# Kidney Function After Radical Nephrectomy: Assessment by Quantitative SPECT of $^{99m}$Tc-DMSA Uptake by the Kidneys

Simona Ben-Haim, Vladimir Sopov, Avi Stein, Boaz Moskovitz, Avi Front, Yoel Mecz, Levy Las, Alexander Kastin, Ofer Nativ, and David Groshar

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

To determine the function of the remaining contralateral kidney after the removal of a functioning kidney, 30 consecutive patients (18 men, 12 women; average age, 67 y; age range, 34–87 y) who were undergoing unilateral radical nephrectomy were evaluated by sequential quantitative $^{99m}$Tc-dimercaptosuccinic acid (DMSA) SPECT (QDMSA) studies. **Methods:** The 30 patients were undergoing radical nephrectomy for renal tumors. The first study was done before surgery. Follow-up studies were performed 2–23 mo after surgery. Clinical evaluations and determinations of serum creatinine level were performed at the same time as the QDMSA studies. **Results:** The relative contribution of the resected kidneys to the global renal function before surgery was 43.2% ± 7.3%. After surgery the uptake of the remaining kidney increased from 13.4% ± 4.0% to 18.3% ± 5.8% ($t$ = 5.7; $P$ = 0.0000). The relative function of the remaining kidney increased from 56.8% ± 7.1% to 79.1% ± 23.6% ($t$ = 4.9; $P < 0.0001$) of the global renal function before nephrectomy. Increases in the renal volume (from 211 ± 62 cm$^3$ to 229 ± 68 cm$^3$; $t$ = 4.5; $P$ = 0.0001) and in the percentage injected dose per cubic centimeter (%ID/cm$^3$) of the remaining kidney (from 0.066 ± 0.02 %ID/cm$^3$ to 0.085 ± 0.03 %ID/cm$^3$; $t$ = 4.6; $P$ = 0.0001) were associated with this change. Nine patients had 2 follow-up studies performed 3–4 mo after surgery and 12–14 mo after surgery. The volume of the remaining kidney (209.22 ± 46.20 cm$^3$ versus 217.88 ± 58.85 cm$^3$; $t$ = 0.962; $P$ = 0.364), the %ID/cm$^3$ (0.09 ± 0.016 %ID/cm$^3$ versus 0.093 ± 0.025 %ID/cm$^3$; $t$ = 0.362; $P$ = 0.726), and the percentage uptake (19.26% ± 4.45% versus 20.11% ± 7.01%) did not change significantly between these 2 QDMSA studies. **Conclusion:** The results of this study suggest that adaptive changes causing hyperfunction of the remaining kidney may occur after nephrectomy of a functioning kidney in adults. These changes occur soon after surgery, persist for at least 1 y, and are evident on QDMSA studies.

**Key Words:** radionuclide imaging; quantitative SPECT; $^{99m}$Tc-DMSA; nephrectomy

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After removal of 1 kidney because of disease, cancer, injury, or transplant donation, functional adaptation and compensatory hypertrophy of the remaining kidney take place. Compensatory renal growth has been shown in studies of animals and humans (*1–4*). Kidney enlargement has been estimated radiologically by an increase in length or in some indices using the length, width, or volume (*1,3,4*). Renal volume determination by sonography has shown a 20%–100% increase in the remaining kidney volume (*3,4*). Functional adaptation of the remaining kidney after unilateral nephrectomy has a rapid onset, more so for glomerular function than for tubular function. The creatinine clearance increases to 70%–75% of the preoperative creatinine clearance within several weeks postoperatively (*5*) and remains stable for more than 10 y after nephrectomy (*6–8*). The serum creatinine level usually increases up to 20% above baseline, remaining within the normal range (*9,10*). The effective renal plasma flow increases by about 30% as early as 1 wk after surgery (*8*) and remains above the prenephrectomy level even after 10 y.

The renal uptake of $^{99m}$Tc-dimercaptosuccinic acid (DMSA) has been shown to correlate well with effective renal plasma flow, glomerular filtration rate, and creatinine clearance (*11–13*). Quantitative SPECT of $^{99m}$Tc-DMSA (QDMSA) uptake by the kidneys has been shown to be useful in separating normal from diseased kidneys (*14*), to correlate well with creatinine clearance and serum creatinine level in patients with single kidneys (*14,15*), and to be a reproducible method to monitor serial changes in individual renal function (*16*). The aim of this investigation was to evaluate the volume and function of the remaining kidney after resection of a functioning kidney by QDMSA studies.

## MATERIALS AND METHODS

### Patient Population

Forty-five patients with renal tumors were enrolled prospectively in the study. Fifteen of these patients were excluded: 5 were lost to follow-up, 2 died after surgery, 2 had diagnoses of benign renal cysts and did not have surgery, 2 had hypofunctioning of the resected kidney, 1 refused surgery, 1 had widespread disease with

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For correspondence or reprints contact: Simona Ben-Haim, MD, DSc, Department of Nuclear Medicine, Carmel Medical Center, Haifa, Israel 34362.

lung metastases and did not have surgery, 1 had partial infiltration of the radiopharmaceutical dose and the study was technically inadequate, and 1 did not have follow-up of his serum creatinine level at the time of the QDMSA study after surgery. The study population consisted of the remaining 30 patients (18 men, 12 women; average age, 67 y; age range, 34–87 y). Twelve (40%) patients had hypertension, 2 (6%) had diabetes, and 1 (3%) had nephrolithiasis of the remaining kidney. All patients underwent radical nephrectomy of a functioning kidney. Twenty-six patients had malignant tumors: 24 had renal cell carcinoma, 1 had a transitional cell carcinoma of the ureter, and 1 had a retroperitoneal liposarcoma. Four patients had benign tumors of the kidney: 1 had a cystic nephroma, 1 had a simple cyst, 1 had multilocular renal cysts, and 1 had perinephric pseudocysts. Each patient had 2 or 3 sequential QDMSA studies. A total of 69 QDMSA studies were evaluated. All patients had a study performed immediately before surgery. A second study was performed 2–23 mo after surgery. In 9 of these patients an early follow-up study was performed 2–6 mo after surgery (early follow-up) and another study was performed 12–17 mo after surgery (late follow-up). At the same time, patients were evaluated clinically, and serum creatinine levels were determined.

### Quantitative SPECT

The technique has been reported in detail (*14*) and is described briefly. Quantitative SPECT of $^{99m}$Tc-DMSA uptake by the kidneys was measured using the same methodology as in previous studies (*14,15,17*). The patient was injected with 75–150 MBq (2–4 mCi) $^{99m}$Tc-DMSA, and SPECT was performed after 4–6 h. The exact dose injected was obtained by measurement of the syringe in the dose calibrator before and after the injection. The amount of radioactivity was corrected for decay from the time of injection to the time the study was actually performed. The studies were performed using a rotating, single-head $\gamma$ camera equipped by an all-purpose, low-energy collimator (Apex 415-ECT; Elscint, Ltd., Haifa, Israel). Data acquisition lasted 20 min, with 120 projections, 3° apart, accumulating 3–5 $\times$ $10^5$ counts per study. The raw data were reconstructed by filtered backprojection using a Hann filter with a cutoff of 0.5 cycle/cm. 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 transaxial reconstruction data using the threshold method. After obtaining a series of phantom measurements using volumes of 30–3800 cm$^3$ and concentrations between 0.375 and 135 kBq/cm$^3$, a threshold value of 43% was found to be optimal for $^{99m}$Tc (*15,18*).

On the transaxial slices the operator identifies the slice to define the kidney and draws a region of interest around the organ. For volume measurements (in cubic centimeters) the number of pixels containing activity greater than the threshold in all sections multiplied by the slice thickness is calculated. For concentration measurements, the threshold value is subtracted from all pixels in the regions of interest in all slices. All nonzero pixels with higher counts than the threshold value are used to calculate the concentration. Counts per voxel are converted into concentration units (in kBq/cm$^3$) using the regression line obtained previously by phantom measurements (*18*). The percentage injected dose per cubic centimeter (%ID/cm$^3$) of renal tissue is calculated using this value corrected for radioactivity decay. Kidney uptake is then obtained by multiplying kidney volume (in cubic centimeters) and %ID/cm$^3$ (*14*). Excellent correlation ($r$ = 0.99) has been found between actual concentration in kidney phantoms and SPECT-measured concentration (*14*), and a coefficient of variation for replicate studies of <2% was also found in phantom studies (*19*), indicating that the method can be used reliably to measure the concentration of $^{99m}$Tc-DMSA in the kidneys.

### Statistical Analysis

The $t$ test and paired $t$ test were used to compare preoperative versus postoperative and remaining versus resected kidney values of volume in cubic centimeters, %ID/cm$^3$, and percentage uptake as well as serum creatinine levels. Values are expressed as mean $\pm$ SD. Linear regression analysis was used to evaluate the correlation between serum creatinine level and renal uptake before and after surgery.

## RESULTS

Patient characteristics and results of QDMSA studies are summarized in Table 1 and Table 2. Before surgery the operated kidneys contributed 43.2% $\pm$ 7.3% to the global renal function (right and left kidneys), and the contralateral kidneys contributed 56.8% $\pm$ 7.3%. The uptake of $^{99m}$Tc-DMSA before surgery in the contralateral kidney was 13.4% $\pm$ 4.0%. This increased to 18.3% $\pm$ 5.8% ($t$ = 5.7; $P$ = 0.0000). This increase was associated with an increase in renal volume from 211 $\pm$ 62 cm$^3$ to 229 $\pm$ 68 cm$^3$ ($t$ = 4.5; $P$ = 0.0001) as well as an increase in %ID/cm$^3$ from 0.066 $\pm$ 0.02 %ID/cm$^3$ to 0.085 $\pm$ 0.03 %ID/cm$^3$ ($t$ = 4.6; $P$ = 0.0001). In the 9 patients who had early and late QDMSA studies performed after surgery there was no significant change in the contralateral kidney uptake (19.26% $\pm$ 4.45% versus 20.11% $\pm$ 7.01%; $t$ = 0.457; $P$ = 0.6599), renal volume (209.22 $\pm$ 46.2 cm$^3$ versus 217.88 $\pm$ 58.85 cm$^3$; $t$ = 0.962; $P$ = 0.364), and %ID/cm$^3$ (0.09 $\pm$ 0.016 versus 0.093 $\pm$ 0.025 %ID/cm$^3$; $t$ = 0.362; $P$ = 0.726) between these 2 examinations. After surgery the function of the remaining kidney increased to 79.1% $\pm$ 23.6% of total (both kidneys) preoperative renal function compared with 56.8% $\pm$ 7.3% preoperatively ($t$ = 4.9; $P$ < 0.001).

Serum creatinine levels before surgery were within normal limits in all patients, except for 2 (6.6%) with creatinine levels of 1.7 and 2.0 mg/dL (patients 1 and 27; Table 1). The average preoperative serum creatinine level was 1.04 $\pm$ 0.28 mg/dL. It increased to 1.55 $\pm$ 0.46 mg/dL after surgery ($t$ = 7.695; $P$ = 0.0000). In the 9 patients who had their creatinine levels determined at early and late follow-up after surgery, no significant change was found between those levels (1.433 $\pm$ 0.40 mg/dL versus 1.45 $\pm$ 0.40 mg/dL; $t$ = 0.80; $P$ = 0.447). Abnormal serum creatinine levels (>1.6 mg/dL) were more common after surgery, occurring in 6 (20%) of the patients. In the 6 patients with elevated creatinine levels after surgery, the uptake of $^{99m}$Tc-DMSA in the nonoperated kidney before surgery was 11.2% $\pm$ 3.0% compared with 14.3% $\pm$ 4.0% in the nonoperated kidneys of patients with postoperative serum creatinine levels < 1.6 mg/dL ($t$ = 2.007; $P$ = 0.0545). Otherwise, no change in the patients' clinical status occurred after surgery.

**TABLE 1**
Patient Characteristics and QDMSA SPECT Data Before and After Nephrectomy

| | | | Creatinine (mg/dL) | | QDMSA: Removed kidney, preop | | | QDMSA: Contralateral kidney, preop | | | QDMSA: Contralateral kidney, postop | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Patient no. | Age (y) | Sex | Preop | Postop | Volume (cm³) | %ID/cm³ | Uptake (%) | Volume (cm³) | %ID/cm³ | Uptake (%) | Volume (cm³) | %ID/cm³ | Uptake (%) | Follow-up (mo) |
| 1 | 71 | M | 1.7 | 2.3 | 143 | 0.025 | 3.55 | 201 | 0.036 | 7.3 | 197 | 0.039 | 7.7 | 8 |
| 2 | 65 | M | 1.0 | 1.6 | 152 | 0.04 | 6.1 | 240 | 0.053 | 12.7 | 250 | 0.062 | 15.6 | 2 |
| 3 | 77 | M | 1.1 | 1.6 | 180 | 0.048 | 8.8 | 198 | 0.048 | 9.5 | 226 | 0.047 | 10.7 | 7 |
| 4 | 65 | F | 1.0 | 1.1 | 179 | 0.08 | 14.4 | 191 | 0.09 | 17.0 | 201 | 0.120 | 24.7 | 2 |
| 5 | 34 | F | 0.4 | 0.9 | 229 | 0.071 | 16.4 | 198 | 0.082 | 16.4 | 232 | 0.101 | 23.5 | 10 |
| 6 | 71 | M | 1.0 | 2.8 | 252 | 0.03 | 7.6 | 328 | 0.046 | 15.2 | 364 | 0.042 | 15.4 | 11 |
| 7 | 63 | M | 1.4 | 1.6 | 220 | 0.06 | 13.2 | 220 | 0.064 | 14.2 | 242 | 0.079 | 19.2 | 3 |
| 8 | 52 | M | 1.1 | 1.3 | 291 | 0.031 | 9.1 | 437 | 0.039 | 17.4 | 471 | 0.029 | 13.9 | 7 |
| 9 | 44 | M | 0.8 | 1.5 | 193 | 0.039 | 7.7 | 256 | 0.037 | 9.54 | 277 | 0.066 | 18.3 | 3 |
| 10 | 68 | M | 1.0 | 1.6 | 240 | 0.056 | 13.5 | 250 | 0.05 | 12.5 | 258 | 0.045 | 11.6 | 12 |
| 11 | 70 | F | 0.9 | 1.3 | 192 | 0.067 | 13.1 | 196 | 0.07 | 13.9 | 208 | 0.091 | 19.0 | 13 |
| 12 | 53 | M | 1.0 | 1.4 | 208 | 0.059 | 12.4 | 225 | 0.081 | 18.2 | 260 | 0.093 | 24.3 | 14 |
| 13 | 87 | M | 1.2 | 2.5 | 220 | 0.046 | 10.3 | 220 | 0.062 | 13.8 | 210 | 0.082 | 17.4 | 23 |
| 14 | 66 | F | 0.8 | 1.4 | 231 | 0.039 | 9.2 | 250 | 0.039 | 9.9 | 259 | 0.058 | 15.3 | 10 |
| 15 | 73 | F | 1.0 | 1.5 | 135 | 0.066 | 9.0 | 121 | 0.079 | 9.6 | 137 | 0.097 | 13.3 | 3 |
| 16 | 75 | M | 1.0 | 1.4 | 174 | 0.056 | 9.8 | 169 | 0.066 | 11.2 | 204 | 0.101 | 20.7 | 14 |
| 17 | 55 | F | 0.9 | 1.1 | 166 | 0.07 | 11.7 | 168 | 0.068 | 11.5 | 211 | 0.072 | 15.1 | 3/12* |
| 18 | 52 | M | 1.1 | 1.4 | 251 | 0.03 | 8.6 | 229 | 0.05 | 12.3 | 270 | 0.098 | 26.6 | 3/14* |
| 19 | 73 | F | 1.0 | 1.4 | 131 | 0.114 | 14.9 | 159 | 0.105 | 16.6 | 185 | 0.169 | 31.2 | 3 |
| 20 | 79 | M | 0.9 | 1.3 | 165 | 0.06 | 9.4 | 180 | 0.06 | 10.4 | 180 | 0.119 | 21.5 | 3/12* |
| 21 | 74 | F | 0.9 | 1.5 | 132 | 0.11 | 14.5 | 159 | 0.11 | 17.0 | 174 | 0.119 | 20.7 | 3/13* |
| 22 | 69 | M | 1.2 | 1.7 | 139 | 0.03 | 4.6 | 196 | 0.05 | 9.2 | 172 | 0.117 | 20.2 | 8 |
| 23 | 80 | M | 1.1 | 1.5 | 125 | 0.11 | 13.9 | 203 | 0.12 | 24.5 | 197 | 0.119 | 23.6 | 3 |
| 24 | 80 | M | 1.2 | 1.9 | 168 | 0.06 | 9.6 | 232 | 0.065 | 15.0 | 210 | 0.100 | 20.6 | 3/12* |
| 25 | 66 | M | 1.0 | 1.2 | 204 | 0.06 | 11.6 | 259 | 0.05 | 12.2 | 310 | 0.046 | 16.5 | 2/11* |
| 26 | 73 | F | 0.9 | 1.2 | 124 | 0.074 | 9.24 | 224 | 0.086 | 19.3 | 288 | 0.119 | 34.0 | 3/17* |
| 27 | 76 | M | 2.0 | 2.3 | 173 | 0.041 | 7.12 | 144 | 0.055 | 7.9 | 135 | 0.081 | 14.3 | 6/12* |
| 28 | 76 | F | 0.8 | 1.0 | 114 | 0.063 | 7.24 | 172 | 0.094 | 16.3 | 155 | 0.112 | 17.3 | 6 |
| 29 | 71 | F | 0.9 | 1.5 | 198 | 0.057 | 11.3 | 159 | 0.052 | 8.37 | 159 | 0.036 | 5.75 | 4 |
| 30 | 46 | F | 0.8 | 1.1 | 145 | 0.09 | 12.4 | 170 | 0.09 | 15.4 | 184 | 0.090 | 16.0 | 3/12* |

*Early/late follow-up.
Preop = preoperative; postop = postoperative.

## DISCUSSION

After removal of 1 kidney compensatory growth changes occur in the remaining kidney (*20*). Increased renal blood flow and glomerular pressures may cause a mechanical stimulation for renal growth. Humoral and neural mechanisms are also possible causative factors (*21,22*). Hyperplasia and hypertrophy are characteristic of the compensatory growth. Several studies have examined the effects of renal donation on the contralateral kidney. Hypertension, mild proteinuria, and a decrease in creatinine clearance may develop in long-term follow-up, but these are no greater than those in the normal population. In spite the known functional and structural changes after nephrectomy, donor renal function remains stable for many years after renal donation (*8,22–25*).

**TABLE 2**
Quantitative DMSA SPECT Before and After Nephrectomy

| Parameter | Resected kidney, preop | Contralateral kidney, preop | Contralateral kidney, postop |
|---|---|---|---|
| Volume (cm³) | 186 ± 45 | 211 ± 62 | 229 ± 68* |
| %ID/cm³ | 0.059 ± 0.02 | 0.066 ± 0.02 | 0.085 ± 0.03* |
| Uptake (%) | 10.3 ± 3.2 | 13.4 ± 4.0 | 18.3 ± 5.8† |

*$P = 0.0000$.
†$P = 0.0001$.
Preop = preoperative; postop = postoperative.

Renal cortical scintigraphy with $^{99m}$Tc-DMSA is being used for functional imaging of the proximal renal tubular mass, which is dependent on renal blood flow and on the proximal tubule cell membrane transport function (*13,26*). Quantitation of $^{99m}$Tc-DMSA uptake in each kidney separately provides a practical index of absolute renal function (*11–15,17,27–30*). Absolute quantitation of $^{99m}$Tc-DMSA uptake by the kidneys has been used in separating normal from diseased kidneys (*14*). A good correlation ($r = 0.76$) between QDMSA and creatinine clearance (*15*) and between QDMSA and serum creatinine (*14,15*) has been reported in patients with a single kidney. QDMSA has also been shown to be a reproducible method that can be used to monitor serial changes in individual renal function with a precision of 7.1% (*16*).

Patients in this group, after nephrectomy because of renal tumor, showed a compensatory response in the remaining kidney. The compensatory increase in the absolute uptake of $^{99m}$Tc-DMSA by the remaining kidney was associated with an increase in the renal volume and an increase in %ID/cm$^3$. The function of the remaining kidney increased to 79.1% of the total preoperative renal function compared with 56.8% before surgery. The compensatory changes seen early after nephrectomy remain unchanged between the early and late follow-up studies, probably reaching a plateau at this time. These findings agree with similar observations made in different patient groups undergoing nephrectomy. Kidney enlargement of 20%–100% was shown by sonography during long-term follow up (*2–4*). Anderson et al. (*8*) measured renal function on $^{131}$I-labeled *o*-iodohippurate scans and found an increase in the effective renal plasma flow of 32.5% by 1 wk and 30.1% within 1 y over the baseline preoperative values after renal donation. The mean postoperative effective renal plasma flow represented 66% of the total preoperative effective renal plasma flow. Pabico et al. (*31*) found a 55% increase in the effective renal plasma flow calculated with *p*-aminohippurate clearance within 10–14 d after donor nephrectomy. Vincenti et al. (*5*) found a creatinine clearance of 72% of the preoperative value 1 wk after nephrectomy.

In 27 patients who were monitored for more than 20 y, Regazzoni et al. (*25*) found an immediate increase in creatinine clearance of about 34%, peaking at 2–6 mo postoperatively and then reaching a plateau. Smith et al. (*32*) monitored 40 patients for 5–30 y (mean, 11.8 y) after unilateral nephrectomy. Serum creatinine levels increased in these patients by 17% (from 1.1 to 1.29 mg/dL), although this increase was not statistically significant. Measures of glomerular function (serum creatinine, creatinine clearance, or inulin clearance) are remarkably stable with time after unilateral nephrectomy. The glomerular filtration rate after donor nephrectomy generally stabilizes at 75%–85% of the predonation values, and serum creatinine increases by approximately 20% (*5–8,10,33–35*). Our findings agree with these reports, which also showed an increase in serum creatinine levels in all patients. However, this increase was more pronounced than that in our patients, reaching to 55% above baseline. This finding may associated with the fact that our patients were older and a significant percentage had other disorders affecting renal function, such as hypertension, diabetes, and nephrolithiasis of the remaining kidney.

This study also assessed the possibility of predicting long-term follow-up results on the basis of the preoperative evaluation of the contralateral kidney function, indicated by the absolute uptake of $^{99m}$Tc-DMSA by that kidney. In the 6 patients who had significant increases in creatinine levels after surgery, reaching the abnormal range (>1.6 mg/dL), the preoperative QDMSA data suggest a relatively reduced preoperative uptake (although not statistically significant) in the nonoperated kidney. If, indeed, it is possible to predict preoperatively the postoperative renal function on the basis of QDMSA, this study may be potentially useful in identifying a subset of patients who may need consideration of a different surgical intervention (e.g., nephron-sparing surgery), a special diet (e.g., dietary restriction of protein and phosphate), a change in medication to prevent renal function deterioration (angiotensin-converting enzyme inhibitors, heparin, or calcium channel blockers), and a closer follow-up for the evaluation of the possible deterioration of renal function after surgery. However, our findings are not statistically significant, possibly because of the small number of patients and overall relatively preserved renal function in this patient group. No patient developed renal failure after surgery.

## CONCLUSION

Compensatory hyperfunction is common after nephrectomy because of renal tumor and can be shown on QDMSA. Compensatory hyperfunction is caused by an increase in renal volume and in %ID/cm$^3$ in the remaining kidney, occurs early after surgery, and remains essentially unchanged for at least 1 y after surgery. The ability to identify preoperatively a high-risk group of patients with significant postsurgical deterioration of renal function needs to be further evaluated.

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