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Radionuclide venography of lower limbs by subcutaneous injection: Comparison with venography by intravenous injection

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We have proved that subcutaneous injection (SC) of a small dose of Tc-99m pertechnetate (1 to 2 mCi: 37 to 74 MBq) at acupuncture points (K-3 and B-60) may offer an alternative method of radionuclide venography (RNV) of the lower limbs. In this study, we compared intraveneous (IV) RNV and SC-RNV in 22 consecutive cases with typical signs and symptoms suggesting venous abnormality of the lower limb(s) from March to May 1988. They are 11 male and 11 female, aged 47.7±15.7 years.

Among the 44 limbs of the 22 cases, 4 were normal, 12 (27.3%) were found to have varicose veins in the legs only, 18 (40.9%) had partial stenosis of the deep veins (14 poplito-tibial and 4 superficial femoral), and 13 (29.6%) had complete stenosis of the deep veins (4 poplito-tibial, 1 superficial femoral and 8 ilio-femoral. SC-RNV showed almost the same results as IV-RNV in 21 (47.7%), superior to IV-RNV in 22 (50%) (including 4.6% failure of IV-RNV), and inferior to IV-RNV in 1 (2.3%).

We conclude that SC-RNV is definitely an alternative method of lower-limb venography. Since it is in most cases superior to IV-RNV, we suggest that it can take the place of IV-RNV in routine work.

Key words: Radionuclide venography, Subcutaneous injection, Acupuncture points

INTRODUCTION

Venous abnormalities of the lower limbs are not uncommon in the southern part of Taiwan in our experience. Among these abnormalities deep venous thrombosis (DVT) is the most serious problem. DVT in the lower limbs, if undiagnosed and untreated, can result in pulmonary emboli and may have a fatal outcome.[1–3] Unfortunately, clinical diagnosis of DVT of the lower limbs has been shown to be unreliable and this remains a diagnostic problem for clinicians.[4–9] Since complications associated with anticoagulation, when they occur, are usually significant, objective diagnostic tests would be of value before starting treatment. Ascending contrast venography is currently considered the diagnostic reference method.[10–12] It is, however, invasive and expensive, often uncomfortable, not uniformly available, and not without morbidity;[9,12–14] it also requires the services of experienced radiologists.[11,15] Because of these disadvantages, several non-invasive methods have been developed during the past decade, including ^{99m}Tc-MAA ascending radionuclide venography,[16] ^{125}I-fibrinogen test,[17,18] ^{123}I-fibrinogen scintigraphy,[19] large-volume ^{99m}Tc-pertechnetate radionuclide venography,[20,21] blood-pool radionuclide venography,[22–26] Doppler ultrasound,[27–31] real-time ultrasound,[32–39] impedance plethysmography,[40–48] and combined impedance plethysmography and ^{125}I-fibrinogen leg scanning.[49,50] All of these have their limitations.[6,35,37–39,45,46,51–55]

In the last 2 years, on researching the relationship of vessels to the meridian, an important part of the traditional concept in Chinese medicine for thousand years, we developed a new method of venography: ascending radionuclide venography of the lower

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limbs by subcutaneous injection at acupuncture points (K-3 and B-60).[56] In the present study, we intend to evaluate the clinical usefulness of this method by comparing it with ascending radionuclide venography by intravenous injection of ^{99m}Tc-MAA.

MATERIALS AND METHODS

Between March and May 1988, 22 consecutive cases (11 male and 11 female, aged 47.7±15.7 year-old) (mean±SD) with typical signs and symptoms suggesting venous disease of the lower limb(s) were referred to us for evaluation. They underwent ascending radionuclide venography by intravenous injection of ^{99m}Tc-MAA (IV-RNV) and by subcutaneous injection of ^{99m}Tc-pertechnetate at the acupuncture points K-3 and B-60 (SC-RNV).

Radionuclide venography by subcutaneous injection
Lying supinely below the detector of a commercially available gamma-camera (Elscint Dymax LF), every patient received subcutaneous injections of a total of 1 mCi (37 MBq) ^{99m}Tc-pertechnetate ($^{99m}TcO_4^-$), in 2 separate doses (each dose of ≤0.5 m*l* in volume), simultaneously at the accupuncture points K-3 and B-60 (Fig. 1) of the diseased or the right foot. The medial view of the leg was then taken at 20 seconds a frame for 5 or more frames. Meanwhile, we watched the monitor; and we moved the bed to take pictures of the knee for about 3 to 10 frames when the popliteal vein and/or its surrounding superficial veins were filled with radionuclide. Images of the superficial femoral vein and the iliac vein were subsequently taken. When testing of the diseased or the right lower limb was finished, the opposite limb was tested in turn in the same manner. Thus, altogether 16 to 32 frames were taken for each limb. A normal result is shown in Fig. 2A.

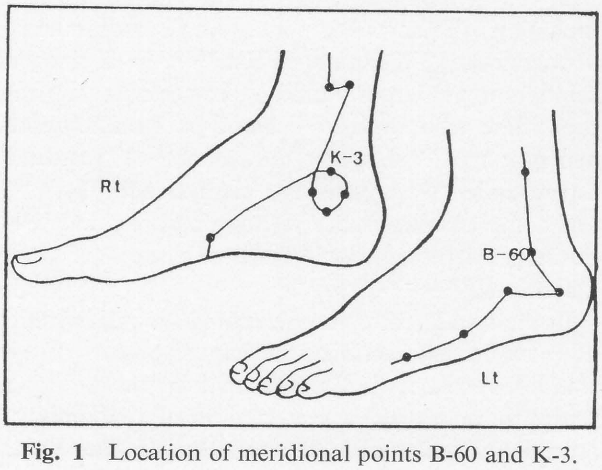

Fig. 1 Location of meridional points B-60 and K-3.

Radionuclide venography by intravenous injection
The IV-RNV was carried out at 30 minutes to 1 hour after the SC-RNV was finished, when the radionuclide of SC-RNV had been already cleared out of the intravascular space into the whole-body soft tissues. The moving scanning bed-gamma camera technique,[57] as decribed in the literature, was used for IV-RNV. About 1/2 of the 1 to 1.5 mCi (37 to 55.5 MBq) ^{99m}Tc-MAA was initially injected into a dorsal vein of one foot, after a tourniquet was applied above the ankle joint. The tourniquet was soon released and a medial view of the leg was taken when the deep veins of the calf filled with radionuclide, as observed on the camera monitor. Then, 1/2 of the remaining radionuclide was injected to fill the deep veins of the knee and the thigh, and an image of the thigh was taken. With injection of the rest of the dose, the common femoral and the iliac veins were finally scanned. Subsequently, a test was performed on the opposite lower limb in the same manner.

A

B

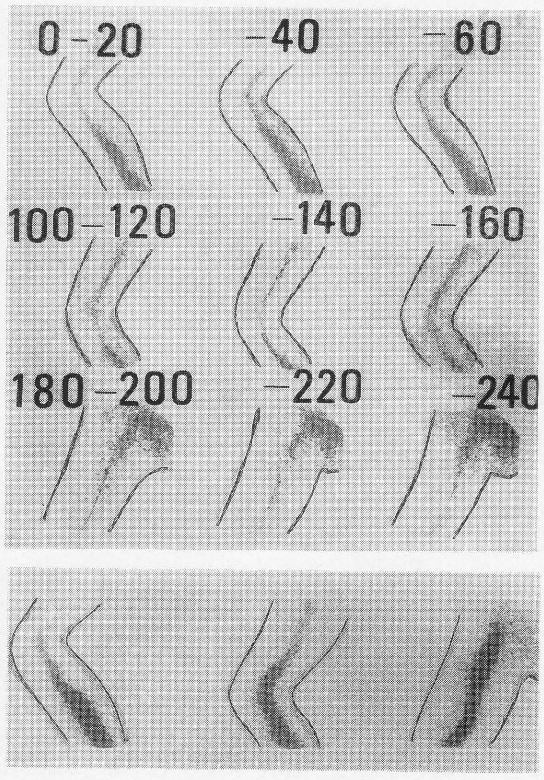

Fig. 2 A 59-year-old man with painful swelling and a localized burning sensation in the left lower limb. A. SC-RNV (medical view) revealed a normal dynamic venous flow in the right lower limb. Venous drainage of the limb was normally through the deep venous system, and began within 20 seconds after subcutaneous injection of $^{99m}TcO_4^-$ at acupuncture points K-3 and B-60. B. IV-RNV (medial view) of the right lower limb demonstrated the same venous flow pattern as SC-RNV did, but less dynamic.

A

B

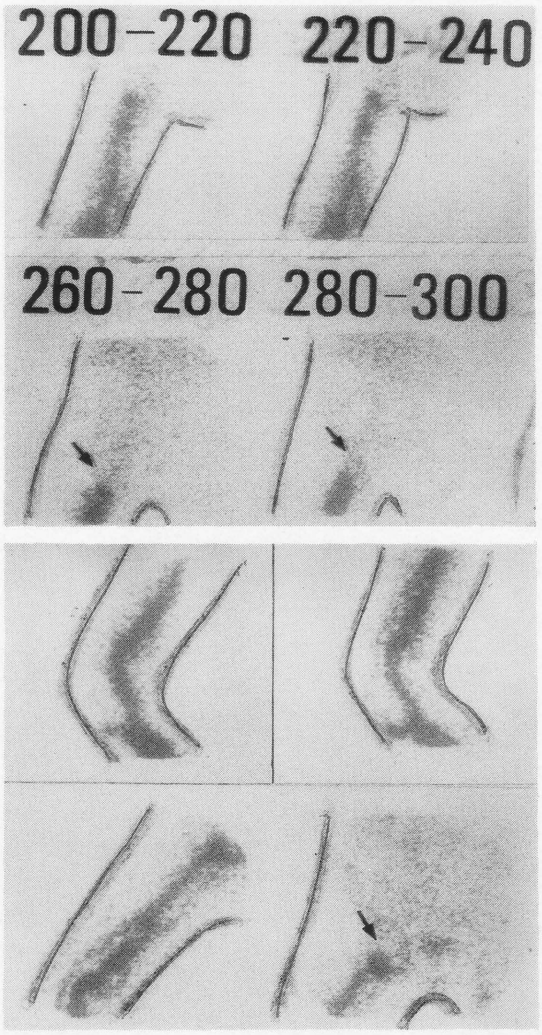

Fig. 3 A 42-year-old woman with bilateral leg edema after receiving postoperative irradiation therapy for cervical carcinoma. A. SC-RNV (medial view) of the right lower limb showed common femoral vein occlusion (arrows). B. IV-RNV (medial view) disclosed the same venous flow pattern (arrow).

A

B

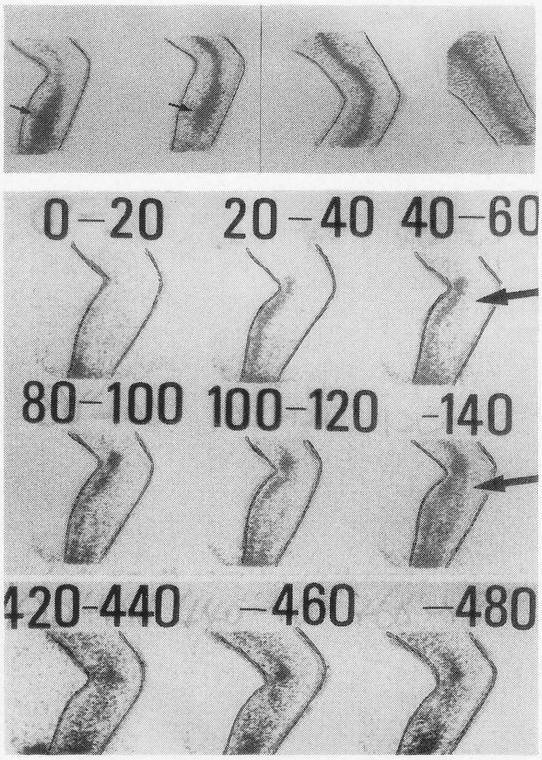

Fig. 4 A 48-year-old woman, suffering from sore calves. A. IV-RNV (medial view) revealed venous toruosity and dilatation in the left leg (arrows), and normal deep venous flow in the knee and the thigh. B. In SC-RNV (medial view), there was generally delayed venous drainage in the leg, and the deep venous flow in the calf region began to appear only late in the 140-second frame (arrows). Tortuous collateral vessels were prominent. These findings indicated partial stenosis of the deep calf vein(s) with superficial varicoses.

RESULTS

Case reports

Case 1. A 59-year-old male patient was admitted to the surgical ward because of painful swelling and a localized burning sensation in the left lower limb. Both SC-RNV and IV-RNV revealed a normal venogram of the right lower limb (Figs. 2A and 2B), and an occlusion at the left ilio-femoral venous junction. Subsequent contrast venography confirmed it.

Case 2. A 42-year-old female patient had received postoperative irradiation therapy for cervical carcinoma before she developed bilateral leg edema. The results of both SC-RNV and IV-RNV demonstrated bilateral deep venous occlusion at the ilio-femoral junction (Figs. 3A and 3B).

Case 3. A 48-year-old female patient suffered from sore calves. The IV-RNV revealed bilateral varicose veins in the calves (Fig. 4A). Sequential SC-RNV images showed delayed venous passage through the deep venous system in the left leg (Fig. 4B). Instead, superficial collateral venous flow was prominent and appeared much earlier (Fig. 4B). The SC-RNV also revealed partial stenosis of the right poplito-tibial vein almost the same as the change in the left limb.

Case 4. A 61-year-old female patient had intermittent attacks of bilateral lower leg edema, accompanied with occasional right flank pain, for nearly 2 years. Both the SC-RNV and IV-RNV demonstrated severe varicose veins in the calves (Figs. 5A and 5B).

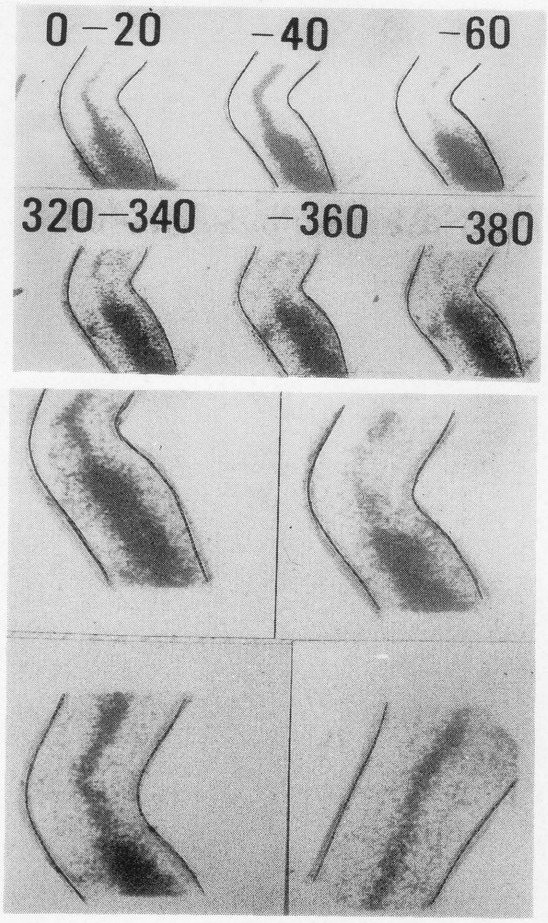

Fig. 5 A 61-year-old woman with intermittent lower leg edema without leg pain. A. SC-RNV (medial view) revealed severely tortuous abd dilated calf veins in the right lower limb, of which the venous draining flow began early in the initial 20 seconds after subcutaneous injection of radionuclide, suggesting no evidence of deep vein stenosis. B. Almost the same change was seen in IV-RNV (medial view).

Case 5. A 36-year-old female patient suffered from right calf soreness for several weeks and was referred for an evaluation of the deep veins of the leg. The IV-RNV did not indicate a definite abnormality (Fig. 6A). In contrast, the SC-RNV showed delayed venous drainage of the leg and prominent varicose veins in the calf region (Fig. 6B).

Case 6. A 42-year-old male patient, a narcotics addict, suddenly developed severe painful swelling and a localized burning sensation in the left leg. We failed to inject the radioactive agent into a dorsal vein of the left foot. However, a SC-RNV revealed complete stenosis of the tibial, popliteal and superficial femoral veins. Venous drainage of that leg was mainly through the superficial collateral veins (Figs. 7A and 7B).

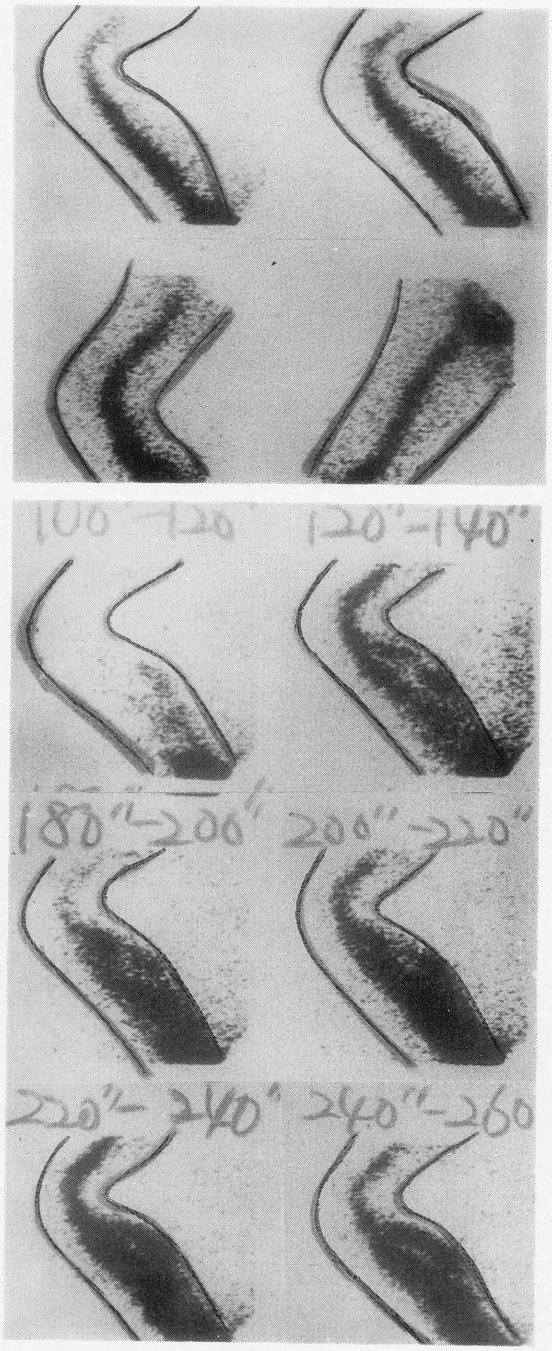

Fig. 6 A 36-year-old woman, suffering from right calf soreness. A. IV-RNV (medial view) of the right leg showed a normal venous flow pattern. B. SC-RNV, however, disclosed delayed venous drainage with prominent calf varicoses veins.

Overview

The overall results are shown in Table 1. Four of the 44 limbs were found to be normal in both SC-RNV and IV-RNV, and were clinically symptom free. Twelve limbs had varicose veins in the calves without evidence of DVT in SC-RNV; IV-RNV failed to

A

B

C

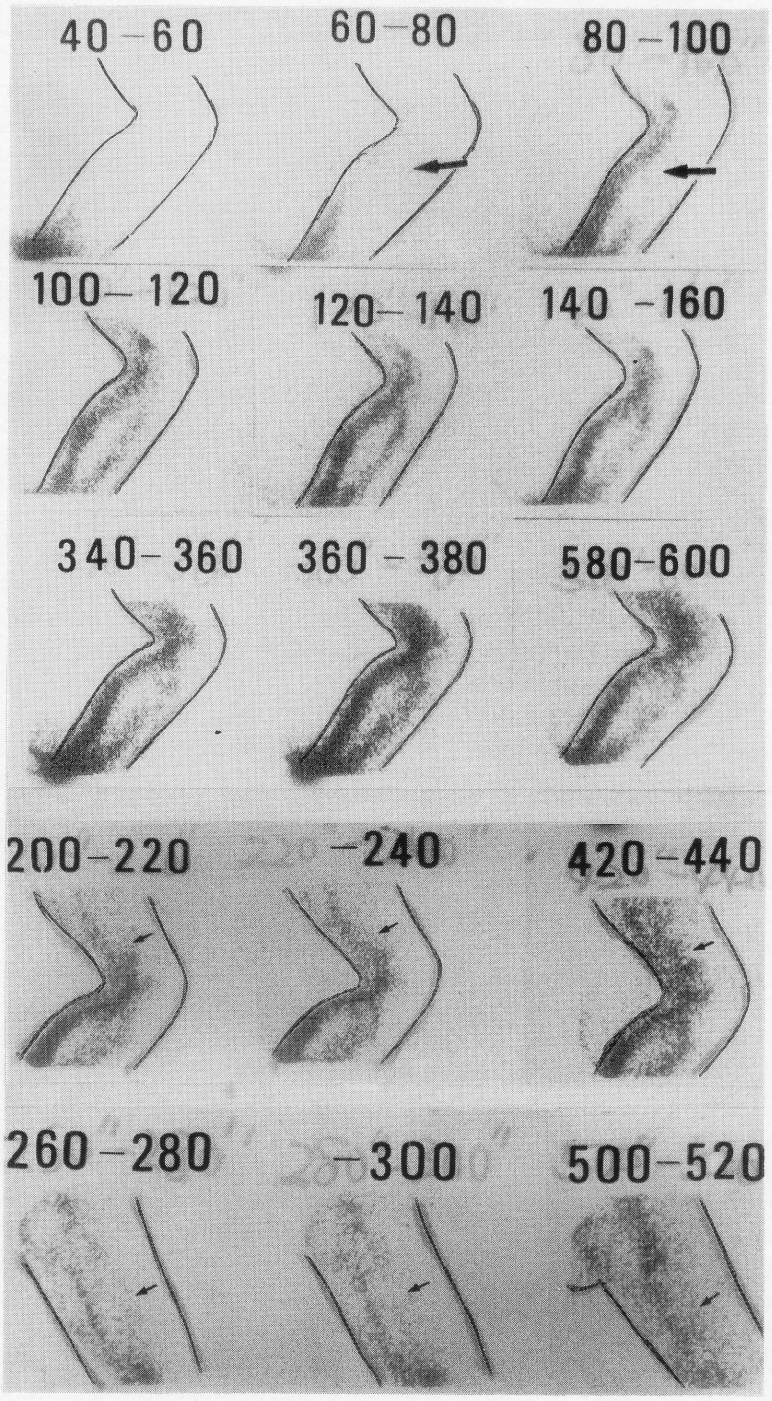

Fig. 7 A 42-year-old man with very painful swelling of the left leg. IV-RNV was not successful since the sole of the foot was extremely swollen. A. SC-RNV (medial view) demonstrated a serial dynamic flow pattern through the superficial veins in the leg. No deep venous flow was visible (arrows). B. SC-RNV of the left knee also revealed occlusion of the popliteal vein (arrows). C. The superficial femoral vein was seen to be occluded (arrows) in SC-RNV.

detect varicose veins in 6 of them. Eighteen limbs were found to have partial stenosis of the deep veins in SC-RNV, 14 in the poplito-tibial veins and 4 in the superficial femoral vein. Detection of poplito-tibial venous partial stenosis by IV-RNV was unreliable, only 4 limbs being detected (28.6%); and the diagnosis of partial stenosis of the superficial femoral vein by IV-RNV (25%, 1/4) was also unreliable. Complete stenosis (occulsion) of the deep veins was diagnosed by both SC-RNV and IV-RNV, with technical failure on injection in 1 (2.3%, 1/44) by IV-RNV. There was complete stenosis of the

Table 1 Venous abnormality of lower limbs in 22 patients (44 limbs) in RNV

	Normal	Leg varicose	Partial stenosis		Complete stenosis		
			PT	SF	PT	SF	IF
SC-RNV	4	12	14	4	4	1	8
IV-RNV	4	6	4	1	4	1	7

IF: Ilio-femoral vein; IV: Intravenous injection; PT: Poplito-tibial vein; RNV: Radionuclide venography; SC: Subcutaneous injection; SF: Superficial femoral vein.
(There are 3 limbs with combined IF and/or SF and/or PT stenosis.)

poplito-tibial veins in 4, the superficial femoral vein in 1, and the ilio-femoral veins in 8. Altogether, IV-RNV failed to provide a diagnostic result in 20 limbs.

DISCUSSION

Although ascending contrast venography remains the most widely acknowledged standard for diagnosis of venous diseases of the lower limbs, it has certain limitations, for example it is relatively technique-dependent and needs some expertise in both testing and reading and usually causes a higher radiation dose.[9–15] For this reason, several non-invasive methods have been gaining importance clinically. Among these the most valuable ones were real-time ultrasound,[32–39] impedance plethysmography,[40–48] and combined impedance plethysmography and ^{125}I-fibrinogen leg scanning.[49–50] Both real-time ultrasound and serial impedance plethysmography are accurate in diagnosing the proximal deep venous diseases (popliteal and femoral veins). However, they cannot detect dynamic change in the whole course of the deep veins. Besides, impedence plethysmography is not a real imaging process. DVT in the calf region less frequently causes fatal complications,[58] though it may predispose to the occurrence of proximal DVT that in turn can result in pulmonary embolism.[54,55] Neither real-time ultrasound nor impedance plethysmography is adequate in diagnosing calf venous disease.[35,37–39,45,46] ^{125}I-fibrinogen leg scanning can detect DVT in the calf veins; yet it has some limitations, e.g. a higher false positive rate.[17,18,52–55] It is, also, not a real imaging assessment. Blood-pool radionuclide venography was not so effective in detecting deep venous diseases of the lower limbs in our own experience. It usually missed cases with partial stenosis of the deep veins and sometimes gave a false positive result.

In researching the meridian, an important concept in traditional Chinese medicine, we have found that subcutaneous injection of ^{99m}Tc-pertechnetate at acupuncture points K-3 and B-60 could result in a rapid-sequenced venography.[56] By this technique, venous drainage of the lower limb is normally through the deep venous system, of which the radioactivity begins to appear in the leg within the first 20 seconds after the injection (Fig. 2A). In cases with calf varicosity, venous drainage of the involved leg may be totally delayed (case 5), or the deep venous drainage remains normally smooth (case 4); in either condition, there should be segmentally tortuous and dilated superficial veins with blood stagnation. In the present study 12 limbs showed such a change in SC-RNV; 1 of them received ascending contrast venography, that demonstrated the same change. Partial stenosis of the deep vein(s) is evidenced by delayed deep venous drainage (case 3) or faint deep venous passage, accompanied with earlier and prominent superficial venous drainage. Three of the 18 limbs, that showed partial stenosis of the deep vein(s), received ascending contrast venography and proved to be deep vein stenosis. Total or complete stenosis of the deep veins usually involved an occluded deep vein with or without a lot of collateral superficial vessels (cases 1, 2 and 6). All the limbs with complete deep venous stenosis showed such a change in SC-RNV, and for one of them ascending contrast venography was employed and gave the same result.

For years ascending radionuclide venography (IV-RNV) was routinely carried out to test all clinically suspected DVTs and other venous diseases of the lower-limbs in our laboratory. It was relatively simple and caused less radiation than ascending contrast venography, and was much more acceptable to the patients. IV-RNV, however, in the present study did not disclose calf varicosity in half of the 12 limbs, all of which were seen to have varicoses and/or telangiectasis over the skin of the leg on inspection. Another pitfall of IV-RNV was that it seemed unable to detect partial stenosis of the deep vein(s) on most occasions. Partial stenosis of the deep vein may be caused by an intraluminal thrombus, extravascular hematoma, Baker's cyst or adjacent masses.[59] Recognizing the presence of the intravascular or non-vascular lesion makes proper management possible. Both IV-RNV and SC-RNV are not adequate for the diagnosis of such a lesion. But, through demonstration of dynamic changes in the venous flow, SC-RNV could detect the site of partial stenosis, indicating where to apply morphological detection, e.g. a duplex ultrasound scan. As with SC-RNV, IV-RNV was also reliable in demonstrating complete stenosis of the deep veins with thrombosis.[57] Indeed, IV-RNV detected 12 of the 13 sites with deep vein thrombosis in the present study, while it did not work in 1 case because of unsuccessful intravenous injection into the severely edematous foot. SC-RNV did not cause any problems of this kind.

As for the mechanism of SC-RNV, several previous important reports should be mentioned. In 1980, Plummer reported the presence of communicating or perforating veins beneath the acupuncture points in the lower limb.[60] Dung also mentioned that there are concomitant arteries and veins coursing along the nerves which reach muscle masses at the neuromuscular attachments, and the 3 components, i.e. nerves, arteries and veins, form so-called neurovascular bundles.[61] Although the physiological role of blood vessels in the formation of acupuncture points was not known, he emphasized that blood vessels in the vicinity of the neuromuscular attachment often cause the points to become tender sooner. These points could be what we usually call in the bed-side language "physiologically tender points." By light and electron microscopy, Watari et al also discovered that there are a lot of vascular elements in the acupuncture points, much more than in those without acupuncture loci.[62] In a word, the above investigators suggested that the acupuncture points might be closely related to the vessels morphologically. In one of our previous studies,[56] we found that either intra-acupuncture point injection or subcutaneous (SC) injection of ^{99m}Tc-pertechnetate at or around the acupuncture points could result in a venography mimicking IV-RNV. If the SC injection was done far from the acupuncture points, the appearance of venous flow could be considerably delayed and not so well visualized. Thus, the acupuncture points might play a role in collecting the tissue fluid and transporting it into the intra-vascular space. Since the ^{99m}Tc-pertechnetate is in an ionic state, it is not surprising that after SC injection it "diffuses" into veins rather than lymphatics. Another important point is why we chose K-3 and B-60 for SC injection. The reasons are: 1. Both K-3 and B-60 are easy to detect. They are the physiologically tender points located behind the medial and lateral malleoli of the ankle, respectively. 2. Since they are located at the ankle joint, accumulation of the subcutaneously injected isotope can cause no interference on the SC-RNV images.

As a whole, SC-RNV may be superior to IV-RNV in diagnosing lower-limb venous disease. It provides functional information associated with the dynamic flow change in both superficial and deep veins of the lower limbs. However, since the images abtained from SC-RNV are mainly functional, certain real morphological imaging procedures, e.g. duplex ultrasound scan, can be used in combination. The latter is known to be highly reliable in detecting proximal venous thrombus, but is poor in diagnosing calf venous disease.[35,37–39] It is technique-dependent and does not demonstrate an entire course of venous images. Therefore, we believe that a combination of SC-RNV and duplex ultrasound scan will become the most reliable imaging method in detecting the lower-limb venous disease. We are going to work on the evaluation of such a combination.

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