4. Bubeck B. Renal clearance determination with one blood sample: improved accuracy and universal applicability by a new calculation principle. *Semin Nucl Med* 1993;23: 73–86.
5. Bland M, Altman D. Statistical methods for assessing agreement between two methods of clinical measurements. *Lancet* 1986;II:307–310.
6. Kotzerke J, Moog F, Kleinschmidt K, Reske SN. New data on the reproducibility of ^{99m}Tc-MAG3-clearance. *Eur J Nucl Med* 1996;23:1074.
7. Møller ML, Widding A. Reproducibility of ^{99m}Tc-MAG3 compared to ^{99m}Tc-DTPA renography: day-to-day variation in estimates of renal function. *Eur J Nucl Med* 1996;23:1189.
8. Grady H, Bullivant E. Renal blood flow varies during normal activity in conscious unrestrained rats. *Am J Physiol* 1992;262:R926–R932.
9. Fauvel J, Hadj-Aissa A, Laville M, et al. Stress-induced renal functional alterations in normotensives. *Am J Hypertens* 1991;4:955–958.
10. Frokiaer J, Knudsen L, Flo C, et al. Reproducibility of iodine-123-hippuran renoscintigraphy in the normal pig at various flow rates. *Scand J Urol Nephrol* 1989; 125(suppl):87–93.
11. Rehling M, Nielsen BV, Pedersen EB, Nielsen LE, Hansen HE, Bacher T. Renal and extrarenal clearance of ^{99m}Tc-MAG3: a comparison with ^{125}I-OIH and ^{51}Cr-EDTA in patients representing all levels of glomerular filtration rate. *Eur J Nucl Med* 1995;22:1379–1384.
12. Wustenberg P, Hortian B, Weirich S, Kerber A, Kuhnle H. Reproducible determination of the glomerular filtration rate (GFR) and the effective renal plasma flow (ERPF) in conscious rats using inulin and *p*-aminohippuric acid. *J Exp Anim Sci* 1991;34:13–20.

Comparison of Radionuclide Scrotal Blood-Pool Index Versus Gonadal Venography in the Diagnosis of Varicocele

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The purpose of our study was to assess the value of a radionuclide scrotal blood-pool index (SBPI) in diagnosing and grading clinical and subclinical varicocele. **Methods:** Scrotal scans were performed on 1360 infertile patients. Thirty fertile patients with a normal scrotum on palpation served as controls. The patients' red blood cells were labeled in vivo by administration of stannous ions of pyrophosphate followed by the intravenous administration of ^{99m}Tc-pertechnetate. The scans initially were inspected visually and, when bilateral varicocele was excluded, a computerized analysis of the ratio of the blood-pool activity in each hemiscrotum (SBPI) permitted accurate grading of the varicocele. A subgroup of 224 patients was selected randomly and had gonadal venography. The results of physical examination, scrotal scan, gonadal venography and semen analysis were compared. **Results:** Normal values of SBPI (0.9–1.1) were derived from the control group. There was a 93.5% correlation between palpation and SBPI grade in diagnosing palpable varicocele. When compared to gonadal venography, subclinical varicocele was demonstrated by scrotal scan in 54.8% of infertile male patients with abnormal semen analysis, normal female partners and no other cause of infertility. Of these patients, 32.6% had, unexpectedly, Grade 2 or 3 varicocele. Right and bilateral varicocele were demonstrated three times as often by scrotal scan than by palpation. SBPI was accurate in diagnosing recurrent varicocele but there was a low correlation (61.1%) between SBPI and gonadal venography grade. There was a high correlation between SBPI grade and sperm analysis grade. **Conclusion:** SBPI grading of varicocele was validated as an accurate, quantitative and noninvasive method of grading varicocele, equivalent to the grading system by palpation in a large group of infertile patients. The main contribution of SBPI was in detecting and grading subclinical varicocele in infertile patients with no other cause of infertility. SBPI also was accurate in diagnosing but not in grading recurrent varicocele.

Key Words: scrotal blood-pool index; gonadal venography; semen analysis; clinical and subclinical varicocele

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Varicocele is defined as a pathologic distention of the veins of the pampiniform plexus. Reflux of blood from the internal spermatic vein (ISV) resulting from the absence or incompetence of the venous valves may be present (*1*).

Varicocele occurs in 8% to 20% of men in the general population (*2–4*) and in 17% of men with proven fertility (*5*). The incidence of varicocele in men attending infertility clinics ranges from 19% to 41% (*6*). In a multicenter study by the World Health Organization (*7*), varicocele was present in 11.7% of the total male population and in 25.4% of the men with abnormal semen parameters who were evaluated for infertility of at least 1 yr duration.

Subclinical varicocele is defined as reflux through the internal spermatic vein without any palpable distention of the pampiniform plexus (*8*). Clinical varicocele is graded as Grade 1, 2 or 3 by the classification of Dubin and Amelar (*9*). Some authors suggest that larger clinical varicoceles are more likely to damage spermatogenesis than smaller clinical varicoceles (*7,10,11*). Progressive deterioration in sperm concentration and motility also was reported (*7*).

The purpose of our study was to assess the value of radionuclide blood-pool imaging of the scrotum in diagnosing and grading infertile patients with clinical or subclinical varicocele. A quantitative evaluation of the results was performed and the results were expressed as the nuclear scrotal blood-pool index (SBPI). The results of scrotal scintigraphy were correlated with the findings on clinical examination, gonadal venography and semen analysis.

MATERIALS AND METHODS

Scrotal scans, performed on 1360 patients (age range 17–52 yr; mean age 30.6 yr) from 1988 to 1994, were evaluated prospectively. The subjects were referred to our nuclear medicine department from infertility clinics and had been infertile for at least 12 mo before the evaluation. All these patients had at least three abnormal semen analyses. Primary palpable varicocele was present in 458 patients and recurrent varicocele in 135 patients. In 767 patients with normal women partners, no apparent cause of infertility was found after an extensive work-up and subclinical varicocele was suspected. From the group of 1360 patients, 224

patients were chosen randomly and had gonadal venography. The control group consisted of 30 patients, who had scintigraphy with in vivo red blood cells labeling for other reasons (cardiac multigated studies and diagnosis of liver hemangiomas). All these patients were under the age of 30, fertile, had at least two normal semen analyses and had no palpable varicocele.

Palpation of the scrotum and grading of varicocele was performed by an experienced staff urologist according to the classification of Dubin and Amelar (*9*).

Scintigraphic evaluation was performed with the patient in the upright position with abduction of the legs. The penis was taped to the midline of the anterior abdominal wall. A lead strip was placed on the median raphe dividing the scrotum into two compartments. The patients performed the valsalva maneuver during data acquisition. The patients' red blood cells were labeled in vivo by injecting 0.15 μg/kg of stannous pyrophosphate 20 min before the intravenous administration of 370 MBq (10 mCi) ^{99m}Tc-pertechnetate. Imaging was performed using a large field-of-view camera equipped with a parallel-hole, low-energy collimator. Twenty minutes after radionuclide administration, a 600–800K static scan was obtained depicting the blood-pool distribution in the scrotal area. Normal scrotal uptake was considered equal to the surrounding soft-tissue value.

An initial visual analysis was performed in all cases by an experienced nuclear medicine physician. The visual analysis enabled a qualitative detection of the presence of subclinical, unilateral or bilateral varicocele. When bilateral varicocele was demonstrated, the scrotal scan was designated positive and the SBPI was not computed.

Bilateral varicocele was assigned a visual grade, which was satisfactory for preoperative evaluation and follow-up in most cases. However, we found that upper hips and crural area cannot serve as normal background due to dilated veins in some patients. A quantitative grade could not be determined confidently in patients with bilateral varicocele. The main purpose of our study was to determine the value of varicocele grading by a quantitative method—SBPI. Therefore, we choose to present the results of scrotal scan in patients with bilateral varicocele as positive or negative and not to present the visual grade.

In patients with unilateral varicocele, the computerized analysis allowed a quantitation of the differential blood-pool activity in each hemiscrotum and grading of varicocele. This was done by using the following formula: SBPI = net counts of the left hemiscrotum/net counts of the right hemiscrotum. Values of 1 ± 0.1 were assumed to be within the normal range (if visual activity was one sided). In cases of right varicocele, the SBPI formula was reversed: SBPI = net counts of right hemiscrotum/net counts of left hemiscrotum.

The results were graded as follows: (a) Grade 0—normal study (SBPI = 1.0 ± 0.1); (b) Grade 1—mild uptake (SBPI = 1.2–1.5); (c) Grade 2—moderate uptake, represented by less than major vascular structures (SBPI = 1.6–2.0); and (d) Grade 3—intense uptake, compared to major normal vascular structures (SBPI > 2). The degree of blood flow was not evaluated because we found that it is a poor criterion for predicting the grade of varicocele. Varicocele grading was performed only on static blood-pool images, because these depicted the varicocele volume.

We assessed the reproducibility of SBPI by repeating the scrotal scans after 3–4 wk in 45 patients. The analysis of the second scans was performed by a nuclear medicine physician blinded to the results of the previous scans. In 27 patients, the results were identical. The second SBPI was 0.1 smaller than the first SBPI in 8 patients, it was 0.2 smaller in 2 patients, it was 0.1 greater in 8 patients and it was 0.2 greater in 1 patient. There was no change in scrotal scan grade in any of these patients. We concluded that SBPI is very reproducible.

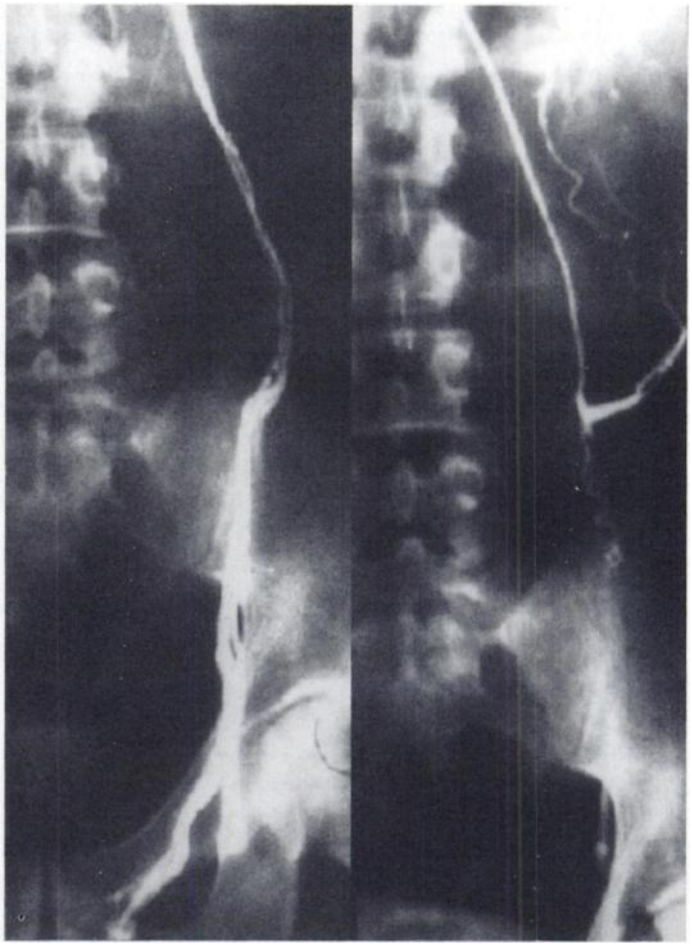

FIGURE 1. Retrograde gonadal venography. Left subclinical varicocele Grade 2. There is reflux into left internal spermatic vein (ISV), which is approximately 1 cm in diameter (left). The reflux disappears after coil embolization of ISV (right). Scrotum was not exposed to reduce irradiation to testes.

Selective gonadal venography was performed by means of a selective catheter, which was usually inserted through the right femoral vein. We injected 10–20 ml contrast medium (2–3 ml/sec) with the patient in the semiupright (30°–50°) position using a Zvitler catheter for the left ISV (Fig. 1) and a side-winder catheter for the right ISV (*12–14*). The results were graded as follows: (a) Grade 0—no reflux, continent valves; (b) Grade 1—reflux in ISV with a diameter less than 5 mm and opacification of a slightly enlarged pampiniform plexus; (c) Grade 2—reflux in the ISV of a diameter between 0.5–1.0 cm and an evident varicocele; and (d) Grade 3—reflux in the ISV with a diameter greater than 1 cm and a large varicocele.

Semen Analysis

At least three semen analyses were available in each patient. The results of the best semen analysis were classified into: (a) Grade 0—more than 20 million sperm/ml, motility and normal cell morphology greater than 50%; (b) Grade 1—between 5 and 20 million sperm/ml and/or motility and normal cell morphology between 20% and 50%; (c) Grade 2—between 1 and 5 million sperm/ml and/or motility and normal cell morphology of less than 20%; and (d) Grade 3—up to 1 million sperm/ml and no motility and abnormal cell morphology in 100%.

Statistical Analysis

The main and sample groups were compared by Student's t-test for differences between the mean age and mean duration of

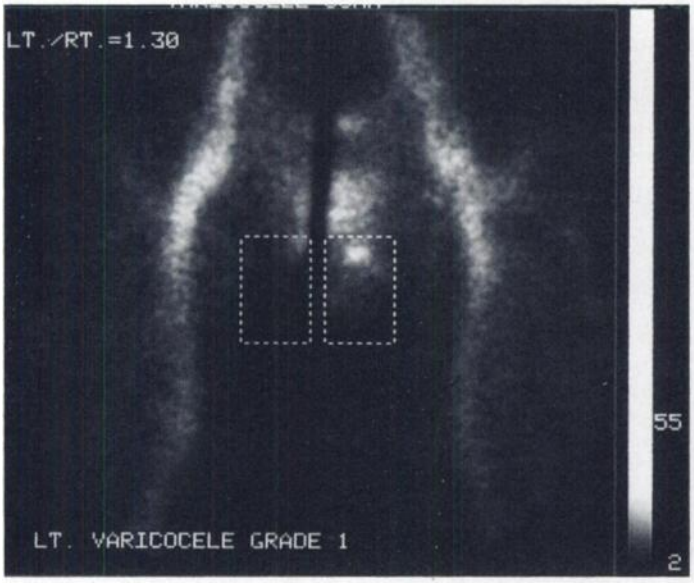

FIGURE 2. Scrotal scan of left varicocele Grade 1; left/right. SBPI = 1.45.

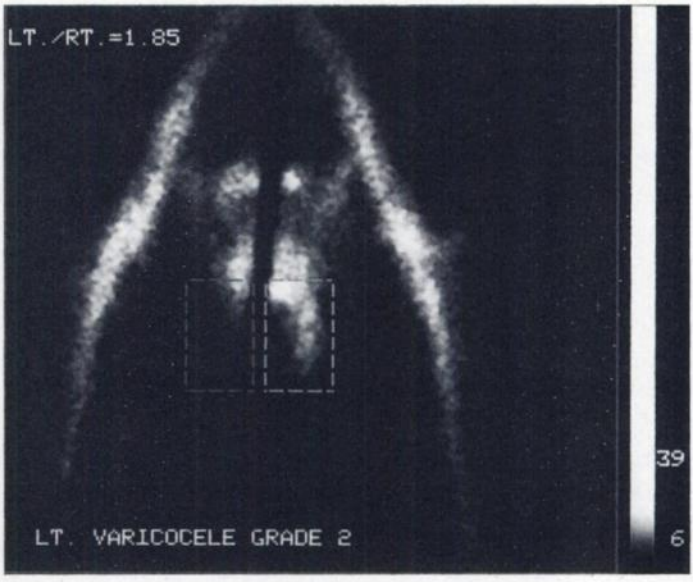

FIGURE 3. Scrotal scan of left varicocele Grade 2; left/right SBPI = 1.81.

infertility. Chi-square analysis was performed to compare the distributions of varicocele groups and to certify random sampling between the varicocele subgroups. Semen analysis grade was compared to SBPI grade by Spearman rank coefficient of correlation. Sensitivity, specificity, accuracy, positive predictive values and negative predictive values in diagnosing varicocele were calculated for palpation and for SBPI compared to gonadal venography.

RESULTS

In the control group, the SBPI ranged from 0.9–1.1, with an average of 1.04. In two control patients (6.6%), the values were 1.25 and 1.42, respectively. These patients with normal spermatograms and normal scrotum probably had subclinical varicocele. Venography was not performed in these patients due to its invasiveness. There was no significant difference between the main and venography sample groups regarding mean patient age, mean duration of infertility or distribution of varicocele grade.

Palpable Left Varicocele

Scrotal scan grade of varicocele was identical to palpatory grade in 87.7%, 87.2% and 100% of Grade 1 (Fig. 2), Grade 2 (Fig. 3) and Grade 3 varicocele (Fig 4), respectively (chi-square, $p = 0.0001$; Table 1). To evaluate 224 patients, we used palpation, scrotal scan and gonadal venography (Table 2). When compared to venography, physical examination had a sensitivity of 45.5% and a specificity of 96.8% and SBPI had a sensitivity of 96.4% and a specificity of 98.1% in diagnosing left varicocele.

Right Varicocele

Right palpable varicocele was confirmed by scrotal scan in 45 of 51 patients (88.2%) and subclinical right varicocele was demonstrated by scrotal scan in 96 patients. When compared to venography, palpation had a sensitivity of 41.2% and a specificity 99.4% and SBPI had a sensitivity of 88.2% and a specificity of 100% in diagnosing right varicocele.

Suspected Subclinical Varicocele

In 420 of 767 patients (54.8%) with suspected subclinical varicocele, scrotal scan demonstrated 283 Grade 1, 110 Grade 2 and 27 Grade 3 left varicoceles (Table 2). The 122 patients with suspected subclinical varicocele also were evaluated by gonadal venography, which demonstrated varicocele in 81 patients (66.4%): left varicocele in 60 patients (49.2%), right varicocele in 10 (8.2%) and bilateral varicocele in 11 patients (9%). There was a 95% sensitivity and 98% specificity of SBPI compared to venography in diagnosing subclinical left varicocele.

Bilateral Varicocele

Bilateral varicocele was demonstrated in 30 of 36 patients with palpable bilateral varicocele (Fig. 5) and subclinical bilateral varicocele was found in 78 patients. When compared to gonadal venography, palpation had a sensitivity of 31.3% and a specificity of 95.7% and scrotal scan had a sensitivity of 75% and a specificity of 99% in diagnosing bilateral varicocele.

Recurrent Varicocele

Eighteen patients with palpable recurrent varicocele were assessed by scrotal scan and gonadal venography and the venograms were normal in four of these patients. When compared to venography, SBPI had a sensitivity of 85.7% and a specificity of 75% and the varicocele grade was identical by the two methods in 11 of 18 patients (61.1%; chi-square, $p = 0.031$).

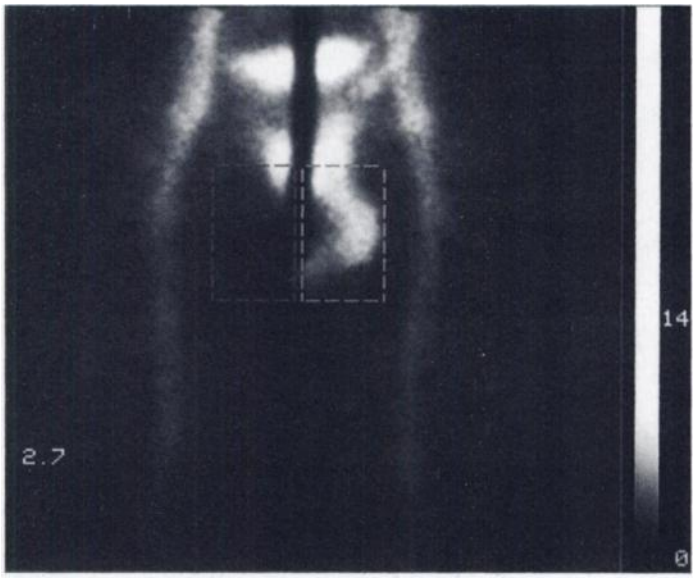

FIGURE 4. Scrotal scan of left varicocele Grade 3; left/right SBPI = 2.7.

TABLE 1
Comparison of Scrotal Blood-Pool Index, Palpation and Semen Analysis

	Scrotal scan scrotal blood-pool index			
	Grade 0	Grade 1	Grade 2	Grade 3
Palpable varicocele				
Grade 1	12	150	9	0
Grade 2	3	6	75	2
Grade 3	0	0	0	55
Subclinical left varicocele	367	283	110	27
Right varicocele	6	105	34	2
Semen analysis				
Grade 1	290	304	74	13
Grade 2	81	191	85	22
Grade 3	22	38	82	50

	Scrotal scan	
	Negative	Positive
Type:		
Bilateral varicocele		
Palpable	6	30
Nonpalpable	—	78

Correlation Between Semen Analysis and Scintigraphic Grading

Deterioration in semen parameters was strongly associated with high-grade varicocele (Table 1). There was a 0.61 Spearman rank correlation between semen analysis grade and SBPI grade of varicocele ($p < 0.001$).

DISCUSSION

We assessed the value of scintigraphy in the evaluation of varicocele in a large series of infertile patients. Thirty fertile patients with normal spermatograms and without palpable varicocele served as control subjects and the normal values for

TABLE 2
Comparison of Palpation, Scrotal Scan and Gonadal Venography in 224 Patients

	Scrotal blood-pool index									
	Grade 0		Grade 1			Grade 2			Grade 3	
	Venography									
	Grade 0	Grade 1	Grade 0	Grade 1	Grade 2	Grade 1	Grade 2	Grade 3	Grade 2	Grade 3
Left palpable varicocele (Grade 1)	1	1	0	24	1	0	0	1	0	0
Left palpable varicocele (Grade 2)	1	0	0	1	0	0	13	0	0	0
Left palpable varicocele (Grade 3)	0	0	0	0	0	0	1	0	0	8
Suspected subclinical left varicocele	50	3	1	30	1	2	14	1	2	7
Right varicocele										
Palpable	1	1	0	5	0	1	0	0	0	0
Nonpalpable	—	1	0	7	1	0	1	0	0	0
Post high-ligation varicocele	1	1	0	1	0	0	1	1	1	0
Post low-ligation varicocele	1	1	1	4	1	0	0	0	0	0
Postembolization varicocele	1	0	0	0	0	0	1	1	0	1

	Scrotal scan			
	Negative		Positive	
	Gonadal venography			
	Negative	Positive	Negative	Positive
Bilateral varicocele				
Palpable	7	1	2	4
Nonpalpable	—	3	0	8

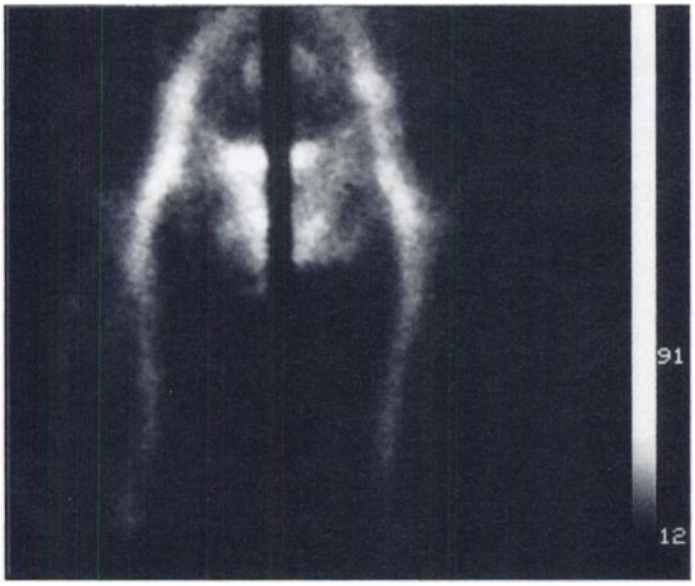

FIGURE 5. Scrotal scan of bilateral varicocele. Scrotal scan is designated positive and no quantitative grades are computed.

SBPI (0.9–1.1) were derived from this group of patients. There was a 89.7% overall grade-for-grade correlation between scrotal scan and physical examination ($p < 0.001$) in evaluating left palpable varicocele. Our results confirm its reported high accuracy (*15, 16*). This finding validates SBPI as an accurate, quantitative method of grading varicocele, which is equivalent to the clinical grading system by palpation of Dubin and Amelar (*9*). When compared to gonadal venography, the overall sensitivity of palpation and of scrotal scan was 50.4% and 94.3%, respectively. The overall specificity was high for both palpation (87.9%) and SBPI (96.6%). The low overall sensitivity of palpation compared to scrotal scan is explained by the high percentage of subclinical varicocele detected by SBPI and gonadal venography.

In 767 of 1360 infertile patients (56.4%), subclinical varicocele was suspected. In 420 of 767 patients, left varicocele was demonstrated by SBPI and there were 110 (26.2%) Grade 2 and 27 (6.4%) Grade 3 cases. SBPI was computed only when there was unilateral varicocele. This series is a highly selected group of infertile men referred for further evaluation by infertility clinics. The presence of high-grade nonpalpable varicocele may be explained by particular anatomic configurations such as a thick scrotal wall, the presence of concomitant hydrocele or a high position of the varicose veins at the external orifice of the inguinal canal or in the inguinal canal.

Recurrent palpable varicocele was analyzed separately from primary left palpable varicocele. The low grade-for-grade correlation (61.1%) between SBPI and gonadal venography probably results from the alteration of normal anatomy and appearance of aberrant varicose venous collaterals, which cannot be graded accurately by SBPI. The scrotal scan seems to be accurate in diagnosing recurrent varicocele, but SBPI may not be suitable for grading recurrent varicocele.

Geatti et al. (*17*) reported on 263 patients with clinical varicocele who were studied with various combinations of techniques. They studied 96 patients by both scrotal scintigraphy and gonadal phlebography. An overall agreement of 71% grade for grade was found. The highest correlation (82%) was found for Grade 3 varicocele. Ramanna et al. (*18*) reported a sensitivity of 92% and a specificity of 97% for scintigraphy versus phlebography.

Color doppler ultrasound of the scrotum emerges as an alternative investigation of varicocele. It is nonivasive and is well tolerated by the patients (*19*). It measures the diameter of ISV and testicular size and depicts reflux into ISV. However, this method is subjective and operator dependent (*19*).

Contrary to the results of Geatti et al. (*17*), we found a statistically significant correlation between the severity of semen deterioration and the scintigraphic grade of varicocele. This difference between the results of the two studies probably resulted from the different populations studied. Our patients had at least three abnormal spermatograms, were infertile, had a normal woman partner and were referred for further evaluation by scrotal scan after an extensive evaluation in an infertility clinic. Geatti et al. (*17*) studied a population of young military recruits presenting with varicocele.

Urologists consider different methods of qualitative grading of varicocele by scrotal scan as cumbersome and subjective. They are relying more on palpation to detect and grade varicocele. The SBPI is accurate, the calculation of varicocele grade is straightforward and more urologists are referring infertile patients for scrotal scan as our large series demonstrates. The large percentage of Grade 2 and 3 left varicocele among the infertile patients with subclinical left varicocele and the high correlation between varicocele grade and severity of spermatogram abnormalities suggest a detrimental role of subclinical varicocele on fertility. Dhabuwala et al. (*20*) found that operative repair of subclinical varicocele resulted in improved spermatograms and a pregnancy rate of 50%. A noninvasive diagnosis of subclinical varicocele, as provided by SBPI, may be beneficial.

Follow-up of pregnancy rates has been gathered prospectively only lately. During previous years, our data were incomplete on this regard and may be biased. We intend, after sufficient follow-up, to analyze pregnancy results and to determine the impact of the scrotal scan on the ultimate goal of therapy—successful pregnancy rate.

CONCLUSION

We found the nuclear SBPI to be an accurate, quantitative and noninvasive method for detecting and grading varicocele, which is equivalent to the grading system by palpation of Dubin and Amelar (*9*). Nuclear SBPI is not necessary for diagnosing and grading clinical varicocele, but it may serve as a quantitative baseline for postoperative comparison, especially in patients with suspected recurrent varicocele. Also, SBPI permits a quantitative assessment of the varicocele grade for research purposes and for interinstitutional comparison. A visual inspection of the scrotal scan before computing SBPI is essential to exclude bilateral varicocele. The main contribution of SBPI is its ability to detect and grade subclinical varicocele, which was present in almost 55% of infertile men with abnormal spermatograms and normal women partners in whom no other cause of infertility was found.

REFERENCES

1. Ivanissevich O. Left varicocele due to reflux. Experience with 4470 operative cases in forty-two years. *J Int Coll Surg* 1960;34:742–755.
2. Steeno O, Knops J, Declerck L, Adimoelja A, Van de-Voorde H. Prevention of fertility disorders by detection and treatment of varicocele at school and college age. *Andrologia* 1976;8:47–53.
3. Verstoppen GR, Steeno OP. Varicocele and the pathogenesis of the associated subfertility. A review of the various thories. II. Results of surgery. *Andrologia* 1977;9:293–305.
4. Greenberg SH. Varicocele and male fertility. *Fertil Steril* 1977;28:699–706.
5. Kursh ED. What is the incidence of varicocele in a fertile population? *Fertil Steril* 1987;48:510–511.
6. Pryor JL, Howards SS. Varicocele. *Urol Clin North Am* 1987;14:499–513.
7. World Health Organization. The influence of varicocele on parameters of fertility in a large group of men presenting to infertility clinics. *Fertil Steril* 1992;57:1289–1293.

8. Monteyne R, Comhaire F. The thermographic characteristics of varicocele: an analysis of 65 positive registrations. *Br J Urol* 1978;50:118–120.
9. Dubin L, Amelar RD. Varicocele size and results of varicocelectomy in selected subfertile men with varicocele. *Fertil Steril* 1970;21:606–609.
10. Fariss BL, Fenner DK, Plymate SR, Brannen GE, Jacob WH, Thomason AM. Seminal characteristics in the presence of a varicocele as compared with those of expectant fathers and prevasectomy men. *Fertil Steril* 1981;35:325–327.
11. Bsat FA, Masabni R. Effectiveness of varicocelectomy in varicoceles diagnosed by physical examination versus doppler studies. *Fertil Steril* 1988;50:321–323.
12. Comhaire F, Kunnen M. Selective retrograde venography of the internal spermatic vein: a conclusive approach to the diagnosis of varicocele. *Andrologia* 1976;8:11–24.
13. Ahleberg NE, Bartley O, Chidekel N. Retrograde contrast filling of the left gonadal vein. *Acta Radiol (Diagn)* 1965;3:385–389.
14. Riedel P. Radiological anatomy of the left testicular vein in varicocele and male infertility. In: Jecht EW, Zeitler E, eds. *Recent advances in diagnosis and therapy*. Berlin: Springer-Verlag, 1982:49–52.
15. Freund J, Handelsman DJ, Bautovich GJ, Conway AJ, Morris JG. Detection of varicocele by radionuclide blood-pool scanning. *Radiology* 1980;137:227–230.
16. Harris JD, McConnell BJ, Lipshultz LI, McConnell RW, Conoley PH. Radioisotope angiography in diagnosis of varicocele. *Urology* 1980;16:69–72.
17. Geatti O, Gasparini D, Shapiro B. A comparison of scintigraphy, thermography, ultrasound and phlebography in grading of clinical varicocele. *J Nucl Med* 1991;32: 2092–2097.
18. Ramanna L, Waxman AD, Yoon J, Hyun M. Evaluation of scrotal varicocele with blood-pool scintigraphy, correlation with contrast gonadal venography. *Radiology* 1990;177:143.
19. Lund L, Nielsen AH. Color doppler sonography in the assessment of varicocele testis. *Scand J Urol Nephrol* 1994;28:281–285.
20. Dhabuwala CB, Hamid S, Moghissi KS. Clinical versus subclinical varicocele: improvement in fertility after varicocelectomy. *Fertil Steril* 1992;57:854–857.

Automatic Three-Dimensional Matching of CT-SPECT and CT-CT to Localize Lung Damage After Radiotherapy

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The aim of this study was to develop a fast and clinically robust automatic method to register SPECT and CT scans of the lungs. **Methods:** CT and SPECT scans were acquired in the supine position from 20 patients with healthy lungs. After partial irradiation of the lungs by radiotherapy, the scans were repeated. Two matching methods were compared: a conventional method with external skin markers and a new method using chamfer matching of the lung contours. In the latter method, a unique value for the SPECT threshold, needed for segmentation of the SPECT lungs, was determined by iteratively applying the chamfer matching algorithm. **Results:** The new technique for CT-SPECT matching could be implemented in a fully automatic manner and required less than 2 min. No large systematic shifts or rotations were present between the matches obtained with the marker method and the lung contour method for healthy or partially irradiated lungs. For healthy lungs, the number of ventilation SPECT counts outside the CT-defined lung was taken as a measure for a good match. This number of outside counts was slightly lower for the new method than for the conventional method, which indicates that the accuracy of the new method is at least comparable to the conventional method. For ventilation, a systematic difference between the results of the matching methods, a small translation in the anterior → posterior direction, could be attributed to an inconsistency of the marker positions (2 mm). For perfusion, a somewhat larger anterior → posterior shift was found, which was attributed to the gravity force. CT-CT correlation on the lung contours using chamfer matching was tested with the same dataset. For accurate matching, the CT slices encompassing the diaphragm had to be deleted. **Conclusion:** The new method based on lung contour matching is a fast, automatic procedure and allows accurate clinical follow-up.

Key Words: SPECT; CT; lung; image registration; chamfer matching

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In nuclear medicine, radiotherapy and oncology, there is a growing interest in combining the information of SPECT and CT or magnetic resonance scans. SPECT is used to map organ function and metabolism and has also been established as useful in the evaluation of tumor staging with radiolabeled monoclonal antibodies (*1,2*). One drawback is that SPECT reveals little anatomical information. In contrast, CT gives accurate anatomical detail but does not provide much information about the function of the tissue. The combination of SPECT and CT can, therefore, lead to a more accurate tumor localization or the exact localization of nonfunctioning tissue (*3*). In recent developments in radiotherapy, lung SPECT is combined with CT. Here, regions of nonfunctional lung tissue are identified with perfusion and ventilation SPECT scans, which gives additional information for the design of a radiation treatment plan based on the CT scan (*4*). Furthermore, it has been shown that lung SPECT is a very sensitive method for monitoring radiation damage after radiotherapy, if it is combined with CT (*5,6*). Of course, the prerequisite for an optimal combination of the information of the different modalities is that the SPECT and CT scans need to be matched spatially (i.e., registered). For clinical application, the matching method should be fast and robust.

In a research project to establish the dose–effect relationship for lung tissue after radiotherapy, several hundred CT-SPECT registrations have to be performed. Previously, the CT-SPECT matching was performed using external markers placed on the skin (*5*). The registration of the scans was performed by minimizing the root mean-square (RMS) distance between the markers. This method has several disadvantages. For the different modalities (CT or SPECT), different markers have to be used. This procedure is inaccurate due to the variation in the positioning of the markers. The markers have to be identified in both scans, which is done manually and is time-consuming. The skin (and markers) can also move with respect to the organ of

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