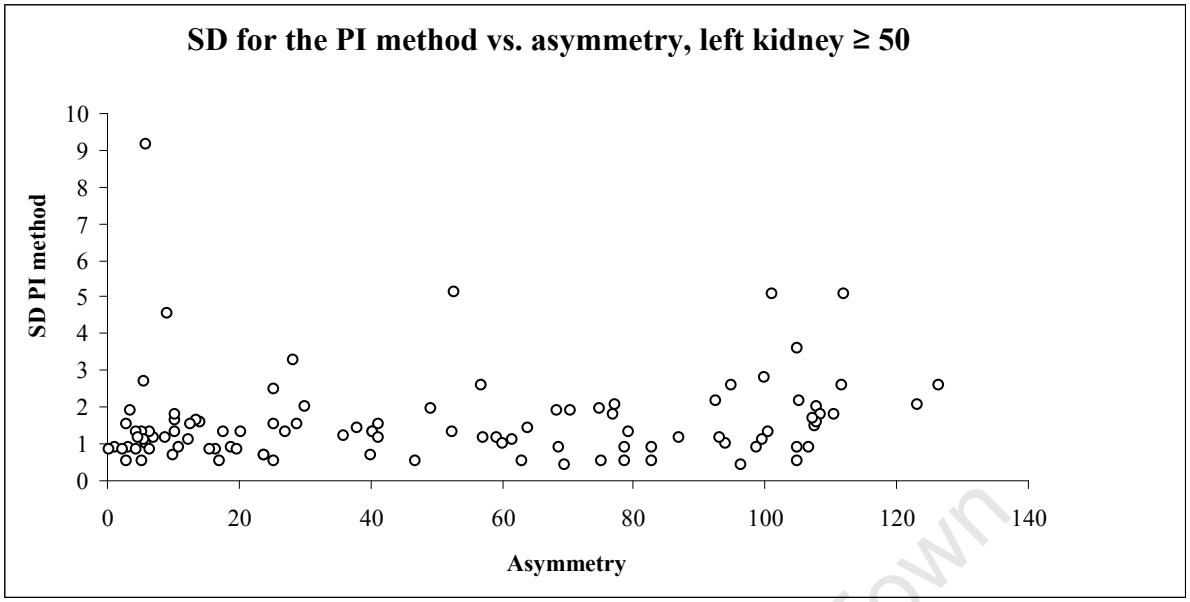

Figure 20: For patients in whom the DRF of the left kidney was greater than or equal to 50, the standard deviation of the PI method was plotted against the asymmetry in renal function. Asymmetry was the difference between the DRF of the left and right kidney.

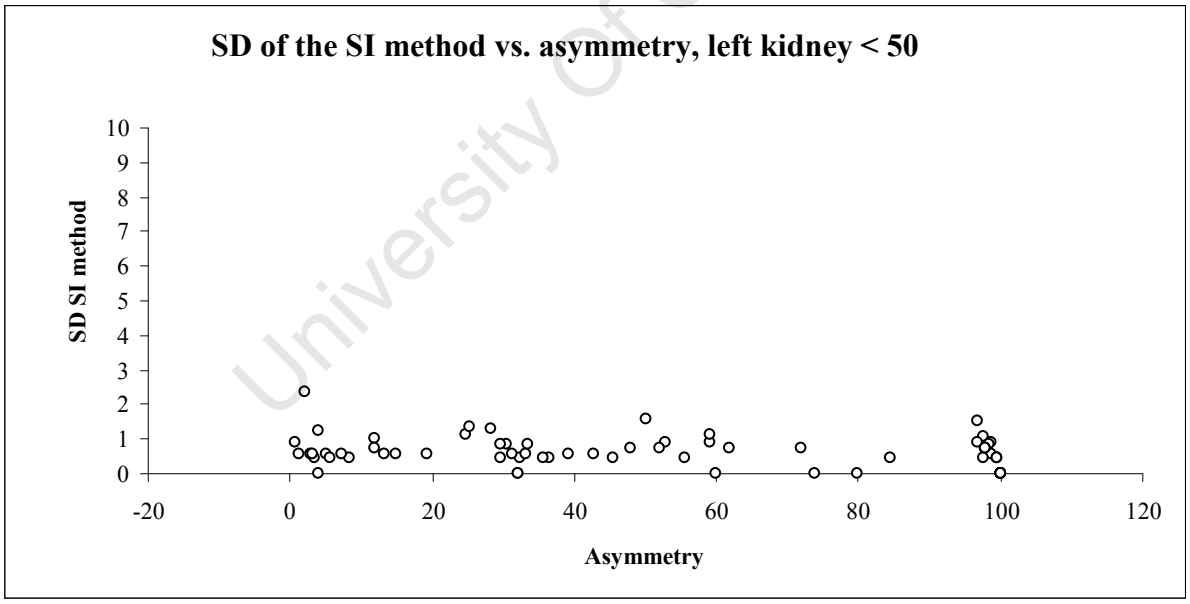

Figure 21 For patients in whom the DRF of the left kidney was less than 50, the standard deviation of the SI method was plotted against the asymmetry in renal function. Asymmetry was the difference between the left and right kidneys.

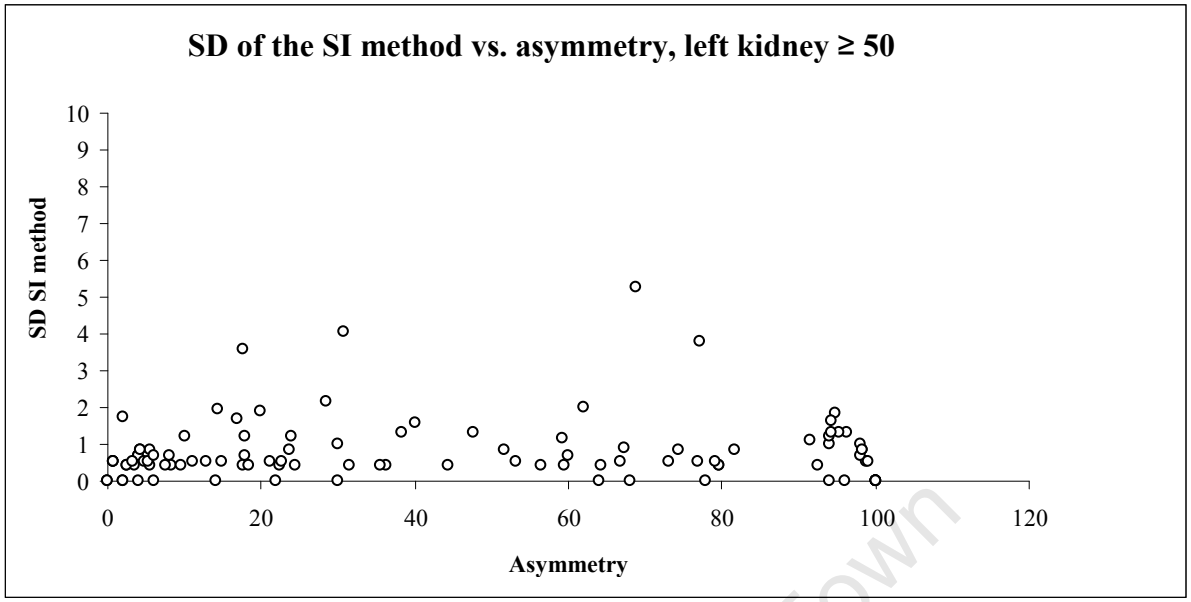

Figure 22: For patients in whom the DRF of the left kidney is greater than or equal to 50, the standard deviation of the SI method was plotted against the asymmetry in renal function. Asymmetry was the difference between the DRF of the left and right kidneys

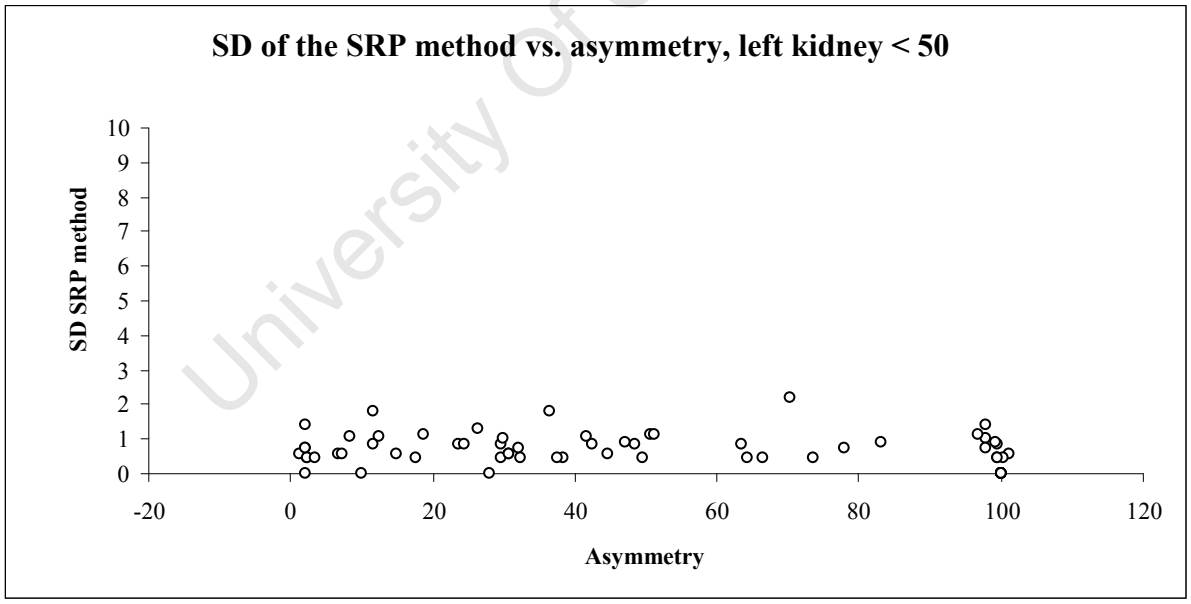

Figure 23: For patients in whom the DRF of the left kidney was less than 50, the standard deviation of the SRP method was plotted against the asymmetry in renal function. Asymmetry was the difference between the DRF of the left and right kidneys.

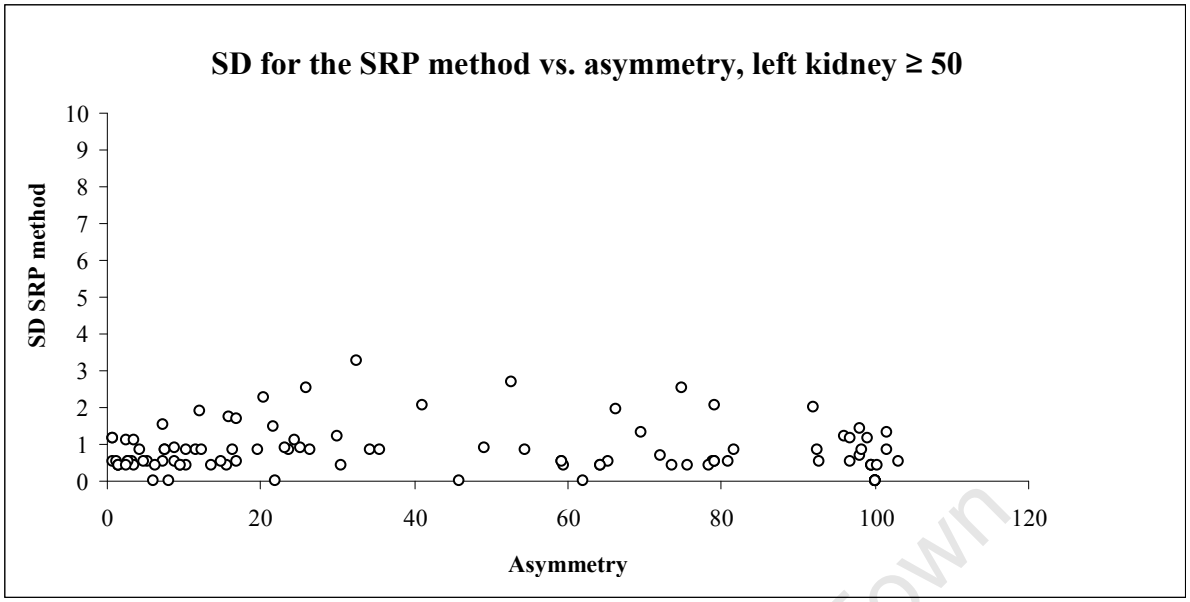

Figure 24: For patients in whom the DRF of the left kidney was greater than or equal to 50, the standard deviation of the SRP method was plotted against the asymmetry in renal function. Asymmetry was the difference between the DRF of the left and right kidneys

There is no trend between the standard deviation and the side of the poorly functioning kidney for any of the three methods.

Further analysis of the studies above the 95th percentile for the standard deviation

Values for SD above 3.39, 1.84 and 1.96 were above the 95th percentile for the PI method, the SI method and SRP plot method respectively.

There are 17 patients who had a SD for one or more method above the 95th percentile.
The details of these patients are listed in **Table 9**. In the column GFR (e) denotes eGFR and (m) mGFR.

Patient number	Age in months	Mean DRF	GFR	SD PI	SD SI	SD SRP
27	3	50	82 (e)	1.30	2.35	0.45
55	0	71	83 (e)	5.13	1.30	0.89
117	41	98	65 (e)	3.58	1.22	2.00
131	91	-2	32 (m)	6.35	0.71	1.14
135	0	2	32 (e)	3.56	0.00	0.00
136	0	100	37 (e)	5.08	0.00	0.00
141	85	42	51 (m)	9.14	1.87	2.28
142	1	46	42 (e)	2.68	1.92	1.67
146	2	64	37 (e)	2.51	1.22	2.07
148	191	68	57 (e)	1.95	2.17	3.27
152	2	70	46 (e)	3.27	1.58	2.70
156	4	46	77 (e)	3.44	1.00	1.10
158	3	91	74 (e)	2.17	3.78	2.51
160	0	19	62 (m)	1.30	0.71	2.17
162	0	69	54 (e)	2.61	4.04	2.55
164	10	90	70 (e)	1.00	5.27	2.07
169	3	46	19 (e)	4.56	3.56	1.73

There was one patient who had a SD above the 95th percentile for all three methods, patient 141. He was a seven year old with a mean DRF of 42% and a mGFR of 51 ml/min/1.73m^2.

Six patients had a SD above the 95th percentile for two of the methods, four of these were for the SI and SRP methods, one was for the PI and SI method and one was for the PI and SRP method.

There was a wide spectrum of ages in this group but 12 of the 17 cases were younger than four months. The mean DRF included the whole spectrum of DRF from -2 to 100%, with no apparent pattern. Two of the 17 patients had a low normal GFR and the rest had GFRs below 78ml/min/1.73m^2. Only five patients had a GFR below the 10th centile for age.

If the 171 patients in this study are categorised in a two by two table on the basis of SD above the 95th percentile and GFR we get the following: **Table 10**

SD from the mean	GFR < 80 ml/min/1.73m^2	GFR > 80 ml/min/1.73m^2
One or more SDs above the 95th percentile	15	2
Remaining patients	37	117

Yates corrected $X^2 = 26.87$ with $p < 0.001$.

If the 171 patients in this study are categorised in a two by two table on the basis of SD above the 95th percentile and age we get the following: **Table 11**

SD from the mean	Under 4 months	Greater than 4 months
Above the 95th percentile	12	5
Remaining patients	18	136

Yates corrected $X^2 = 21.17$ with $p < 0.001$.

A GFR below 80 ml/min/1.73m^2 is associated with a high SD. Age under four months is also associated with a high SD.

Accuracy of the individual methods

To determine the accuracy of the methods we processed the renograms of the 37 patients with solitary kidneys as if there were two kidneys. Any value other than 100% or 0%, depending on the side of the absent kidney reflects inaccuracy.

With the PI method only one of the 37 patients had an accurate value. He had a DRF of 100% for his solitary left kidney. The remaining 18 children with a solitary left kidney had values between 97.4 and 111% while the 18 patients with an absent left kidney had values between -8.6 and 4.8%. Twenty two of the 37 patients had a mean DRF greater than one SD from the expected value of 0 or 100; i.e. above 2.39 or 102.39 or below -2.39 or 97.61,

Thirteen of the 37 patients with solitary kidneys had a value of 0 or 100% with the SI method. We do not know how many of these were calculated values and how many were replaced with 0 because they were less than 0. The remaining 24 cases had mean values between 0.2- 1.6% and 96.2-99.6%, but only five of these patients did not have a zero or 100 value as one of the individual measurements. Any replacements would introduce a bias in the calculation of the means and SDs.

With the SRP plot method 14 cases had a value of 0 or 100% and the remaining 22 cases had values between – 0.6% and 1.6% and 96-100.8%. Of these 13 patients had a mean DRF greater than one SD from the expected value, below -0.58 or 99.42 or greater than 0.58 or 100.58.

Discussion

Introduction

Differential renal function calculated on the MAG3 renogram is frequently used in the clinical decision making process in children with renal abnormalities. However there is very little data in the literature on the reproducibility of the results of processing a ^{99m}Tc MAG3 renogram with a particular method or of the reproducibility of different methods.

Method

Current literature reports a small difference in the differential renal function obtained by the methods recommended in the EANM guidelines and International Scientific Committee of Radionuclides in Nephrourology (ISOCORN) consensus reports (12,31). It is also reported that the reproducibility of the methods is good (14, 17, 18). These studies were done on relatively small numbers of patients and all the studies only included a small number of patients that were at the extremes of age, DRF and had low GFRs.

We could not find any literature that investigates how the interactions between age, GFR, level of asymmetry and method of processing affect the reproducibility of the renogram in the individual patient.

Although the mathematical principles of the two methods used in this study are well described we do not have access to the source code used by the programmers and do not know if all the manufactures apply the mathematics in a similar fashion. Does the same method implemented by different software packages perform equally well? Do different methods give similar results?

Image acquisition and processing

We use a 40 minute imaging protocol for both the diuretic renogram and the indirect cystogram. When performing a diuretic renogram furosemide is administered at 20 minutes after MAG3 injection.

There are three accepted ways for drawing the perirenal background region of interest, C-shaped, perirenal and rectangular. We used a C-shaped perirenal background 1 pixel away from the renal ROI. This C-shaped background was automatically placed by the Philips software but it could be manipulated to ensure that it did not extend outside the body outline and that it did indeed include a representative background.

On the experimental software packages the background was automatically assigned, the background was one pixel wide placed one pixel distance from the manually drawn renal ROIs.

The time intervals used to calculate DRF with the different methods varied slightly. The EANM guidelines recommend that the DRF be calculated between 60 and 120 seconds from the peak in the cardiac curve. The PI method used the 60-120 second time interval. We could not manipulate the time interval for the SI method which was set to be from 60-150 seconds. The time interval for the SRP method differed slightly form patient to patient depending on the best straight line fit to the linear part of the Rutland Patlak plot. It never exceeded 180 seconds, the cut off for the end point in the calculations.

As we did not perform F0 or F-15 studies the time interval for the SRP method should not be a problem.

Patient selection

The studies by Leziac (18) and Ozcan(14) both had poorer precisions in very young children than in older children. In clinical practice we occasionally encounter a study where the values for DRF cannot be reproduced on repeated processing. These problems are usually encountered with very young patients or patients with a low GFR. We selected a stratified sample to ensure that the patients with the low GFRs and the extremes for DRF were included.

The most frequent indications were hydronephrosis and vesico-ureteric reflux. The other indications included dysplastic kidneys, posterior urethral valves, Takayasu's arteritis and neuropathic bladders. This distribution of diagnoses reflects the pattern of referrals at this hospital.

The ages of the children included in this study range from under one month to 16 years, with a median age of 33 months. Our hospital, a dedicated paediatric hospital, sees all children up to 12 years age and selected adolescents. The two main groups of children referred to our department are those younger than two years with hydronephrosis, for initial assessment and follow up, and those older than three years with recurrent urinary tract infections (UTI's) and vesico-ureteric reflux (VUR) who are sent for indirect cystograms.

We only included children on whom we could find a measured GFR (mGFR) or calculate a GFR (eGFR) within two months from the renogram date and we did not have any reason to suspect a change in renal function. We used the Schwartz nomogram to estimate the eGFR. The error when using this method in predicting the true clearance can be considerable. When comparing it to calculating GFR from unlabelled iothalamate urinary excretion the 95% limits of agreement are between -42 ml/min/1.73m^{2}to + 56 ml/min/1.73 m^2 It has the greatest error at higher levels of GFR (23, 29, 30).

It is not standard practice in our hospital to measure GFR on the day of the MAG3 renogram in all patients. We had to calculate the GFR (eGFR) in the majority of the patients as a measured GFR (mGFR) was only available for the 12% of patients. As mGFR get requested in the more complex cases and those patients with suspected low GFRs we cannot comment on the relationship between mGFR and reproducibility.

Exclusions

Of the 1416 studies performed in our department during the 8 year period 172 patients were included in the project. The vast majority, 745, of the patients were not included due to the absence of a recent creatinine or GFR. 189 studies were also excluded because the patient was used before and 141 were not used because the predefined groups were already full.

There were 11 cases where the studies could not be processed in a satisfactory manner so there was no differential renal function in the original report. We also found that 5 patients whose studies had been processed for the original report could not be processed with the study software. There were two distinct groups of patients. With the largest group the reason for the difficulty in processing the renogram was very poor target to background ratio. This was due to globally poor uptake or a poorly functioning kidney where there were scattered islands of functioning tissue. The second group had severe hydronephrosis. The kidneys extended to the margin of the body and acceptable background ROIs could not be drawn. This means that 1.1% of all the studies performed in our department could not be processed due to patient factors. These problems in processing are well described in the literature (12, 13, 16)

One extreme outlier was seen when the studies were analysed by the Philips integral method. The values obtained were clearly wrong, the DRF values were between 111 and 180 for a solitary kidney, with a mean DRF of 139. We did not experience any problems with the other two methods. This extreme outlier would have skewed the data for the PI method and was excluded from the study. If this study was included in the analysis, the SD of the PI method would have been even higher.

Possible explanations for this outlier are that this patient had a very low GFR of 20 ml/min/1.73m^2 at the time of study and that we could not clearly identify the kidney from the background. However, both experimental packages gave correct results for this solitary kidney. This difference in results between the two integral methods may be due to the truncation applied by the SI method. The values with the SRP method were an accurate estimate the true value.

Results

The mean differential renal function of the left kidney

The mean DRF for the SI method and the SRP plot method were very similar, 52.4 and 52.6%. This difference between the two methods was comparable to the data published by Piepsz (17) where they found a mean difference of less the 0.3% for numerous methods and Ozcan (14) who found a mean difference of -0.8% between the Rutland Patlak plot method and the integral method.

The PI method gives a significantly higher mean DRF of 55.2%. This is a far greater difference between the methods than is described in the literature. The differences between the two integral methods are of concern. Assuming both integral methods employ the same mathematical principles, differences in background subtraction may be the explanation.

The differential renal function of individual patients and methods:

There was no gold standard to compare the DRF results with. The mean of all three results was used as a reference value.

The patient mean differential renal function of all three methods were plotted against the study specific mean DRF for each patient. For all three methods there was agreement between the individual mean DRF and the mean DRF of all three methods across the whole range of DRF.

Bland-Altman plots of the PI and SI, the PI and SRP methods and finally the SI and SRP methods show that there were very similar results for both the SI method and SRP plot for all ranges of DRF. The agreement between the PI method and the other two methods were not as good with the PI method systematically giving higher values for the left kidney than the SI and SRP methods. This implies that there was an over subtraction of the background activity for the right kidney or under subtraction from the left kidney with the PI method. The difference in background ROI size between the two methods, one pixel wide vs. three pixels wide may also account for this.

The precision of the methods

The mean standard deviation was calculated for all three methods. The mean standard deviation of the SI and SRP methods was similar, 0.71 and 0.75. The PI had a significantly higher mean Standard deviation of 1.68. The SDs of the SI and SRP methods are far lower than the data published by Piepsz (17) were the SD for the integral method was 1.7 and the SD for the Rutland Patlak plot was 2.8. Although the SD for the PI method was higher than the SI and SRP methods, the SD for the PI method is similar the above mentioned published SD for the integral method. The published SD was also calculated on a group of healthy volunteers where we would expect a low SD (17). This study therefore yielded a good SD for all three methods if we take into account that the patient population was selected to include a large proportion of patients at the extremes for GFR and DRF. We had a good SD for the vast majority of patients regardless of indication and the SD only increased in the type of patient where we sometimes have difficulty in processing the study

The precision was determined by calculating the standard deviation of the standard deviation. This is similar to the study of Piepsz (17) were the standard deviation of the differences between two measurements was used to define the precision when repeated MAG3 studies were done on the same group of healthy volunteers. The SRP had very good precision with an SD of 0.58%, the highest SD observed was 3.3% and the SI method had a SD of 0.73 with the highest SD observed 5.3%. The 95^{th} centile of individual patients for these methods were 1.96 for the SRP method and 1.84 for the SI method. These values imply that for these

methods of processing a change greater than two% from the previous study is most likely due to patient factors and not processing.

The precision of the Philips integral method is not as good. The highest observed standard deviation with the PI method is 9.1%, with the 95th centile for SD at 3.39%. Thus a change in DRF of 4 % would be regarded as significant. This is still below the 5% to 10 % value used in most clinical settings.

The reproducibility of measurement of individual patients and differential renal function

There is very little data available in the literature on the reproducibility of DRF at different levels of DRF. The only study that looked at this was the one by Leziac (18) who divided the patients into two groups according to DRF, a group 45-55% DRF and another 30-70% DRF but the patients from the first group was not excluded from the second group. There was no significant difference between SDs from these two groups.

We found that there was no correlation between high standard deviation and DRF for any of the three methods.

The reproducibility of measurement of individual patients and age

Visually the XY scatter plots suggested a trend between high SD and age below 6 months for the PI and SI methods. There were a number of higher SD values in the older children with the PI method as well suggesting that age wass not the only risk factor for high SDs.

The data did not have a normal distribution. We did non-parametric testing on the data. For all three methods there was a correlation between age and SD. However visual inspection of the scatter plots was used to divide the patients into age groups. Only the PI method had a correlation between SD and distinct age groups. There was a correlation between SD and age in children under 6 months as well as in children younger than twelve months. However there was no correlation between SD and age in children older than 6 months. A possible explanation for this may be that the studies in children under 12 months included the group younger than six months and that the correlation stems from the presence of younger children in both calculations.

The tendency for higher SDs at younger age groups has been described by Ozscan who found high SDs in children under 9 months, with the highest SD in children under three months, 7.1 (14). The higher SDs were attributed to difficulties in delineating the kidney ROI, renal immaturity and inappropriate background subtraction.

The reproducibility of measurement of individual patients and global renal function

There was a clear trend between GFR and SD for the PI method, the patients with the higher standard deviation all had a GFR below 80 ml/min/1.73m^2. The patients who had SDs above 2 when analysed by the SI and SRP method all had a GFR below 80 ml/min 1.73m^{2}but, the numbers were small.

The relationship between SD and GFR was tested with the Rank Spearman Correlation coefficient and there was a relationship between low GFR and high SD for each of the three methods. Sub dividing the patients into age groups, GFR and SD had a strong relationship in all the age groups with the PI method but with not with the SI and SRP methods.

The GFR corrected for surface area increases as the child matures. A GFR of 40ml/min/1.73m^2 is normal in a one month old baby and abnormal in a six month old. The children with low GFR were separated into two groups, normal for age and renal insufficiency, depending on the GFR for age using the normal values published by Piepsz (27). Renal insufficiency was defined as a GFR below the 10th centile for age.

In the 21 children with renal insufficiency the relationship between high SD and GFR for age was tested by Rank Spearman correlation. There was a strong relationship between renal insufficiency and SD with the PI method but no relationship with the other two methods.

Of the 17 patients who had SDs greater than the 95th centile for SD with one or more of the methods, 15 had GFR corrected for surface area below 80 ml/min/1.73m^2 but only five had GFR below the 10th centile for age.

Low GFR was an independent risk factor for high SD, when analysing the studies with the PI method. In the other two methods the high SD can be attributed to immaturity with the associated problems of drawing accurate ROIs in small babies rather than just low GFR.

These results were also reflected in the Chi square analysis of the seventeen patients that had a SD above the 95th centile for one or more of the methods. A GFR below 80ml/ min/1.73m^2 and age below four months had a strong association with the higher SDs for all three methods.

.

The reproducibility measurement of individual patients and asymmetry of renal function and side of affected kidney

We could not find published literature describing a relationship between the side of the poorly functioning kidney, or degree of individual renal impairment and high SD.

There was no association between SD and the degree of asymmetry between the two kidneys for any of the three methods. The side of the affected kidney also had no association with SD.

The accuracy of the methods

To determine the accuracy of the three methods we processed the studies of children with solitary kidneys as if they had two kidneys. These children were selected to include a similar number of solitary left and solitary right kidneys and wide ranges of GFR and age. This group consisted of 37 patients.

The approach assumes that if the calculation gives a value different form 100 or 0% depending on the side of the absent kidney this reflects a problem with the accuracy of the method. This was also done in the study by Lythgoe (22).

The PI method had a poor accuracy in the sense that only one patient had a mean DRF of 100% for the left kidney. The remaining 36 patients had values that ranged from -8.6 to 4.8% and 97.4 to 111%.

The study design did not foresee that the data at these extreme values may have been truncated. There were no values below 0 or above 100 with the SI method. The values below 0 were truncated by the software. We do not know how many of the 0 or 100 values were due to truncation but 24 cases had a value other than 0 or 100. The truncation of data introduced a bias in the analysis and we cannot comment further on the accuracy of this method.

The practice of truncating values is done in different software packages. It introduces a serious problem in reporting. If a method gives a result of 10 % function for a poorly functioning kidney, it is accepted and used in the patients report but if the same method gives a value of -10% it is automatically changed to 0%. If the package does not warn the user by differentiating between a calculated 0 and truncated 0 it creates a false sense of accuracy. It may be more useful not to truncate the values, so that the reporting physician can process the study several times and report the mean DRF. The mean DRF would be a better reflection of the true DRF.

Fourteen patients had either a 0 or 100% value with the SRP method. The Rutland Patlak plot method uses the best line fit to the graph in the Rutland Patlak space. This should theoretically not allow a negative fit to the graph but graphs with a very slight negative incline could be missed by the person doing the processing. This study would support the study by Lythgoe (22) that concluded that the Rutland Patlak plot method had better accuracy than most other methods,

Conclusions

The mean DRF and reproducibility differ between methods that should theoretically give the same results. This means all methods used to process renograms should be validated before clinical use.

The majority of patients attending our department could be processed with very reproducible results with each of the methods. Only 1.1% of the study population could not be processed by any of the methods.

The DRF calculated on the MAG3 renogram using the SI method and SRP method were the most reproducible for the vast majority of the patients.

The reproducibility of the Philips integral method was not as good, particularly if the GFR was below 80 ml.min/1,73m^2. Further studies using mGFR are needed to establish exactly at what level of GFR the decrease in reproducibility becomes of clinical importance.

We used eGFR and mGFR corrected for surface area to stratify our patients.We had hoped to use a model to determine the relative impact of factors such as age and GFR on reproducibility. We were unable to do this due to the distribution of the data. In future studies the possibility of stratifying patients on the basis of GFR for age should be considered. If at all possible future studies should also use mGFR rather than eGFR to stratify the patients.

We suggest that all renograms be processed more than once by different methods and different software packages and the mean value of repeated processing be used as the value given in the report. This is of particular importance in children younger than six months and children with low GFR.

Performing truncation of data makes it impossible to improve the accuracy by using repeated measurements at the extremes for DRF. There should at the very least be a clear distinction between a calculated value of 0 (or 100) and a truncated value. It would probably be better if truncation was not done by the package.

References

1. Brown SCW. The urologist's view.In: Prigent A, Piepsz A, editors. Functional imaging in nephro-urology. United Kingdom: Taylor and Francis; 2006. p. 67.
2. Peters CA. Urinary tract obstruction in children. J Urol. 1995;154:1874-1884.
3. Koff SA. Problematic ureteropelvic junction obstruction. J Urol 1987;138:390.
4. Chertin B, Rolle U, Farkas A, Puri P. Does delaying pyeloplasty affect renal function in children with a prenatal diagnosis of pelvi-ureteric junction obstruction? BJU Int. 2002;90:72-75.
5. Onen A, Jayanthi VR, Koff SA. Long- term follow-up of prenatally detected severe bilateral hydronephrosis initially managed nonoperatively. J Urol. 2002;168:1118-1120.
6. Piepsz A. Antenatally detected hydronephrosis. Semin Nucl Med. 2007;3:249-260.
7. Thorup J, Joleka R, Cortes D, Nielsen OH. The results of 15 years of consistent strategy in treating antenatally suspected pelvi-ureteric junction obstruction. BJU Int. 2003;91:850-852.
8. Gordon I, Colarinha P, Fettich J, Fischer S, Frökier J, Hahn K. Guidelines for indirect radionuclide cystography. Eur J Nuc Med. 2001;28(3):BP16-20.
9. Ritchie G, Wilkinson AG, Prescott RJ. Comparison of differential renal function using technetium-99m mercaptoacetyltriglycine (MAG3) and technetium-99m dimercaptosuccinic acid (DMSA) renography in a paediatric population. Pediatr Radiol. 2008;38:857-862.
10. Patzer L, Seeman T, Luck C, Wühl E, Janda J, Misselwitz J. Day- and night –time blood pressure elevation in children with higher grades of renal scarring. J Pediatr. 2003;142:117-122.
11. Gordon I, Anderson PJ, Lythgoe MF, Orton M. Can technetium-99m-mercaptoacetylglycine replace technetium-99m-dimercapto-succinic acid in the exclusion of a focal renal defect? J Nucl Med 1992;33:2090-2093.
12. Gordon I, Colarinha P, Fettich J, Fischer S, Frökier J, Hahn K. Guidelines for standard and diuretic renography in children. Eur J Nuc Med. 2001;28(3):BP21-30.
13. Eskild-Jensen A, Gordon I, Piepsz A, Frøkiær J. Interpretation of the renogram: problems and pitfalls in hydronephrosis in children. BJU Int 2004;94(6):887- 892.
14. Ozcan Z, Anderson PJ, Gordon I. Robustness of estimation of differential renal function in infants and children with unilateral prenatal diagnosis of a hydronephrotic kidney on dynamic renogram: How real is the supranormal kidney? Eur J Nucl Med Mol Imaging. 2006;33:738-744.
15. Šámal M, Nimmon CC, Britton KE, Bergmann H. Relative renal uptake and transit time measurements using functional factor images and fuzzy regions of intrest. Eur J Nucl Med 1998;25(1):48- 54.
16. Sennewald K, Taylor A. A pitfall in calculating differential renal function in patients with renal failure. Clin Nucl Med. 1993;18:377-381.
17. Piepsz A, Tondeur M, Ham H. Relative ^{99m}Tc – MAG3 renal uptake: reproducibility and accuracy. J Nucl Med. 1999;40(6):972-976.

18. Lezaic L, Hodolic M, Fettich J, Grmek M, Milcinski M. Reproduciblitiy of ^{99m}Tc-Mecaptoacetyltriglycine renography: population comparison. Nucl Med Commun. 2008;29(8):695- 704.
19. Bland JM, Altman DG. Measurement error. Br Med J. 1996;313:744.
20. Piepsz A, Colarinha P, Gordon I, Hanh K, Olivier P, Roca I. Guidelines for ^{99m}Tc-DMSA scintigraphy in children. Eur J Nucl Med. 2001;28(3):BP 37-41.
21. Lythgoe MF, Gordon I, Anderson PJ. Effect of renal maturation on the clearance of technetium- 99m mercaptoacetyltriglycine. Eur J Nucl Med. 1994;21:1333-1337.
22. Lythgoe MF, Gordon I, Khader Z, Smith T, Anderson PJ. Assessment of various parameters in the assessment of differential renal function using technetium-99m mercaptoacetyltriglycine. Eur J Nucl Med. 1999;26(2):155-162.
23. Schwartz GJ, Furth S. Glomerular filtration measurement and estimation in chronic kidney disease. Pediatr Nephrol. 2007;22:1839-1848.
24. Piepsz A, Colarinha P, Gordon I, Hahn K, Olivier P, Roca I, et al. Guidelines for glomerular filtration rate determination in children. Eur J Nucl Med. 2001;28(3):BP 31-36.
25. Jacobs F, Thierens H, Piepsz A, Bacher K, Van der Wiele C, Ham H, et al. Optimized tracer-dependant dosage cards to weight-independent effective doses. Eur J Nuc Med Mol Imaging. 2005;32(5):581-8.
26. StatSoft, Inc. (2008). STATISTICA (data analysis software system), version 8.0. www.statsoft.com.
27. Piepsz A, Tondeur M, Ham H. Revisiting normal ^{51}Cr-ethylenediaminetraacetic acid clearance values in children. Eur J Nucl Med Mol imaging. 2006;33:1477-1482.
28. Tabachnick, B.G, Fidell, L.S. Multilevel linear modelling. In: Using multivariate statistics. 5th ed. Boston: Allyn and Bacon; 2007. p. 835-838.
29. Piepsz A, Ham H.R. Pediatric applications of renal nuclear medicine. Semin Nucl Med.2006;36:16-35.
30. Prigent A. Monitoring renal function and limitations of renal function tests. Semin Nucl Med.2008;38:32-46.
31. Prigent A, Cosgriff, Gates GF, Granerus G, Fine EJ Itoh K. Consensus report on quality control of quantitative measurement of renal function obtained from the renogram. International consensus committee from the scientific committee of radionuclides in nephrourology. Semin Nucl Med.1999;29:146-159.

Appendix

The indications for the renograms in the 172 patients

Table A.1: Children with symmetrical DRF and GFR ≥ 80 ml/min/1.73m^2 (n = 30)

Indications	Number of patients
Hydronephrosis, left	13
Hydronephrosis, right	3
Hydronephrosis, bilateral	3
Vesico-ureteric reflux	5
Posterior urethral valves	1
Takayasu's arteritis	1
Urinary tract infection	1
Dysplastic kidneys	1
Duplex kidneys	1
Stricture right ureter	1

Table A.2: Children with asymmetrical DRF and GFR ≥ 80 ml/min/1.73m^2 (n = 68)

Indications	Number of patients
Hydronephrosis, left	10
Hydronephrosis, right	9
Hydronephrosis, bilateral	9
Vesico ureteric reflux	16
Posterior urethral valves	3
Takayasu's arteritis	4
Neuropathic bladder	2
Duplex kidneys	3
Hypoplastic kidneys	3
Renal artery stenosis	1
Bilateral nephroblastoma	1
Renal cyst	2
Infection	1
Renal caculi	1
Possible urinary leak	1
Mega ureter	1
No record of indication	1

Table A.3: Children with asymmetrical DRF and a GFR below 80ml/min/1.73m2 (n=36)

Indications	Number of patients
Hydronephrosis, right	10
Hydronephrosis, left	10
Hydronephrosis, bilateral	6
Posterior uretral valves	4
Takayasu's arteritis	1
Neuropathic bladder	1
Hypoplastic kidney	1
Renal transplant work-up	1
Vasculopathy	1
Renal vein thrombosis	1

Table A.4: Children with a solitary kidney (n=38)

Indications	Number of patients
Multicystic kidney, right	3
Multicystic kidney, left	2
Hydronephrosis left, multicystic kidney right	4
Hydronephrosis left, solitary kidney	2
Hydronephrosis left, right nephrectomy	2
Hydronephrosis right, multicystic kidney left	3
Hydronephrosis right, solitary kidney	3
Hydronephrosis right, left nephrectomy	3
Vesico-ureteric reflux and solitary kidney	7
Takayasu's arteritis with nephrectomy	2
Posterior urethral valves solitary kidney	2
Neuropathic bladder	1
Dysplastic kidney	2
Recurrent UTI	1
Trauma	1

Thirty normal studies

The values for the left and right kidney are the differential renal function values recorded in the original report.

Table A.5: Demographic information of the first 30 patients

anon num	D.O.B	study date	age in months	L	R	GFR
1	1998/11/12	2001/01/11	25.99	54	46	86
2	1998/04/28	2001/02/16	33.68	51	49	111
3	1997/02/23	2001/02/23	48.00	52	48	135
4	1992/04/29	2001/04/06	107.24	50	50	140
5	1994/12/27	2001/08/17	79.67	47	53	130
6	2000/03/04	2001/11/05	20.07	50	50	82
7	1990/11/15	2001/12/07	132.73	50	50	139
8	1988/01/01	2001/12/11	167.33	48	52	112
9	2000/08/24	2002/05/03	20.27	55	45	85
10	1999/10/23	2002/05/10	30.55	51	49	100
11	1998/05/13	2002/07/19	50.20	47	53	138
12	1989/07/09	2002/08/02	156.78	50	50	115
13	1996/04/03	2002/10/29	78.85	48	52	187
14	2001/09/01	2002/12/06	15.15	55	45	133
15	2002/03/18	2003/04/11	12.78	46	54	120
16	2003/02/02	2003/05/27	3.75	52	48	110
17	1997/02/18	2003/11/20	81.02	48	52	128
18	2003/03/10	2004/02/06	10.94	52	48	100
19	2002/01/26	2004/03/05	25.26	50	50	145
20	1991/06/01	2004/04/08	154.25	54	46	175
21	2004/02/05	2004/06/08	4.07	47	53	90
22	2004/01/06	2004/07/23	6.54	51	49	95
23	2002/05/23	2004/07/23	26.02	51	49	122
24	1994/09/25	2004/07/27	118.05	51	49	160
25	1995/07/26	2004/12/03	112.30	49	51	88
26	2003/07/25	2004/12/09	16.53	53	47	112
27	2004/10/02	2005/01/11	3.32	49	51	82
28	1997/04/17	2005/02/22	94.23	53	47	147
29	1996/12/30	2005/03/01	98.00	49	51	166
30	2003/07/29	2005/03/18	19.65	52	48	152

Average age = 58 months (standard deviation = 52 months).
Average value left kidney = 51% (standard deviation = 2.4%).
Average GFR = 123 ml/min/1.73m^2 (standard deviation = 29 ml/min/1.73m^2).

Table A.6: Raw data of the first normal studies

Pt num	PI 1	PI 2	PI 3	PI 4	PI 5	PRP 1	PRP 2	PRP 3	PRP 4	PRP 5	SI 1	SI 2	SI 3	SI 4	SI 5	SRP 1	SRP 2	SRP 3	SRP 4	SRP 5
1	51	50	50	52	50	52	52	51	55	49	50	50	50	50	50	49	50	49	49	50
2	48	49	49	48	49	50	50	51	50	50	49	49	49	49	49	48	49	48	48	48
3	54	54	52	53	53	54	48	52	45	54	52	52	52	52	52	54	53	53	54	54
4	54	52	51	53	52	49	50	47	52	49	50	50	50	50	50	52	51	51	51	51
5	51	51	52	53	51	49	49	49	49	49	51	50	50	51	51	51	51	51	51	51
6	54	52	52	54	52	48	49	50	51	49	51	51	51	51	51	52	51	52	51	51
7	51	51	53	52	54	51	53	52	50	52	51	52	52	51	52	53	53	53	53	54
8	47	48	50	48	49	46	46	46	46	45	46	46	47	46	47	45	45	45	45	45
9	55	56	58	56	56	53	54	54	53	53	53	53	53	52	53	53	53	53	53	53
10	53	52	52	55	54	52	51	51	53	52	53	53	52	53	52	51	51	50	51	51
11	48	48	49	47	50	46	45	46	46	46	46	46	46	46	45	46	47	46	47	47
12	59	58	57	58	57	52	52	52	53	53	55	55	55	54	55	55	55	55	55	54
13	50	48	49	49	49	47	48	50	48	47	48	48	48	48	48	49	49	50	49	50
14	47	48	48	47	47	48	48	47	45	49	47	47	47	47	47	47	48	48	47	47
15	48	48	48	46	47	41	41	41	41	40	43	43	44	43	44	43	43	42	42	43
16	57	54	57	56	58	53	52	55	55	45	52	53	52	53	52	48	51	50	50	49
17	49	48	49	50	50	44	44	44	45	46	47	48	47	48	47	46	47	46	47	46
18	52	54	53	52	54	51	52	51	53	51	52	52	53	52	51	53	53	52	52	52
19	50	50	51	49	51	46	46	46	45	45	46	47	47	48	47	46	46	46	46	46
20	55	56	54	53	54	50	51	45	45	43	52	52	52	51	52	49	50	50	49	50
21	47	49	48	46	51	44	42	43	41	41	43	44	45	44	44	43	42	46	46	44
22	51	52	51	50	55	49	52	51	50	50	50	50	50	50	49	49	52	53	53	52	51
23	52	50	51	51	52	48	49	49	48	48	49	50	50	50	49	49	49	49	50	49
24	47	47	48	48	49	44	44	44	44	43	44	45	45	44	44	46	45	45	48	48
25	51	50	50	49	49	47	47	48	48	50	48	48	48	49	48	49	49	48	49	49
26	57	55	55	55	55	52	51	52	52	51	54	53	52	53	52	55	54	53	54	53
27	53	52	53	50	53	47	46	47	47	45	50	51	50	45	49	48	49	48	48	48
28	55	53	54	52	54	51	52	51	52	52	51	52	52	48	52	52	52	53	50	52
29	50	50	50	48	48	47	46	48	47	47	48	47	47	47	47	49	50	48	49	49
30	51	51	51	53	52	36	45	45	45	35	48	49	49	49	49	41	46	44	44	45

Asymmetrical renal function

Differential renal function falling between 40 -44% and 56-60%

Table A.7: Demographics of the 40-44% and 56%-60% group

Pt number	D.O.B	Study date	Age in months	L	R	GFR
31	1989/12/28	2001/06/08	138.0	59	41	131
32	1992/11/14	2002/05/24	114.0	56	44	165
33	2002/05/30	2002/11/05	6.0	56	44	126
34	2002/11/25	2003/01/07	2.0	59	41	103
35	2001/03/15	2004/03/12	36.0	56	44	97
36	1997/10/05	2004/11/16	85.0	57	43	137
37	2000/06/19	2006/07/18	73.0	40	60	86
38	2004/07/19	2005/03/15	8.0	60	40	116
39	2001/08/03	2005/05/06	45.0	60	40	106
40	1993/01/20	2005/10/12	153.0	56	44	175

Table A.8: Raw data of the 40-44% and 56-60% group

Pt number	I-1	I-2	I-3	I-4	I-5	S-I1	S-I2	S-I3	S-I4	S-I5	S-R/P1	S-R/P2	S-R/P3	S-R/P4	S-R/P5
31	60	59	59	61	60	57	57	57	57	57	58	57	58	57	57
32	58	59	58	59	57	54	54	54	53	54	55	55	56	55	55
33	59	60	58	57	60	56	56	55	55	53	51	51	52	52	51
34	56	57	53	54	56	50	49	49	50	50	51	50	51	53	51
35	56	55	56	58	59	54	54	55	54	54	54	54	55	54	55
36	58	57	56	59	55	52	52	51	53	53	52	51	51	52	52
37	41	41	41	40	42	40	41	41	40	40	44	44	42	44	45
38	59	59	61	59	59	59	59	60	59	59	59	57	58	58	59
39	62	63	62	62	61	61	61	61	61	61	62	63	63	64	64
40	57	57	54	53	55	54	55	54	54	53	55	55	55	55	54

Differential renal function falling between 35-39% and 61-65%

Table A.9: Demographic of the 35-39% and 61-65% group

Pt number	D.O.B.	Study date	Age in months	Lt	Rt	GFR
41	1994/09/26	2003/11/07	109.37	61	39	180
42	1998/04/23	2005/08/30	88.25	62	38	114
43	1997/12/22	2004/02/17	73.86	64	36	165
44	1995/10/06	2007/05/11	139.14	36	64	97
45	2002/09/14	2005/06/17	33.08	36	64	230
46	2005/01/09	2005/11/18	10.28	36	64	90
47	2005/06/30	2005/11/18	4.63	36	64	99
48	1996/03/17	2007/06/15	134.93	36	64	114
49	2002/07/29	2003/07/25	11.86	38	62	144
50	2003/07/26	2007/05/08	45.40	36	64	80

Table A.10: Raw data of the 35-39% and 61-65% group

Pt number	P-I1	P-I2	P-I3	P-I4	P-I5	S-I1	S-I2	S-I3	S-I4	S-I5	RP-1	RP-2	RP-3	RP-4	RP-5
41	63	62	63	65	65	62	61	61	61	62	61	61	61	61	61
42	60	61	61	61	58	59	59	59	58	59	58	59	59	58	58
43	61	62	62	65	63	60	59	59	59	58	58	57	58	58	58
44	37	36	38	36	37	34	34	34	35	35	37	39	38	38	37
45	40	38	39	39	38	35	35	38	35	36	35	35	35	35	36
46	38	36	36	35	37	34	34	33	33	33	36	36	36	36	36
47	35	37	37	37	37	35	36	34	34	35	36	36	34	35	35
48	38	37	36	36	38	35	38	38	38	38	39	40	41	41	42
49	37	37	36	36	39	35	34	36	36	35	34	34	36	35	36
50	33	33	33	32	33	34	34	32	33	33	35	35	34	34	35

Differential renal function falling between 30-34% and 66-70%

Table A.11: Demographic of the 30-34% and 66-70% group

Pt number	D.O.B.	Study Date	Age in months	L	Rt	GFR
51	15/11/2004	05/07/2005	8	33	67	83
52	14/02/2005	22/09/2005	7	34	66	85
53	18/06/1997	02/04/2004	81	34	66	90
54	08/04/1995	07/10/2003	102	34	66	91
55	21/04/2003	02/05/2003	0	67	33	83
56	11/09/2000	01/08/2006	71	66	34	102
57	08/04/2000	31/03/2006	72	69	31	98
58	07/09/2003	14/07/2006	34	68	32	115
59	30/10/2002	05/12/2006	49	33	67	113
60	06/09/2000	13/04/2007	79	69	31	84

Table A.12: Raw data of the 30-34% and 66-70% group

Pt number	L	Rt	GFR	P-I1	P-I2	P-I3	P-I4	P-I5	S-I1	S-I2	S-I3	S-I4	S-I5	RP-1	RP-2	RP-3	RP-4	RP-5
51	33	67	83	31	32	35	32	33	31	30	30	30	31	31	30	31	31	31
52	34	66	85	36	35	34	34	34	34	34	34	34	34	34	35	35	34	35
53	34	66	90	38	36	41	37	38	32	32	31	32	32	34	30	30	33	32
54	34	66	91	38	36	36	35	36	32	33	32	32	32	34	33	34	34	34
55	67	33	83	71	72	83	80	76	75	75	74	73	72	63	63	63	61	63
56	66	34	102	65	65	62	64	66	61	61	60	61	60	62	62	64	61	62
57	69	31	98	69	71	69	67	69	67	68	68	68	68	67	67	69	68	68
58	68	32	115	69	70	71	72	71	65	66	66	66	66	62	63	61	61	61
59	33	67	113	33	33	34	34	34	34	34	34	34	33	36	39	36	37	36
60	69	31	84	67	68	70	67	68	65	65	65	65	65	66	65	65	65	65

Differential renal function falling between 25-29% and 71-75% group

Table A.13: Demographic of the 25-29% and 71-75% group

Pt number	D.O.B.	Study date	Age in months	Lt	Rt	GFR
61	1990/06/24	2003/03/14	152.64	27	73	143
62	2004/03/13	2005/04/22	13.31	29	71	89
63	2000/01/16	2004/03/30	50.43	26	74	88
64	1997/12/18	2004/04/16	75.93	71	29	147
65	2003/04/09	2006/05/09	36.99	73	27	135
66	1997/11/02	2007/07/10	116.21	71	29	135
67	2006/05/21	2008/03/25	22.14	29	71	88
68	2005/09/05	2008/02/19	29.47	71	29	81

Table A.14: Raw data of the 25-29% and 71-75% group

Pt number	I-P1	I-P2	I-P3	I-P4	I-P5	S-I1	S-I2	S-I3	S-I4	S-I5	RP-1	RP-2	RP-3	RP-4	RP-5
61	27	28	27	27	28	27	27	27	27	28	28	27	28	28	27
62	29	30	31	29	29	28	29	29	28	29	28	29	29	29	31
63	25	19	24	23	20	25	24	27	23	26	26	24	25	25	23
64	58	58	59	59	59	57	56	56	56	57	57	56	56	55	57
65	73	73	74	73	74	72	72	72	73	72	73	73	73	73	73
66	72	69	70	71	69	68	69	68	68	68	67	68	67	68	66
67	27	27	27	27	28	27	26	26	26	25	26	25	24	24	23
68	70	70	70	69	71	61	61	63	62	62	61	59	60	61	63

Differential renal function falling between 20-24% and 76-80%

Table A.15: Demographic of the 20-24% and 76-80% group

Pt number	D.O.B.	Study date	Age in months		Lt	Rt	GFR
69	1998/02/11	12/05/2003		63	79	21	116
70	2001/06/19	24/08/2004		38	79	21	112
71	1998/01/29	20/08/2003		67	21	79	84
72	2000/11/25	17/09/2003		34	24	76	108
73	1996/07/01	14/10/2008		147	78	22	116
74	1989/10/16	26/04/2001		138	23	77	112
75	2005/03/21	04/05/2007		25	22	78	89
76	1994/05/28	12/10/2007		160	22	78	95

Table A.16: Raw data of the 20-24% and 76-80% group

Pt number	P-I1	P-I2	P-I3	P-I4	P-I5	S-I1	S-I2	S-13	S-I4	S-I5	R-P1	R-P2	R-P3	R-P4	R-P5
69	79	81	80	81	79	80	80	80	79	80	81	81	81	81	81
70	79	81	81	81	82	80	80	80	81	79	80	80	80	80	79
71	26	26	25	25	28	22	22	22	22	23	28	28	29	30	29
72	25	24	25	24	25	24	25	24	24	23	27	27	26	27	25
73	78	79	80	77	79	77	77	76	77	76	79	80	80	80	79
74	22	22	22	20	23	20	20	20	20	20	17	18	18	18	18
75	23	20	21	20	22	20	19	21	20	22	25	26	26	25	27
76	23	23	24	21	22	25	24	23	23	23	26	25	25	25	25

Differential renal function falling between 15-19% and 81-85%

Table A.17: Demographic of the 15-19% and 81-85% group

Pt number	D.O.B	Study date	Age in months	Lt	Rt	GFR
77	2002/05/26	2003/08/19	15	19	81	117
78	2002/02/15	2003/06/13	16	15	85	118
79	2003/11/14	2004/03/30	5	85	15	109
80	2005/01/16	2005/10/28	9	81	19	121
81	1998/01/12	2005/10/10	93	83	17	112
82	1996/01/21	2007/02/20	133	85	15	127

Table A.18: Raw data of the 15-19% and 81-85% group

Pt number	P-I1	P-I2	P-I3	P-I4	P-I5	S-I1	S-I2	S-I3	S-I4	S-I5	RP-1	RP-2	RP-3	RP-4	RP-5
77	23	21	23	20	25	20	21	21	21	19	18	19	19	18	17
78	13	14	14	13	13	13	13	13	13	13	14	13	13	13	13
79	93	95	93	92	94	91	90	92	91	90	90	90	90	89	89
80	78	79	80	81	80	78	78	79	78	78	77	78	77	76	78
81	86	84	84	84	84	84	83	83	83	84	83	83	82	82	83
82	85	85	85	84	85	84	84	84	84	84	82	82	82	83	82

Differential renal function falling between 10-14% and 86-90%

Table A.19: Demographic of the 10-14% and 86-90% group

Pt number	D.O.B.	Study date	Age in months	Lt	Rt	GFR
83	2004/08/15	2005/01/14	5	11	89	93
84	1996/01/18	2008/06/27	149	10	90	105
85	2007/07/24	2007/10/12	3	90	10	80
86	2004/08/27	2006/03/23	19	90	10	141
87	1997/04/12	2004/03/16	83	90	10	119
88	2005/12/17	2007/12/04	24	90	10	118
89	2003/05/02	2008/02/19	58	89	11	92

Table A.20: Raw data of the 10-14% and 86-90% group

Pt number	P-1	P-2	P-3	P-4	P-5	SI-1	SI-2	SI-3	SI-4	SI-5	RP-1	RP-2	RP-3	RP-4	RP-5
83	8	8	8	10	11	14	14	14	15	13	17	16	17	17	17
84	10	10	10	10	10	10	10	10	10	10	10	11	12	11	11
85	89	89	89	89	91	89	88	88	89	88	91	91	90	92	90
86	89	90	90	89	89	89	90	90	89	90	90	91	91	90	90
87	90	92	91	92	92	90	90	90	90	89	89	89	90	90	89
88	89	89	89	92	89	88	87	88	87	86	88	88	88	88	87
89	91	86	90	87	89	89	89	89	89	89	89	89	89	89	90

Differential renal function falling between 1-9% and 91-99%

Table A.21: Demographic of the 1-9% and 91-99% group

Pt number	D.O.B	Study date	Age in months	Lt	Rt	GFR
90	26/12/2003	20/02/2004	2	7	93	94
91	21/04/2003	08/06/2004	14	8	92	91
92	10/08/1990	21/11/2006	195	98	2	81
93	13/12/2002	23/01/2004	13	95	5	89
94	11/04/1997	07/03/2006	107	98	2	144
95	18/06/2007	18/01/2008	7	92	8	80
96	03/02/2003	05/02/2008	60	92	8	119
97	31/03/1994	08/09/2006	149	96	4	117
98	06/09/1999	21/12/2006	87	1	99	142

Table A.22: Raw data of the 1-9% and 91-99% group

Pt number	P-1	P-2	P-3	P-4	P-5	SI-1	SI-2	SI-3	SI-4	SI-5	RP-1	RP-2	RP-3	RP-4	RP-5
90	11	13	17	13	12	0	0	0	0	0	0	0	0	0	0
91	7	6	8	5	8	8	7	8	8	8	9	8	9	9	7
92	99	101	99	99	101	97	97	97	97	97	96	96	97	96	97
93	95	96	97	98	97	94	96	96	97	96	95	96	96	97	97
94	98	99	98	98	98	98	98	98	98	98	98	98	98	99	99
95	86	89	88	91	88	80	78	82	83	82	84	80	84	83	85
96	91	92	92	91	91	90	90	89	90	90	89	90	90	90	89
97	100	99	98	100	100	97	98	98	98	95	98	98	99	100	97
98	-1	0	-1	-1	-1	2	0	1	1	1	0	0	0	0	0

Solitary kidneys

Patients with a GFR between 80-120ml/min/1.73m^2 and solitary kidneys

Table A.23: Demographics of the normal GFR group

Pt number	D.O.B	Date of study	Age in months	Kidney	GFR
99	19/07/1999	07/10/2003	51	L	87
100	03/08/2003	09/07/2004	11	L	86
101	01/12/1993	20/07/2004	128	L	88
102	12/04/1996	29/04/2005	109	L	118
103	04/04/1994	30/08/2005	137	L	114
104	25/01/2006	26/07/2006	6	L	83
105	08/03/2003	07/10/2005	31	L	121
106	18/07/1989	25/03/2003	164	L	112
107	07/05/1995	13/09/2005	124	L	94
108	30/12/1994	09/05/2006	136	L	90
109	12/08/1999	12/01/2007	89	L	119
110	11/05/1999	12/09/2003	52	R	111
111	27/12/2001	03/12/2002	11	R	95
112	14/10/1999	10/02/2004	52	R	110
113	20/06/2002	13/07/2005	37	R	97
114	16/08/2006	24/07/2007	11	R	83
115	05/05/1999	16/03/2007	94	R	104
116	18/11/1999	26/10/2007	95	R	101

Table A.24 Raw data of the normal GFR group

Pt number	P-1	P-2	P-3	P-4	P-5	S-I1	S-I2	S-I3	S-I4	S-I5	RP1	RP2	RP3	RP4	RP5
99	105	103	99	103	103	100	100	100	100	100	100	100	100	100	100
100	106	105	109	102	107	100	100	100	100	100	100	100	100	100	100
101	113	113	112	112	108	100	99	99	100	98	100	99	98	100	99
102	103	103	101	102	103	99	100	100	100	99	100	100	100	100	101
103	102	103	104	104	104	99	99	100	99	98	100	100	100	100	99
104	95	101	95	99	97	97	97	100	97	97	100	99	100	100	100
105	102	103	102	102	103	100	100	100	100	100	100	100	100	100	100
106	104	105	105	101	103	98	100	98	99	100	101	100	102	101	100
107	102	105	103	104	106	100	99	99	100	99	100	100	100	99	100
108	103	105	103	107	103	99	95	98	98	96	100	97	98	98	97
109	106	103	104	104	102	95	97	100	97	98	98	101	99	100	100
110	99	100	99	99	100	98	98	100	98	100	101	101	100	101	100
111	101	101	101	101	100	100	100	100	100	99	100	100	100	100	100
112	99	102	99	99	99	100	100	100	100	100	100	100	100	100	100
113	101	100	98	99	100	100	100	100	100	100	100	100	100	100	100
114	98	98	97	98	98	100	99	99	100	99	100	99	99	100	101
115	101	100	101	100	99	100	100	100	100	100	100	100	100	100	100
116	102	99	101	102	104	100	99	100	100	100	100	99	100	100	99

Patients with a GFR between 60-80ml/min/1.73m^2

Table A.25: Demographics of the group with GFR falling between 60-80ml/min/1.73m^2

Pt number	D.O.B.	Date of Study	Age in months	Kidney	GFR
117	2002/03/02	2005/08/05	41	L	65
118	1996/12/14	2004/03/19	87	L	65
119	2000/09/26	2004/08/13	47	L	79
120	2002/12/02	2003/03/04	3	L	70
121	2003/01/27	2005/07/19	30	L	63
122	2000/08/11	2004/03/12	43	R	67
123	2005/06/24	2006/03/09	8	R	72
124	2004/03/27	2007/11/09	43	R	67

Table A.26: Raw data of the group with GFR falling between 60-80ml/min/1.73m^2

Pt number	P-1	P-2	P-3	P-4	P-5	S-I 1	S-I 2	S-I-3	S-I4	S-I 5	R-P 1	R-P2	R-P3	R-P4	R-P5
117	103	101	106	105	97	98	98	97	95	97	98	97	97	93	95
118	111	107	103	93	107	100	99	99	95	99	99	98	99	100	98
119	102	106	106	102	104	96	98	96	97	98	101	98	100	98	98
120	100	102	99	101	99	99	99	96	99	98	99	99	98	99	100
121	116	113	114	114	109	99	99	98	100	100	102	102	102	101	101
122	101	102	101	101	100	100	100	100	100	100	100	100	100	100	100
123	95	97	95	95	94	99	99	99	98	99	100	98	100	99	98
124	102	102	106	106	105	100	100	100	100	99	100	100	100	100	100

Patients with a GFR between 40-60ml/min/1.73m^2

Table A.27: Demographics of the group with GFR falling between 40-60ml/min/1.73m^2

Pt number	D.O.B.	Date of Study	Age in months	Kidney	GFR
125	01/02/2003	07/04/2006	38	R	50
126	14/08/1996	22/05/2007	129	R	46
127	12/08/2007	30/10/2007	3	L	53
128	14/12/1996	01/02/2008	134	L	59
129	21/02/2007	24/08/2007	6	R	46

Table A.28: Raw data of the group with GFR falling between 40-60ml/min/1.73m^2

Pt number	P-1	P-2	P-3	P-4	P-5	S-I 1	S-I 2	S-I-3	S-I4	S-I 5	R-P 1	R-P2	R-P3	R-P4	R-P5
125	96	98	96	97	98	98	100	100	100	99	101	100	100	100	100
126	105	99	103	97	103	100	100	100	100	100	100	100	100	100	100
127	102	97	97	101	103	100	100	100	100	100	100	100	100	100	100
128	108	101	101	107	113	100	100	100	100	100	100	100	100	100	100
129	99	101	101	101	96	100	100	99	98	99	99	99	100	98	99

Patients with a GFR below 40ml/min/1.73m^2

Table A.29: Demographics of the group with GFR falling between 20-40ml/min/1.73m^2

pt number	D.O.B.	Date of Study	age in months	Kidney	GFR
130	1998/10/14	2004/04/08	66	L	20
131	1996/04/29	2003/12/05	91	R	32
132	2005/10/01	2005/10/27	1	R	22
133	2004/04/24	2006/10/12	30	R	25
134	2007/01/18	2007/03/06	2	R	39
135	2007/12/26	2008/01/08	0	R	32
136	2008/05/21	2008/06/03	0	L	37

Table A.30: Raw data of the group with GFR below 40ml/min/1.73m^2

pt number	P-1	P-2	P-3	P-4	P-5	S-I 1	S-I 2	S-I-3	S-I4	S-I 5	R-P 1	R-P2	R-P3	R-P4	R-P5
130	111	141	113	180	154	100	100	100	100	100	100	100	100	100	100
131	107	111	106	101	118	98	99	100	99	99	98	100	98	99	97
132	101	103	96	99	95	100	100	100	100	100	100	100	100	100	100
133	98	97	98	101	97	98	99	99	99	100	98	101	98	98	100
134	99	100	95	97	94	100	98	98	98	98	100	100	100	100	99
135	93	92	100	93	98	100	100	100	100	100	100	100	100	100	100
136	108	100	102	99	94	100	100	100	100	100	100	100	100	100	100

Patients with abnormal GFR values and asymmetric differential renal function

Table A.31: Demographics of the abnormal GFR and asymmetrical differential renal function group

Anon num	D.O.B	study date	age in months	L	R	Asymmetry	GFR
137	2003/01/02	2003/01/10	0.26	66	34	32	63
138	2006/08/31	2006/10/09	1.28	68	32	36	58
139	2006/04/19	2006/05/11	0.72	74	26	48	63
140	2001/09/21	2002/02/28	5.26	49	51	-2	70
141	1994/10/22	2001/11/09	84.60	55	45	10	51
142	2003/01/13	2003/02/06	0.79	54	46	8	42
143	2004/05/14	2004/07/02	1.61	47	53	-6	64
144	2004/03/24	2004/07/30	4.21	48	52	-4	75
145	2004/08/29	2004/09/14	0.53	47	53	-6	60
146	2002/09/01	2002/10/17	1.51	60	40	20	37
147	2007/08/25	2007/11/09	2.50	2	98	-96	48
148	1990/12/20	2006/11/10	190.69	71	29	42	57
149	1992/02/18	2007/01/12	178.79	88	12	76	59
150	2007/01/31	2008/03/25	13.77	82	18	64	64
151	2004/03/01	2004/04/06	1.18	23	77	-54	39
152	2003/01/28	2003/03/18	1.61	74	26	48	46
153	2004/05/07	2004/05/07	0	86	14	72	77
154	2005/01/05	2006/06/06	16.99	36	64	-28	71
155	2000/01/09	2006/03/31	74.68	37	64	-27	79
156	2008/05/27	2008/09/12	3.55	38	62	-24	77
157	2005/01/07	2006/02/03	12.88	44	56	-12	65
158	2007/07/12	2007/09/28	2.56	95	5	90	74
159	2007/10/14	2008/06/13	7.98	84	16	68	68
160	2008/04/09	2008/04/18	0.30	24	76	-52	62
161	2008/06/26	2008/08/12	1.54	71	29	42	61
162	2008/04/01	2008/04/15	0.46	75	25	50	54
163	2006/12/29	2007/08/21	7.72	85	15	70	59
164	2007/11/30	2008/09/19	9.66	98	2	96	70
165	2007/06/04	14/08/2007	2.33	56	44	12	63
166	1997/01/31	28/03/2008	133.85	56	44	12	63
167	2002/06/22	28/09/2007	63.21	64	36	28	68
168	2005/10/28	06/02/2006	3.32	64	36	28	58
169	2005/03/30	08/07/2005	3.29	55	45	10	19
170	2005/04/23	2005/07/19	2.86	83	17	66	79
171	2001/07/05	01/10/2004	38.90	51	49	2	78
172	2006/02/15	11/04/2006	1.81	50	50	0	58

Table A.32: Raw data of the abnormal GFR and asymmetrical differential renal function group

Pt number	I-1	I-2	I-3	I-4	I-5	S-I 1	S-I 2	S-I 3	S-I 4	S-I 5	S-RP1	S-RP2	S-RP3	S-RP4	S-RP5
137	78	77	76	75	75	69	70	70	70	67	65	66	66	63	65
138	63	64	68	66	64	62	63	62	62	62	53	53	55	54	54
139	70	72	69	69	71	63	63	62	62	60	57	55	56	56	55
140	46	45	47	47	46	51	52	52	51	52	53	49	51	51	51
141	53	43	40	39	60	40	40	39	38	43	42	42	38	40	37
142	50	53	53	51	57	40	43	44	42	45	40	44	42	40	42
143	60	54	52	53	54	48	48	49	49	49	51	50	52	51	51
144	61	61	58	59	53	51	50	49	49	49	44	45	45	43	44
145	51	50	49	51	53	48	48	49	46	49	51	51	52	51	51
146	62	62	65	59	65	60	60	59	57	59	72	71	71	72	67
147	9	3	3	3	3	2	0	3	0	3	0	0	0	0	2
148	77	74	74	72	76	62	66	63	67	63	66	70	63	69	63
149	88	88	87	88	87	87	87	87	86	86	87	86	87	87	87
150	84	80	82	82	82	82	83	82	82	82	82	83	82	82	82
151	54	55	55	60	51	38	36	37	39	38	39	38	38	37	39
152	66	63	59	67	66	72	69	71	68	70	81	75	76	76	74
153	86	90	86	89	86	75	76	77	76	75	75	74	74	74	76
154	36	36	37	39	38	34	34	34	34	34	32	31	31	31	31
155	37	36	37	38	37	36	35	35	35	35	33	35	34	34	34
156	49	50	45	43	51	43	45	43	45	44	45	47	45	47	45
157	44	45	44	44	43	43	43	42	42	43	41	41	42	41	41
158	93	98	97	95	98	90	89	91	82	91	89	89	88	83	88
159	84	85	86	88	83	82	82	82	82	82	80	79	80	80	79
160	22	24	21	24	23	19	19	18	20	19	17	12	13	16	16
161	69	70	71	70	73	65	66	66	64	64	61	63	62	61	62
162	80	80	78	80	74	64	63	68	61	71	65	62	64	59	65
163	81	84	85	85	86	79	81	80	78	80	84	84	87	84	85
164	98	96	98	96	97	79	82	83	93	85	86	90	90	91	91
165	55	56	53	56	56	52	52	51	53	52	48	49	51	50	50
166	55	54	55	55	56	51	51	51	52	51	51	51	51	51	50
167	62	63	62	61	62	57	58	57	58	57	57	57	57	57	56
168	63	63	63	62	62	61	62	61	61	61	61	59	60	60	59
169	61	53	53	49	57	45	44	37	42	38	42	43	43	43	39
170	82	82	81	81	82	85	83	83	84	83	87	86	86	86	85
171	53	49	52	52	51	48	48	47	49	47	45	46	45	47	45
172	54	51	52	54	52	40	42	44	40	42	44	45	46	45	44

Table A.33: Individual values of the children with DRF between 45 and 55% and GFR > 80 ml/min/1.73m^2 using all four methods

Anon num	I-mean	I-stdev	I-asym	P-RP mean	P-RP stdev	P-RP asym	S-I mean	S-I stdev	S-I asym	S-RP mean	S-RP stdev	S-RP asym
1	50.6	0.89	1.2	51.8	2.17	3.6	50	0.00	0	49.4	0.55	1.2
2	48.6	0.55	2.8	50.2	0.45	0.4	49	0.00	2	48.2	0.45	3.6
3	53.2	0.84	6.4	50.6	3.97	1.2	52	0.00	4	53.6	0.55	7.2
4	52.4	1.14	4.8	49.4	1.82	1.2	50	0.00	0	51.2	0.45	2.4
5	51.6	0.89	3.2	49	0.00	2	50.6	0.55	1.2	51	0.00	2
6	52.8	1.10	5.6	49.4	1.14	1.2	51	0.00	2	51.4	0.55	2.8
7	52.2	1.30	4.4	51.6	1.14	3.2	51.6	0.55	3.2	53.2	0.45	6.4
8	48.4	1.14	3.2	45.8	0.45	8.4	46.4	0.55	7.2	45	0.00	10
9	56.2	1.10	12.4	53.4	0.55	6.8	52.8	0.45	5.6	53	0.00	6
10	53.2	1.30	6.4	51.8	0.84	3.6	52.6	0.55	5.2	50.8	0.45	1.6
11	48.4	1.14	3.2	45.8	0.45	8.4	45.8	0.45	8.4	46.6	0.55	6.8
12	57.8	0.84	15.6	52.4	0.55	4.8	54.8	0.45	9.6	54.8	0.45	9.6
13	49	0.71	2	48	1.22	4	48	0.00	4	49.4	0.55	1.2
14	47.4	0.55	5.2	47.4	1.52	5.2	47	0.00	6	47.4	0.55	5.2
15	47.4	0.89	5.2	40.8	0.45	18.4	43.4	0.55	13.2	42.6	0.55	14.8
16	56.4	1.52	12.8	52	4.12	4	52.4	0.55	4.8	49.6	1.14	0.8
17	49.2	0.84	1.6	44.6	0.89	10.8	47.4	0.55	5.2	46.4	0.55	7.2
18	53	1.00	6	51.6	0.89	3.2	52	0.71	4	52.4	0.55	4.8
19	50.2	0.84	0.4	45.6	0.55	8.8	47	0.71	6	46	0.00	8
20	54.4	1.14	8.8	46.8	3.49	6.4	51.8	0.45	3.6	49.6	0.55	0.8
21	48.2	1.92	3.6	42.2	1.30	15.6	44	0.71	12	44.2	1.79	11.6
22	51.8	1.92	3.6	50.4	1.14	0.8	49.6	0.55	0.8	52.2	0.84	4.4
23	51.2	0.84	2.4	48.4	0.55	3.2	49.6	0.55	0.8	49.2	0.45	1.6
24	47.8	0.84	4.4	43.8	0.45	12.4	44.4	0.55	11.2	46.4	1.52	7.2
25	49.8	0.84	0.4	48	1.22	4	48.2	0.45	3.6	48.8	0.45	2.4
26	55.4	0.89	10.8	51.6	0.55	3.2	52.8	0.84	5.6	53.8	0.84	7.6
27	52.2	1.30	4.4	46.4	0.89	7.2	49	2.35	2	48.2	0.45	3.6
28	53.6	1.14	7.2	51.6	0.55	3.2	51	1.73	2	51.8	1.10	3.6
29	49.2	1.10	1.6	47	0.71	6	47.2	0.45	5.6	49	0.71	2
30	51.6	0.89	3.2	41.2	5.22	17.6	48.8	0.45	2.4	44	1.87	12

Table A. 34: Results of the children with DRF between 45 and 55% and GFR > 80 ml/min/1.73m^2 using all four methods

Variable	Mean	Median	Variance	Std.Dev.
I-mean	51.44	51.60	8.05	2.84
I-stdev	1.05	0.95	0.11	0.32
I- asym	5.09	4.40	13.95	3.73
P-RP mean	48.29	48.70	11.96	3.46
P-RP stdev	1.31	0.89	1.59	1.26
P-RP asym	5.96	4.00	23.25	4.82
S-I mean	49.34	49.60	8.26	2.87
S-I stdev	0.52	0.55	0.24	0.49
S-I asym	4.71	4.00	11.91	3.45
S-RP mean	49.31	49.40	10.15	3.19
S-RP stdev	0.63	0.55	0.21	0.46
S-RP asym	5.28	4.60	13.75	3.71

Table A.35: The demographic details of the four patients with the extreme values in the Philips Rutland Patlak Plot.

Patient number	DRF left kidney	Indication	GFR	Age in months
3	52	VUR grade 3	135	48
16	52	Left hydronephrosis and right renal calculus	110	4
20	54	Stricture distal right ureter	175	154
30	52	Right hydronephrosis and hydroureter	152	20

Table A.36: The mean and SD values of the four methods, for the four patients with unexpected extreme values on the Philips Rutland Patlak plot method.

Patient number	PI Mean	PI SD	P-RP Mean	P-RP SD	SI Mean	SI SD	S-RP Mean	S-RP SD
3	53.2	0.84	50.6	3.97	50	0	53.6	0.55
16	56.4	1.52	52	4.12	52.4	0.55	49.6	1.14
20	54.4	1.44	46.8	3.49	51.8	0.45	49.6	0.55
30	51.6	0.89	41.2	5.22	48.8	0.44	44	1.87

Statistical analysis

Table A. 37: Results of all the patients: (n = 172)

Variable	Mean	Median	Minimum	Maximum	Lower Quartile	Upper Quartile	10th Percentile	90th Percentile	Variance	Std. Dev.	Skewness	Kurtosis
Age in months	52.2	33.7	0.0	195.4	7.1	87.9	1.6	136.3	2741.0	52.4	0.9	-0.4
GFR	95.4	91.0	19.0	230.0	68.0	117.0	53.0	142.0	1290.5	35.9	0.5	0.6
I-mean	55.7	54.6	-8.6	139.8	36.7	80.4	4.2	100.2	1017.6	31.9	-0.1	-0.6
I-stdev	1.68	1.18	0.00	29.01	0.84	1.84	0.55	2.68	5.71	2.39	9.14	101.45
I-asymmetry	51.1	43.2	0.4	179.6	12.6	92.0	4.4	104.8	1577.2	39.7	0.4	-1.0
S-mean	52.7	51.6	0.0	100.0	34.0	78.9	1.2	97.2	914.0	30.2	-0.1	-0.8
S-stdev	0.71	0.55	0.00	5.27	0.45	0.87	0.00	1.34	0.53	0.73	2.90	12.70
S-asymmetry	48.0	38.8	0.0	100.0	12.4	93.2	3.6	99.6	1364.8	36.9	0.2	-1.5
RP-mean	52.9	51.2	-0.6	101.6	34.8	79.6	1.0	99.0	925.8	30.4	-0.1	-0.8
RP-stdev	0.75	0.55	0.00	3.27	0.45	0.89	0.00	1.41	0.34	0.58	1.39	2.84
RP-asymmetry	48.0	38.0	0.8	103.2	11.6	92.6	2.8	100.0	1417.3	37.7	0.2	-1.6

Table A.38: Results of all the patients, excluding patient 130 (n = 171)

Variable	Mean	Median	Minimum	Maximum	Lower Quartile	Upper Quartile	10th Percentile	90th Percentile	Variance	Std. Dev.	Skewness	Kurtosis
Age in months	52.2	33.7	0.0	195.4	7.0	88.3	1.6	136.3	2756.1	52.5	0.9	-0.4
GFR	95.8	91.0	19.0	230.0	68.0	117.0	54.0	142.0	1264.5	35.6	0.5	0.6
I-mean	55.2	54.6	-8.6	113.2	36.6	80.0	4.2	100.0	981.7	31.3	-0.2	-0.7
I-stdev	1.52	1.14	0.00	9.14	0.84	1.82	0.55	2.68	1.32	1.15	2.96	13.19
I-asymmetry	50.3	41.2	0.4	126.4	12.4	91.6	4.4	103.2	1488.7	38.6	0.3	-1.4
S-mean	52.4	51.6	0.0	100.0	34.0	78.2	1.2	97.2	906.2	30.1	-0.1	-0.8
S-stdev	0.72	0.55	0.00	5.27	0.45	0.89	0.00	1.34	0.53	0.73	2.90	12.72
S-asymmetry	47.7	38.4	0.0	100.0	12.0	92.4	3.6	99.2	1356.8	36.8	0.2	-1.5
RP-mean	52.6	51.2	-0.6	101.6	34.6	79.6	1.0	98.4	918.1	30.3	-0.1	-0.8
RP-stdev	0.75	0.55	0.00	3.27	0.45	0.89	0.00	1.41	0.34	0.58	1.40	2.86
RP-asymmetry	47.7	37.6	0.8	103.2	11.6	92.4	2.8	100.0	1409.6	37.6	0.3	-1.5

Table A.39: Results of the children with DRF between 45 and 55% and GFR > 80 ml/min/1.73m^2 (n = 30)

Variable	Mean	Median	Minimum	Maximum	Lower Quartile	Upper Quartile	10th Percentile	90th Percentile	Variance	Std. Dev.	Skewness	Kurtosis
Age in months	58.4	32.1	3.3	167.3	16.	98.0	5.3	143.5	2694.5	51.9	0.8	-0.8
GFR	122.8	121.0	82.0	187.0	100.0	140.0	85.5	163.0	826.4	28.8	0.4	-0.6
I-mean	51.4	51.6	47.4	57.8	49.0	53.2	48.0	55.8	8.1	2.8	0.4	-0.5
I-stdev	1.05	0.95	0.55	1.92	0.84	1.14	0.77	1.41	0.11	0.32	1.24	2.04
I-asymmetry	5.1	4.4	0.4	15.6	2.8	6.4	1.4	11.6	14.0	3.7	1.3	1.4
S-mean	49.3	49.6	43.4	54.8	47.2	51.8	45.1	52.7	8.3	2.9	-0.3	-0.5
S-stdev	0.52	0.55	0.00	2.35	0.45	0.55	0.00	0.77	0.24	0.49	2.17	6.83
S-asymmetry	4.7	4.0	0.0	13.2	2.0	6.0	0.8	10.4	11.9	3.5	0.9	0.4
RP-mean	49.3	49.4	42.6	54.8	46.6	51.8	44.6	53.4	10.2	3.2	-0.3	-0.7
RP-stdev	0.63	0.55	0.00	1.87	0.45	0.71	0.00	1.33	0.21	0.46	1.28	1.90
RP-asymmetry	5.3	4.6	0.8	14.8	2.0	7.2	1.2	10.8	13.8	3.7	0.8	0.0

Table A .40: Results of the group with 40 - 44% and 56 - 60% DRF and GFR > 80 ml/min/1.73m^2 (n = 10)

Variable	Mean	Median	Minimum	Maximum	Lower Quartile	Upper Quartile	10th Percentile	90th Percentile	Variance	Std. Dev.	Skewness	Kurtosis
Age in months	66.0	59.0	2.0	153.0	8.0	114.0	4.0	145.5	3096.4	55.7	0.4	-1.3
GFR	124.2	121.0	86.0	175.0	103.0	137.0	91.	170.0	834.0	28.9	0.6	-0.4
I-mean	56.3	57.6	41.0	62.0	55.2	59.4	48.1	60.9	33.5	5.8	-2.4	6.7
I-stdev	1.19	1.10	0.71	1.79	0.84	1.64	0.71	1.72	0.19	0.44	0.17	-2.10
I-asymmetry	16.3	17.0	10.4	24.0	13.6	18.8	10.4	21.8	18.1	4.3	0.2	-0.2
S-mean	53.6	54.1	40.4	61.0	52.2	57.0	45.0	60.1	32.5	5.7	-1.3	2.9
S-stdev	0.52	0.50	0.00	1.22	0.45	0.71	0.00	1.03	0.13	0.36	0.30	0.70
S-asymmetry	11.3	9.2	0.8	22.0	7.6	18.4	2.6	20.6	47.5	6.9	0.2	-1.0
RP-mean	54.1	54.6	43.8	63.2	51.4	57.4	47.5	60.7	26.7	5.2	-0.3	1.4
RP-stdev	0.69	0.55	0.45	1.10	0.55	0.84	0.45	1.10	0.06	0.25	0.79	-0.99
RP-asymmetry	10.7	10.0	2.4	26.4	3.2	14.8	2.6	21.4	54.6	7.4	0.9	1.1

Table A.41: Results of the group with 35 - 39% and 61 - 65% DRF and GFR > 80 ml/min/1.73m^2 (n = 10)

Variable	Mean	Median	Minimum	Maximum	Lower Quartile	Upper Quartile	10th Percentile	90th Percentile	Variance	Std. Dev.	Skewness	Kurtosis
Age in months	65.1	59.6	4.6	139.1	11.9	109.4	7.5	137.0	2648.8	51.5	0.9	-1.6
GFR	134.3	129.0	80.0	230.0	97.0	165.0	85.0	205.0	2259.8	47.	0.8	0.2
I-mean	44.2	37.0	32.8	63.6	36.6	60.2	34.6	63.1	156.3	12.5	1.0	-1.2
I-stdev	1.05	1.07	0.45	1.52	0.84	1.30	0.64	1.43	0.10	0.31	-0.47	0.12
I-asymmetry	26.2	26.2	20.4	34.4	25.2	27.2	21.4	30.8	13.2	3.6	0.9	3.0
S-mean	42.3	35.5	33.2	61.4	34.4	58.8	33.3	60.2	145.9	12.1	1.0	-1.2
S-stdev	0.80	0.77	0.45	1.34	0.55	0.84	0.50	1.32	0.10	0.31	0.95	-0.14
S-asymmetry	27.0	29.0	17.6	33.6	22.8	31.2	17.8	33.4	34.5	5.9	-0.7	-0.9
RP-mean	43.2	36.9	34.6	61.0	35.2	57.8	34.8	59.7	124.2	11.2	1.0	-1.2
RP-stdev	0.58	0.55	0.00	1.14	0.45	0.84	0.00	1.07	0.15	0.38	-0.27	-0.70
RP-asymmetry	24.6	26.2	15.6	30.8	18.8	29.6	16.2	30.4	34.6	5.9	-0.5	-1.6

Table A.42: Results of the group with 30 - 34% and 66 - 70% DRF and GFR > 80 ml/min/1.73m^2 (n = 10)

Variable	Mean	Median	Minimum	Maximum	Lower Quartile	Upper Quartile	10th Percentile	90th Percentile	Variance	Std. Dev.	Skewness	Kurtosis
Age in months	50.4	59.9	0.4	102.0	7.6	79.2	3.8	91.7	1308.9	36.2	-0.2	-1.5
GFR	94.4	90.5	83.0	115.0	84.0	102.0	83.0	114.0	147.6	12.2	0.8	-0.8
I-mean	52.3	51.2	32.6	76.4	34.6	69.0	33.1	73.5	344.7	18.6	0.1	-2.3
I-stdev	1.63	1.32	0.55	5.13	1.10	1.52	0.72	3.50	1.64	1.28	2.68	7.88
I-asymmetry	34.7	33.8	24.0	52.8	28.8	38.0	25.8	47.0	66.8	8.2	1.1	1.9
S-mean	49.5	47.3	30.4	73.8	32.2	65.8	31.1	70.8	335.4	18.3	0.1	-2.3
S-stdev	0.46	0.45	0.00	1.30	0.45	0.55	0.00	0.93	0.13	0.36	1.20	3.54
S-asymmetry	34.2	34.0	21.2	47.6	31.6	36.4	25.6	43.4	46.1	6.8	0.1	2.0
RP-mean	48.7	49.2	30.8	67.8	33.8	62.6	31.3	66.5	260.8	16.2	0.0	-2.4
RP-stdev	0.87	0.87	0.45	1.79	0.45	1.10	0.45	1.55	0.19	0.44	1.00	0.75
RP-asymmetry	30.3	30.6	23.2	38.4	25.2	35.6	23.8	37.4	29.1	5.4	0.1	-1.5

Table A.43: Results of the group with 25 - 29% and 75 - 79% DRF and GFR > 80 ml/min/1.73m^2 (n = 8)

Variable	Mean	Median	Minimum	Maximum	Lower Quartile	Upper Quartile	10th Percentile	90th Percentile	Variance	Std. Dev.	Skewness	Kurtosis
Age in months	62.1	43.7	13.3	152.6	25.8	96.1	13.3	152.6	2446.4	49.5	1.1	-0.0
GFR	113.3	112.0	81.0	147.0	88.0	139.0	81.0	147.0	839.1	29.0	0.0	-2.6
I-mean	47.3	44.1	22.2	73.4	27.3	70.1	22.2	73.4	513.1	22.7	0.1	-2.5
I-stdev	0.95	0.63	0.45	2.59	0.55	1.10	0.45	2.59	0.52	0.72	2.12	4.64
I-asymmetry	41.5	43.0	17.2	55.6	40.2	46.2	17.2	55.6	121.7	11.0	-1.6	4.1
S-mean	45.7	42.5	25.0	72.2	26.6	65.0	25.0	72.2	433.4	20.8	0.2	-2.4
S-stdev	0.70	0.55	0.45	1.58	0.45	0.77	0.45	1.58	0.15	0.38	2.17	5.00
S-asymmetry	38.0	43.6	12.8	50.0	30.0	46.8	12.8	50.0	173.0	13.2	-1.3	0.6
RP-mean	45.4	42.7	24.4	73.0	26.1	64.0	24.4	73.0	434.8	20.9	0.2	-2.3
RP-stdev	0.89	0.97	0.00	1.48	0.69	1.14	0.00	1.48	0.20	0.45	-0.98	1.35
RP-asymmetry	37.9	43.2	12.4	51.2	28.0	48.4	12.4	51.2	199.8	14.1	-1.0	-0.1

Table A.44: Results of the group with 20 - 24% and 76 - 80% DRF and GFR > 80 ml/min/1.73m^2 (n = 8)

Variable	Mean	Median	Minimum	Maximum	Lower Quartile	Upper Quartile	10th Percentile	90th Percentile	Variance	Std. Dev.	Skewness	Kurtosis
Age in months	84.2	64.8	25.4	160.5	35.9	142.9	25.4	160.5	3090.1	55.6	0.5	-2.0
GFR	104.0	110.0	84.0	116.0	92.0	114.0	84.0	116.0	162.6	12.8	-0.7	-1.4
I-mean	44.5	25.3	21.2	80.8	22.2	79.3	21.2	80.8	859.5	29.3	0.6	-2.2
I-stdev	1.07	1.12	0.55	1.30	1.05	1.18	0.55	1.30	0.05	0.23	-1.96	4.72
I-asymmetry	55.8	56.8	48.0	61.6	52.8	58.8	48.0	61.6	20.5	4.5	-0.7	-0.2
S-mean	43.3	23.8	20.0	80.0	21.3	78.2	20.0	80.0	865.9	29.4	0.6	-2.2
S-stdev	0.61	0.63	0.00	1.14	0.45	0.80	0.00	1.14	0.12	0.34	-0.32	0.89
S-asymmetry	56.6	57.4	52.0	60.0	53.0	59.8	52.0	60.0	12.4	3.5	-0.2	-2.3
RP-mean	45.6	27.6	17.8	81.0	25.5	79.7	17.8	81.0	830.1	28.8	0.6	-2.2
RP-stdev	0.56	0.50	0.00	0.89	0.45	0.84	0.00	0.89	0.09	0.30	-0.69	0.49
RP-asymmetry	54.1	54.4	42.4	64.4	47.8	60.8	42.4	64.4	66.0	8.1	-0.1	-1.8

Table A .45: Results of the group with 15 - 19% and 81 - 85% DRF and GFR > 80 ml/min/1.73m^2 (n = 6)

Variable	Mean	Median	Minimum	Maximum	Lower Quartile	Upper Quartile	10th Percentile	90th Percentile	Variance	Std. Dev.	Skewness	Kurtosis
Age in months	45.1	15.3	4.5	133.0	9.4	92.9	4.5	133.0	2942.0	54.2	1.2	-0.5
GFR	117.3	117.5	109.0	127.0	112.0	121.0	109.0	127.0	41.1	6.4	0.3	-0.2
I-mean	63.0	82.0	13.4	93.4	22.4	84.8	13.4	93.4	1248.3	35.3	-0.9	-1.7
I-stdev	1.02	1.02	0.45	1.95	0.55	1.14	0.45	1.95	0.29	0.54	0.97	1.18
I-asymmetry	68.8	69.2	55.2	86.8	59.2	73.2	55.2	86.8	124.2	11.2	0.6	0.5
S-mean	61.6	80.8	13.0	90.8	20.4	84.0	13.0	90.8	1232.9	35.1	-0.9	-1.8
S-stdev	0.45	0.50	0.00	0.89	0.00	0.84	0.00	0.89	0.15	0.39	-0.23	-1.90
S-asymmetry	67.7	67.4	56.4	81.6	59.2	74.0	56.4	81.6	86.8	9.3	0.3	-0.6
RP-mean	60.5	79.7	13.2	89.6	18.2	82.6	13.2	89.6	1222.3	35.0	-0.9	-1.8
RP-stdev	0.61	0.55	0.45	0.84	0.45	0.84	0.45	0.84	0.03	0.18	0.71	-1.87
RP-asymmetry	66.7	64.8	54.4	79.2	63.6	73.6	54.4	79.2	74.5	8.6	0.2	0.0

Table A.46: Results of the group with 10 - 14% and 86 - 90% DRF and GFR > 80 ml/min/1.73m^2 (n = 7)

Variable	Mean	Median	Minimum	Maximum	Lower Quartile	Upper Quartile	10th Percentile	90th Percentile	Variance	Std. Dev.	Skewness	Kurtosis
Age in months	48.6	23.6	2.6	149.3	5.0	83.1	2.6	149.3	2823.4	53.1	1.3	1.3
GFR	110.3	105.0	92.0	141.0	93.0	119.0	92.0	141.0	296.6	17.2	0.8	0.5
I-mean	66.8	89.4	9.	91.4	10.0	89.6	9.0	91.4	1531.5	39.1	-1.2	-0.8
I-stdev	1.02	0.89	0.00	2.07	0.55	1.41	0.00	2.07	0.44	0.67	0.05	0.28
I-asymmetry	79.8	79.2	77.2	82.8	78.8	82.0	77.2	82.8	3.8	2.0	0.5	-0.6
S-mean	66.9	88.4	10.0	89.8	14.0	89.6	10.0	89.8	1406.4	37.5	-1.2	-0.8
S-stdev	0.44	0.55	0.00	0.84	0.00	0.71	0.00	0.84	0.11	0.33	-0.59	-1.07
S-asymmetry	77.1	78.0	72.0	80.0	74.4	79.6	72.0	80.0	8.9	3.0	-1.0	-0.2
RP-mean	67.9	89.2	11.0	90.8	16.8	90.4	11.0	90.8	1365.2	37.0	-1.2	-0.8
RP-stdev	0.57	0.55	0.45	0.84	0.45	0.71	0.45	0.84	0.02	0.15	1.13	0.20
RP-asymmetry	77.1	78.4	66.4	81.6	75.6	80.8	66.4	81.6	26.0	5.1	-1.9	4.0

Table A.47: Results of the group with 1 - 9% and 91 - 99% DRF and GFR > 80 ml/min/1.73m^2 (n = 9)

Variable	Mean	Median	Minimum	Maximum	Lower Quartile	Upper Quartile	10th Percentile	90th Percentile	Variance	Std. Dev.	Skewness	Kurtosis
Age in months	70.5	60.1	1.8	195.4	13.3	106.8	1.8	195.4	4846.2	69.6	0.7	-0.7
GFR	106.3	94.0	80.0	144.0	89.0	119.0	80.0	144.0	623.5	25.0	0.6	-1.3
I-mean	65.9	91.4	-0.8	99.8	13.2	98.2	-0.8	99.8	2016.6	44.9	-0.9	-1.6
I-stdev	1.11	1.10	0.45	2.28	0.55	1.30	0.45	2.28	0.39	0.63	0.79	-0.03
I-asymmetry	89.9	93.2	73.6	101.6	82.8	98.8	73.6	101.6	107.9	10.4	-0.5	-1.4
S-mean	63.1	89.8	0.0	98.0	7.8	97.0	0.0	98.0	2066.1	45.5	-0.8	-1.7
S-stdev	0.67	0.45	0.00	2.00	0.00	1.10	0.00	2.00	0.47	0.69	0.88	0.13
S-asymmetry	88.9	94.0	62.0	100.0	84.4	96.0	62.0	100.0	143.8	12.0	-1.6	2.6
RP-mean	63.4	89.6	0.0	98.4	8.4	96.4	0.0	98.4	2094.7	45.8	-0.8	-1.7
RP-stdev	0.72	0.55	0.00	1.92	0.55	0.89	0.00	1.92	0.35	0.59	0.86	1.33
RP-asymmetry	89.7	92.8	66.	100.0	83.2	96.8	66.4	100.	128.2	11.3	-1.2	0.9

Table A. 48: Results for the solitary left kidney group and GFR 80-140 ml/min/1.73m^2 (n = 11)

Variable	Mean	Median	Minimum	Maximum	Lower Quartile	Upper Quartile	10th Percentile	90th Percentile	Variance	Std. Dev.	Skewness	Kurtosis
Age in months	89.6	108.6	6.0	164.2	31.0	136.3	11.2	136.9	3107.4	55.7	-0.4	-1.4
GFR	101.1	94.0	83.0	121.0	87.0	118.0	86.0	119.0	238.7	15.5	0.2	-2.1
I-mean	103.8	103.6	97.4	111.6	102.4	104.2	102.4	105.8	11.2	3.3	0.8	3.9
I-stdev	1.67	1.67	0.55	2.61	0.89	2.19	0.89	2.59	0.47	0.68	-0.19	-0.91
I-asymmetry	107.5	107.2	94.8	123.2	104.8	108.4	104.8	111.6	44.6	6.7	0.8	3.9
S-mean	99.0	99.2	97.2	100.0	97.6	100.0	97.4	100.0	1.1	1.1	-0.8	-1.0
S-stdev	0.77	0.71	0.00	1.82	0.00	1.34	0.00	1.64	0.41	0.64	0.30	-0.98
S-asymmetry	97.9	98.4	94.4	100.0	95.2	100.0	94.8	100.0	4.5	2.1	-0.8	-1.0
RP-mean	99.8	99.8	98.0	100.8	99.6	100.0	99.2	100.2	0.5	0.7	-1.5	4.0
RP-stdev	0.53	0.45	0.00	1.22	0.00	0.84	0.00	1.14	0.19	0.44	0.25	-1.03
RP-asymmetry	99.5	99.6	96.	101.6	99.2	100.0	98.4	100.4	2.0	1.4	-1.5	4.0

Table A. 49: Results for the solitary right kidney group and GFR 80-140 ml/min/1.73m^2 (n = 7)

Variable	Mean	Median	Minimum	Maximum	Lower Quartile	Upper Quartile	10th Percentile	90th Percentile	Variance	Std. Dev.	Skewness	Kurtosis
Age in months	50.4	51.9	11.2	95.2	11.2	94.4	11.2	95.2	1200.8	34.7	0.3	-1.4
GFR	100.1	101.0	83.0	111.0	95.0	110.0	83.0	111.0	93.5	9.7	-0.8	0.5
I-mean	0.1	0.4	-1.6	2.2	-0.8	0.6	-1.6	2.2	1.4	1.2	0.4	0.9
I-stdev	0.94	0.84	0.45	1.82	0.45	1.34	0.45	1.82	0.27	0.52	0.74	-0.53
I-asymmetry	99.7	99.2	95.6	103.2	98.8	101.6	95.6	103.2	5.7	2.4	-0.4	0.9
S-mean	0.3	0.2	0.0	1.2	0.0	0.6	0.0	1.2	0.2	0.5	1.7	2.4
S-stdev	0.36	0.45	0.00	1.10	0.00	0.55	0.00	1.10	0.16	0.40	0.91	0.58
S-asymmetry	99.4	99.6	97.6	100.0	98.8	100.0	97.6	100.0	0.8	0.9	-1.7	2.4
RP-mean	-0.0	0.0	-0.6	0.2	0.0	0.2	-0.6	0.2	0.1	0.3	-2.0	4.6
RP-stdev	0.26	0.00	0.00	0.84	0.00	0.55	0.00	0.84	0.12	0.35	0.83	-1.00
RP-asymmetry	100.1	100.0	99.6	101.2	99.6	100.0	99.6	101.2	0.3	0.5	2.0	4.6

Table A.50: Results for the solitary left kidney group and GFR 60-79 ml/min/1.73m^2 (n = 5)

Variable	Mean	Median	Minimum	Maximum	Lower Quartile	Upper Quartile	10th Percentile	90th Percentile	Variance	Std. Dev.	Skewness	Kurtosis
Age in months	37.4	41.1	3.0	66.0	29.7	47.2	3.0	66.0	542.4	23.3	-0.6	0.8
GFR	68.0	65.0	63.0	79.0	63.0	70.0	63.0	79.0	46.0	6.8	1.4	1.4
I-mean	105.0	104.0	100.2	113.2	102.4	105.2	100.2	113.2	24.5	5.0	1.5	2.6
I-stdev	2.25	2.00	1.30	3.58	1.79	2.59	1.30	3.58	0.76	0.87	0.88	0.53
I-asymmetry	110.0	108.0	100.4	126.4	104.8	110.4	100.4	126.4	98.1	9.9	1.5	2.6
S-mean	97.5	97.0	96.2	99.2	97.0	98.2	96.2	99.2	1.4	1.2	0.6	-0.7
S-stdev	0.96	1.00	0.45	1.30	0.84	1.22	0.45	1.30	0.12	0.34	-0.84	0.13
S-asymmetry	95.0	94.0	92.4	98.4	94.0	96.4	92.4	98.4	5.6	2.4	0.6	-0.7
RP-mean	99.3	99.0	96.0	101.6	99.0	100.8	96.0	101.6	4.7	2.2	-0.8	0.7
RP-stdev	1.19	1.30	0.55	2.00	0.71	1.41	0.55	2.00	0.34	0.58	0.31	-0.97
RP-asymmetry	98.6	98.0	92.0	103.2	98.0	101.6	92.0	103.2	18.6	4.3	-0.8	0.7

Table A.51: Results for the solitary right kidney group and GFR 60-79 ml/min/1.73m^2 (n = 3)

Variable	Mean	Median	Minimum	Maximum	Lower Quartile	Upper Quartile	10th Percentile	90th Percentile	Variance	Std. Dev.	Skewness	Kurtosis
Age in months	31.9	43.0	8.5	44.1	8.5	44.1	8.5	44.1	410.3	20.3	-1.7	
GFR	67.3	67.0	67.0	68.0	67.0	68.0	67.0	68.0	0.3	0.6	1.7	
I-mean	-0.1	-1.0	-4.2	4.8	-4.2	4.8	-4.2	4.8	20.8	4.6	0.8	
I-stdev	1.28	1.10	0.71	2.05	0.71	2.05	0.71	2.05	0.48	0.69	1.14	
I-asymmetry	100.3	102.0	90.4	108.4	90.4	108.4	90.4	108.40	83.3	9.1	-0.8	
S-mean	0.5	0.2	0.0	1.2	0.0	1.2	0.0	1.2	0.4	0.6	1.6	
S-stdev	0.30	0.45	0.00	0.45	0.00	0.45	0.00	0.45	0.07	0.26	-1.73	
S-asymmetry	99.1	99.6	97.6	100.0	97.6	100.0	97.6	100.0	1.7	1.3	-1.6	
RP-mean	0.3	0.0	0.0	1.0	0.0	1.0	0.0	1.0	0.3	0.6	1.7	
RP-stdev	0.33	0.00	0.00	1.00	0.00	1.00	0.00	1.00	0.33	0.58	1.73	
RP-asymmetry	99.3	100.0	98.0	100.0	98.0	100.0	98.0	100.0	1.3	1.2	-1.7	

Table A.52: Results for the solitary kidney group and GFR 40-59 ml/min/1.73m^2 (n = 5)

Variable	Mean	Median	Minimum	Maximum	Lower Quartile	Upper Quartile	10th Percentile	90th Percentile	Variance	Std. Dev.	Skewness	Kurtosis
Age in months	61.9	38.1	2.6	133.6	6.1	129.2	2.6	133.6	4217.8	64.9	0.4	-3.1
GFR	50.8	50.0	46.0	59.0	46.0	53.0	46.0	59.0	29.7	5.5	0.9	-0.1
I-mean	41.6	3.0	-1.4	106.0	0.4	100.0	-1.4	106.0	3148.6	56.1	0.6	-3.3
I-stdev	2.88	2.83	1.00	5.10	2.19	3.29	1.00	5.10	2.28	1.51	0.49	0.93
I-asymmetry	101.6	100.0	94.0	112.0	99.2	102.8	94.0	112.0	43.9	6.6	1.0	1.8
S-mean	40.3	0.8	0.00	100.0	0.6	100.0	0.0	100.0	2972.2	54.5	0.6	-3.3
S-stdev	0.35	0.00	0.00	0.89	0.00	0.84	0.00	0.89	0.23	0.47	0.62	-3.28
S-asymmetry	99.4	100.0	98.4	100.0	98.8	100.0	98.4	100.0	0.6	0.8	-0.8	-2.5
RP-mean	40.2	1.0	-0.2	100.0	0.0	100.0	-0.2	100.0	2984.2	54.6	0.6	-3.3
RP-stdev	0.23	0.00	0.00	0.71	0.00	0.45	0.00	0.71	0.11	0.33	0.95	-1.39
RP-asymmetry	99.7	100.0	98.0	100.4	100.0	100.0	98.0	100.4	0.9	1.0	-2.0	4.4

Table A.53: Results for the solitary kidney group and GFR below 40 ml/min/1.73m^2 (n = 7)

Variable	Mean	Median	Minimum	Maximum	Lower Quartile	Upper Quartile	10th Percentile	90th Percentile	Variance	Std. Dev.	Skewness	Kurtosis
Age in months	27.1	1.5	0.4	91.2	0.4	65.8	0.4	91.2	1396.4	37.4	1.1	-0.4
GFR	29.6	32.0	20.0	39.0	22.0	37.0	20.0	39.0	54.3	7.4	-0.1	-1.7
I-mean	34.7	3.0	-8.6	139.8	1.2	100.6	-8.6	139.8	3561.2	59.7	1.4	0.1
I-stdev	7.36	3.56	1.64	29.01	2.55	6.35	1.64	29.01	93.56	9.67	2.50	6.42
I-asymmetry	110.9	97.6	90.4	179.6	94.0	117.2	90.4	179.6	991.1	31.5	2.3	5.3
S-mean	29.1	1.0	0.0	100.0	0.0	100.0	0.0	100.0	2347.1	48.5	1.2	-0.8
S-stdev	0.33	0.00	0.00	0.89	0.00	0.71	0.00	0.89	0.17	0.42	0.47	-2.45
S-asymmetry	99.0	100.0	96.8	100.0	98.0	100.0	96.8	100.0	1.8	1.3	-0.7	-1.3
RP-mean	29.0	1.0	0.0	100.0	0.0	100.0	0.0	100.0	2354.7	48.5	1.2	-0.8
RP-stdev	0.43	0.00	0.00	1.41	0.00	1.14	0.00	1.41	0.37	0.61	1.04	-0.82
RP-asymmetry	99.2	100.0	96.8	100.0	98.0	100.0	96.8	100.0	1.7	1.3	-1.5	0.9

Table A.54: Results of the group with 45 - 55% DRF and GFR 60 -79 ml/min/1.73m^2 (n = 4)

Variable	Mean	Median	Minimum	Maximum	Lower Quartile	Upper Quartile	10th Percentile	90th Percentile	Variance	Std. Dev.	Skewness	Kurtosis
Age in months	12.5	4.7	1.6	38.9	2.9	22.1	1.6	38.9	312.3	17.7	2.0	3.9
GFR	71.8	72.5	64.0	78.0	67.0	76.5	64.0	78.0	37.6	6.1	-0.6	-1.1
I-mean	52.7	53.0	46.2	58.4	48.8	56.5	46.2	58.4	26.7	5.2	-0.4	-0.2
I-stdev	2.19	2.32	0.84	3.29	1.18	3.21	0.84	3.29	1.46	1.21	-0.25	-4.40
I-asymmetry	9.1	8.4	2.8	16.8	5.2	13.0	2.8	16.8	33.8	5.8	0.7	1.4
S-mean	49.4	49.1	47.8	51.6	48.2	50.6	47.8	51.6	2.7	1.6	0.9	0.5
S-stdev	0.71	0.69	0.55	0.89	0.55	0.87	0.55	0.89	0.03	0.19	0.08	-5.52
S-asymmetry	2.8	3.0	0.8	4.4	1.8	3.8	0.8	4.4	2.2	1.5	-0.8	1.5
RP-mean	48.0	48.3	44.2	51.0	44.9	51.0	44.2	51.0	12.7	3.6	-0.1	-5.2
RP-stdev	0.96	0.87	0.71	1.41	0.77	1.15	0.71	1.41	0.10	0.31	1.61	2.93
RP-asymmetry	6.1	5.4	2.0	11.6	2.0	10.2	2.0	11.6	23.7	4.9	0.3	-4.4

Table A.55: Results of the group with 45 -55% DRF and GFR 40-59 ml/min/1.73m^2 (n = 4)

Variable	Mean	Median	Minimum	Maximum	Lower Quartile	Upper Quartile	10th Percentile	90th Percentile	Variance	Std. Dev.	Skewness	Kurtosis
Age in months	21.9	1.3	0.5	84.6	0.7	43.2	0.5	84.6	1745.8	41.8	2.0	4.0
GFR	52.8	54.5	42.0	60.0	46.5	59.0	42.0	60.0	66.3	8.1	-0.9	-0.7
I-mean	50.8	51.7	47.0	52.8	48.9	52.7	47.0	52.8	7.2	2.7	-1.4	1.5
I-stdev	3.66	2.08	1.34	9.14	1.41	5.91	1.34	9.14	13.69	3.70	1.85	3.43
I-asymmetry	4.6	5.4	1.6	6.0	3.4	5.8	1.6	6.0	4.1	2.0	-1.9	3.5
S-mean	43.1	42.2	40.0	48.0	40.8	45.4	40.0	48.0	12.0	3.5	1.4	2.1
S-stdev	1.67	1.77	1.22	1.92	1.45	1.90	1.22	1.92	0.10	0.32	-1.39	1.51
S-asymmetry	13.8	15.6	4.0	20.0	9.2	18.4	4.0	20.0	48.0	6.9	-1.4	2.1
RP-mean	44.4	43.2	39.8	51.2	40.7	48.0	39.8	51.2	25.1	5.0	1.1	0.7
RP-stdev	1.31	1.25	0.45	2.28	0.64	1.98	0.45	2.28	0.68	0.83	0.26	-2.64
RP-asymmetry	12.5	13.6	2.4	20.4	6.4	18.6	2.4	20.4	62.4	7.9	-0.6	-1.0

Table A.56: Results of the group with 35 - 44% and 56 - 65% DRF and GFR 60 -79 ml/min/1.73m^2 (n = 7)

Variable	Mean	Median	Minimum	Maximum	Lower Quartile	Upper Quartile	10th Percentile	90th Percentile	Variance	Std. Dev.	Skewness	Kurtosis
Age in months	43.9	17.0	2.3	133.9	3.6	74.7	2.3	133.9	2408.9	49.1	1.1	0.5
GFR	69.4	68.0	63.0	79.0	63.0	77.0	63.0	79.0	42.6	6.5	0.6	-1.4
I-mean	48.3	47.6	37.0	62.0	37.2	55.2	37.0	62.0	91.7	9.6	0.1	-1.4
I-stdev	1.27	0.71	0.71	3.44	0.71	1.30	0.71	3.44	0.99	1.00	2.24	5.24
I-asymmetry	16.1	12.0	4.8	26.0	10.0	25.6	4.8	26.0	77.5	8.8	0.1	-2.2
S-mean	45.2	44.0	34.0	57.4	35.2	52.0	34.0	57.4	77.5	8.8	-0.0	-1.4
S-stdev	0.53	0.55	0.00	1.00	0.45	0.71	0.00	1.00	0.09	0.30	-0.32	1.80
S-asymmetry	15.7	14.8	2.4	32.0	4.0	29.6	2.4	32.0	131.3	11.5	0.5	-1.1
RP-mean	44.2	45.8	31.2	56.8	34.0	50.8	31.2	56.8	86.0	9.3	-0.2	-1.2
RP-stdev	0.68	0.45	0.45	1.14	0.45	1.10	0.45	1.14	0.10	0.32	0.93	-1.30
RP-asymmetry	15.9	13.6	0.8	37.6	1.6	32.0	0.8	37.6	204.5	14.3	0.6	-1.1

Table A.57: Results of the group with 25 - 34% and 66 - 75% DRF and GFR 60-79 ml/min/1.73m^2: (n = 3)

Variable	Mean	Median	Minimum	Maximum	Lower Quartile	Upper Quartile	10th Percentile	90th Percentile	Variance	Std. Dev.	Skewness	Kurtosis
Age in months	0.8	0.7	0.3	1.5	0.3	1.5	0.3	1.5	0.4	0.7	0.8	
GFR	62.3	63.0	61.0	63.0	61.0	63.0	61.0	63.0	1.3	1.2	-1.7	
I-mean	72.3	70.6	70.2	76.2	70.2	76.2	70.2	76.2	11.3	3.4	1.7	
I-stdev	1.37	1.30	1.30	1.52	1.30	1.52	1.30	1.52	0.02	0.12	1.73	
I-asymmetry	44.7	41.2	40.4	52.4	40.4	52.4	40.4	52.4	45.0	6.7	1.7	
S-mean	65.4	65.0	62.0	69.2	62.0	69.2	62.0	69.2	13.1	3.6	0.5	
S-stdev	1.18	1.22	1.00	1.30	1.00	1.30	1.00	1.30	0.02	0.16	-1.25	
S-asymmetry	30.8	30.0	24.0	38.4	24.0	38.4	24.0	38.4	52.3	7.2	0.5	
RP-mean	60.9	61.8	55.8	65.0	55.8	65.0	55.8	65.0	21.8	4.7	-0.9	
RP-stdev	0.97	0.84	0.84	1.22	0.84	1.22	0.84	1.22	0.05	0.22	1.73	
RP-asymmetry	21.7	23.6	11.6	30.0	11.6	30.0	11.6	30.0	87.3	9.3	-0.9	

Table A.58: Results of the group with 25 - 34% and 66 - 75% DRF and GFR 40-59 ml/min/1.73m^2 (n = 4)

Variable	Mean	Median	Minimum	Maximum	Lower Quartile	Upper Quartile	10th Percentile	90th Percentile	Variance	Std. Dev.	Skewness	Kurtosis
Age in months	48.5	1.5	0.5	190.7	0.9	96.2	0.5	190.7	8984.3	94.8	2.0	4.0
GFR	53.8	55.5	46.0	58.0	50.0	57.5	46.0	58.0	29.6	5.4	-1.5	1.9
I-mean	70.6	69.8	64.2	78.4	64.6	76.5	64.2	78.4	49.7	7.1	0.2	-4.5
I-stdev	2.46	2.30	1.95	3.27	1.97	2.94	1.95	3.27	0.38	0.62	0.89	-1.07
I-asymmetry	41.1	39.6	28.4	56.8	29.2	53.0	28.4	56.8	198.9	14.1	0.2	-4.5
S-mean	65.5	64.8	62.2	70.0	63.2	67.7	62.2	70.0	10.9	3.3	1.1	1.6
S-stdev	2.06	1.87	0.45	4.04	1.01	3.10	0.45	4.04	2.25	1.50	0.68	1.06
S-asymmetry	30.9	29.6	24.4	40.0	26.4	35.4	24.4	40.0	43.8	6.6	1.1	1.6
RP-mean	64.9	64.6	53.8	76.4	58.4	71.3	53.8	76.4	86.9	9.3	0.2	0.9
RP-stdev	2.34	2.63	0.84	3.27	1.69	2.99	0.84	3.27	1.10	1.05	-1.46	2.67
RP-asymmetry	29.7	29.2	7.6	52.8	16.8	42.6	7.6	52.8	347.7	18.7	0.2	0.9

Table A.59: Results of the group with 1- 24% and 76 - 99% DRF and GFR 60-79 ml/min/1.73m^2 (n = 7)

Variable	Mean	Median	Minimum	Maximum	Lower Quartile	Upper Quartile	10th Percentile	90th Percentile	Variance	Std. Dev.	Skewness	Kurtosis
Age in months	5.3	2.9	0.0	13.8	0.3	9.7	0.0	13.8	27.4	5.2	0.7	-1.0
GFR	70.6	70.0	62.0	79.0	64.0	77.0	62.0	79.0	41.3	6.4	-0.0	-1.5
I-mean	78.9	85.2	22.8	97.0	81.6	96.2	22.8	97.0	650.5	25.5	-2.3	5.7
I-stdev	1.47	1.41	0.55	2.17	1.00	1.95	0.55	2.17	0.34	0.58	-0.43	-0.86
I-asymmetry	73.3	70.4	54.4	94.0	63.2	92.4	54.4	94.0	224.9	15.0	0.5	-1.1
S-mean	73.7	82.2	19.0	88.6	75.8	84.4	19.0	88.6	595.4	24.4	-2.5	6.5
S-stdev	1.71	0.84	0.00	5.27	0.45	3.78	0.00	5.27	3.99	2.00	1.32	0.27
S-asymmetry	65.0	64.4	51.6	77.2	62.0	68.8	51.6	77.2	59.7	7.7	-0.3	1.8
RP-mean	73.5	82.2	14.8	89.6	74.6	87.4	14.8	89.6	694.7	26.4	-2.5	6.2
RP-stdev	1.34	0.89	0.45	2.51	0.55	2.17	0.45	2.51	0.77	0.88	0.37	-2.34
RP-asymmetry	67.0	70.4	49.2	79.2	59.2	74.8	49.2	79.2	105.1	10.3	-0.8	0.1

Table A. 60: Results of the group with 1 - 24% and 76 - 99% DRF and GFR 40 - 59 ml/min/1.73m^2 (n = 3)

Variable	Mean	Median	Minimum	Maximum	Lower Quartile	Upper Quartile	10th Percentile	90th Percentile	Variance	Std. Dev.	Skewness	Kurtosis
Age in months	63.0	7.7	2.5	178.8	2.5	178.8	2.5	178.8	10062.2	100.3	1.7	
GFR	55.3	59.0	48.0	59.0	48.0	59.0	48.0	59.0	40.3	6.4	-1.7	
I-mean	58.7	84.2	4.2	87.6	4.2	87.6	4.2	87.6	2227.9	47.2	-1.7	
I-stdev	1.72	1.92	0.55	2.68	0.55	2.68	0.55	2.68	1.17	1.08	-0.82	
I-asymmetry	78.4	75.2	68.4	91.6	68.4	91.6	68.4	91.6	142.2	11.9	1.1	
S-mean	55.9	79.6	1.6	86.6	1.6	86.6	1.6	86.6	2226.3	47.2	-1.7	
S-stdev	1.07	1.14	0.55	1.52	0.55	1.52	0.55	1.52	0.24	0.49	-0.65	
S-asymmetry	76.4	73.2	59.2	96.8	59.2	96.8	59.2	96.8	361.1	19.0	0.7	
RP-mean	57.3	84.8	0.4	86.8	0.4	86.8	0.4	86.8	2432.1	49.3	-1.7	
RP-stdev	0.88	0.89	0.45	1.30	0.45	1.30	0.45	1.30	0.18	0.43	-0.13	
RP-asymmetry	80.8	73.6	69.6	99.2	69.6	99.2	69.6	99.2	257.9	16.1	1.6	

Results of the remaining groups

Four of the groups had only one patient per group and one group, below 40ml/min/1.73m^2 and 25-35% differential renal function, had no patients.

Table A.61: Results for groups with only one patient each

Group	L kidney	Age	GFR	PI-mean	PI-stdev	PI- assym	SI-mean	SI-stdev	SI-assym	SRP-mean	SRP-stdev	SRP - assym
DRF 45-55% And GFR< 40	55	3.29	19	54.6	4.56	9.2	41.2	3.56	17.6	42	1.73	16
DRF 35-45% and GFR 40 – 59	64	7.13	58	62.6	0.55	25.2	61.2	0.45	22.4	59.8	0.84	19.6
DRF 35-45% and GFR < 40	60	1.51	37	62.6	2.51	25.2	59	1.22	18	70.6	2.07	41.2
DRF < 25% and GFR < 40	23	1.18	39	55	3.24	10	37.6	1.14	24.8	38.2	0.84	23.6