

## Radionuclide venography of lower limbs by subcutaneous injection: A clinical evaluation

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SC-RNV, radionuclide venography by subcutaneous injection of Tc-99m pertechnetate at acupuncture points K-3, a new alternative of lower limb venography, was recently developed in our clinical laboratory. In some of the previous studies, we have proved its superiority to radionuclide venography by intravenous injection. The current investigation was conducted to understand the reliability of SC-RNV in the diagnosis of deep vein thrombosis (DVT). Fifty-seven cases with lower leg edema, from Nov., 1989 through Oct., 1990, received both SC-RNV and duplex US for causative evaluation. As a result of duplex US, 26 were considered normal (non-DVT), 19 were classified as unilateral DVT, and 12 as bilateral DVT. In nineteen cases (61%, 19/31) with DVT also a XCT and/or a CV (contrast venography) was taken, that showed compatible results. All of the non-DVT had a normal pattern of SC-RNV, all of the unilateral DVT had unilateral impairment of deep vein drainage in SC-RNV, and all of the bilateral DVT had impaired deep venous drainage bilaterally in SC-RNV. It is therefore concluded that SC-RNV is one of the best choices among available non-invasive lower-limb venographic methods.

**Key words:** radionuclide venography, subcutaneous injection, acupuncture points

### INTRODUCTION

RADIONUCLIDE VENOGRAPHY of the lower limbs by subcutaneous injection of Tc-99m pertechnetate at acupuncture points (SC-RNV),<sup>1</sup> an alternative type of lower-limb venography, was recently developed in our clinical laboratory. It was recognized to be easier and simpler, yet more accurate than radionuclide venography by intravenous injection.<sup>1,2</sup> In the present study, we intend to evaluate the reliability of the SC-RNV in the diagnosis of deep vein thrombosis of the lower limbs (DVT).

### MATERIALS AND METHODS

From Nov., 1989 through Oct., 1990, 57 cases with lower leg edema were referred to us for evaluation of the cause of the leg edema. A SC-RNV and a color

duplex ultrasound (duplex US) were carried out for every one of them on the same day.

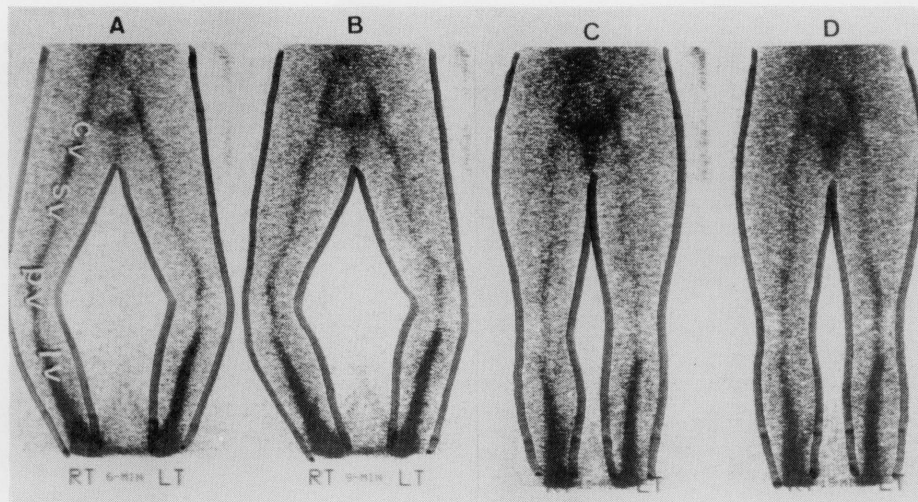
#### *Radionuclide venography by subcutaneous injection (SC-RNV)*

A Toshiba GCA-90B Digital Gamma Camera was used for the SC-RNV. The SC-RNV technique has already been described in the literature,<sup>1,2</sup> and in the present study the procedure was modified. After subcutaneous (SC) injection of 18.5-37 MBq (0.5-1 mCi) Tc-99m pertechnetate at acupuncture point K-3 in each foot, we had the patient lie supinely under the detector of the gamma camera. Lower body scans, from the pelvis to the feet, were then taken with the legs semi-flexed at 6 and 9 minutes after SC injection. At 12 and 15 minutes, another 2 lower body scans were taken with the legs straight.

Interpretation of the SC-RNV was done by both the authors. The intra-observer variation found by the 1st author was 1.1% (2/179, data unpublished), and the inter-observer difference between the 2 authors' findings was 3.4% (6/179, data unpublished). Normally, in SC-RNV there are deep venous images

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**Fig. 1** Normal SC-RNV of a 38 year-old woman. A. At 6 minutes after subcutaneous injection of Tc-99m pertechnetate at acupuncture points K-3, there is smooth deep venous drainage in the lower limbs, through the calf deep veins (lv), the popliteal vein (pv), the superficial femoral vein (sv) and common femoral vein (cv). Superficial venous drainage is not visible normally. B. At 9 minutes after injection is almost the same pattern of deep venous drainage. By 12 minutes (C) and 15 minutes (D), the deep venous drainage may persist, or become a little faint.

at 6 minutes and 9 minutes, as shown in Fig. 1. Besides, the soft tissue of the lower extremities is demarcated to tell the anatomical location of the deep veins. At 12 minutes and 15 minutes, the deep venous drainage may become less prominent than the earlier phases, i.e. at 6 minutes and 9 minutes, and occasionally there may be evidence of some superficial venous drainage in the calf or calves. In cases with DVT, the affected limb usually shows impaired deep venous drainage, i.e. poor or non-visualization of the deep vein(s), and prominent collateral superficial venous drainage, as shown in Figs. 4, 6, 7 and 8.

#### *Duplex ultrasound (duplex US)*

An ACUSON 128 computed ultrasound scanner was used for duplex US, with an L-538 transducer. When the patient lay supinely, the transducer was put over the common femoral vein (CFV), the superficial femoral vein (SFV) and the popliteal vein (pop. v) to record the duplex US. Normally, by color Doppler US the deep vein is demonstrated as a complete band encoded with blue color (Fig. 2a). With Doppler signal recording, the deep venous flow undergoes normal phasic change with respiration, i.e. increased flow rate in the expiratory phase and decreased flow rate in the inspiratory phase, as shown in Fig. 2b. On proximal compression there is cessation of deep venous flow, and after release of the compression there is transient augmentation of the flow rate (Fig. 2c). And on squeezing, i.e. distal compression,

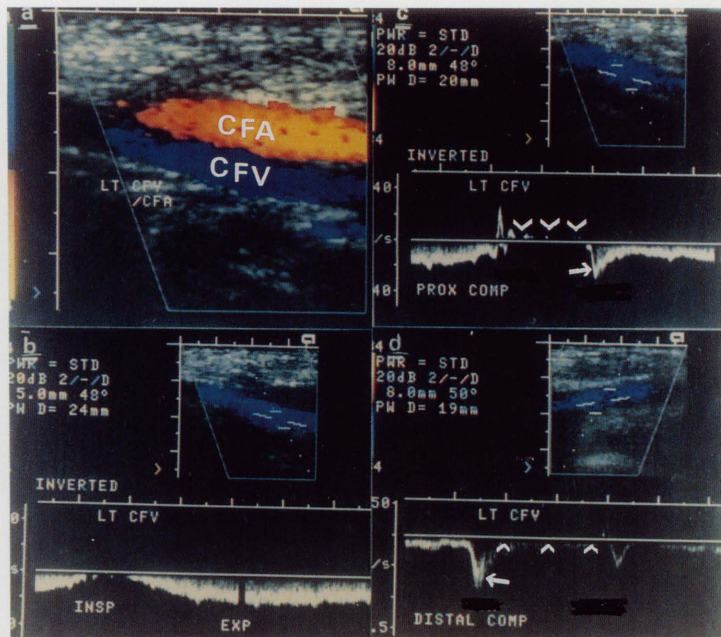
there is initial augmentation followed by cessation of the flow (Fig. 2d). By color Doppler US, in cases with DVT, usually there is low or poor echogenic thrombus instead of color flow in the deep vein(s) (Fig. 3a to 3c); or, in cases of DVT with recanalization there is partial thrombus in the deep vein(s) having segmented color-coded flow that is antegrade or reversed (Fig. 5).

#### *Grouping of patients*

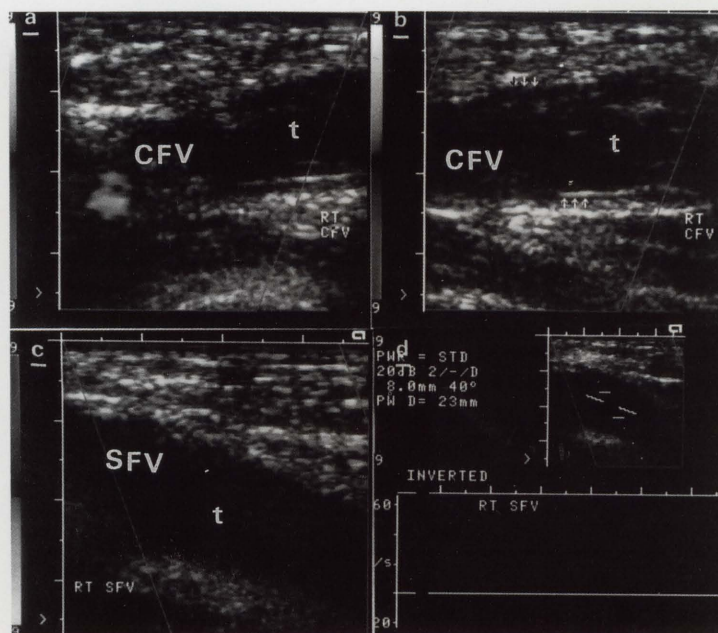
Since duplex US is a reliable diagnostic tool for the diagnosis of DVT,<sup>3-9</sup> the patients were classified into 3 groups according to the findings of duplex US. The diagnostic criteria of duplex US for DVT are: (1). echogenic substance(s) in the deep veins with no Doppler signal, (2). loss of phasic change in deep venous flow with respiration, and (3). loss of normal response of deep venous flow and caliber to compression.

- Group 1 (normal): Twenty-six patients were considered normal, since no evidence of DVT was obtained by duplex US. They were 11 males and 15 females, aged 28 to 77 years.
- Group 2 (unilateral DVT): Nineteen patients (8 males, 11 females) had unilateral DVT (involving CFV, SFV and/or pop. v) by duplex US, aged 23 to 77 years.
- Group 3 (bilateral DVT): Twelve patients (5 males, 7 females, aged 28 to 69 years) had bilateral DVT by duplex US.

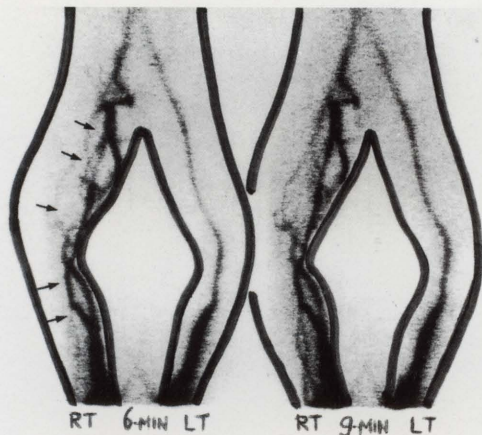
Among the patients in groups 2 and 3, 19 (61%,



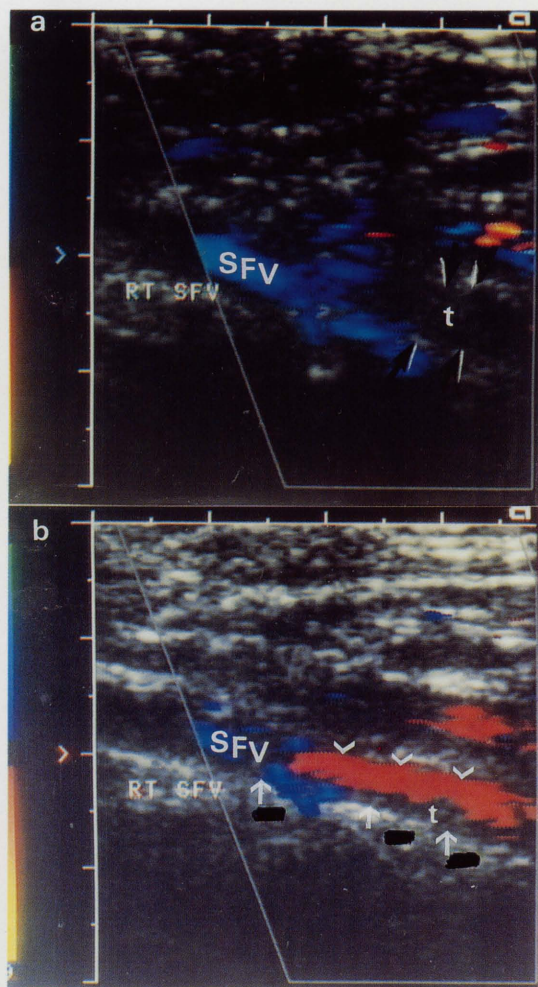
**Fig. 2** Normal duplex US of a 38-year-old female. a. In the normal color flow map, the left common femoral artery (CFA) was encoded with orange-red color, and the left common femoral vein (CFV) was encoded with green-blue color. b. The Doppler signal of the left CFV showed phasic change of blood flow rate with respiration normally, that is lower rate at inspiration and higher rate at expiration. c. With proximal compression of the left CFV, the blood flow was suddenly interrupted (white arrow heads); and after release of the compression, there was normally transient augmentation of blood flow (white arrow). d. On distal compression (squeeze), there was initially augmentation (white arrow) followed by transient decrement/ceasation (white arrow heads) of blood flow in a normal deep vein.



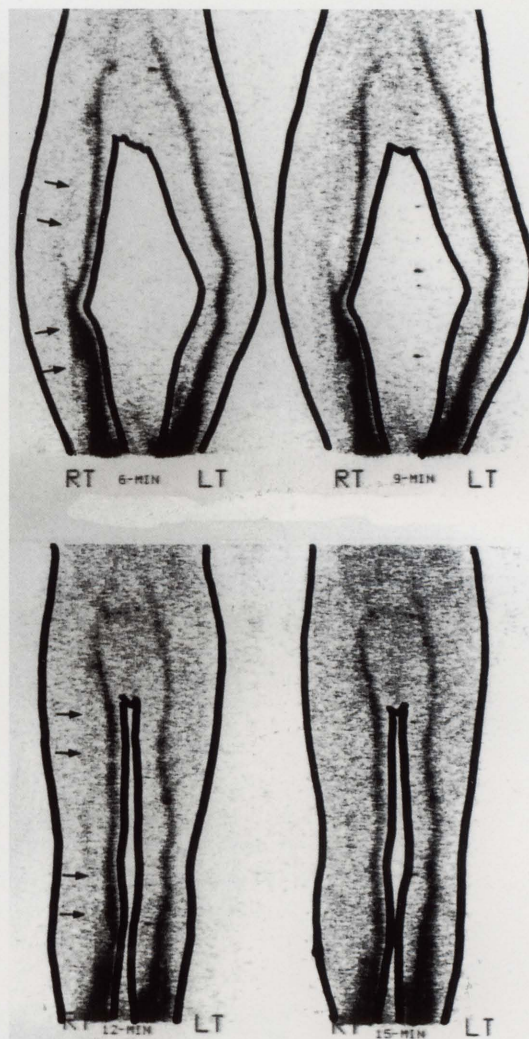
**Fig. 3** Case 1: A 38-year-old male patient with right lower leg edema. The color Doppler ultrasound (a to c) revealed no visible color flow in the right common femoral vein (CFV) and superficial femoral vein (SFV); instead, there was a low echogenic thrombus (t) in those vessels. By duplex ultrasound (d) was no Doppler signal to be detected.



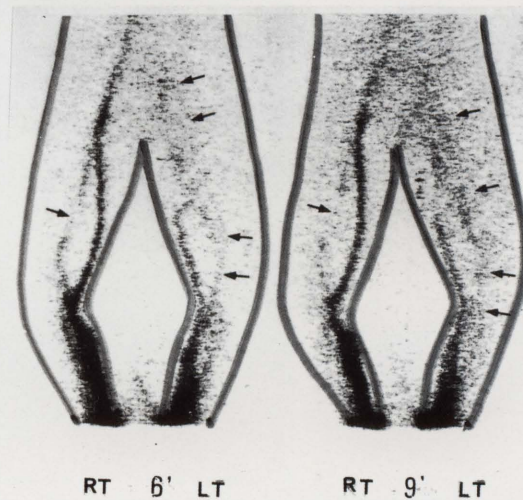
**Fig. 4** Case 1. The SC-RNV revealed non-visualization of the right CFV, SFV, popliteal vein and calf deep veins (arrows) with prominent superficial collateral circulations.



**Fig. 5** Case 2. A 67-year-old male patient with right leg edema. a. The color Doppler ultrasound revealed some echogenic thrombi (t, arrows) in the right SFV. b. On Valsalva maneuver, there was reversed flow (white arrow heads, encoded with red color) through the SFV (white arrows), indicating partial recanalization. (t=thrombus)



**Fig. 6** Case 2. The SC-RNV showed non-visualization of the deep veins of the right lower extremity (arrows) with prominent collateral circulation through the greater saphenous vein.



**Fig. 7** Case 3. A 71-year-old female patient with bilateral lower limb edema. The SC-RNV revealed impaired deep venous drainage (arrows) through the right SFV, and left CFV, SFV, popliteal vein and calf deep veins.

19/31) had also received contrast venography (CV) and/or x-ray computed tomography of the pelvis and thighs (XCT). The results of CV/XCT were compatible with those of duplex US.

## RESULTS

### Overall

All of the normal subjects (group 1) had a normal SC-RNV pattern of deep venous drainage (as shown in Fig. 1). All of those with unilateral DVT (group 2) had ipsilaterally impaired deep venous drainage (Figs. 4 and 6). All of those with bilateral DVT (group 3) showed bilaterally impaired deep venous drainage (as shown in Figs. 7 and 8).

### Case report

**Case 1** A 38-year-old man experienced right lower leg edema for 7 months following a traffic accident, and was hospitalized when the swollen leg became painful. A duplex US revealed echogenic thrombi in the right CFV and SFV with no Doppler signal to be detected (Fig. 3). The result of SC-RNV showed non-visualization of deep venous flow through the right deep calf veins, pop. v, SFV and CFV. Instead, there was prominently superficial collateral circulation in the right lower extremity (Fig. 4). The deep venous drainage of the left lower extremity looked normal.

**Case 2** A 67-year-old diabetic male patient suffered from right leg edema for 2 weeks before admission. A duplex US demonstrated deep vein thrombi in the right SFV, and on Valsalva maneuver the flow was reversed, indicating partial recanalization (Fig. 5).

On SC-RNV, there was no deep venous flow through the right calf deep veins, pop. v, SFV and CFV. But collateral flow through the right greater saphenous vein was evident. Deep venous drainage was normal on the left side (Fig. 6).

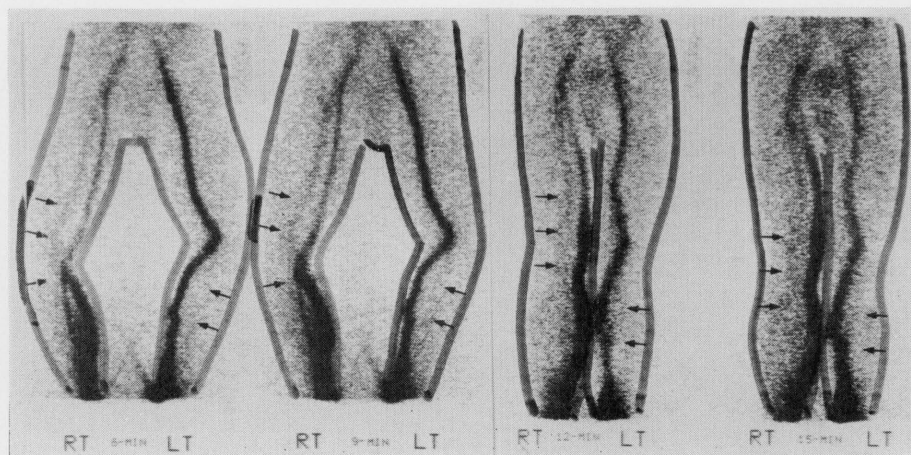
**Case 3** A 71-year-old female, having uterine cervical carcinoma noticed for years and undergoing radiotherapy, suffered from edema of the bilateral lower extremities for 4 months intermittently. A duplex US showed DVT in the left CFV/SFV and the right SFV. On SC-RNV, there were bilateral DVTs with prominent superficial collateral circulation (Fig. 7).

**Case 4** A 63-year-old male CVA (cerebro vascular accident) patient suffered from painful right leg edema and left calf soreness for a couple of days. A duplex US revealed DVT in the right SFV and the left pop. v. The SC-RNV demonstrated impaired deep venous drainage through the right pop. v and SFV, and through the left calf deep veins and pop. v. (Fig. 8).

## DISCUSSION

DVT involving the lower extremity remains a severe clinical problem, as it may predispose to pulmonary embolism.<sup>10-12</sup> Diagnosis should therefore be done early, before its proximal propagation or even the severe complication, pulmonary embolism, occurs. Contrast venography is currently considered the standard method of diagnosis.<sup>13-15</sup> However, it is invasive and expensive, often uncomfortable, not uniformly available, and not without morbidity.<sup>15-18</sup>

In the past decade, some non-invasive assessments

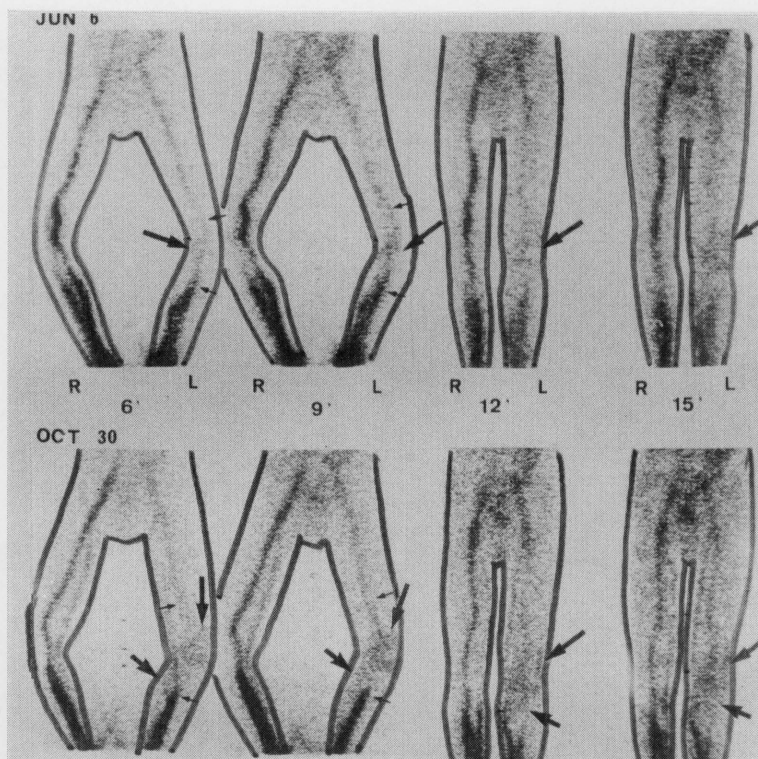


**Fig. 8** Case 4. A 63-year-old male patient with painful right leg edema and left calf soreness. The SC-RNV revealed impaired deep venous drainage through the right popliteal vein and SFV, and through the left calf deep veins and popliteal vein.

have been developed and are gaining more and more importance.<sup>1-6,19-26</sup> Among these, SC-RNV is the most recent one, and was developed in our clinical laboratory.<sup>1,2</sup> Compared with the ascending radionuclide venography (IV-RNV), SC-RNV possesses several advantages. First, in SC-RNV the radionuclide absorbed is finally distributed into the soft tissue of whole body to be an anatomical landmark telling the deep veins from the superficial veins; thus, a false negative result from misreading a superficial as a deep vein can be prevented. The latter is not uncommon in IV-RNV, since the radionuclide utilized in IV-RNV is usually Tc-99m MAA (macroaggregated albumin) that after injection into a pedal vein accumulates in the lungs, and thereby the soft tissue of the body cannot be contoured as the landmark. Second, since in IV-RNV there is usually a higher concentration of radionuclide within the deep vein(s), a vessel having a thrombus with recanalization could be visualized as normal patency. Previously such an experience was not unusual in our routine work. By mean of SC-RNV, it is easy to prevent false reading in such a case, because the diseased vein is demonstrated as a faintly or non-visualized vessel accompanied with prominent col-

lateral superficial venous drainage, as shown in Fig. 6 (case 2). Finally, on IV-RNV the procedure may be very time-consuming, esp. in cases of moderate-to-severe foot edema; and, occasionally there is failure on IV injection.<sup>1</sup>

In the present study, the clinical availability of SC-RNV was settled. It was as sensitive and accurate as duplex US for the diagnosis of DVT. All of those with US evidence of DVT had a positive SC-RNV result (group 2 and group 3), and all of those without US evidence of DVT had a normal result. However, duplex US is a complicated technique, and is more technique-dependent and less time-saving than SC-RNV. By duplex US, the vein(s) could be visualized only segmentally; and, for most sonographers, it is difficult to observe the entire course of the deep veins of the lower limbs. In fact, duplex US is efficacious in the diagnosis of proximal (i.e. above-knee) DVT, while its role in detection of distal (i.e. below-knee) DVT is uncertain.<sup>24,27</sup> During the last 2 years, we set up a qualified duplex US technique for the diagnosis of proximal DVT, but have frequently been unable to tell a distal DVT by duplex US only. In the present study, among the 6 cases in which the SC-RNV revealed evidence of combined proximal and

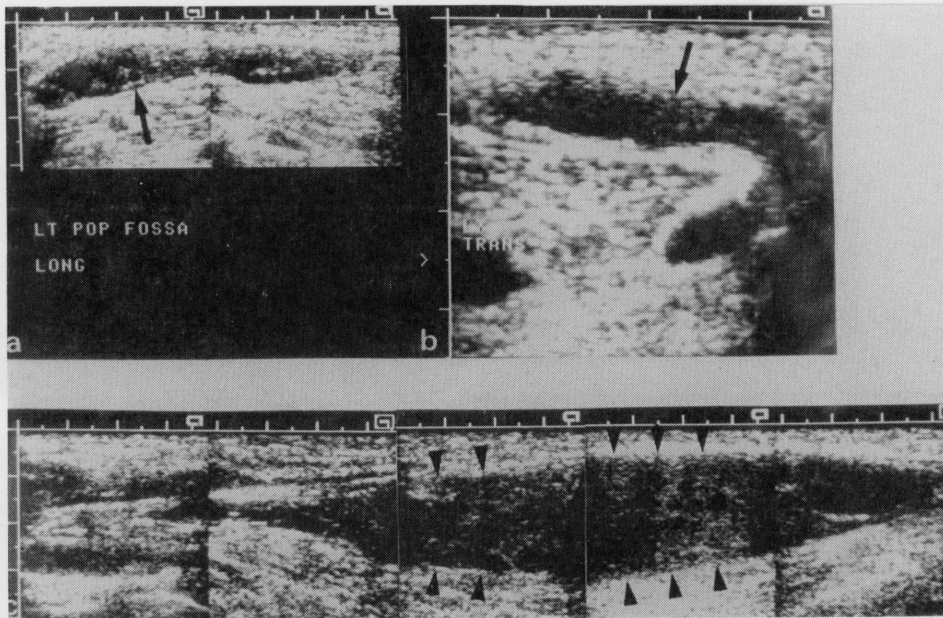


**Fig. 9** A case of pyogenic arthritis of knee and calf cellulitis compressing the deep vein (a 68-year-old man). The SC-RNV on Jun. 6, 1990 revealed abnormally soft tissue accumulation of radioactivity in the left knee (long arrows), that extended into the left upper calf region (short arrows) on Oct. 30 the same year, after inadequate treatment. However, the deep venous drainage of the left lower extremity remained normal (small arrows).

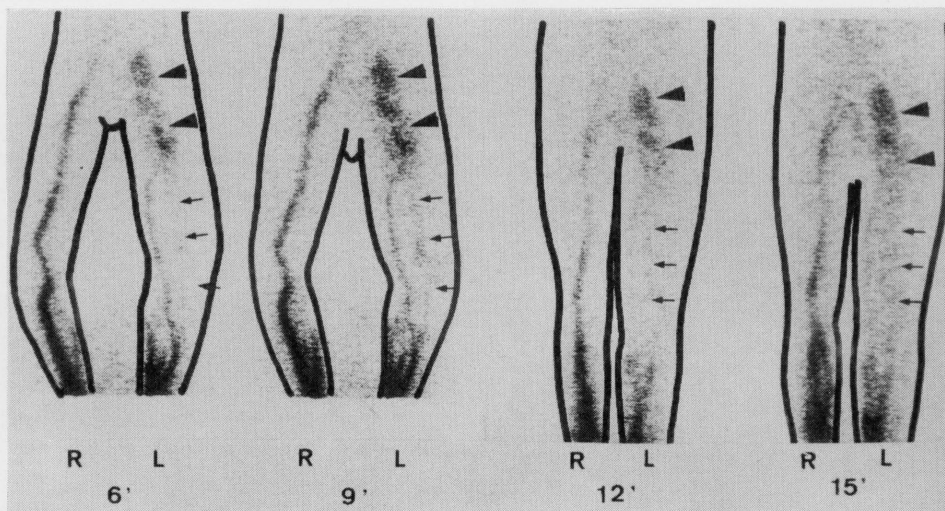
distal DVTs, duplex US revealed only proximal DVT in 4. Nevertheless, distal DVT is seldom a critical clinical problem;<sup>10-12</sup> and in the present study, none of the cases referred to us showed evidence of simple distal DVT in SC-RNV, duplex US, CV and/or XCT.

Another problem is whether SC-RNV could distinguish impaired deep venous drainage due to

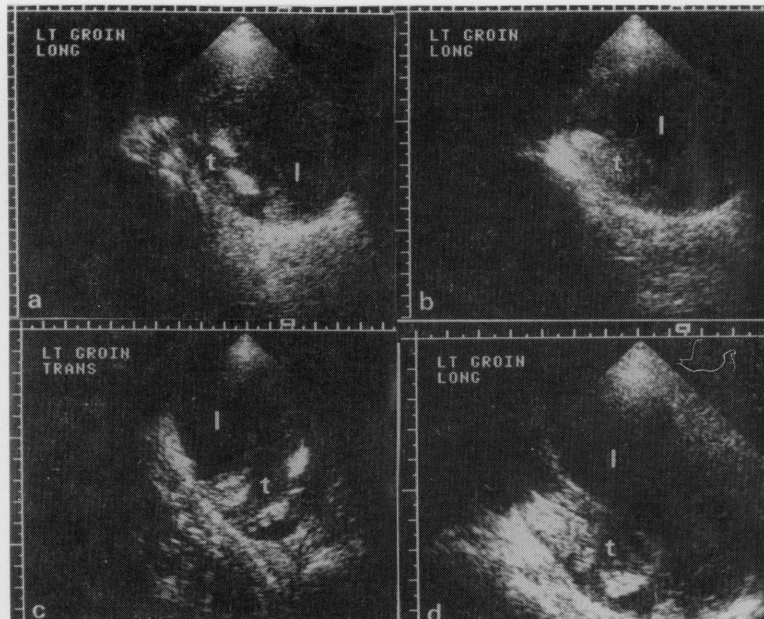
DVT from venous disturbance due to external compression. Two of our recent cases with lower leg edema may offer an answer; one was a case of left leg edema from pyogenic arthritis and calf cellulitis compressing the left popliteal vein (Figs. 9 and 10), and the other was a case of left common femoral arterial pseudo-aneurysm compressing the left CFV and causing edematous swelling of the left lower



**Fig. 10** The same case as in Fig. 9. The real-time ultrasound revealed a focus of low and heterogeneous echogenicity (arrows) in the joint space of the left knee (a: longitudinal scan, b: transverse scan). In the calf region was the other focus of the same echogenic characteristics (c: longitudinal scan), indicating cellulitis.



**Fig. 11** A case of pseudo-aneurysm of the left common femoral artery (a 63-year-old woman). The SC-RNV revealed soft tissue swelling, impaired deep venous drainage (arrows), and abnormal accumulation of radioactivity at the groin region (arrow-heads) of the left lower extremity. The abnormal accumulation at the groin region is not a sign of DVT, and is indicative of some vascular mass compressing the left common femoral vein.



**Fig. 12** The same case as in Fig. 11. A real-time ultrasound of the left groin region revealed a vascular mass with lumen (1) and circumferential thrombus (t), that by contrast angiography was a pseudo-aneurism of the left common femoral artery.

extremity (Figs. 11 and 12). A SC-RNV of the former one showed increased soft tissue radioactivity at the left knee joint and in the upper left calf region, and there was smooth deep venous drainage both proximal and distal to the left knee (Fig. 9); a real-time US revealed intra-articular fluid collection in the left knee and hypoechoic necrotizing material in the left calf muscle layers (Fig. 10). In the latter case, a SC-RNV demonstrated soft tissue swelling of the left lower extremity, interruption of deep venous drainage through the left popliteal vein and the left SFV with collateral circulation via the greater saphenous vein, and extra-vascular accumulation of radionuclide in the soft tissue of the left groin region (Fig. 11); a duplex US revealed aneurysmal dilatation of the left common femoral artery (CFA) and no evidence of DVT in the left CFV or SFV. Besides, in real-time US there was tortuous and segmentally dilated CFA with a thrombus formation in the latter case (Fig. 12). The major distinguishing point is the extravascular accumulation of radioactivity in the soft tissue around the compressed deep veins in the non-DVT cases. However, there still may be few cases showing impaired deep venous drainage with a cause undetermined by SC-RNV. In such a situation, the duplex US could afford a certain aid for causative diagnosis, although it is undoubtedly more time-consuming.

Our conclusion is that SC-RNV is clinically reliable in the diagnosis of DVT. Since it is simple to perform, less technique-dependent and more

time-saving, we recommend it as one of the most available, non-invasive methods for routine use in the diagnosis of DVT.

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#### REFERENCES

1. Wu CC, Jong SB: Radionuclide venography of lower limbs by subcutaneous injection: Comparison with venography by intravenous injection. *Ann Nucl Med* 3: 125-133, 1989
2. Wu CC, Jong SB, Yang CC, Peng GT, Wu DK: Clinical evaluation of a new alternative venography: Radionuclide venography of lower-limbs by subcutaneous injection at acupuncture points B-60 and K-3. *Kaohsiung J Med Sci* 4: 688-699, 1988 (full text in Chinese)
3. Ragjendra BN, Horvi SC, Hilton S, et al: Deep venous thrombosis: Detection by probe compression of veins. *J Ultrasound Med* 5: 89-95, 1986
4. Appleman AT, DeJons TE, Lampmen LE: Deep venous thrombosis of the leg: US findings. *Radiology* 163: 743-746, 1987
5. Vogel P, Laing FC, Jeffrey RB, et al: Deep venous thrombosis of the lower extremity: US evaluation. *Radiology* 163: 747-751, 1987



6. O'Leary DH, Kane RA, Chase BM: A prospective study of the efficacy of B-Scan sonography in the detection of deep venous thrombosis in the lower extremities. *J Clin Ultrasound* 16: 1-8, 1988
7. Aikken AGF, Godden DJ: Real-time ultrasound diagnosis of deep vein thrombosis: A comparison with venography. *Clin Radiol* 38: 309-313, 1987
8. Rosner NH, Doris PE: Diagnosis of femoropopliteal venous thrombosis; Comparison of duplex sonography and plethysmography. *Am J Roentgenol* 150: 623-627, 1988
9. White EM: Duplex sonography of the lower extremity venous system. In Grant EG, White EM (ed.): *Duplex sonography*. New York, Berlin, Heidelberg, London, Tokyo, Springer-verlag New York Inc., pp. 239-259, 1988
10. Sevitt S: Venous thrombosis and pulmonary embolism. *Am J Med* 33: 703-704, 1962
11. Dalen JE, Alpert JS: Natural history of pulmonary embolism. *Prog Cardiovasc* 17: 259-270, 1975
12. Lundh B, Fagher B: The clinical picture of deep vein thrombosis correlated to the frequency of pulmonary embolism. *Acta Med Scand* 210: 353-356, 1981
13. Rabinov K, Paulin S: Roentgen diagnosis of venous thrombosis in the leg. *Arch Surg* 104: 134-144, 1972
14. Thomas ML: Phlebography. *Arch Surg* 104: 145-151, 1972
15. Albrechtsson U, Olsson CG: Thrombotic side-effects of the lower-limb phlebography. *Lancet* i: 723-724, 1976
16. Hull R, Hirsch J, Sackett DL, et al: Cost effectiveness of clinical diagnosis, venography and non-invasive testing in patients with symptomatic deep vein thrombosis. *N Engl J Med* 304: 1561-1567, 1981
17. Bettman MA, Paulin S: Leg phlebography: The incidence, nature, and modification of undesirable side effect. *Radiology* 122: 101-104, 1977
18. Bettman MA: Contrast phlebography: Methods in hematology. In Hirsh J (ed.): *Venous thrombosis and pulmonary embolism diagnostic methods*. New York, Churchill Livingstone Inc., pp 20-32, 1987
19. Rosenthal L: Combined inferior vena cavography, iliac venography and lung imaging with Tc-99m albumin macroaggregates. *Radiology* 98: 623-626, 1971
20. Kakka V: The diagnosis of deep-vein thrombosis using the I-125 fibrinogen test. *Arch Surg* 104: 152-159, 1972
21. DeNardo SJ, DeNardo GL: Iodine-123 fibrinogen scintigraphy. *Semin Nucl Med* 7: 245-251, 1977
22. Sy WM, Lao RS, Bay R, et al: Ec-99m pertechnetate radionuclide venography-large volume injection without tourniquet. *J Nucl Med* 19: 1001-1006, 1978
23. Beswick W, Chimel R, Booth R, et al: Detection of deep venous thrombosis by scanning of Tc-99m labelled red-cell venous pool *Br Med J* 1: 82-84, 1979
24. Sumner DS, Lambeth A: Reliability of Doppler ultrasound in the diagnosis of acute venous thrombosis both above and below the knee. *Am J Surg* 138: 205-210, 1979
25. Hull RD, Hirsch J, Carter CJ, et al: Diagnostic efficacy of impedance plethysmography for clinically suspected deep-vein thrombosis: A randomized trial. *Ann Intern Med* 102: 21-28, 1985
26. Huisman MV, Buller HR, ten Cate JW, et al: Serldi impedance plethysmography for suspected deep venous thrombosis in outpatients. *N Engl J Med* 314: 823-828, 1986.
27. Polak JF: Venous thrombosis/Chronic venous thrombosis and venous insufficiency. In: *Peripheral vascular sonography. A practical guide*. Hong Kong, Williams & Wilkins, pp 155-246, 1992