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Quantitative SPECT of DMSA uptake by the kidneys: Assessment of reproducibility
Technical Note

David Groshar, Boaz Moskovitz, Elias Issaq, and Ofer Nativ

Departments of Nuclear Medicine and Urology, Bnai Zion Medical Center, Faculty of Medicine, Technion-Israel Institute of Technology, Haifa, Israel

Since its introduction in the early 1970s [1], the technetium dimercapto-succinic acid (Tc-DMSA) scan has been used as a static imaging agent to detect cortical defects in the kidneys [2–7]. Scintigraphy provides an image of the functional renal parenchyma, and the renal uptake of Tc-DMSA has been shown to correlate well with the effective renal plasma flow (ERPF), glomerular filtration rate (GFR) and creatinine clearance [8–10]. Thus, the renal uptake of Tc-DMSA provides a practical index for evaluation of individual renal function.

Measurement of the individual Tc-DMSA uptake by the kidneys has been described using planar and single photon emission tomography (SPECT) techniques [9, 11–18]. Quantitative SPECT of Tc-DMSA uptake by the kidneys (QDMSA) is a relatively simple technique, easily standardized and allows determination of individual and global renal function [12, 19]. In previous studies QDMSA was useful in separating normal from diseased kidneys [12]. Also, a good correlation was found between QDMSA and renal function measured by creatinine clearance in patients with a single kidney, validating the measurements in each kidney separately [19]. In the present report the precision of the method was evaluated to determine the reproducibility of QDMSA in the same patient.

METHODS

Patient population

Fifteen volunteers (4 females and 11 males), mean age 45-years-old (range 23- to 78-years-old), without known renal disease and having normal serum creatinine, were studied by two sequential quantitative SPECT examinations with a mean interval of four days apart (range 2 to 7 days). The studies were performed 4 to 6 hours after the intravenous injection of 2 mCi of the radiopharmaceutical. The exact dose injected was obtained by measuring the syringe in a dose calibrator before and after injection. Images of the injection site was obtained to detect extravascular injection of the radiopharmaceutical. Renal functional volume (cc), percentage of injected dose per cc of renal tissue (%ID/cc) and percent of individual renal uptake (%) of 30 normal kidneys were studied.

Key words: Tc-DMSA, effective renal plasma flow, DMSA, SPECT.

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Quantitative SPECT

Quantitative SPECT of DMSA uptake by the kidneys was measured using the same methodology as in previous studies [12, 19]. The amount of radioactivity was corrected for decay from the time of preparation to the time the study was actually performed. The studies were performed using a rotating gamma camera and an all-purpose, low energy collimator. Data acquisition lasted 20 minutes and required 120 projections (3° apart), and the entire study accumulated 3 to 5 $\times$ 10^5 counts. Raw data were reconstructed by filtered backprojection with a Hanning filter with a cutoff point of 0.5 cycle/cm. Data were analyzed and stored on an Elscint SP-1 computer with an optical disk. This 32-bit computer utilized our software program for quantitative SPECT calculations. After reconstruction, each image was sectioned at 1-pixel (0.68 cm) intervals in the transaxial, coronal and sagittal planes using a 64 $\times$ 64 byte matrix. Kidney volumes and radioactive concentration measurements were calculated on the reconstruction data using the threshold method. A threshold of 43% has been found to be highly reliable in a variety of phantoms and human tissues [20]. The study required only 20 minutes, and data analysis was practically automated and operator independent, with very low intra- and interobserver variability [20]. The method does not deny that tissue attenuation is present but assumes that cancellation of attenuation effects occurs. Consideration of the theoretical role of attenuation and the inability to correct for it has led us to use the empirical threshold method and to demonstrate its usefulness and reliability by extensive phantom studies and by the only meaningful gold standard: the *in vivo/in vitro* correlation [20].

In brief, the operator chooses the slice to define the kidney and draws a region of interest (ROI) around the organ. For volume measurements (cc) the number of pixels in all sections multiplied by the slice thickness is summed. For concentration measurements, the threshold value was subtracted from all pixels in the ROI in all slices. All the nonzero pixels that have higher counts than the threshold value are used to calculate the concentration. Counts per voxel are converted into concentration units (μCi/cc)

Table 1. Results of quantitative SPECT of DMSA uptake by the kidneys

	Quantitative SPECT						Differences					
	First			Second			1st-2nd			%		
Kidneys	Vol	%ID	Uptake	Vol	%ID	Uptake	Vol	%ID	Uptake	Vol	%ID	Uptake
1	232	6.3	14.6	229	6.5	14.9	3.0	−0.2	−0.3	1.3	−3.1	−2.0
2	213	5.0	10.6	213	4.7	10.0	0.0	0.3	0.6	0.0	6.2	6.2
3	157	10.8	17.0	162	9.4	15.2	−5.0	1.4	1.7	−3.1	13.8	10.7
4	240	4.2	10.1	215	4.2	9.0	25.0	0.0	1.1	10.9	0.0	10.9
5	251	5.1	12.8	227	5.9	13.4	24.0	−0.8	−0.6	10.0	−14.5	−4.5
6	264	5.6	14.7	262	5.8	15.3	2.0	−0.2	−0.6	0.76	−3.5	−4.0
7	220	6.3	14.1	225	5.5	12.5	−5.0	0.8	1.6	−2.2	13.6	12.0
8	266	7.7	20.5	281	7.0	19.8	−15.0	0.7	0.7	−5.5	9.5	3.5
9	282	5.3	15.2	272	5.2	14.2	10.0	0.1	1.0	3.6	1.9	6.8
10	172	12.6	21.8	176	11.0	19.4	−4.0	1.6	2.4	−2.3	13.6	11.6
11	198	8.2	16.3	189	8.7	16.7	9.0	−0.5	−0.4	4.6	−5.9	−2.4
12	194	10.4	20.3	201	10.0	20.3	−7.0	0.4	0.0	−3.5	3.9	0.0
13	176	11.1	19.6	179	12.0	21.5	−3.0	−0.9	−1.9	−1.6	−7.8	−9.2
14	207	9.7	20.3	214	8.7	18.7	−7.0	1.0	1.6	−3.3	10.9	8.2
15	235	8.6	20.2	242	7.5	18.4	−7.0	1.1	1.8	−2.9	13.7	9.3
16	216	7.2	15.5	202	6.8	13.8	14.0	0.4	1.8	6.7	5.7	12.4
17	194	5.0	9.7	192	5.0	9.6	2.0	0.0	0.1	1.0	0.0	1.0
18	160	10.2	16.3	158	9.5	15.0	2.0	0.7	1.3	1.3	7.1	8.4
19	254	4.5	11.4	260	4.4	11.4	−6.0	0.1	0.0	−2.3	2.5	0.1
20	253	5.3	13.4	237	6.0	14.2	16.0	−0.7	−0.8	6.5	−12.4	−5.7
21	257	5.5	14.1	254	5.7	14.6	3.0	−0.2	−0.5	1.2	−3.6	−3.5
22	228	7.6	17.6	237	6.9	16.5	−9.0	0.7	1.1	−3.9	9.6	6.4
23	279	6.9	19.4	288	6.1	17.8	−9.0	0.8	1.6	−3.2	12.3	8.6
24	278	5.5	15.4	272	5.2	14.2	6.0	0.3	1.2	2.2	5.6	8.1
25	159	12.1	19.3	161	10.4	16.8	−2.0	1.7	2.5	−1.2	15.0	13.8
26	183	9.0	16.6	184	8.9	16.4	−1.0	0.1	0.2	−0.5	1.1	1.2
27	168	11.2	18.8	155	11.8	18.4	13.0	−0.6	0.4	8.0	−5.2	2.1
28	167	11.0	18.5	185	11.5	21.4	−18.6	−0.5	−2.9	−10.5	−4.4	−14.5
29	228	9.9	22.7	216	9.5	20.6	12.0	0.4	2.1	5.4	4.1	9.7
30	189	8.5	16.0	196	7.4	14.4	−7.0	1.1	1.6	−3.6	14.0	10.5
mean	217	7.9	16.4	216	7.6	15.8	1.2	0.3	0.6	0.4	3.4	3.8
± SD	39	2.5	3.4	38.0	2.3	3.3	10.3	0.7	1.2	4.8	8.1	7.1

Abbreviations are: vol, volume; %ID, percent of injected dose per cc (X100); uptake, absolute kidney uptake (%); 1st-2nd, first minus second study; %, difference between first and second study expressed as a % of the mean value of both studies.

using the regression line obtained previously by phantom measurements. The percentage of injected dose per cc of renal tissue (%ID/cc) was calculated using this value corrected for radioactivity decay. Kidney uptake is then obtained by multiplying kidney volume (cc) and %ID/cc.

Statistical analysis

Values are expressed by their mean ± 1 SD. For each pair of quantitative SPECT determinations of volume, %ID/cc and uptake, the difference between first and second studies and the least square linear regression coefficient were determined. Also, the difference between the first and second studies was expressed as a percentage of the mean value of the two studies. The precision of the method is represented by the SD of these differences [21].

RESULTS

Volume

The mean volume value was 217 cc ± 39 cc (range 157 cc to 282 cc) for the first study and 216 cc ± 38 cc (range 155 cc to 288 cc) for the second study. A good correlation was found between first and second studies ($y = 0.94x + 11.0$; $r = 0.96$). The mean difference between first and second studies was 1.2 cc ± 10.3 cc (range −18cc to 25cc), and the mean difference between the first and second studies as a percentage of the mean value of the two studies was 0.46% ± 4.8 (range −10.5% to 10.9%). In 22 kidneys the difference was less than 5%, in five kidneys it was between 5% and 9.9%, and in three kidneys the change was between 10% and 11% (Table 1).

%ID/cc

The mean %ID/cc (X100) value was 7.88 ± 2.5 (range 4.2 to 12.6) for the first study and 7.57 ± 2.33 (range 4.2 to 12) for the second study. A good correlation was found between first and second studies ($y = 0.896x + 0.005$; $r = 0.96$). The mean difference between first and second studies was 0.3 ± 0.69 (range −0.9 to 1.7), and the mean difference between the first and second studies as a percentage of the mean value of the two studies was 3.4% ± 8.1 (range −14.5% to 15%). In 11 kidneys the difference was less than 5%; in nine kidneys it was between 5% and 9.9% and in 10 kidneys the change was between 10% and 15% (Table 1).

Uptake

The mean uptake value was 16.4% ± 3.4% (range 9.7% to 22.7%) for the first study and 15.8% ± 3.3% (range 9% to 21.5%) for the second study. A good correlation was found between the first and second studies ($y = 0.91x + 0.89$; $r = 0.93$). The mean

difference between first and second studies was 0.62% ± 1.2% (range −2.9% to 2.5%), and the mean difference between the first and second studies as a percentage of the mean value of the two studies was 3.8% ± 7.1 (range −14.5% to 15%). In 11 kidneys the difference was less than 5%, in eleven kidneys it was between 5% and 9.9%, and in 8 kidneys the change was between 10% and 15% (Table 1).

DISCUSSION

Rather than accurate measurement of the renal function, serial monitoring of renal function is the major concern in the management of patients with renal disease [22–24]. Several radionuclide techniques have been proposed to evaluate individual kidney function [4, 8, 22, 24]. The use of radionuclides in the study of the kidneys relies on their functional ability to provide quantitative measurement information [23]. The main applications are in the determination of residual renal function, serial measurements of renal function when some intervention is planned or monitoring renal function to detect progressive loss of function [4, 23, 24].

Renal cortical scintigraphy using Tc-DMSA has been used for detecting renal cortical defects [3, 24–26]. Functional imaging of the proximal renal tubular mass is obtained that is dependent on the renal blood flow and proximal tubular cell membrane transport function [8]. The quantitation of Tc-DMSA uptake in each kidney separately provides a practical index of absolute renal function [8]. Quantitation of Tc-DMSA uptake by the kidneys using planar scintigraphy has been reported [9, 11, 13–18]. However, the need for correction for depth and background limits the usefulness and prevents widespread acceptance of planar scintigraphy for quantitation of Tc-DMSA uptake by the individual kidney [23].

The application of quantitative SPECT of DMSA uptake in the kidneys to evaluate the individual renal function has been reported [12, 15, 19]. Absolute quantitation by SPECT is feasible and has been shown to be a clinically reliable and useful technique [12, 19, 27–29]. It can be considered in two levels: measurement of volumes and measurement of absolute radionuclide concentrations. Thus, QDMSA provides information concerning the percent of injected dose per cc of renal tissue and functional kidney volumes, and by multiplying these two parameters individual kidney uptake is obtained. It has been shown that the individual kidney uptake of DMSA measured by SPECT is useful in separating normal from diseased kidneys [12]. Also, a good correlation was found between quantitative SPECT of DMSA uptake in single kidneys and renal function measured by creatinine clearance (r = 0.76) [19] and serum creatinine (r = 0.83 to 0.89) [12, 19], validating the measurements in each kidney separately.

In a recent report of the radionuclides in the nephrourology committee on renal clearance [24], Cr-51-EDTA was suggested as the agent of choice for renal function evaluation. However, this technique provides information on global renal function, has poor imaging characteristics and lacks commercial availability [24]. Also, the blood and urine sampling requirements and the length of the study limit the routine use of these method [22, 24]. In another recent report on the precision of repeated plasma clearance measurements of Cr-51-EDTA on healthy volunteers it was found that the overall precision of the measurements was 8.4% [30]. In 9 out of 12 volunteers (75%) the difference between the first and second measurements was less than 10%, and in the remaining three volunteers the change was less than 18% [30]. These findings were considered better than those obtained with any method based on urine samples of inulin or creatinine [30].

In the present report the precision (reproducibility) of QDMSA was studied. To evaluate the precision of the method, QDMSA was performed twice with a mean interval of four days apart in normal volunteers. A precision similar to that obtained with the plasma clearance of Cr-51-EDTA [30] was found when measuring the QDMSA parameters twice in the same patient. For volume measurements, 27 out of 30 kidneys (90%) showed less than 10% difference between the first and second studies, with a precision of 4.8%. For %ID/cc measurements, 20 out of 30 kidneys (67%) showed less than 10% difference and the remaining 10 kidneys showed a difference of less than 15% between the first and second study with an overall precision of 8.1%. For the uptake determination used as the index of renal function, 22 out of 30 kidneys (73%) showed less than a 10% difference and the remaining 8 kidneys showed a difference of less than 15% between the first and second studies, with an overall precision of 7.1%.

In conclusion, quantitative SPECT measurement of Tc-DMSA uptake by the kidneys is a reproducible method that can reliably be used to monitor serial changes in individual renal function.

Reprint requests to Dr. D. Groshar, Department of Nuclear Medicine, Bnai Zion Medical Center, POB 4940, Haifa, Israel, 31048.

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