# OPTIMISATION OF INDICES OF EXTERNAL PNEUMATIC COMPRESSION FOR PROPHYLAXIS AGAINST DEEP VEIN THROMBOSIS: RADIONUCLIDE GATED IMAGING STUDIES

BY

ROGER KAMM, RICHARD BUTCHER, JERRY FROELICH, MARK JOHNSON, EDWIN SALZMAN, ASCHER SHAPIRO, H WILLIAM STRAUSS

# Optimisation of indices of external pneumatic compression for prophylaxis against deep vein thrombosis: radionuclide gated imaging studies

ROGER KAMM,* RICHARD BUTCHER,† JERRY FROELICH,† MARK JOHNSON,*
EDWIN SALZMAN,‡ ASCHER SHAPIRO,* H WILLIAM STRAUSS†

*From the \*Massachusetts Institute of Technology, Cambridge; the †Massachusetts General Hospital, Boston; and the ‡Beth Israel Hospital, Boston, Massachusetts, USA.*

SUMMARY    The amount and rate of blood expelled with different modes of intermittent external pneumatic compression applied to the lower leg were studied on a regional basis in a series of experiments on healthy human volunteers. Radionuclide imaging of the labelled blood pool, with acquisition of counts synchronised to the pressurisation cycle, provided data on regional blood volumes in the leg in relation to time. To determine the changes in blood volume of the lower leg resulting from external pneumatic compression labelled red blood cell counts were determined during 10 different types of compression cycle. Since venous stasis is considered to be a major cause of venous thrombosis the red blood cell counts were used to calculate regional values of the fraction of blood ejected as well as comparative indices proportional to regional flow rate, regional velocity, and regional wall shear stress. All these indices should be maximised for optimal prophylaxis against deep vein thrombosis. The four compartment cuff in each compression mode applied a mean pressure of 45 mm Hg, but different combinations of values were used for intercompartmental pressure gradation ($\triangle p$) and for intercompartmental time sequencing to the onset of compression ($\triangle t$). Uniform compression ($\triangle p=0$; $\triangle t=0$) was substantially inferior to cycles with gradation and sequencing. The optimal values of $\triangle p$ were in the range 5-10 mm Hg and of $\triangle t$ in the range 0-0.5 seconds.

The risk of deep vein thrombosis in patients treated with bed rest, such as those undergoing surgical and orthopaedic procedures and acute myocardial infarction, can be reduced by periodically compressing the veins of the legs with an external pneumatic compression device.[1-5] Depending on a variety of factors, including the particular clinical setting, external pneumatic compression as currently practiced reduces the incidence of thrombus formation by roughly 80%,[6] as determined by ^{125}I-fibrinogen scanning; it is therefore not totally effective. The procedure also probably lessens the risk of pulmonary embolism, although direct proof remains to be provided.

Address for correspondence and reprints: Professor Ascher H Shapiro, Room 3-254, Massachusetts Institute of Technology, 77 Massachusetts Avenue, Cambridge, MA 02139, USA.

The usual mechanism cited for the effectiveness of external pneumatic compression in providing protection against deep vein thrombosis is the elimination of venous stasis.[1] The rate and amount of blood moved by external pneumatic compression, however, as well as other pertinent haemodynamic quantities, depend on a number of pressurisation cycle variables whose effects have not been well characterised. These variables include whether pressure should be applied (*a*) uniformly along the leg, (*b*) in a graded fashion, (*c*) sequentially in a wave like manner, or (*d*) in some combination of the latter two.

Theoretical and laboratory studies of hydraulic models[7][8] predicted that uniform compression would produce an occlusive throat (fig 1) in the proximal portion of the vein undergoing compression and that this narrowing would limit the flow speeds and shear stresses produced by external pneumatic compression in veins distal to the throat. The theoretical studies also indicated that this problem could be alleviated by the
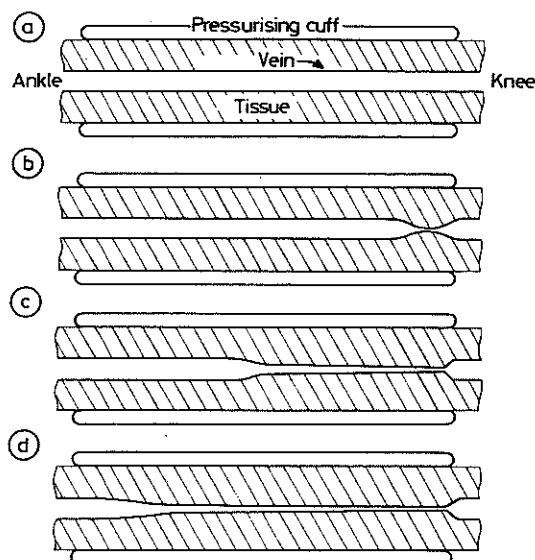
FIG 1 *Time sequence diagrams of leg vein showing that when external compression is applied uniformly to a segment of vessel having a high distal impedance it collapses first at the proximal end (a). A wave of emptying (b,c,d) then proceeds distally but more and more slowly. The ever increasing proximal impedance limits the rate of emptying distal to the occlusive throat.*

use of either graded compression, with pressure decreasing from ankle to knee, or sequential compression, with pressure applied in a wave like fashion from ankle to knee, or by the combination of graded and sequential compression. These theoretical predictions were confirmed by hydraulic model experiments[9] and by non-invasive studies of healthy volunteers using circumferential strain gauges and Doppler ultrasound measurements of the proximal flow pulse.[10][11]

The present studies were performed to obtain a more detailed understanding of the rate and site of blood expelled from the lower leg with various external pneumatic compression cycles as a preliminary to selecting an optimal cycle for subsequent clinical trials. The procedure used for determining the temporal variation in local blood volume is similar to that used for multigated cardiac blood pool imaging except that the recording was triggered by the compression device.

## Material and methods

Twenty three healthy volunteers, between 18 and 35 years of age, of either sex, and free of evidence of cardiac or peripheral vascular disease by history and physical examination, were studied. Informed consent

was obtained under a protocol approved by the subcommittee on human studies of the committee on research of the Massachusetts General Hospital. Twelve of these subjects took part in the first series of experiments (series A) and 11 in the second (series B).

RADIONUCLIDE LABELLING
Twenty minutes after the administration of stannous pyrophosphate (Pyrolite, New England Nuclear) intravenously, 3-5 ml of the subject's blood was withdrawn into a heparinised shielded syringe containing 15 mCi (555 mBq) of $^{99m}TcO_4$ (half life 6 hours). After 10 minutes' incubation the labelled blood sample was reinjected into the subject. This labelling technique has been shown to produce 90% efficiency for tagging the red cells[12] and provides a stable blood pool indication with minimal non-vascular background. Imaging was carried out at least 15 minutes after injection to permit the labelled cells to equilibrate within the subject's blood pool.

TEST PROCEDURE
With the subject lying supine and horizontal a compression cuff with four separate compression compartments was loosely fitted below the knee to one leg by means of Velcro fasteners; we found that even a trace of tightness diminished significantly the baseline volume of blood. A folded towel raised the ankle sufficiently to eliminate calf compression by the table. Cobalt markers were taped to the subject's medial malleolus and patella for image orientation. The air pressurisation and control system allowed independent control of the start and duration of compression and the inflation pressure of each compartment. The pressure rise time (time required to reach two thirds of maximum pressure) was approximately 0.5 s in each compartment depending on the size of the leg and the looseness with which the cuff was applied.

Using a large field of view gammacamera (Technicare 410 with an all purpose collimator) linked to a dedicated computer (Technicare 560) with gated acquisition capability, imaging was performed during repetitive 10 s cycles of compression, each of which was followed by 30-50 s of vein refilling time. A signal generated 0.5 s before the onset of each successive compression cycle triggered the gating mechanism, at which time image acquisition was begun. Counts were acquired for 16 image frames (time windows), each of 0.5 s duration, during the first 7.5 s of each compression cycle; the first 0.5 s of imaging before compression gave a baseline value. Periodic compression and decompression and data acquisition were continued, using the gating mechanism to superimpose the counts of each additional compression phase on the previously acquired image

data, until an accumulated count density of about 15 000 counts per frame was attained. The applied pressure in each cuff segment was maintained for approximately 10 s; this was approximately twice as long as the time required to attain an equilibrated collapse. The refill time between compression cycles, subsequent to depressurisation, was established in a preliminary trial for each subject by imaging the refill period after a single long compression and then choosing a time at which three consecutive 2 s images showed no significant increase in counts. A summary of the sequence of steps for each pressurisation cycle is shown in table 1.

COMPRESSION CYCLES

A total of 10 different pressurisation cycles was tested. Table 2 gives the details of pressures and timing used in the different pressurisation cycles. The tests were divided into two groups — series A and series B.

*Series A* — Each of 12 subjects underwent serial testing with four different compression cycles: (*a*) uniform compression, (*b*) graded compression with pressure within each compartment being 10 mm Hg greater than in the adjacent more proximal compartment; (*c*) sequential compression, with a time delay of 0.75 s between compartments in the onset of compression, and (*d*) combined graded and sequential compression. with pressure intervals $\triangle p = 10$ mm Hg and time delays $\triangle t = 0.75$ s. These indices were selected because our preliminary non-invasive studies suggested that they would not be far from optimal with respect to the resulting haemodynamic indices. All pressurisation cycles had a mean pressure across the four compartments of 45 mm Hg since previous studies had shown that higher pressures did not significantly increase the volume of venous blood displaced from the lower leg.[10][11] The uniform compression mode tested here is an optimised one,

TABLE 1 *Sequence of steps followed for each pressurisation cycle*

| Time from beginning of compression (s) | Event |
|---|---|
| Before test | Cuff applied to one leg of supine subject |
| Before test | Preliminary trial to determine vein refilling time necessary for each subject (usually 30-50 s) |
| −0.5 | No pressure in cuff segments; veins full; baseline counts for 0.5 s |
| 0 | Pressurisation cycle started acquired (table 2) |
| 0.5 | Counts acquired for first 0.5 s time window of pressurisation |
| 1.0 | Counts acquired for second 0.5 s time window |
| 7.5 | Counts acquired for a total of 15 successive 0.5 s time windows of pressurisation; then acquisition ceased |
| 10.0 | Pressure released in all cuff segments |
| 40-60 | Veins allowed to refill according to time determined in preliminary trial above; this completes one compression-decompression cycle |
| −0.5 to 40-60 | } Second complete cycle |
| −0.5 to 40-60 | } Third complete cycle |
| | Application of complete cycles continued, accumulating counts in each 0.5 s time window, until a total of about 15 000 counts per time window is attained (usually about 20 cycles total) |

TABLE 2 *Indices of pressure and timing*

| Test series | Cycle No | Cycle type | Compartment pressure (mm Hg) | | | | $\triangle p$ (mm Hg) | $\triangle t$ (s) |
|---|---|---|---|---|---|---|---|---|
| | | | 1 | 2 | 3 | 4 | | |
| A | A1 | U | 45 | 45 | 45 | 45 | 0 | 0 |
| A | A2 | G | 60 | 50 | 40 | 30 | 10 | 0 |
| A | A3 | S | 45 | 45 | 45 | 45 | 0 | 0.75 |
| A | A4 | G-S | 60 | 50 | 40 | 30 | 10 | 0.75 |
| B | B1 | S | 45 | 45 | 45 | 45 | 0 | 0.50 |
| B | B2 | S | 45 | 45 | 45 | 45 | 0 | 1.00 |
| B | B3 | G-S | 52.5 | 47.5 | 42.5 | 37.5 | 5 | 0.375 |
| B | B4 | G-S | 52.5 | 47.5 | 42.5 | 37.5 | 5 | 0.875 |
| B | B5 | G | 60 | 50 | 40 | 30 | 10 | 0 |
| B | B6 | G-S | 60 | 50 | 40 | 30 | 10 | 0.25 |
| B | B7 | G-S | 60 | 50 | 40 | 30 | 10 | 0.50 |

U=uniform compression; G=graded compression; S=sequential compression; G-S=combined graded and sequential compression; $\triangle p$=pressure difference between adjacent cuff compartments; $\triangle t$=time delay for pressure application to successive compartments. Mean pressure=45 mm Hg for all compression cycles; rise time for pressure application to each cuff compartment=approximately 0.5 s; total time of pressure application=10 s; refilling time=30-50 s depending on particular subject.

based on our previous work.[11] It differs from most of the commercially available units primarily in terms of the pressure rise time. Our studies as well as those of other investigators,[1] suggest that the rise time should be as short as possible. In these tests, the rise time in each compartment was approximately 0.5 s.

*Series B* — The procedure was essentially the same as in series A, but seven combinations of indices (table 2) were used with each of 11 subjects. The cycles were applied in random order. Cycle B5 had the same indices as cycle A2, thereby linking series B with series A. The combinations of pressure and timing were selected after review of the results of series A, with the aim of finding an optimal combination.

METHODS OF DATA ANALYSIS

For each subject an experiment with a particular type of compression cycle included about 15-30 successive cycles. The digital data from the image sequence were analysed to determine the changes in activity in each of eight segments of the leg. To set the regions the distance from the ankle to the knee was divided into eight equal segments perpendicular to the long axis of the leg (fig 2b). These same regions were then used for the analysis of all data from a given subject. The initial image of each sequence (fig 2a), immediately before the onset of compression, was used as a baseline. We corrected for radioactive decay by normalising the baseline counts for each test.

Typical accumulated counts per frame varied from 400 in region 1 (distal) to 1000 in region 8 (proximal). Because the former count was so low, producing errors of about 10% for the expected Poisson distribution,
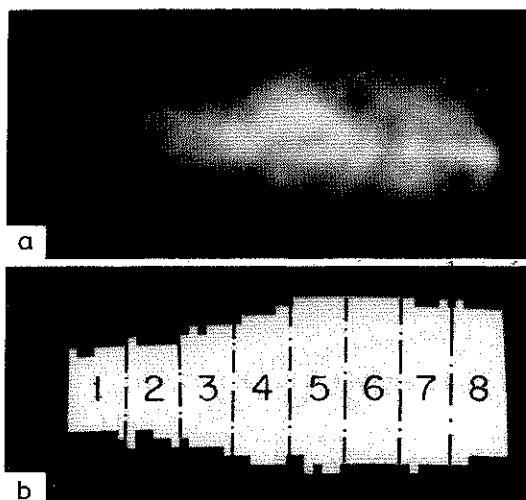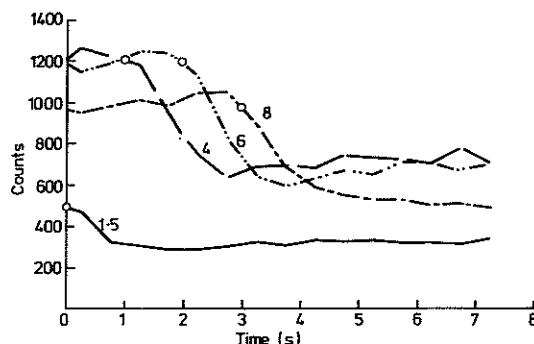


FIG 3 *Individual summed counts in successive time windows for regions 1.5, 4, 6, 8, with cycle B2, sequential compression, $\Delta t = 1$ s. (O) time in cycle when pressure is applied to the corresponding cuff compartment in each region.*

regions 1 and 2 were treated as a single unit, identified as region 1.5. Time windows of 0.25 s duration, which might have given finer time resolution, resulted in unacceptably high noise levels owing to the lower count levels.

*Performance indices*

The methods by which we analysed the data to obtain the results described below are detailed in the Appendix.

*Blood volume vs time* — The counts for all pixels within a region of interest were summed for each time window. For a particular subject the changes in regional sums reflected the changes in total blood volume within each region. Figure 3, for instance, shows that in sequential compression regions 4, 6, and 8 first dilated slightly as blood flowed in from more distal regions; then they deflated rapidly when external pressure was applied.

*Fraction of venous blood ejected* — For each subject different pressurisation cycles were compared by treating count values as blood volumes. With this interpretation, we found that depending on the pressure cycle and the subject from 30% to 60% of the initial blood volume was expelled from each region. Most of the ejection occurred in 2-4 s from the start of the compression cycle. Using the estimate that 25% of the baseline blood resides in the arteries and capillaries,[13] (this amount was assumed not to change significantly during compression because all applied pressures were well below diastolic) we computed from data such as those in fig 3, and for each region of interest, the fraction of venous blood ejected as a function of time. From these results we determined for each compression cycle the maximum percentage of venous blood ejected from each region for a particular subject.

*Indices of compression cycle performance* — Analysis of data on regional counts in relation to time



FIG 2 *(a) A typical baseline radionuclide image of the lower leg, with the ankle at left; (b) shows regions 1-8, as defined from the same baseline image.*

(details given in the Appendix) provided indices that for a particular subject were proportional to regional volumetric flow rate, regional blood velocity, and regional wall shear stress. By means of these indices different compression cycles were compared for a particular subject. Since the haemodynamic indices varied with time the maximum value attained by each index in each region was used as a measure of the scale of the corresponding index in each region. The several maxima generally occurred at different times during the compression cycle.

*Statistical treatment of data* — An analysis of variance[14] was applied to the performance indices. Test series A and B were treated as separate groups since they had different subject populations. The value of a particular maximum index in each region for a particular subject was first normalised to the mean value in that region for the several compression cycle modes applied to that subject (four modes in series A, seven modes in series B). These normalised values were then averaged over the 12 subjects of series A and the 11 subjects of series B. This procedure minimised the effects of intersubject variations.

## Results

Typically, a pressurised region emptied in 2-4 s (for example fig 3). Since the venous refilling time was 30-40 s the blood flow rate induced by external compression was many times the normal resting flow rate. This very high degree of pulsatility was associated with the short rise time (~0.5 s) used in these tests.

As indicated, the data may be manipulated in many ways to determine results of haemodynamic significance. Figures 4 and 5 show different types of
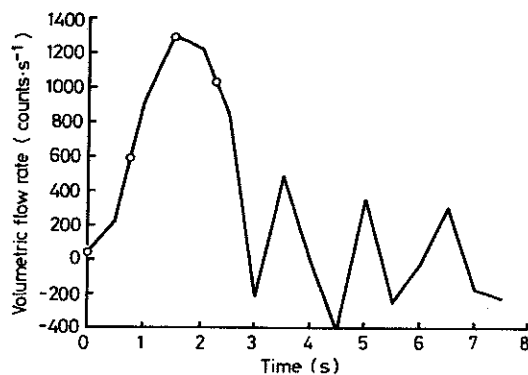


FIG 4   *Individual example of volumetric flow rate index in relation to time at the exit of region 8 (entering the thigh) using cycle A4, combined graded and sequential compression* $\Delta t = 0.75$. *(O) times at which the successive cuff segments are pressurised.*
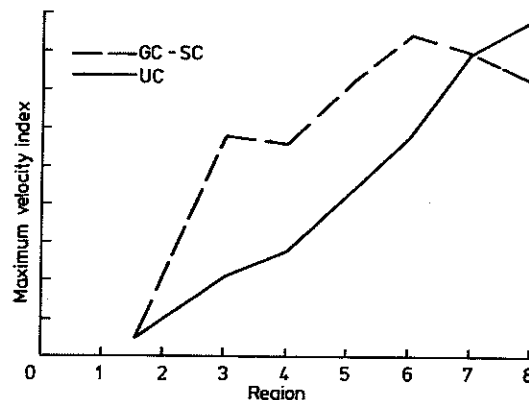


FIG 5   *Comparison of uniform compression (UC; cycle A1) with combined graded and sequential compression (GC-SC; cycle A4) in terms of the maximum velocity index attained in each region in one subject. The index is proportional to the ordinate.*

calculated results for one subject. Figure 4 shows how the volumetric flow index at the exit of region 8 — that is, entering the thigh region — varied with time during sequential compression. The ordinate is proportional to the volumetric blood flow rate for the particular subject. Several increments in flow rate are evident, corresponding to the inflation of successive compartments. The shape of this curve differed from subject to subject and depended also on the pressurisation cycle used. Figure 5 shows the maximum regional values of the velocity index during uniform compression and combined graded and sequential compression. Except near the knee combined compression produced a much higher peak velocity than uniform compression. Comparative regional values of the laminar shear stress show similar behaviour but even greater differences between the two cycles are evident. Graded compression and sequential compression, when compared with uniform compression applied to the same subject, showed improvements similar to those in fig 5. The relatively poor performance of uniform compression — with low levels of velocity and shear stress everywhere except at the knee — was a consequence of the partially occlusive proximal throat shown in fig 1 and agrees with our earlier theoretical predictions.

SERIES A
The first objective was to establish whether uniform compression, although the simplest and least expensive mode, is indeed substantially inferior to graded compression, sequential compression, and combined graded compression and sequential compression.

Figure 6a compares the four compression modes with respect to the maximum percentage of venous
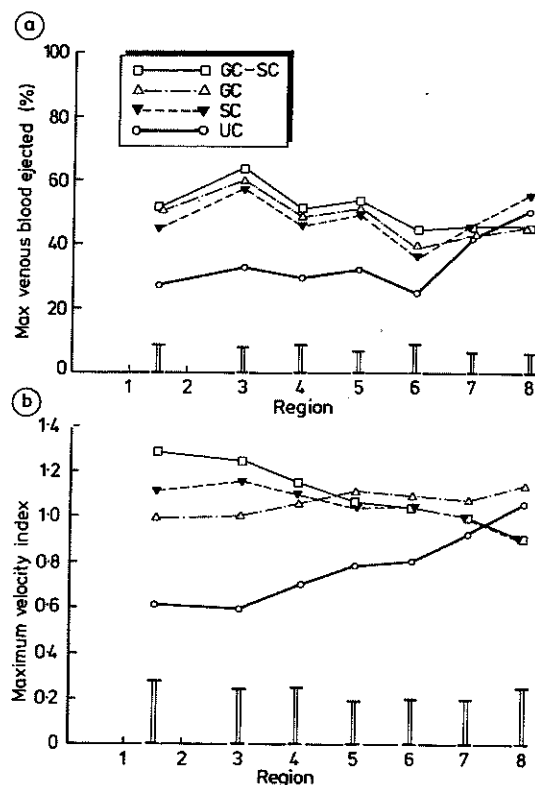
FIG 6 *(a) Mean maximum percentage of venous volume ejected from each region and (b) mean normalised maximum velocity index in each region for 12 subjects of series A. Vertical double bars indicate significant difference at 95% confidence level. GC = graded compression; SC = sequential compression; GC-SC = combined graded and sequential compression; UC = uniform compression.*

blood ejected, averaged for the 12 subjects of series A. Except in the more proximal regions, uniform compression was significantly inferior to graded compression, sequential compression, and combined compression. Figure 6b compares the four compression modes with respect to the maximum velocity index, again averaged for the 12 subjects of series A; the ordinate for each region is normalised so that the mean value for the four compression cycles is 1.0. Again, except in the more proximal regions, uniform compression was significantly inferior to graded compression, sequential compression, and combined compression. The same conclusion is drawn when the four compression modes are compared with respect to the index of maximum flow and the index of maximum turbulent shear stress. When judged on the basis of the index of maximum laminar shear stress, the inferiority of uniform compression is even more pronounced.

SERIES A AND B IN COMBINATION

Although we used our previous experience to select the indices of pressure difference ($\Delta$p) and timing delay ($\Delta$t) for the four compression modes of series A, we could not be certain that each compression mode was individually optimised. Hence, except for the obvious inferiority of the uniform compression mode, decisive comparisons of haemodynamic efficacy among the other three modes required further tests — namely, those of series B. Moreover, our earlier work had shown that mean applied pressures above 45 mm Hg, or modest reductions, would not make any significant difference in the volume of blood expelled[15] and had further identified the importance of a short pressure-rise time ($\leq 0.5$ s). Consequently, the chief indices relevant to the compression phase are the pressure interval, $\Delta$p, and the timing delay, $\Delta$t, to the onset of pressurisation, both referring to adjacent cuff compartments. To minimise the number of cycle types, both $\Delta$p and $\Delta$t were made uniform between neighbouring compartments.

To compare the data for the various cycles, we imagined for each index of performance a three dimensional surface with $\Delta$p and $\Delta$t as axes in the horizontal plane and the index of merit plotted vertically above. Such a three dimensional plot would, in principle, supply values, $\Delta$p and $\Delta$t, corresponding to the highest point of the surface. An immediate complication of this idealised procedure is that there is more than one index of performance and there are many regions of the leg. Consequently, no unique pair of values, $\Delta$p and $\Delta$t, is in every respect optimal. Fortunately, however, the performance indices for maximum percentage ejected, maximum flow rate, maximum velocity, and maximum shear stress yielded comparative results that were generally concordant with each other. Variations along the leg were analysed by dividing the leg into two zones: the lower (regions 1-4) and the upper (regions 5-8). We gave greater weight to the upper zone because thrombi are most likely to form[16] in that region.

A summary of the relative haemodynamic merits of all different compression cycles used in series A and B is shown in fig 7, using $\Delta$p and $\Delta$t as axes, according to the schema mentioned above. Each box enclosed by solid lines is labelled as in table 2 and represents a four compartment compression mode having the values of $\Delta$p and $\Delta$t corresponding to the coordinates of the box. The seven numbers in each box represent the indices of merit arranged according to the key diagram. The numerical ratings are on a comparative basis, ranging from 0 for distinctly poorer than average to 4 for distinctly better than average.

The peak of the index of merit surface was expected to be broadly plateau like rather than sharp because gradation and sequencing would be traded off against
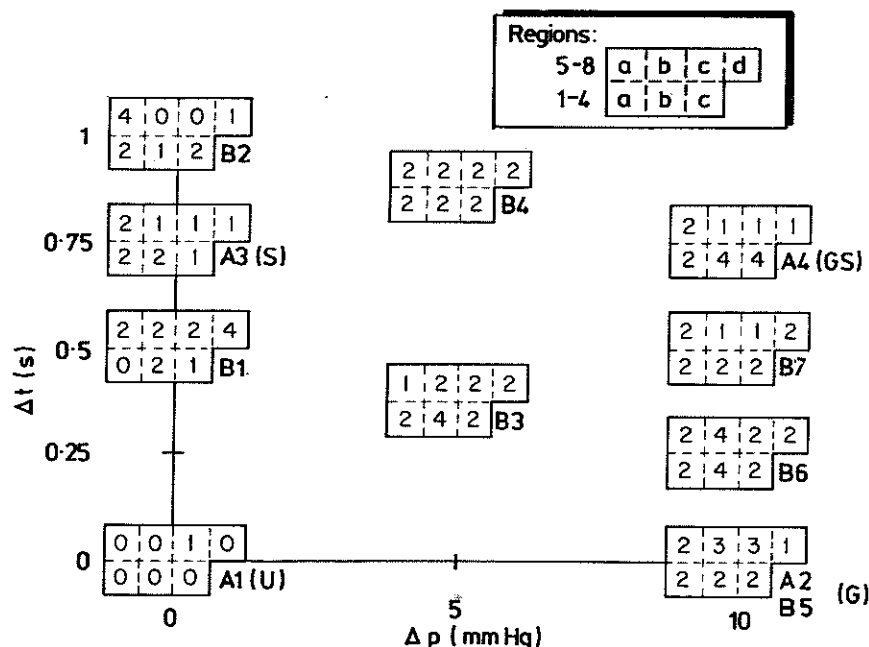
Regions:
| 5-8 | a | b | c | d |
|-----|---|---|---|---|
| 1-4 | a | b | c | |

FIG 7   *Relative rating of different compression cycles (A1-4, B1-7) characterised by the pairs of values of $\Delta p$ (gradation) and $\Delta t$ (sequencing): 0=distinctly poorer than average; 2=average; 4=distinctly better than average. Key: a=maximum fraction ejected; b=maximum velocity; c=maximum laminar shear stress; d=maximum flow rate into thigh. S=sequential (compression); U=uniform; GS=combined graded-sequential; G=graded.*

each other. The results shown in fig 7 were even more plateau like because of several other factors: (a) the data were averaged over the subject population; (b) there were several measures of performance; (c) several regions of the leg were relevant; and (d) the numerical code ratings representing relative efficacy were coarsely graded, partly because of recognition of experimental error and partly because some subjectivity enters into the assignment of these ratings.

## Discussion and conclusions

The precise physiological reasons for the protection that external pneumatic compression provides against deep vein thrombosis are not definitively known at present. We chose several factors that we could evaluate quantitatively as plausible indicators of merit. Firstly, the maximum proportion of venous blood ejected is directly related to the degree of collapse, to the emptying of the valve sinuses and other regions in which blood might tend to pool, to the reduction of residence time in the sinuses and muscular veins, and to the mechanical working of the vessel walls, which might act to release fibrinolytic agents.[17] Secondly, the maximum velocity index represents the level of motion produced, and its square is directly proportional to the turbulent shear stress index

available for mechanically stripping seeds of thrombi off the endothelium by direct mechanical traction. Thirdly, the maximum laminar shear stress index is like the turbulent index but is applicable when the flow is laminar rather than turbulent. Finally the maximum volumetric flow index entering the thigh is a measure of the levels of velocity and shear stress in the large veins of the thigh and thus may be relevant to the effectiveness of external pneumatic compression in preventing the development of thrombi in the superficial femoral vein and the propagation of calf thrombi into the thigh.

Using these indices of performance the comparative merits of different combinations of gradation ($\Delta p$) and sequencing ($\Delta t$) are shown in fig 7 for the upper and lower zones of the region of the lower leg covered by the cuff. Although the comparative ratings do not show a sharp optimum, several distinct conclusions may be drawn.

Firstly, some degree of gradation or sequencing produced substantial improvements over uniform compression ($\Delta p=0$, $\Delta t=0$). The latter mode was distinctly inferior and would have been even more so if longer pressure rise times had been used, as in current commercial versions of external pneumatic compression devices. Secondly, although the optimal cycle almost certainly has some combination of

gradation and sequencing, pure gradation ($\triangle t=0$) was comparatively better than pure sequencing ($\triangle p=0$). Thirdly, the optimal combinations of $\triangle p$ and $\triangle t$ appeared to lie within the area generally bounded by compression cycles B3, B7, and B5 (fig 7). Thus the optimal values of $\triangle p$ were in the range 5-10 mm Hg and of $\triangle t$ in the range 0-0.5 s.

In analysing the data (see Appendix) several assumptions were used in passing from the raw data on counts to the results: (*a*) the counts were a measure of total blood volume, with none coming from the tissues and lymph; (*b*) 25% of the baseline blood volume was in the arteries and capillaries; and (*c*) the volume of blood in the arteries and capillaries did not change appreciably during compression.

Although all of these assumptions introduced some error in an absolute sense, the comparative results were relatively insensitive to the expected levels of deviation from the assumptions. As a result the conclusions are unlikely to be altered by any such deviations.

Nicolaides and colleagues studied the effects of gradation and sequencing on blood velocity in the femoral vein and also conducted a clinical trial in which combined graded and sequential compression was compared with uniform compression.[18] They apparently did not vary the sequencing time interval, $\triangle t$, which in their unit was about 1 s. The rise time in each cuff compartment was on the scale of $\geqslant 4$ s. Our results, on the other hand, suggest that for optimal performance the rise time should be less by a factor of nearly $10^{10}$ [11] and that the sequencing time $\triangle t$ should be not more than about 0.5 s.

## Appendix

Volume index: the accumulated number of counts $N_j$ measured in each region j (from 1 to 8) during a particular time window is proportional to the volume of blood in that region, $V_j$ at the mean time t:

$$V_j(t)=C\,N_j(t) \tag{1}$$

where C, normalised for radiopharmaceutical decay, is a constant for each subject during a series of consecutive tests. Thus $N_j(t)$ is a regional volume index which is proportional to regional blood volume for that particular subject.

Volumetric flow index: the difference between the volumetric flow rates into and out of any region is equal to the rate of change of blood volume within that region:

$$Q_{j-1}(t) - Q_j(t)= \frac{dV_j(t)}{dt} \tag{2}$$

The relatively small amount of flow into each venous region from the capillaries was approximated from the data of Hollars.[11] Since the Q's were not measured in an absolute fashion, we calculated from equation (2) a volumetric flow index in terms of the rate of change of the regional count levels. For a particular subject this is proportional to the actual flow rate. $dV_j/dt$ was approximated as $\triangle V_j/\triangle t$ during each 0.5 s time window and can be attributed to the venous blood volume alone since the applied pressures were insufficient to alter arterial volume significantly. For each successive time window the application of equation (2) serially from the ankle to the knee led to the volumetric flow index in each region as a function of time (for example, fig 4).

Velocity index: the average venous velocity in region j is $U_j(t)=Q_j(t)/A_j^*(t)$ where $A_j^*$ is the mean venous cross sectional area. Moreover,

$$A_j(t)=V_j(t)/L_j= \frac{C}{L_j}N_j(t) \tag{3}$$

where $L_j$ is the length of region j, which remains essentially constant during the compression process. Thus $N_j$ is a measure also of the total vascular cross sectional area in region j. It represents an area index which includes arterial and capillary blood as well as venous blood. We assume that 25% of the baseline vascular volume of each region before compression, corresponding to 0.25 $N_j(0)$, is occupied by arterial and capillary blood,[13] and that leg compression at the pressures used expels mainly venous blood. The value of $[N_j(t)-0.25N_j(0)]$ is taken to be the venous area index. Since the length of each region is unchanged the venous volume index is the same as the venous area index. From the venous volume index as a function of time we may determine the maximum proportion of venous volume ejected from each region (for example fig 6). The velocity index in each region is found as a function of time by dividing the volumetric flow index by the venous area index. Figure 5 shows the maximum velocity index attained in each region during two different pressurization cycles.

Laminar and turbulent shear stress indices: as with velocity we can form indices of shear stress level which, for a particular subject, are proportional to the shear stress and thus usable for purposes of comparing different pressurisation cycles. The shear stress exerted by the flowing blood on the venous walls depends on whether the flow is laminar or turbulent. If the flow is turbulent the shear stress varies nearly as the square of the velocity and, to adequate approximation, is independent of vessel diameter. Accordingly, the turbulent shear stress index is defined as the square of the velocity index. If the flow is laminar the shear stress is proportional to velocity and inversely proportional to vessel diameter. Since the vessel diameter is proportional to the square root of the venous area index the laminar shear stress index is defined as the ratio of the velocity index to the square root of the venous area index.

## References

1 Roberts VC, Cotton LT. In: Ruckley CV, Macintyre IMC, eds. *Venous thromboembolic disease*. Edinburgh: Churchill Livingstone, 1975: 11-30.
2 Harris WH, Railes J, Athanasoulis C, *et al.* External pneumatic compression versus warfarin in reducing

thrombosis in high-risk hip patients. In: Madden JL, Hume
M, eds. *Venous thromboembolism: prevention and
treatment.* New York: Appleton-Century-Crofts,
1976:51–60.

3 Coe NP, Collins REC, Klein LA, *et al.* Prevention of deep
vein thrombosis in urological patients: a controlled
randomized trial of low-dose heparin and external pneumatic
compression boots. *Surgery* 1978;**83**:230–4.

4 Skillman JJ, Collins REC, Coe NP, *et al.* Prevention of deep
vein thrombosis in neurosurgical patients: a controlled
randomized trial of external pneumatic compression boots.
*Surgery* 1978;**83**:354–8.

5 Salzman EW, Sobel M, Lewis J, *et al.* Prevention of venous
thromboembolism in unstable angina pectoris. *N Engl J Med*
1982;**306**:991.

6 Cotton LT, Roberts VC. The prevention of deep vein
thrombosis with particular reference to mechanical methods
of prevention. *Surgery* 1977;**81**:228–35.

7 Kamm RD, Shapiro AH. Unsteady flow in a collapsible tube
subjected to external pressure or body forces. *J Fluid Mech*
1979;**95**:1–78.

8 Kamm RD. Bioengineering studies of periodic external
compression as prophylaxis against deep vein thrombosis.
Part I: numerical studies. *ASME J Biomech Engineering*
1982;**104**:87–95.

9 Olson DA, Kamm RD, Shapiro AH. Bioengineering studies
of periodix external compression as prophylaxis against deep
vein thrombosis. Part II: experimental studies on a simulated
leg. *ASME J Biomech Engineering* 1982;**104**:96–104.

10 Hollars MG, Kamm RD, Shapiro AH. Comparison of
intermittent external compression methods. *32nd Annual
Conference on Engineering in Medicine and Biology,*
Denver, Colorado, 1979;151.

11 Hollars MG. Prevention of deep vein thrombosis; external
compression experiments on healthy volunteers, *SM thesis,*
MIT, Cambridge, 1980.

12 Callahan RJ, Froelich JW, McKusick KA, *et al.* A modified
method for the in vivo labeling of red blood cells with
technetium-99m: concise communication. *J Nucl Med*
1982;**23**:315–8.

13 Conrad MC. *Functional anatomy of the circulation to the
lower extremities.* Chicago: Year Book Medical Publishers,
1971.

14 Box GEP, Hunter WG, Hunter JS. *Statistics for
experimenters.* New York: John Wiley & Sons, 1978.

15 Thirsk RB, Kamm RD, Shapiro AH. Changes in venous
blood volume produced by external compression of the lower
leg. *Med Bio Eng Comput* 1980;**18**:650–6.

16 Nicolaides AN, Kakkar VV, Field ES, *et al.* The origin of
deep vein thrombosis: a venographic study. *Br J Radiol*
1971;**44**:653–63.

17 Knight MTN, Dawson R. Effect of intermittent compression
of the arms on deep venous thrombosis in the legs. *Lancet*
1976;**ii**:1265–7.

18 Nicolaides AN, Fernandes e Fernandes J, Pollock AV.
Intermittent sequential pneumatic compression of the legs in
the prevention of venous stasis and post-operative deep
venous thrombosis. *Surgery* 1980;**87**:69–76.