Scintigraphic Recording of Blood Volume Shifts

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A scintigraphic device consisting of small scintillation probes tightly fixed to the skin was developed to record intravascular blood volume shifts continuously and simultaneously at several sites. The aim of the present study was to ascertain the reliability of the measurements obtained, show the blood shifts induced by common daily activities in healthy subjects and clarify the mechanisms responsible for hemodynamic changes. **Methods:** Measurements were made in three fields of the right lung, the liver, thighs and calves of 16 men during Valsalva maneuver, hyperventilation, various posture changes and treadmill walking. Some tests were repeated. **Results:** The measured blood volume shifts were always in the expected direction and in accordance with those reported in the literature; they also were reproducible. Therefore, the measurements were reliable. A pattern of blood volume changes peculiar to some common daily activities was recorded in subjects moving freely. Insights were obtained on the mechanisms responsible for the blood volume shifts. **Conclusion:** Our noninvasive technique provides reliable continuous measurements of blood volume changes at several sites during common daily activities and could be applied not only in healthy subjects but also in patients.

Key Words: blood shifts; lung; liver; lower limbs; equilibrium blood-pool scintigraphy

J Nucl Med 1995; 36:2022–2031

It is well established that blood volume displacements in an organ or limb can be reliably assessed by equilibrium blood-pool scintigraphy as local intravascular volume shifts are reflected by local changes in radioactivity (*1–4*). The scintillation camera, usually applied to detect these changes, is not suited for measurements in subjects moving freely, whereas in this condition miniature scintillation probes so light that they can be fixed to the patient's skin may be suitable. We therefore developed a device using this type of probe (*5,6*) and performed the present study to assess the reliability of the measurements obtained, show the blood shifts induced by common daily activities in the lung, liver, thighs and calves of healthy subjects and clarify the mechanisms responsible for hemodynamic changes.

MATERIALS AND METHODS

Subjects

Sixteen healthy men (aged 46 ± 12, range 24–69 yr) were studied. Each subject gave informed consent and the study protocol was approved by the Institutional Committee on Human Research.

Monitoring Equipment

The characteristics of the device we used to record the gamma activity of ^{99m}Tc have been previously reported (*5,6*). The apparatus includes four nonimaging probes (Quartz Alfa Silice, Holland B.V. Zazak-Demezn, The Netherlands). Each detector (external dimensions 27 × 35 mm, weight, 32 g) consists of a thallium-drifted CsI crystal (10 × 10 × 10 mm^3, Harshaw, Holland B.V. Zazak-Demezn), photodiode and hybrid preamplifier (voltage required, 24 volts). It was placed inside a 3-mm thick lead container which completely shielded the detector from unwanted radioactivity, except at the base from which a cylindrical collimator (internal dimensions 4 × 15 mm in diameter) protruded. Identical collimators were used throughout the study. The base of each lead container was stiffly inserted into a plastic disk (50 × 15 mm in diameter). The total weight of each probe was about 347 g.

Figure 1 depicts a probe and the instrumentation block diagram which includes, in addition to four probes: four digital-to-analog conversion amplifiers in a separate box fastened with a belt to the subject's waist; a 5-m cable; a pulse-height analyzer with the energy window set at 140 kcV ± 20%; a multiscaler ratemeter which monitored the amplified and filtered signals automatically and provided 1-sec counts in continuous succession; a personal computer which stored the counts of the four probes on a spreadsheet and displayed the corresponding time-activity curves in real time in four colors; and a multichannel analyzer to check window width and verify the energy spectrum in real time. Dedicated software was used for data management.

In vivo experiments were preceded by in vitro studies. The detection sensitivity was calculated using a system of plastic bags and sponges and a ^{99m}Tc solution to simulate radiolabeled blood volumes in lungs, liver, heart and surrounding tissues and their effect on gamma radiation absorption. The count rate efficiency for each detector was 4 × 10^5 cps for each MBq/cm^3 of ^{99m}Tc solution in a simulated leg of a reference phantom, in the 30° solid angle defined by the collimator. We did not record images; we measured relative count rate changes in a fixed geometry so that any variation of recorded radioactivity is due to a blood volume increase or decrease within the solid angle. To ensure a tight connection of the detector to the subject's skin, the base of the plastic cylinder was stuck to a large thick layer of adhesive tape

Received Feb. 6, 1995; revision accepted Jul. 5, 1995.

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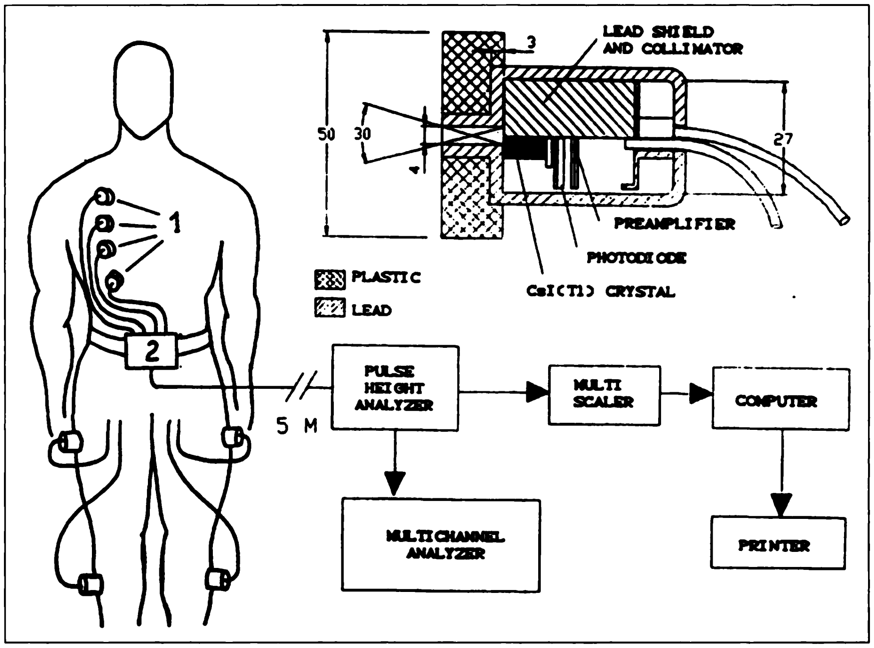

FIGURE 1. Instrumentation block diagram.

covering the skin, and the device was then fastened with abundant adhesive tape to this layer and the surrounding skin. For the lower limbs, adhesive tapes were positioned only along their length to not hinder blood circulation.

The four probes were fixed along the right midclavicular line with the collimator holes positioned at the 2nd, 4th, 6th and 10th intercostal spaces to record radioactivity in the upper, middle and lower fields of the right lung and in the liver. To record radioactivity in the thighs and calves, the four probes were fixed to the lateral side of the lower limbs, about 15 cm above the knees, and the middle of the calves.

Blood Shift Measurements

Each subject's own erythrocytes were labeled in vivo with 20 mCi ^{99m}Tc according to standard techniques. All patients were studied about 30 min after radiotracer injection in a laboratory with a room temperature of about 22°C. They had fasted and abstained from smoking for at least 12 hr. Radioactivity in three fields of the right lung and in the liver was measured continuously during Valsalva maneuver, posture changes, hyperventilation, and treadmill walking. During the Valsalva maneuver (performed twice) during which the subjects were supine, subjects blew a mercury column, raising its level to 40 mm and maintaining this height for 25 sec. The subjects then performed the following posture changes from recumbency: (a) to passive elevation of both legs to about 40°, (b) to sitting up on the bed with legs straight out, (c) to sitting on the bed with legs dangling and (d) to standing. The last change was repeated once. Each posture was maintained for 2 min and preceded and followed by 2-min periods during which the subjects rested supine on the bed. At this point, the subjects were asked to breathe as deeply and frequently as they could for 1 min while standing still. They then sat for 2 min on a chair placed on the treadmill, stood still for another 2 min and afterwards performed a walking test during which the treadmill slope was kept constant at 10° while the speed was increased by 1 kmph every 3 min from 1 to 6 kmph. The subjects always started and stopped walking abruptly. After stopping, the subjects first stood still for 3 min and then sat on a chair to rest for about 15 min. The walking test was then repeated. During both walking tests, blood pressure and heart rate were measured by cuff-sphygmomanometry and continuous EKG recording, respectively.

Radioactivity was also measured in the thighs and calves during changes in posture, from recumbency to sitting on the bed up with straight legs, sitting on the bed with legs dangling and standing still, in this order. Measurements were also performed during two walking tests. In the first (walking A), the subjects walked twice on the treadmill at a steady speed of 3 kmph, the first time for 30 sec and the second time for 90 sec; subjects stood still for 4 min between the two walking periods. During the second walking test (walking B), subjects walked sequentially at three increasing speeds, 1, 3 and 5 kmph; each walking speed was maintained for 3 min. In both walking tests, the treadmill slope was kept constant at 10°, and starting and stopping were always abrupt.

Furthermore, blood volume shifts in the three fields of the right lung were measured as subjects changed from a recumbent to erect posture and while walking at 2 kmph for 1 min before and after arresting blood circulation to the lower limbs. Blood circulation was arrested by inflating two pneumatic cuffs 17 cm wide and 83 cm long wrapped around the thighs at as high a level as possible. While the subjects were standing with cuffs inflated, they also hyperventilated for 1 min.

Data Analysis

From the original 1-sec counts, corrected for physical decay of ^{99m}Tc, the means of the values in each 10 sec of data (5 sec for the Valsalva maneuver) were calculated sequentially throughout the period preceding each test, the test itself and recovery. The starting value for the calculation was always that at the start of the experimental condition. To convert such 10- or 5-sec means into values representing the change from baseline, they were divided by the mean of the counts recorded during the 60 sec immediately preceding the start of the experimental condition. The ratios obtained in all subjects in a given test were compared by one-way analysis of variance and the Bonferroni method in each field. The hemodynamic effect of each experimental condition was also evaluated by comparing the means of the values in 30 sec (15 and 20 sec, respectively, for the Valsalva maneuver and walking test A) measured in each field before and during the test. Paired t-test or analysis of variance and the Bonfer-

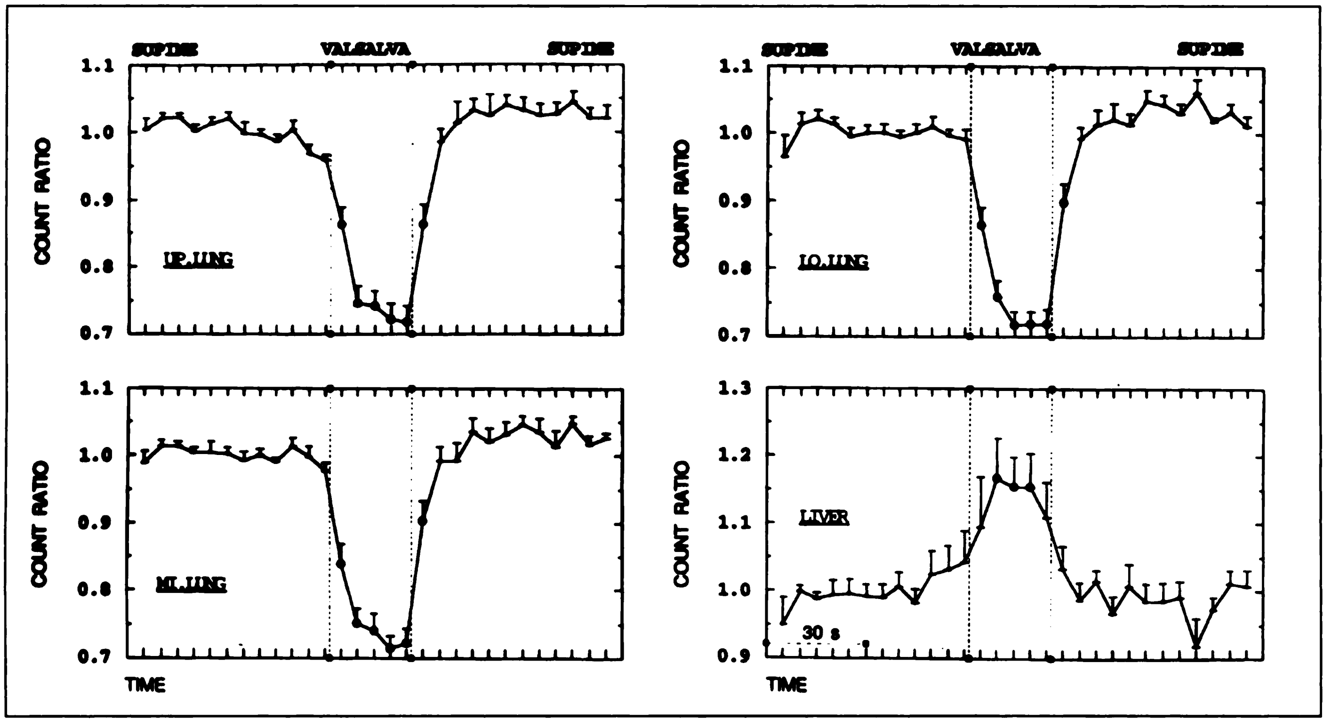

FIGURE 2. Radioactivity changes induced by the Valsalva maneuver in the upper (UP.LUNG), middle (MI.LUNG) and lower field (LO.LUNG) of the right lung and in the liver of supine subjects (n = 8). The mean of two Valsalva maneuvers are shown. Values are the mean + s.e.m. of the computed ratios. Closed circles indicate statistical significance, $p < 0.05$, and the vertical dashed lines define the start and end of the test.

roni method in cases of multiple comparisons were used to evaluate results. A p value <0.05 was statistically significant.

RESULTS

Blood Volume Changes in the Right Lung and Liver

Effects of the Valsalva Maneuver. During this maneuver (Fig. 2, Table 1), the blood volume fell rapidly and markedly in all three fields of the right lung and transiently increased in the liver. When blowing was stopped, the blood volume quickly returned to basal values at all sites. This hemodynamic picture did not differ when the Valsalva maneuver was repeated.

Effects of Posture Changes. Lung blood volume increased slightly in the upper and middle fields but not in the lower field during leg elevation (Table 2). It decreased in all the other changes of posture (Fig. 3, Table 2), with the largest decrease when a supine subject stood up (p = 0.001). This posture change was the only one to induce a similar decrease in blood volume in all three fields of the right lung. In fact, in the lower field, no shift of blood and only a slight decrease, smaller than in the upper field (p = 0.013), occurred when a subject sat up on the bed with, respectively, legs straight or dangling. Blood volume remained unchanged in the upper

TABLE 1
Blood Volume Changes in Eight Subjects during Two Valsalva Maneuvers*

	Upper field of the right lung	p	Middle field of the right lung	p	Lower field of the right lung	p	Liver	p
Test 1								
(B)	1.006 ± 0.023		0.996 ± 0.017		0.987 ± 0.024		1.006 ± 0.037	
(T)	0.729 ± 0.078	0.001	0.733 ± 0.064	0.001	0.723 ± 0.057	0.001	1.166 ± 0.127	0.026
Test 2								
(B)	1.004 ± 0.023		1.001 ± 0.032		1.011 ± 0.018		0.982 ± 0.06	
(T)	0.725 ± 0.061	0.001	0.717 ± 0.06	0.001	0.710 ± 0.063	0.001	1.151 ± 0.156	0.056
Means of tests								
(B)	1.005 ± 0.019		0.999 ± 0.017		0.999 ± 0.015		0.997 ± 0.049	
(T)	0.727 ± 0.065	0.001	0.725 ± 0.056	0.001	0.717 ± 0.052	0.001	1.158 ± 0.139	0.041

*All values are mean radioactivity count ratios ± s.d.
B = baseline and T = midway through the manouver.

TABLE 2
Blood Volume Shifts before (B) and during (T) Posture Changes*

		No.	Upper field of the right lung	p	Middle field of the right lung	p	Lower field of the right lung	p	Liver	p
Supine position to leg elevation	(B)	14	1.002 ± 0.014		1.002 ± 0.009		1.003 ± 0.013		0.999 ± 0.011	
	(T)		1.036 ± 0.042	0.005	1.033 ± 0.037	0.014	1.010 ± 0.048	0.566	1.051 ± 0.048	0.003
Supine position to sitting up	(B)	14	0.997 ± 0.013		0.996 ± 0.011		0.996 ± 0.012		0.998 ± 0.012	
with legs straight	(T)		0.864 ± 0.102	0.001	0.904 ± 0.077	0.001	0.934 ± 0.163	0.180	1.123 ± 0.296	0.132
Supine position to sitting up on	(B)	6	1.003 ± 0.012		0.997 ± 0.009		1.003 ± 0.005		1.001 ± 0.006	
bed with legs dangling	(T)		0.810 ± 0.044	0.001	0.871 ± 0.049	0.003	0.913 ± 0.062	0.015	1.109 ± 0.209	0.269
Supine position to standing										
Test 1	(B)	14	1.001 ± 0.019		0.999 ± 0.014		1.001 ± 0.009		0.994 ± 0.014	
	(T)		0.801 ± 0.1	0.001	0.778 ± 0.067	0.001	0.797 ± 0.071	0.001	1.034 ± 0.215	0.497
Test 2	(B)	13	1.004 ± 0.011		1.000 ± 0.012		0.998 ± 0.014		1.003 ± 0.011	
	(T)		0.778 ± 0.094	0.001	0.763 ± 0.061	0.001	0.791 ± 0.08	0.001	1.046 ± 0.176	0.399
Means of tests	(B)	13	1.004 ± 0.012		0.999 ± 0.01		1.000 ± 0.007		0.999 ± 0.01	
	(T)		0.784 ± 0.092	0.001	0.769 ± 0.064	0.001	0.793 ± 0.072	0.001	1.046 ± 0.192	0.391
Sitting on a chair to standing										
Test 1	(B)	12	1.007 ± 0.013		0.997 ± 0.013		1.001 ± 0.017		1.000 ± 0.012	
	(T)		0.955 ± 0.083	0.068	0.929 ± 0.091	0.017	0.902 ± 0.093	0.003	0.916 ± 0.122	0.031
Test 2	(B)	12	0.994 ± 0.017		0.999 ± 0.017		0.994 ± 0.012		1.002 ± 0.017	
	(T)		0.955 ± 0.089	0.147	0.911 ± 0.095	0.009	0.890 ± 0.097	0.003	0.978 ± 0.158	0.594
Means of tests	(B)	12	1.000 ± 0.007		0.998 ± 0.011		0.998 ± 0.009		1.001 ± 0.012	
	(T)		0.955 ± 0.083	0.091	0.920 ± 0.087	0.007	0.896 ± 0.088	0.002	0.947 ± 0.127	0.160

*All values are mean radioactivity count ratios ± s.d.

field when the subject stood erect from sitting on a chair. Whenever a blood volume shift occurred, it always presented the same pattern: a rapid increase or decrease at assumption of a new posture, a plateau and finally a rapid return to baseline when the basal posture was resumed.

In contrast, hepatic blood volume (Fig. 3, Table 2) was usually unaffected by posture changes, except leg elevation which induced a small increase. In all three fields of the lung and in the liver blood volume presented the same pattern when a change of posture was repeated, that is assuming the supine posture, and standing from recumbency and from sitting on a chair.

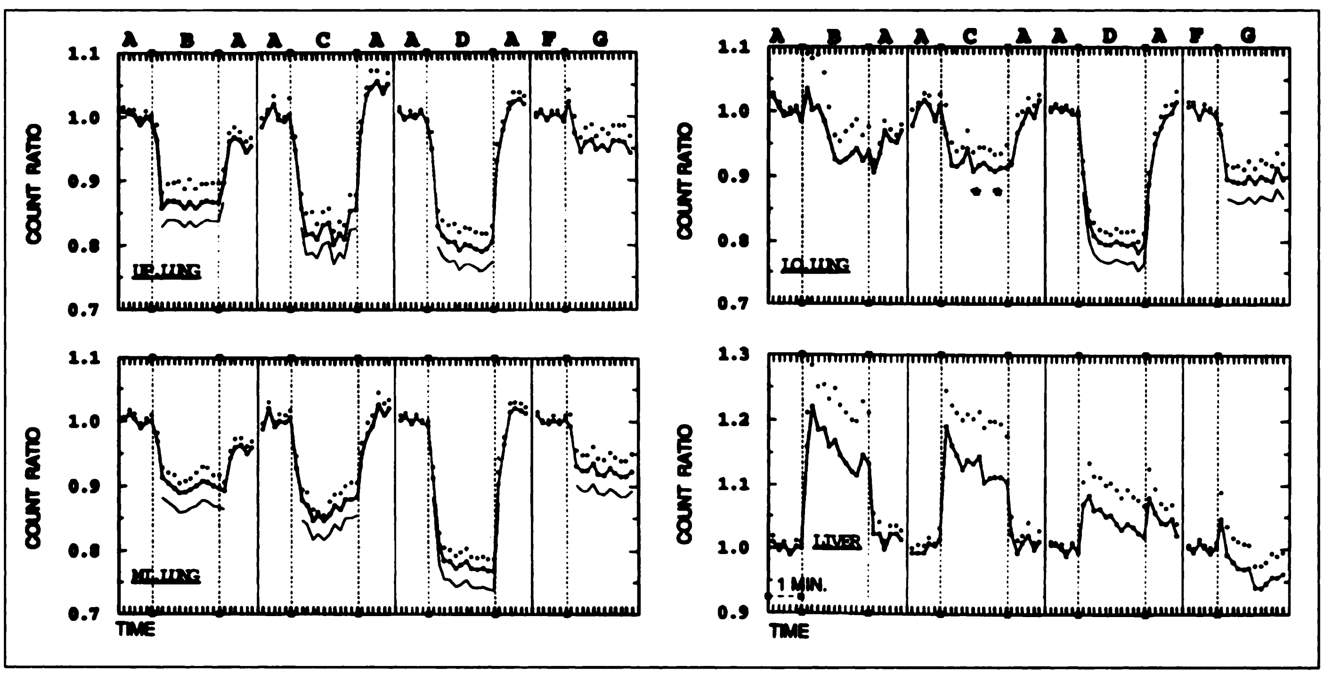

FIGURE 3. Radioactivity changes recorded in three right lung fields and the liver when subjects performed the following posture changes: supine (A) to sitting up with legs straight (B) (n = 14); supine (A) to sitting with legs dangling (C) (n = 6); supine (A) to standing (D) (values are the means obtained in two tests in 14 subjects); and sitting on a chair (F) to standing up (G) (values are the means obtained in two tests in 13 subjects). Small closed circles indicate s.e.m. and an asterisk or lower line indicates statistical significance, $p < 0.05$.

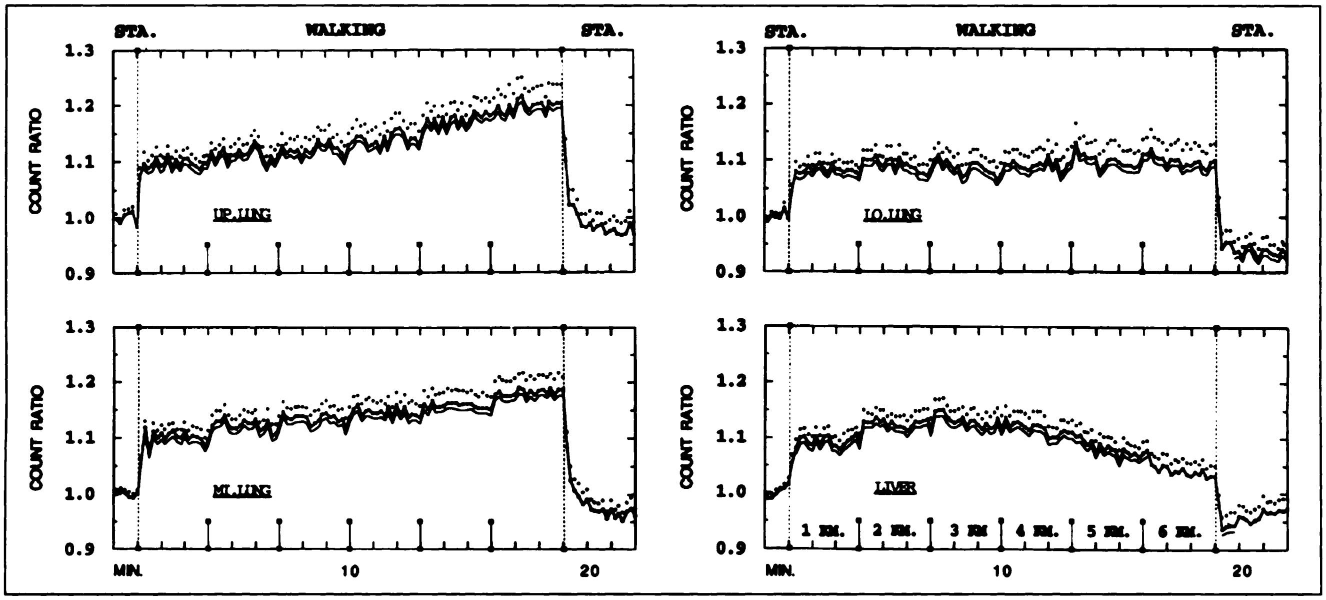

FIGURE 4. Blood volume changes in the three fields of the right lung and the liver (13 subjects) during treadmill walking. Values are the mean of two tests.

Effects of Treadmill Walking. At the start of walking, blood volume increased suddenly and similarly in all three fields of the right lung and in the liver (Fig. 4, Table 3). Lung blood volumes remained stable until the speed reached 3 kmph and increased progressively in the upper and middle fields (p = 0.001 at 5 and 6 kmph) but not in the lower field at higher walking speeds. Hepatic blood volume tended to rise slightly from 1 to 3 kmph and thereafter decreased progressively returning to baseline at 6 kmph. When walking was stopped, blood volume fell rapidly to the basal value in the upper and middle fields of the right lung and under the basal value in the lower field and in the liver.

These changes in blood volume, like those in systolic and diastolic blood pressure and heart rate, were similar in both tests. The highest values reached by the last three variables were, respectively, 169 ± 18 mmHg, 106 ± 7 mmHg and 135 ± 14 bpm.

Effects of Hyperventilation. During hyperventilation (Fig. 5, Table 4), blood volume decreased in the right lung and increased in the liver. The changes were similar in magni-

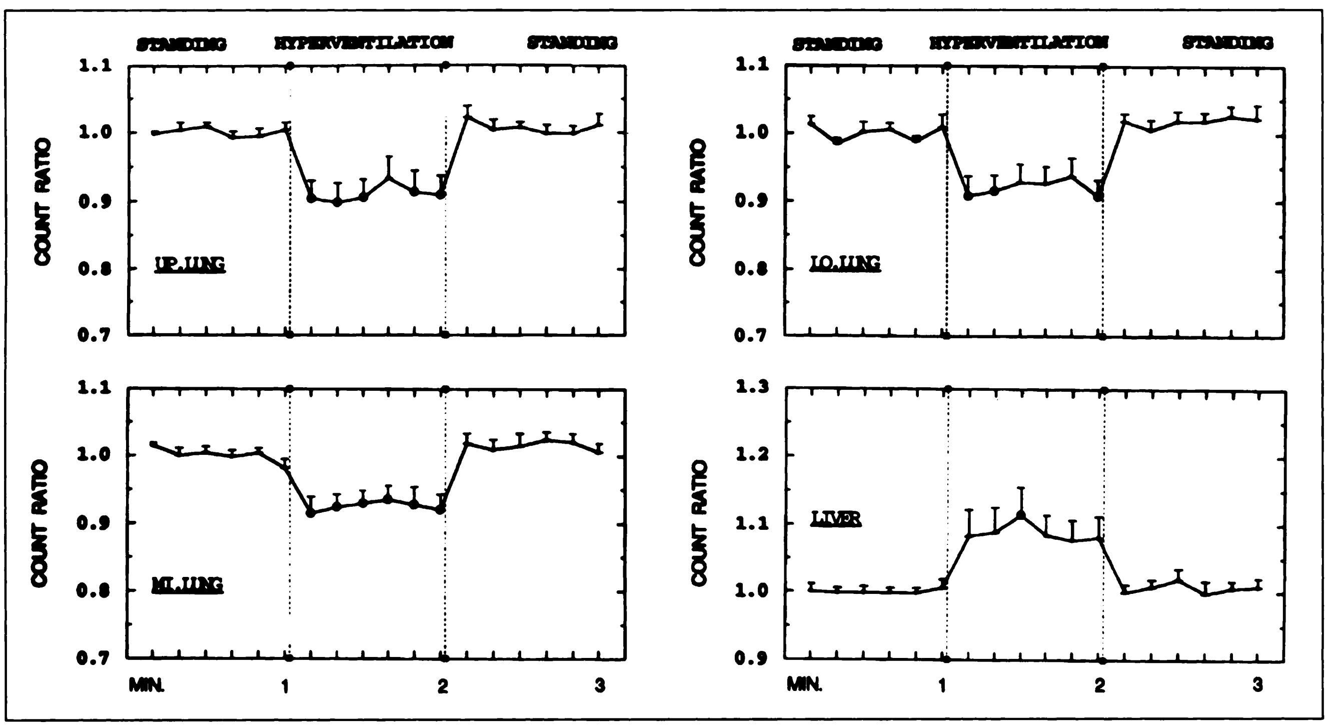

FIGURE 5. Blood volume changes in the three right lung fields and the liver during hyperventilation in standing subjects (n = 13).

TABLE 3
Blood Volume Changes during Treadmill Walking*

	Upper field of right lung (n = 12)	p	Middle field of right lung (n = 13)	p	Lower field of right lung (n = 13)	p	Liver (n = 13)	p
Test 1								
Baseline	0.996 ± 0.009		0.994 ± 0.016		1.002 ± 0.017		0.994 ± 0.013	
1 kmph	1.103 ± 0.043	0.029	1.106 ± 0.053	0.005	1.085 ± 0.041	ns	1.089 ± 0.058	0.050
2 kmph	1.108 ± 0.052	0.017	1.115 ± 0.057	0.001	1.090 ± 0.051	0.037	1.143 ± 0.07	0.001
3 kmph	1.118 ± 0.075	0.005	1.131 ± 0.063	0.001	1.084 ± 0.06	0.047	1.125 ± 0.081	0.001
4 kmph	1.138 ± 0.082	0.001	1.146 ± 0.085	0.001	1.090 ± 0.073	0.035	1.114 ± 0.071	0.003
5 kmph	1.191 ± 0.098	0.001	1.147 ± 0.083	0.001	1.096 ± 0.065	0.015	1.077 ± 0.067	ns
6 kmph	1.200 ± 0.106	0.001	1.177 ± 0.09	0.001	1.092 ± 0.077	0.026	1.031 ± 0.064	ns
Recovery 1	1.020 ± 0.089	ns	1.014 ± 0.099	ns	0.950 ± 0.097	ns	0.941 ± 0.104	ns
Recovery 2	0.980 ± 0.072	ns	0.960 ± 0.067	ns	0.938 ± 0.07	ns	0.949 ± 0.094	ns
Recovery 3	0.970 ± 0.074	ns	0.961 ± 0.059	ns	0.928 ± 0.067	ns	0.966 ± 0.077	ns
Test 2								
Baseline	1.001 ± 0.013		0.999 ± 0.012		0.993 ± 0.011		0.988 ± 0.023	
1 kmph	1.080 ± 0.059	0.008	1.096 ± 0.072	0.005	1.087 ± 0.047	0.006	1.098 ± 0.071	0.001
2 kmph	1.097 ± 0.062	0.001	1.119 ± 0.069	0.003	1.091 ± 0.054	0.004	1.116 ± 0.066	0.001
3 kmph	1.122 ± 0.071	0.001	1.137 ± 0.082	0.001	1.094 ± 0.06	0.002	1.118 ± 0.085	0.001
4 kmph	1.143 ± 0.089	0.001	1.143 ± 0.093	0.001	1.097 ± 0.078	0.001	1.104 ± 0.073	0.001
5 kmph	1.193 ± 0.086	0.001	1.162 ± 0.093	0.001	1.092 ± 0.064	0.003	1.070 ± 0.051	ns
6 kmph	1.219 ± 0.12	0.001	1.189 ± 0.108	0.001	1.094 ± 0.074	0.002	1.041 ± 0.071	ns
Recovery 1	1.022 ± 0.086	ns	1.007 ± 0.071	ns	0.949 ± 0.083	ns	0.939 ± 0.071	ns
Recovery 2	0.986 ± 0.064	ns	0.981 ± 0.05	ns	0.951 ± 0.057	ns	0.952 ± 0.062	ns
Recovery 3	0.973 ± 0.072	ns	0.963 ± 0.051	ns	0.936 ± 0.051	ns	0.969 ± 0.058	ns
Means of tests								
Baseline	0.998 ± 0.01		0.997 ± 0.011		0.998 ± 0.008		0.991 ± 0.014	
1 kmph	1.092 ± 0.045	0.030	1.101 ± 0.057	0.006	1.086 ± 0.041	0.015	1.093 ± 0.06	0.003
2 kmph	1.103 ± 0.054	0.004	1.117 ± 0.061	0.001	1.090 ± 0.05	0.008	1.130 ± 0.062	0.001
3 kmph	1.120 ± 0.071	0.001	1.134 ± 0.066	0.001	1.089 ± 0.058	0.009	1.121 ± 0.078	0.001
4 kmph	1.141 ± 0.084	0.001	1.145 ± 0.085	0.001	1.094 ± 0.074	0.004	1.109 ± 0.066	0.001
5 kmph	1.192 ± 0.091	0.001	1.154 ± 0.08	0.001	1.094 ± 0.064	0.004	1.073 ± 0.055	0.050
6 kmph	1.210 ± 0.109	0.001	1.183 ± 0.093	0.001	1.093 ± 0.074	0.005	1.036 ± 0.064	ns
Recovery 1	1.021 ± 0.085	ns	1.010 ± 0.078	ns	0.949 ± 0.088	ns	0.940 ± 0.08	ns
Recovery 2	0.983 ± 0.063	ns	0.971 ± 0.051	ns	0.944 ± 0.062	ns	0.951 ± 0.67	ns
Recovery 3	0.972 ± 0.071	ns	0.962 ± 0.051	ns	0.932 ± 0.054	ns	0.967 ± 0.064	ns

*All values are mean radioactivity count ratios ± s.d.

tude at all sites and started and ended rapidly at the start and cessation of hyperventilation.

Blood Volume Changes in the Thigh and Calf

Effects of Posture Changes. Blood volumes in the thigh and calf remained unchanged when subjects were supine (Fig. 6, Table 5). In the thigh, blood volume did not vary when subjects sat with their legs dangling, and it increased similarly when they sat with their legs straight and then stood. In the calf, blood volume always increased; the increase was smallest with the change to sitting with straight legs, greater with the change to standing and greatest with the change to sitting with dangling legs ($p = 0.031$). Blood volume increases in the calf were more marked than those in the thigh ($p = 0.001$). In both the thigh and calf, however, the increases were rather slow, which contrasts with the rapid decreases induced by a return to the supine posture.

TABLE 4
Blood Volume Changes in Thirteen Subjects During Hyperventilation (Mean Radioactivity Count Ratios ± s.d.)

	Upper field of right lung	Middle field of right lung	Lower field of right lung	Liver
Baseline	0.999 ± 0.016	1.002 ± 0.018	0.998 ± 0.024	0.999 ± 0.014
Test	0.912 ± 0.102	0.930 ± 0.065	0.922 ± 0.088	1.097 ± 0.119
p	⟨0.011⟩	⟨0.002⟩	⟨0.016⟩	⟨0.013⟩

Effects of Treadmill Walking. Each time subjects walked at 3 kmph (Fig. 7, Table 6). Abruptly starting and stopping walking caused a sudden decrease and sudden increase, respectively, in blood volume in the lower limbs, although the changes were less marked in the thigh than in the leg ($p = 0.001$). When subjects rested while standing, blood volume did not change in the whole lower limb.

A similar pattern of blood volume changes in the lower limb was observed in walking test B (Fig. 8, Table 6), which

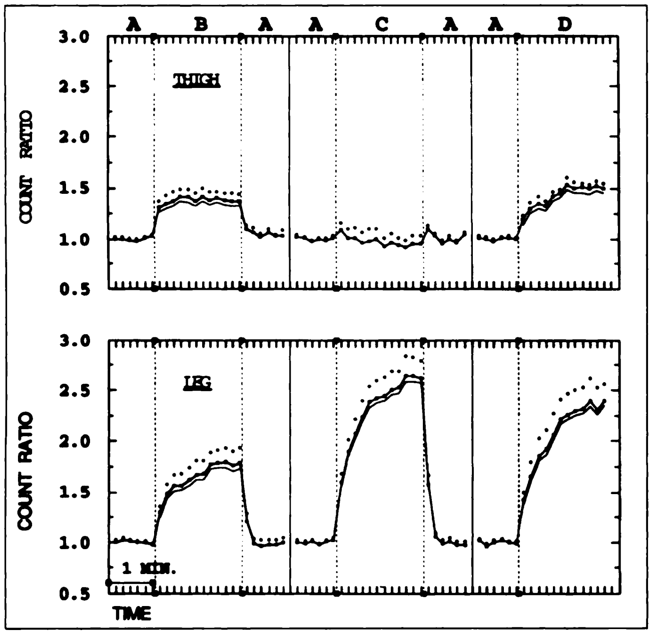

FIGURE 6. Radioactivity changes recorded in the thigh (n = 14) and leg (n = 14) during the following posture changes: supine (A) to sitting up with legs straight (B); supine (A) to sitting with legs dangling (C); and supine (A) to standing (D).

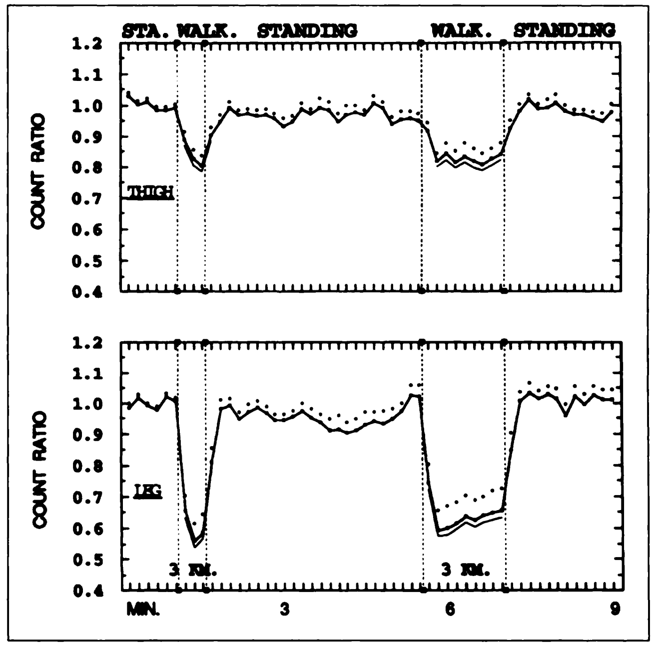

FIGURE 7. Blood volume changes in the thigh (n = 14) and leg (n = 14) during two treadmill walking tests at 3 kmph.

also showed that the blood volume decrease in the thigh and calf tended to become more marked from 1 to 3 kmph and smaller from 3 to 5 kmph.

Effects of Arrest of Blood Circulation to the Lower Limbs on Blood Volume Changes Induced in the Right Lung when Standing, Hyperventilating and Walking. When the cuffs were not inflated, standing from the supine posture (Fig. 9, Table 7) and walking (Fig. 10, Table 7) produced changes in blood volume in all fields of the right lung identical to those already reported. Cuff inflation to over systolic pressure did not change blood volume in the right lung when the subjects were supine and increased it when the subjects were standing still. Arresting the blood circulation to the lower limbs made the decrease in blood volume in the right lung slower during standing. It prevented the blood volume decrease in the upper and lower fields of the right lung and reduced that in the middle field during hyperventilation. It reduced the initial increase in blood volume in all three fields of the right lung during walking.

DISCUSSION

Reliability of Measurements

Blood volume shifts were recorded by our device only when the tests were performed. They were always in the expected direction and agreed with reported measurements in the literature. Thus, lung blood volume was increased by leg elevation (*3*), compression of the thighs in standing subjects, assumption of the supine posture from sitting and standing (*4,7,8*), changing posture from standing to sitting and walking. In the last condition, our measurements agreed with those obtained during bicycle exercise (*9,10*).

TABLE 5
Blood Volume Changes in the Lower Limbs of Seven Subjects before (B) and during (T) Posture Changes*

	Thigh (n = 14)	p	Leg (n = 14)	p
Supine position to sitting up with legs straight				
(B)	0.989 ± 0.033		1.000 ± 0.032	
(T)	1.397 ± 0.216	0.001	1.776 ± 0.532	0.001
Supine position to sitting up on bed with legs dangling				
(B)	0.989 ± 0.031		0.995 ± 0.030	
(T)	0.939 ± 0.293	0.528	2.627 ± 0.696	0.001
Supine position to standing				
(B)	0.997 ± 0.026		1.007 ± 0.018	
(T)	1.503 ± 0.133	0.001	2.366 ± 0.840	0.001

*All values are mean radioactivity count ratios ± s.d.

TABLE 6
Blood Volume Changes in the Lower Limbs during Treadmill Walking Repeated Once*

Test	Thigh	p	Leg	p
Walking A (n = 14)				
Standing A	0.988 ± 0.017		1.014 ± 0.037	
3 kmph A	0.814 ± 0.11	0.001	0.572 ± 0.217	0.001
Standing B	0.955 ± 0.077	ns	1.023 ± 0.123	ns
3 kmph	0.831 ± 0.11	0.001	0.596 ± 0.25	0.001
Walking B (n = 22)				
Standing	1.002 ± 0.026		1.010 ± 0.02	
1 kmph	0.911 ± 0.099	ns	0.590 ± 0.16	0.001
3 kmph	0.890 ± 0.13	0.014	0.581 ± 0.137	0.001
5 kmph	0.939 ± 0.176	ns	0.683 ± 0.188	0.001
Recovery	1.061 ± 0.08	ns	1.069 ± 0.119	ns

*Walking test A was at a steady speed (seven subjects); walking test B was at increasing speeds (eleven subjects). All values are mean radioactivity count ratios ± s.d.

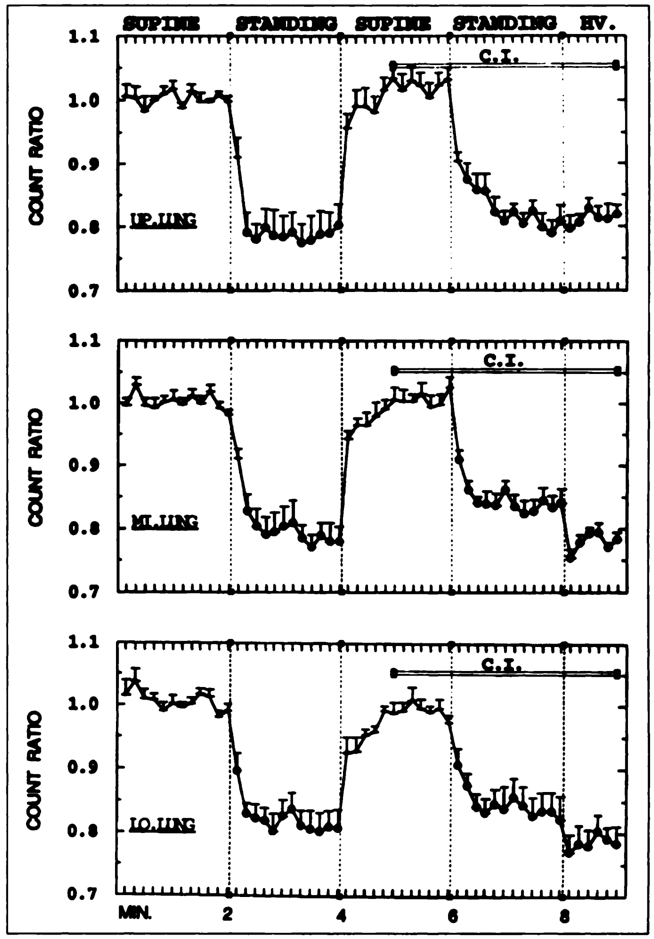

FIGURE 9. Blood volume changes in three right lung fields (n = 7) induced by standing up from recumbency with cuffs not inflated (left), by cuff inflation (CI) and standing up from recumbency and hyperventilation (HV) with cuff inflated (right).

Lung blood volume was decreased by the Valsalva maneuver (*4,11*), hyperventilation, by sitting or standing (*7,8*) from recumbency and by standing from sitting. As expected, blood volume shifts with similar characteristics were recorded in all three fields of the right lung during the Valsalva maneuver, hyperventilation and standing from the supine position. The blood volume changes we recorded in the lower limbs during posture changes and walking were in the opposite direction of the blood shifts in the lung and agreed with previously reported values (*7,8,12,13*).

The lack of change in hepatic blood volume during most of the posture changes confirmed a previous hypothesis (*7*) and its decrease to basal values during treadmill walking was in line with the changes observed during bicycle exercise (*9,10*). Moreover, our continuous radioactivity recording showed that the changes in counts were never erratic but followed a pattern peculiar to a given experimental condition. These results suggest that our measurements always reflected actual changes in blood volume. In addition, reproducibility of our measurements was demonstrated by the finding that all repeated experimental conditions (i.e., assumption of supine posture, standing, sitting on a chair, walking and the Valsalva maneuver) were associated with blood volume shifts similar in direction, magnitude and time course in each of the several fields where radioactivity was measured. The consistency of our measurements was also indicated by the coefficients of variation (5.55%–8.55%, 5.67%–10.03% and 6.11%–6.41%) for blood volume changes recorded in the lung and liver during the Valsalva maneuver, standing from recumbency and walking, respectively. On the basis of all these observations, the measurements obtained by our device are reliable, as expected, because scintillators have been successfully applied in human studies (*10*). Furthermore, our device allowed blood volume changes to be measured at several sites

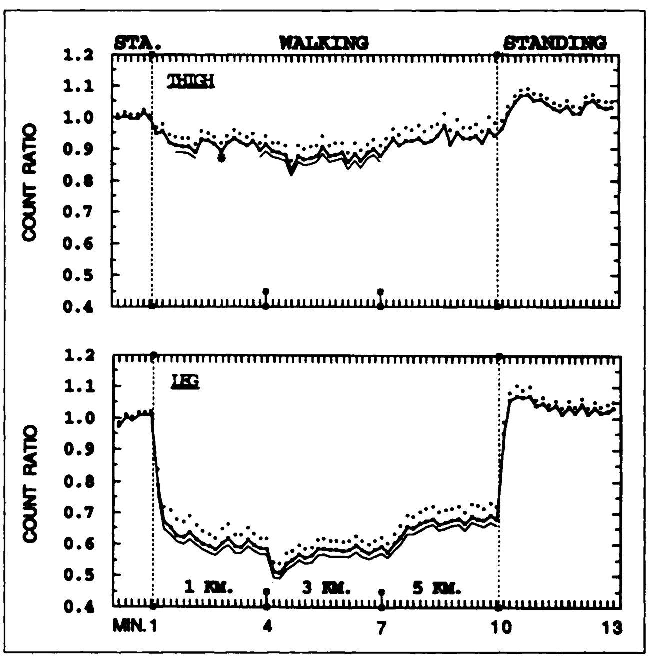

FIGURE 8. Radioactivity changes in the thigh (n = 22) and leg (n = 22) during walking at increasing speeds.

TABLE 7
Effect of Arresting Blood Circulation to the Lower Limbs on Blood Volume Changes in the Right Lung During Standing, Hyperventilation and Treadmill Walking*

Parameter	Upper field of right lung	p	Middle field of right lung	p	Lower field of right lung	p
Supine A (1)	1.001 ± 0.013		1.003 ± 0.011		1.004 ± 0.008	
Standing A (2)	0.780 ± 0.089	(1,2) 0.001	0.781 ± 0.049	(1,2) 0.001	0.806 ± 0.073	(1,2) 0.001
Supine B (3)	1.016 ± 0.042	(1,3) ns	1.002 ± 0.046	(1,3) ns	0.994 ± 0.023	(1,3) ns
Standing B (4)	0.809 ± 0.047	(3,4) 0.001	0.832 ± 0.045	(3,4) 0.001	0.836 ± 0.075	(3,4) 0.001
Supine A—Standing A (5)	0.221 ± 0.093		0.222 ± 0.055		0.198 ± 0.07	
Supine B—Standing B (6)	0.207 ± 0.054	(5,6) ns	0.170 ± 0.073	(5,6) ns	0.158 ± 0.081	(5,6) ns
Hyperventilation B (7)	0.816 ± 0.04	(4,7) ns	0.788 ± 0.023	(4,7) 0.020	0.789 ± 0.067	(4,7) ns
Standing A (1)	0.989 ± 0.019		0.986 ± 0.014		0.995 ± 0.007	
Walking A (2)	1.146 ± 0.087	(1,2) 0.002	1.119 ± 0.06	(1,2) 0.001	1.095 ± 0.059	(1,2) 0.004
Standing B (3)	1.097 ± 0.09	(1,3) 0.018	1.092 ± 0.064	(1,3) 0.003	1.069 ± 0.042	(1,3) 0.005
Walking B (4)	1.156 ± 0.106	(3,4) 0.003	1.117 ± 0.09	(3,4) ns	1.090 ± 0.097	(3,4) ns
Walking A—Standing A (5)	0.157 ± 0.082		0.132 ± 0.059		0.101 ± 0.06	
Walking B—Standing B (6)	0.060 ± 0.034	(5,6) 0.019	0.025 ± 0.047	(5,6) 0.002	0.021 ± 0.077	(5,6) 0.005

*All values are mean radioactivity count ratios ± s.d. (n = 7).
A = cuffs not inflated; B = cuffs inflated. Numbers in parentheses indicate the condition.

simultaneously and continuously in subjects moving freely in the laboratory so that the time course, direction and magnitude of blood volume displacements could be recorded during walking, hyperventilation and the natural movements associated with posture changes.

Mechanisms for Blood Volume Shifts

Such recordings provided some new insights into the mechanisms responsible for blood volume shifts. When the force of gravity was directed towards the feet, the effect of the different heights of the three lung fields above the hydrostatic indifferent point was discernible during the assumption of the two sitting postures from recumbency. It was masked during the change to standing from sitting, because blood volume was already reduced in the upper field, and also during assumption of the erect from the supine position, because the capacity of the vascular beds receiving blood was markedly increased. The blood discharged from the thorax filled not only the veins of the lower limbs but also other venous beds because the vessels in the lung emptied rapidly, whereas those in the lower limbs filled slowly. Moreover, arresting blood circulation to the lower limbs only slowed the decrease in blood volume in the lung as induced by a change in posture: from recumbency to standing. The extent of the filling of veins in the lower limbs was determined by the opposite actions of hydrostatic pressure and the vascular compression exerted on the thigh by the edge of the bed during sitting with the legs dangling and on both thigh and leg by higher muscle tone during standing. Although the percent increase in blood volume was always larger in the calf than the thigh (*12*), the amount of blood that accumulated in the thighs during standing was large, as shown by the rise in lung blood volume induced by compression of the thighs. Whenever the supine

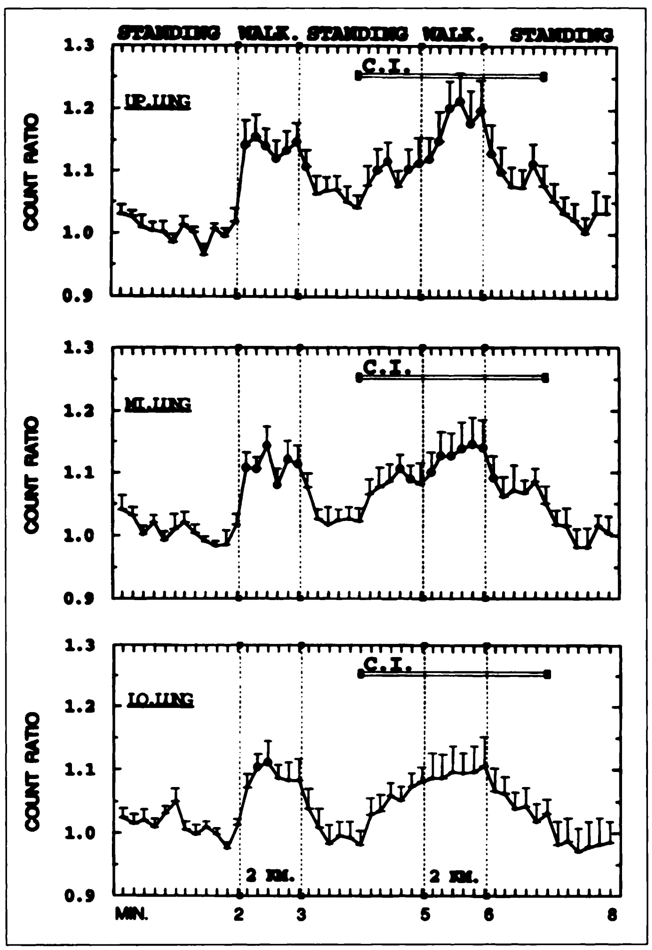

FIGURE 10. Blood volume changes in the three right lung fields (n = 7) induced by treadmill walking (left side) and cuff inflation and treadmill walking with cuffs inflated (right side).

posture was resumed, blood displacement from the lower limbs was fast due to the powerful elastic recoil of the venous walls and low venous resistance to flow so that blood volume in the lung increased rapidly. Leg elevation further increased blood volume in the lung, except in the lower field, which was probably compressed by the diaphragm.

Hyperventilation decreased lung blood volume by a nervous reflex, as suggested by the time course of the shift. In a standing subject, the effect of hyperventilation added to that produced by assumption of the erect posture, and the decrease in lung blood volume was therefore huge, even equaling that caused by the reduced venous return (*11*) due to Valsalva maneuver. Stroke volume probably decreases and contributes, along with muscle arterial dilatation, to the fall in arterial blood pressure and any faints (*11*). Not only the arteries, however, but also the veins in the lower limbs were dilated by the reflex, as suggested by the effects of arresting blood circulation to the lower limbs during hyperventilation.

Lung blood volume was increased by lower limb muscle pumps during walking, as shown by the time course of the changes in blood volume in the lung, thigh and calf at the start and cessation of walking and by the results of arresting blood circulation to the lower limbs. Also, the thoraco-abdominal pump acts during walking, and its function depends on filling of the abdominal cavity veins by blood propelled by muscle pumps of the lower limbs, as indicated by hyperventilation. The progressive rise in blood volume, however, in the upper and middle fields of the right lung at speeds higher than 3 kmph was not due to displacement of blood from the lower limbs because the muscle pumps were unable to cope with the huge arterial flow occurring at higher walking speeds. The blood was displaced to the lung from the liver, as clearly indicated by the time course of the blood shifts. During walking, hepatic blood volume showed unique changes, being first increased and then reduced. The increase might be caused by spleen contraction (*9,10*), augmented intra-abdominal pressure (*13*) and/or constriction of the splanchnic arteries and veins mediated by sympathetic nervous activity (*14,15*).

Because activity of the latter system increases with elevated exercise workload and is accompanied by higher blood concentrations of catecholamines (*15*), the capacity of the hepatic vascular bed was progressively reduced. An additional increase in nervous sympathetic activity probably occurred after walking was stopped and was responsible for the decrease of hepatic blood volume to below basal values. This pattern might indicate that increases in liver blood volume recorded during the Valsalva maneuver and hyperventilation represent the initial phase of involvement of the hepatic blood pool in reflexes directed at maintenance of circulatory homeostasis. In contrast, liver blood volume was usually not modified by posture changes, probably because of weaker activated reflexes and the location of the liver with respect to the hydrostatic indifferent point (*7,8*). The increase in hepatic blood volume during leg elevation was probably due to marked intra-abdominal pressure.

CONCLUSION

Our noninvasive device measures local changes in intravascular blood volume for about 4 hr in subjects moving freely. The device could be used in healthy subjects to record blood volume shifts caused by various conditions and drugs so that the physiology of the cardiovascular system might be further clarified. It could also be used in patients with diseases that induce derangements of blood volume distribution, such as arterial hypotension associated with assumption of the erect posture, heart failure (*6*) and venous insufficiency in the lower limbs, to ascertain the disease severity, its changes and the response to therapy.

ACKNOWLEDGMENTS

The authors thank Professor Alberto Zanchetti for his criticism, Professor Mario Bergonzi (Nuclear Medicine, Fatebenefratelli Hospital, Milan) for his valuable help, Ms. Alix Green for preparing the manuscript, Ms. Paola Boccaccini for typing the manuscript, Mr. Riccardo Sarri for photography and Ms. Giuliana Melegari for her nursing assistance.

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