THE ASSESSMENT OF AORTOILIAC NARROWING

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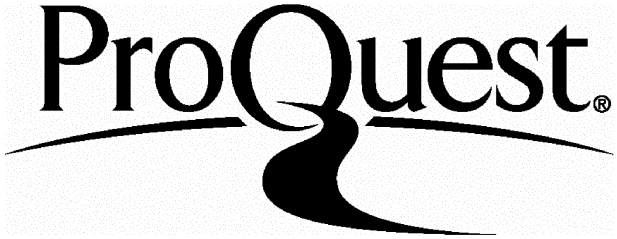


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INTRODUCTION

Occlusive arterial disease is a condition of unknown aetiology and is the major cause of adult mortality in the western world. Most of these deaths are from cardiovascular and cerebrovascular disease, but all arteries from the aorta down to those of 1-2 mm diameter can be affected and those supplying blood to the lower limb are frequently involved in what must be considered a generalised disease process. Fortunately, occlusive arterial disease progresses at different rates in different parts of the arterial tree; this allows surgical treatment of many individual symptomatic lesions to take place in the knowledge that it may be years before the disease starts producing symptoms elsewhere.

Clinical experience has shown that surgical intervention in patients with certain patterns of occlusive arterial disease of the lower limb can bring excellent results, while in others there is little that surgery can offer. Many patients, however, fall into a middle group where a satisfactory outcome can only be anticipated in a proportion of cases. One of the major problems is knowing at which level the most

haemodynamically significant lesion is situated; for example, correction of an occlusion in the thigh will be unlikely to give good results if there is a moderate stenosis in the iliac segment (1). Similarly, if iliac and femoro-popliteal occlusions co-exist in claudicant patients, at least 25% will not be improved if only the proximal lesion is corrected (2).

If some type of vascular reconstruction is indicated, recourse is normally made to arteriography to define the intravascular architecture of the diseased segment. This technique, however, only gives anatomical information and tells little about the flow down an individual vessel. In the aortoiliac segment, in particular, single plane views tend to underestimate any arterial narrowing and biplanar films, while offering greater accuracy, are not obtainable in the majority of hospitals.

Symptoms of occlusive arterial disease are due, initially, to flow disturbances preventing an adequate supply of metabolites getting to part or all of a limb and occurring either at rest or on exercise. This has led many workers to seek a test which could reliably confirm the adequacy of the aortoiliac segment, based on some flow related measurement. One such method, examination of the femoral pulse with Doppler ultrasound, is the main subject of this thesis. This technique utilises the change in frequency of reflected sound waves as they impinge on moving particles, in this case the

erythrocytes; the frequency shift is related to the velocity of blood flowing in an underlying vessel. Advantages of the method are the ability to look at all the velocities across the blood vessel by spectral analysis, so that quite subtle changes in profile can be visualised. It is also noninvasive and safe at conventional levels of ultrasound activity. Disadvantages are the price of the equipment, the relatively small changes in flow patterns produced by quite marked stenoses under resting flow conditions and the lack of uniformity of equipment in many vascular laboratories.

Previous investigators using this method have had to find a standard with which to compare their results; usually this has been arteriography (3) which has inherent disadvantages such as its invasive nature and, more importantly, the recognised difficulty in assessing narrowing especially in the iliac arteries. This, after all, is the main reason for looking for another test.

The present work has set out to assess the reliability of continuous wave Doppler ultrasound, both in patients and in an animal model, with particular reference to the quantification of aortoiliac narrowing. In the animal experiments it was possible to obtain 'hard' pressure and flow data simultaneously and so provide a better standard for comparison with Doppler waveform shapes. In the patient studies, arteriograms were still the main reference material, but in most

cases direct femoral artery pressure studies were performed at rest and during hyperaemia, and in a few cases pressure and flow measurements were obtained at operation, so providing additional data for comparison with Doppler changes.

In any such study it is important to have some understanding of the pathogenesis of the underlying disease, and this is reviewed in Chapter 1; in addition an outline of the current place of medical and surgical therapy is presented. Arteriography, which is the only investigation of vascular disease universally in use and still provides the best material for comparison with non-invasive tests, is described in Chapter 2. Haemodynamics, and in particular the effect of stenosis on pressure and flow in diseased arteries, is discussed in Chapter 3; diagnostic tests exploiting these effects are also outlined. Tests employing Doppler ultrasound are reviewed in Chapter 4.

The experimental work begins at Chapter 5 with a description of the equipment used in the animal and patient studies, and an outline of the data processing techniques. In particular, three methods of objective analysis of Doppler waveform shape are described. The animal experiments were in two parts: the first series related changes in Doppler waveform shape to varying degrees of proximal arterial stenosis at a fixed distance downstream, while the second investigated the propagation of disordered flow patterns at varying

distances below a proximal stenosis. These experiments are described and their results presented in Chapters 6 and 7.

The method of patient assessment is described in Chapter 8 and the results of the patient studies including comparisons of Doppler waveform changes with arteriography and pressure studies are in Chapter 9. A summary and important conclusions from the work will be found in Chapter 10.

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Chapter 1

OCCLUSIVE ARTERIAL DISEASE - THE PROBLEM

In this introductory chapter I shall attempt to review the aetiology and pathogenesis of atherosclerosis, outline the clinical presentation of patients with vascular disease and summarise the treatment of the disease as it affects the lower limb.

A. WHAT IS ATHEROSCLEROSIS?

Advances in therapy and preventive measures usually follow the acquisition of knowledge of the aetiology and pathogenesis of a particular disease. This is well illustrated by the improved survival of patients with infective disorders, many of which were lethal a few decades ago. Occasionally, as with vaccination for smallpox, a major advance occurs almost by chance, with very little knowledge of the nature of the underlying condition. Such events are rare, however, and it is more usual for developments to take place only after a long period of investigative work at both basic scientific and clinical levels.

Patients suffering from occlusive vascular disease are therefore at a considerable disadvantage because it is only in the last few years that progress has been made in understanding the aetiology of these disorders. Certain risk factors, hereditary, acquired and environmental, have been identified for many years and some effort has been made to control some aspects of the disease, for example by lowering blood pressure in patients with hypertension or persuading smokers to stop; however, advances in therapy have come relatively slowly.

It cannot be said that the rate of progress in vascular research is related to any lack of work directed towards solving the problems. Because of the prevalence of vascular disease in the developed countries and the huge clinical work load involved in caring for patients with these conditions, a great deal of time and effort has been spent in an attempt to improve knowledge at both clinical and more basic levels. Many disciplines have been involved, and as many aetiologies proposed for this very widespread disorder; perhaps one of the reasons for the lack of progress has been this multidisciplinary approach where one group of workers may proceed along a line of thought and research with very little reference to other work in a parallel subject which nevertheless has the same goal.

This goal has to be the definition of the initiating

factor or factors in the development of atherosclerosis. Without this knowledge it is unlikely that preventive measures will ever be wholly successful and therapy will be at best empirical. To trace developments in this area it is necessary to return to the middle of the last century and the well known rivalry between Virchow and Rokitansky.

(i) The lipogenic theory

Virchow (4) has been credited with the early popularity of the imbibition theory - in other words, that a 'loosening' of the intimal ground substance was followed by an increased passage of abnormal blood constituents into the subendothelial space. Thrombosis was thought to be very much a secondary, 'accidental', phenomenon which accompanied the process of thickening. He felt that the loosening of the subendothelial connective tissue might well be due to mechanical stress in the arterial wall. The imbibed tissue then underwent a fatty metamorphosis to give rise to the typical raised plaques seen in advanced atherosclerosis. He also recognised, however, that fatty change was not necessarily bound to be followed by plaque formation, but that this sclerotic phase happened selectively, and could be accompanied by ulceration. A crucial factor was the need for an intact endothelium which was thought to be incapable of regeneration.

(ii) The thrombogenic theory

Rokitansky (5), on the other hand, considered the disease to be one of fibrin deposition on the vascular endothelium accompanied by intimal hypertrophy. A primary abnormality of blood coagulation might therefore be the initiating factor. This approach was revived in the present century by Duguid (6) as a result of direct observation of the merging of surface thrombus into mural plaque in coronary arteries.

The lipogenic school received much support from animal studies which showed that lesions in some respects similar to those found in man could be produced by feeding diets with very high cholesterol contents (7). As a result of these rather unsatisfactory models, a great deal of research proceeded in an attempt to define the importance of dietary lipids for atherosclerosis development in man. At the same time, the role of thrombosis was somewhat neglected. Clearly there is an association between lipids and atheroma, but whether a lipid abnormality is the much sought after initiating factor seems unlikely except in a small minority of patients with hereditary disorders of lipid metabolism.

(iii) The monoclonal theory

A recent much needed advance in what had become a cir-

cular argument was the discovery that atheromatous plaques in patients with a genetic mosaic make-up tended to contain cells with a single mosaic marker. The system investigated by Benditt (8) made use of the finding that females tend to be mosaics with one or other X-chromosome being suppressed in the Barr body (9). Benditt investigated plaques in the aortae of black women who were heterozygous for glucose 6-phosphate dehydrogenase. It was possible to examine cells in different plaques for enzyme activity and it was found that most plaques contained one or other iso-enzyme but not both. These plaques were, in effect, clones of a single original cell which had been stimulated specifically to multiply much as might happen in a benign tumour such as a uterine fibroid. Tissue from unaffected parts of the aorta contained a mixture of both types of cell. This approach to the problem leads inevitably to a search for the factor responsible for local proliferation of intimal cells with emphasis on substances known to promote neoplasia elsewhere. It also highlights the importance of smooth muscle cells which appear to be a constant feature of developing plaques (10,11).

(iv) Haemodynamic factors

Although many workers have accepted that 'stress' may affect the distribution of atherosclerotic plaques and possibly their severity, Texon (12,13) considers this to be the

initiating factor. His evidence is at best circumstantial, and most workers are content to use haemodynamics to explain the predilection for plaques to form at certain sites, notably around the mouths of branches and at bifurcations. Some stress factor may also explain why the arteries supplying the legs are involved much more frequently than those supplying the arms. The exact mechanism responsible for this localisation is still being debated. Certainly areas of disturbed flow are more likely to produce thrombosis, but such disturbances are usually secondary to atherosclerotic changes already present. Both areas of low shear and high shear have been implicated (14,15), and the present position is still one of uncertainty.

(v) Factors in the vessel wall

Large arteries in humans are supplied by the adventitial vasa vasorum to a depth of about half way through the media; intramural pressure would cause any deeper vessels to collapse. The inner media and intima are therefore supplied with metabolic requirements by passive diffusion either from the lumen or from the vasa vasorum. Lymphatics are also notably absent from this area for the same reason. It is probable that in arteries more stressed, such as those of hypertensive patients, one of the factors for increased atherogenesis is the relatively wider zone of avascularity in the vessel wall (16) causing an area of hypoxia. Experi-

mentally, hypoxia can certainly accelerate plaque formation in rabbits (17).

(vi) Platelets, thromboxanes and prostaglandins

One of the most exciting developments in relation to vascular disease has been the elucidation of the inter-relationships between these elements and the endothelium. Not only does this theory provide a mechanism for the normal response to injury, but it can explain the way in which such a response, by getting out of control, might give rise to atherosclerotic lesions. The subject has been extensively reviewed by Gryglewski (18) who has also contributed to much of the original work, and the clinical implications have recently been analysed by Mitchell (19). The updated version of the thrombogenic theory had already described the incorporation of thrombus (including platelets) into a developing plaque. Now we are perhaps getting nearer to the level of the initiating factor.

In brief, both platelets and endothelial cells are able to perform the early stages of the prostaglandin synthetic pathway from the basic arachidonic acid. Platelets, however, tend to form thromboxanes which, when liberated, have powerful platelet aggregatory properties. The endothelium, on the other hand, manufactures prostacyclin which is extremely anti-aggregatory and is in addition a strong vaso-

dilator. Normally there appears to be a balance between these two effects in much the same way as between thrombosis and fibrinolysis. By either overactivity of the platelet system or inhibition of the endothelial system an imbalance could occur with release of the platelet stimulatory factor of Ross (20) to initiate the subendothelial proliferation of smooth muscle cells.

Although details remain to be worked out, the importance of the role of prostaglandins has already stimulated clinical work both in prevention and therapeutics. For example, early results of treating severe lower limb ischaemia with prostacyclin (21) have been most encouraging and trials of aspirin and sulphinpyrazone in post-infarction patients are suggestive of a beneficial effect, although limitations of the trials make any judgement premature (22).

In conclusion, the most likely site of action for the initiating factor is the endothelial cell itself. Possibly by direct action of toxic substances (eg lipids or cigarette smoke factors) and at sites dictated by haemodynamic stress, platelets can stick at a point of injury. An imbalance in the local prostacyclin/thromboxane system allows significant platelet accumulation to occur with the penetration of stimulating factors and the incorporation of platelet thrombus into the intima. Smooth muscle cell proliferation is an early and probably reversible phenomenon which is later com-

plicated by the extracellular deposition of lipid. Resolution may be impossible by now, especially as these changes are occurring in a relatively avascular zone deficient in metabolites and oxygen. Subsequent ulceration, thrombus formation and incorporation can then proceed according to the thrombogenic theory.

B. THE CLINICAL MANIFESTATIONS OF ATHEROSCLEROSIS

Whatever the role of thrombosis in the aetiology of the atheromatous plaque, there seems no doubt of its place in the complications of the disease. Myocardial infarction is typically caused by thrombosis in an already diseased coronary system. Narrowing alone may be responsible for angina, and similarly for claudication in the legs. Thrombosis can also occur in the leg vessels, most notably in the superficial femoral artery where it is the final step between stenosis and complete occlusion. This may be mistaken for an embolic episode but is usually rather less acute in effect.

The relationship of these manifestations to thrombosis and atherogenesis was well discussed by Sir George Pickering (23) in an article which included a translation of some of Virchow's original work; the position is essentially the same 18 years later. The subject of this thesis is the investigation of atherosclerosis as it affects the arteries

supplying the legs. Patients present in two main ways: with intermittent claudication or with ischaemic pain at rest, sometimes complicated by incipient or frank gangrene.

(i) Intermittent claudication

This pain, like angina pectoris, classically comes on with exercise and disappears with rest. The exact mode of pain production is still unknown; the stimulus which irritates the pain fibres is probably a metabolite rather than hypoxia itself, a conclusion going back to the experiments of Lewis in the early 1930's (24). Substance P, as it was called, is still not identified. Pain in any one patient tends to come on after a certain distance and providing that the test conditions are well controlled, this can be reproduced in the laboratory with fair reliability. The pain is most commonly felt in the calf, but it can also spread into the thigh or buttock or even start there with a suitably proximal major stenosis or occlusion.

Intermittent claudication is in many cases a benign condition. Indeed, if relatively conservative methods are adopted such as stopping smoking and taking regular exercise, there is now good evidence that symptomatic improvement can be expected in the majority (25,26). However some patients with severe claudication are on the verge of rest pain and their investigation and treatment may need to be undertaken

with a greater degree of urgency.

Resting blood flow in claudicant patients is usually within normal limits whatever the site of the major occlusion, and therefore diagnostic tests based on blood flow must either be fairly sophisticated or utilise a hyperaemic response if they are to be of quantitative value (27). This is a function of peripheral resistance which is reset in the presence of proximal disease to maintain resting flow rates.

(ii) Rest pain

Here the pain is present at rest and frequently comes on in bed at night. Although total limb blood flow is often normal at rest, there is ischaemia in areas supplied by the more peripheral parts of the circulation which can often be relieved by allowing the limb to rest dependently. This gives a significant but temporary haemodynamic advantage (28). If rest pain is present, however, there is considerable urgency to try to improve blood flow as distal tissue necrosis is imminent. Although it is possible to have rest pain as a result of a single major arterial stenosis or occlusion, it is much more usual to find disease at several levels which makes the prospect of surgical improvement less encouraging.

C. TREATMENT OF LOWER LIMB ISCHAEMIA

Because the arteries supplying the lower limb are affected by atherosclerosis at different rates, it is possible to correct localised occlusions or narrowings with some hope of success; the whole of vascular surgery hinges on this concept. The aim must be to attempt to restore the blood pressure on the upstream side of a resistance bed to its normal level; by doing so, an adequate flow of blood, and consequently oxygen and metabolites, will be restored. In the presence of proximal narrowing, distal beds automatically dilate and it is not surprising that medical measures aimed at causing further dilatation or improved blood rheology have no measurable effect on symptoms (29). Sympathectomy can certainly alter cutaneous blood flow but has little place in the management of intermittent claudication. In severe ischaemia, however, there is good anecdotal evidence that ulcer healing is promoted and pain relieved although, in theory at least, dilatation of more proximal beds might well reduce the perfusion of the already compromised distal regions. Clinical trials of sympathectomy have rarely shown objective evidence of improved blood flow particularly to muscle (30) and usually lack an adequate control group.

(i) Conservative measures

In animal experiments, acute occlusion of the femoral

artery causes an immediate fall in peripheral arterial pressure and flow which return to almost normal levels within a few minutes (31) and a similar pattern has been seen in human studies such as those of Dornhorst and Sharpey-Schafer (32), although the 'immediate' response takes over 24 hours to develop fully. After this acute opening up of collateral vessels already present, there follows a much longer period of new collateral development with a time course of months or years. This process consists of increasing the diameters of existing vessels and increasing the number of anastomoses between the proximal and distal circulations. It is well known that foot pulses can return following acute occlusion of the superficial femoral artery in man, and that the resting ankle pressure may be normal. However, even in the best developed collateral system there is usually an abnormal distal pressure response to exercise.

Although many factors are involved in the development of occlusive arterial disease, disuse of the lower limb is one which is often neglected. An interesting observation in patients with one leg severely disabled by polio or stroke is that radiological atheroma seems more advanced on the affected side. The corollary of this is that exercise may slow the rate of progression of established disease and possibly increase the rate of collateral development. This approach has been applied therapeutically with considerable success, especially in the Scandinavian countries (33,34) although

controls have often been unsatisfactory. Fitzgerald et al (35) did however demonstrate significant improvement in both exercise tolerance and maximal calf blood flow in their treated group.

The mechanism for the improvement in symptoms with physical training is likely to be by collateral vessel development but changes in muscle cell metabolism may also be important (36). Key glycolytic enzymes are found to have enhanced activity not only in physically fit normal subjects but also in claudicant patients who have undergone a controlled training scheme. Whatever the mechanism, the published results all favour an increase in exercise level, preferably in a controlled regime, for patients with claudication who are not in imminent danger of tissue necrosis.

Smoking is a well recognised risk factor and patients with vascular disease are often told to stop. The evidence that this will improve symptoms is hard to find, but a few small trials are suggestive of a beneficial effect (37). What is certain, however, is that a satisfactory outcome of a vascular reconstruction is seriously compromised by continued smoking (38) and the available evidence would support considerable investment of resources to try to reduce smoking for both therapeutic and preventive reasons.

(ii) Surgical methods

Although patients with mild to moderate claudication can, and almost certainly should, be treated conservatively, those with severe claudication and rest pain are much closer to developing irreversible tissue damage and it is for these patients that surgery holds out the only real hope of improvement. Surgery can bypass or remove occlusions and stenoses, or dilate them using percutaneous transluminal angioplasty (PTA). This latter technique was developed by Dotter (39), but good results have only recently been obtained with the improved balloon catheter of Grüntzig (40). The method offers a relatively safe way of improving flow without open operation and is especially suitable for unfit patients or when there is both proximal and distal disease where one lesion may be dilated and the other (usually distal) is bypassed. Ideally stenoses or occlusions should be short; the method is still at an evaluation stage and a recent review by Dacie (41) summarises the present situation. What is clear is that just as for successful bypass surgery, haemodynamic data are needed to assess the severity of a lesion and to monitor the response to treatment.

For direct arterial surgery to be successful, three essential requirements must be met (42). In the first place, the inflow must be adequate: in other words, the section of arterial tree between the heart and the proximal

anastomosis of a bypass must not be severely stenosed. Secondly, the blood flow down the graft must be correct: there should not be a large pressure drop either at rest or during hyperaemia, but at the same time the flow must be adequate to maintain patency. Thirdly, run-off resistance distal to the graft must not be too high. Clearly these last two factors are closely related. If these three conditions are met, a bypass graft should function and the arterial pressure at the distal anastomosis should return to close to systemic levels. However, if the distribution of blood beyond the distal anastomosis is not satisfactory, for example in the presence of severe tibial disease but a good collateral system around the knee, a graft may function but symptoms may not be much improved.

The aim of the work described in this thesis is to try to improve the assessment of the first of these conditions, proximal narrowing. If there is reliable knowledge of any significant proximal impedance, a more rational approach to surgery may be planned. Traditionally, clinical examination of the femoral pulse combined with arteriography provide the only information and both can be misleading. What is needed is a simple, preferably noninvasive method of assessing proximal disease in addition to the standard clinical and radiological methods.

Chapter 2

ARTERIOGRAPHY - THE 'GOLD STANDARD'

Arteriography remains the single most useful investigation for the patient with peripheral vascular disease. Not only does it give an anatomical map of the major arteries of interest and any areas of disease, but it can also show significant deviations from the normal pattern of supply to abdominal organs and to the lower limbs. By modern methods it is possible, with a single injection, to demonstrate all vessels upon which operations are possible using multiple exposures as the contrast medium goes down the legs.

The major limitation of the technique is its invasive nature and although complications are rare, when they do occur they are often serious (43). There is general acceptance, therefore, that arteriography should be reserved for those cases who are likely to have an operation if the investigation confirms the clinical findings and shows that surgery is technically feasible. In spite of this, many arteriograms are still requested apparently for 'routine' purposes even though surgical intervention seems an unlikely sequel (44,45).

Arteriograms have set the standard by which all other tests of aortoiliac disease have been compared, and this reflects the enormous quantity of useful information available in a good examination. However, although in the smaller vessels of the leg serious lesions are unlikely to be missed, in the iliac arteries the common posterior plaques are often underestimated in conventional AP views (1). The importance of routinely performing aortography, rather than femoral arteriography, has been stressed by several workers (46,47) who appreciated the frequency of unexpected proximal disease.

Other ways of assessing aortoiliac disease depend either on isotope imaging or some direct or indirect method of measuring arterial pressure or flow.

(i) Translumbar aortography

The technique presently in use is derived, with few modifications, from that of dos Santos (48). Either local or general anaesthesia is employed but in the UK the latter is more common. The patient is intubated and lies prone, and the aorta is punctured directly through the left loin with much the same approach as for a chemical lumbar sympathectomy. Because the contrast medium is injected into a large

vessel, the technique is relatively non-selective, all distal vessels being demonstrated if necessary but with a relatively low concentration of contrast in the blood. Timing of the exposures is very important and more difficult with this method than by the Seldinger technique.

Complications are usually the result either of the anaesthetic or of faulty placement of the needle, often in a tributary of the aorta rather than the main lumen. Extravasation may occur, and a sizeable haematoma is common. The method is, however, fairly quick and comfortable for the patient. It is difficult to perform associated haemodynamic measurements unless the catheter modification is employed (49).

(ii) Seldinger arteriography

Here a catheter is passed into the aorta, usually from a femoral artery puncture. The technique, as described by its originator (50), is beautiful in its simplicity and can be performed easily under local anaesthesia especially when the modern non-irritant types of contrast medium are used. High aortograms can be achieved, and its only limitation in patients with aortoiliac disease is that it may not be possible to negotiate a tortuous or markedly stenosed iliac artery. In such cases a trans-axillary approach may be made, but it

is more usual to proceed to a translumbar aortogram.

Major advantages are that several runs are possible using different exposure times, and that by withdrawing the catheter distally, more contrast medium can be introduced allowing better visualisation of small vessels. Pressure measurements may be made at the same session (51) and it is easier to perform oblique views of, for example, the profunda femoris artery. However, for biplanar iliac artery imaging, special equipment is needed which is not at present available in the majority of hospitals in the UK.

Complications are limited to those of medium sensitivity, bleeding and haematoma at the puncture site and the occasional disruption of a plaque as the catheter is passed up a diseased artery. In practice, such local complications are rare in patients with occlusive arterial disease, being much commoner following the investigation of younger patients with cardiac problems(52).

(iii) Intravenous arteriography

Although visualisation of the heart and great vessels has been achieved by injecting large volumes of contrast medium into peripheral veins (53), the resolution has been inadequate for imaging peripheral arteries. Several att-

empts have been made to improve this method in order to avoid the complications of direct arterial puncture and also to obtain pictures using a lower concentration of dye with consequently less discomfort for the patient. The use of Xeroradiography (54) has been partially successful in both these respects, but because of inadequate sensitivity of the plates it is confined to studies of peripheral vessels and has not been widely adopted. A recent report, however, has given encouraging results in patients with popliteal aneurysms (55).

The advent of digital vascular imaging (56) must surely herald the beginning of a new era in diagnostic procedures for patients with peripheral vascular disease. An intravenous injection is given and an augmented image is built up using a computer. The resolution is adequate to make conventional arteriography unnecessary in certain cases and improvements in the method will almost certainly reduce this need still further. Although not as yet widely available in the UK, digital vascular imaging is already in regular use in the United States.

(iv) Other imaging techniques

Ultrasound and Doppler imaging, while undoubtedly useful in studies of superficial arteries such as the carotid, are

not suitable for examining the iliac arteries because of inadequate resolution and the presence of bowel gas. Isotope imaging has been more widely studied; once again an intravenous injection can be made and computer enhancement is used to provide better resolution (57). It is not sufficiently accurate for the assessment of non-occlusive aortoiliac disease but it can provide useful information about the common femoral and more distal vessels (58).

CONCLUSIONS

Arteriography remains the most useful method of investigating the patient with peripheral vascular disease if surgery is contemplated. Its limitations, especially in the aortoiliac segment, are well recognised. The wider use of haemodynamic studies, possibly at the time of arteriography, would allow more information to be obtained with no extra morbidity for the patient. The safety of digital vascular imaging and the prospect of using it to follow patients sequentially make it of great interest at the present time, although whether it will eventually provide adequate resolution of all necessary arterial segments is as yet not known.

Chapter 3

THE EFFECT OF STENOSIS ON PRESSURE AND FLOW

Other tests used in the assessment of aortoiliac narrowing measure blood flow, velocity or pressure either directly or indirectly. In order to understand them and appreciate their limitations, it is necessary to examine some of the complex haemodynamic events taking place within the diseased arterial system.

A. HAEMODYNAMICS OF ARTERIAL STENOSIS

When blood flows through a narrowed arterial segment, energy is lost in a number of ways: frictional losses, losses due to a sudden contraction of the stream and losses due to expansion in the post-stenotic region (59). This energy loss is apparent as a reduction in the arterial pressure beyond the narrowed segment. The relationship between flow through and pressure across a stenosis is therefore extremely complex, especially when the pulsatile nature of blood flow is taken into account.

The effect of stenoses on flow and pressure has been extensively investigated both in vitro and in animal and human experiments. Surgeons in particular have been interested in the idea of 'critical stenosis': although difficult to define with accuracy, there seems little doubt that it is an important concept in certain clinical situations. Critical stenosis is usually understood as that level of lumen area reduction which, if reduced slightly further, would produce a marked fall in blood flow through the stenosed segment. The exact value of critical stenosis varies in different parts of the arterial tree and is mainly dependent on the flow rate at a particular site which in turn is dependent on downstream resistance (60).

Interestingly, the earliest work on this subject was not directly concerned with diseased arteries. Mann et al (61) thought that the application of a flow probe to a vessel might itself cause a slight constriction which could reduce the measured flow and so invalidate the results. They performed studies in vitro using tubes and also in vivo employing internal and external constrictions of the carotid arteries in dogs. Their conclusions were that a 50% area reduction produced only a minimal change in steady flow; flow did not change much until a stenosis of between 70% and 80% area reduction was used (with a length of 8-10mm). It was therefore perfectly acceptable to use a flow probe which caused a slight constriction of the vessel wall. Almost as

an afterthought, it was stated that in arterial repair procedures a good result might be expected even when it was not possible to reconstitute the lumen completely.

Shipley and Gregg (62), in a series of investigations in many ways similar, came to rather different conclusions; in particular they established the importance of peripheral resistance (PR) as a factor determining flow through a stenosis. At physiological values of PR, however, and when allowance is made for the difficulty in assessing true area reduction when employing an external constriction, there is marked agreement between these two studies.

The advent of reconstructive vascular surgery revived interest in the physiology of blood flow through narrowed arteries. Crawford et al (63) looked at both flow through and pressure drop across diseased carotid bifurcations in man, and in artificially stenosed carotid arteries in dogs. The classical inverse relationship between these two measurements was found; in addition the effect of increasing the length of a stenosis was appreciated but not accurately quantified. For a stenosis of 6mm length in the canine carotid system it was found that an area reduction of at least 60% was needed before any appreciable effect on flow or pressure gradient could be found (Fig 1). This study was essentially clinically orientated, the aim being to decide at what level of carotid stenosis surgery should be undertaken.

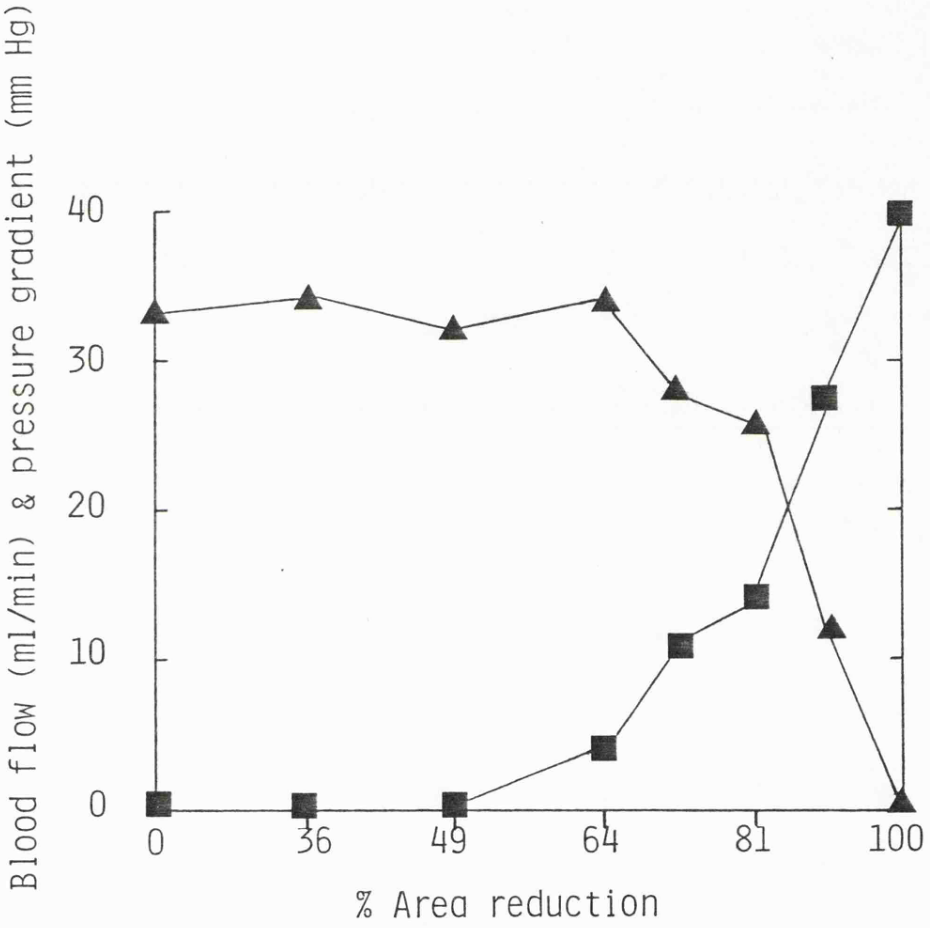


Figure 1. The effect of increasing the area reduction of a stenosis on pressure gradient and flow. The stenosis was 6mm in length and was externally applied; ▲—▲ - blood flow, ■—■ - pressure gradient. After Crawford et al (63).

The work of May and colleagues (64,65) attempted to explain these findings on a more mathematical basis using a canine model essentially similar to that used in the animal experiments in this thesis. They confirmed the concept of critical stenosis for a certain set of conditions, once more finding that an area reduction of about 80% over a 10mm length of artery was needed before any significant reduction of flow occurred. They clearly appreciated the interrelationship of flow and PR: in an artery with a high normal flow rate (and low peripheral resistance), such as the internal carotid, the value of critical stenosis would be smaller.

In the appendix to their first paper (64) they attempted to quantify the various pressure losses at a stenosis by derivations from Poiseuille's law. Although the problem of pulsatility was ignored, and also the fact that turbulence was likely to be induced by such a narrowing, this was really the first attempt to put the haemodynamics of flow through a stenosis on a firm foundation; their experimental results were in broad agreement with values predicted by their equations.

In their second paper (65) they concentrated on the problem of critical stenosis making the point that this will change for different sets of conditions mainly related to PR and also to the size of the unstenosed vessel. Sympathec-

tomy, by decreasing PR, would reduce the value of iliac critical stenosis from 80% to 60% (Fig 2). In smaller vessels, such as the coronaries, predicted values for critical stenosis might be as low as 21% area reduction because of the smaller size and lower PR.

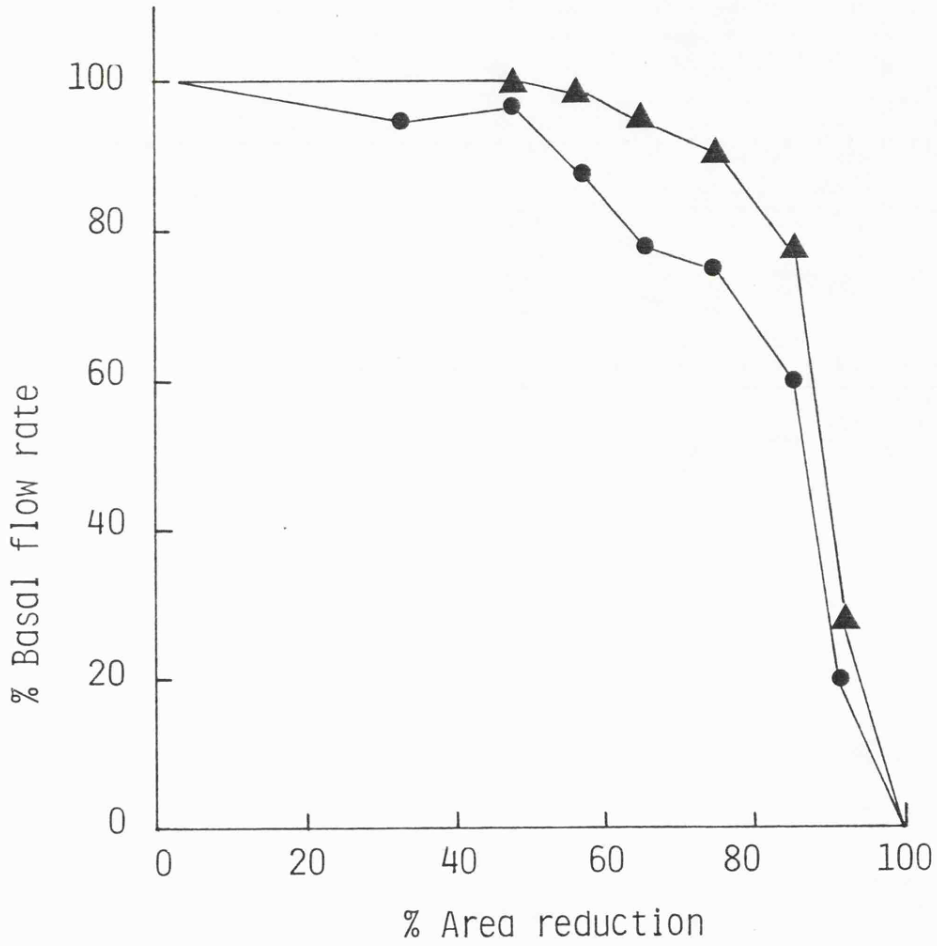


Figure 2. The effect of sympathectomy on arterial blood flow in an animal model with increasing stenosis. Ipsilateral ganglionectomy had increased resting blood flow by 176%. The reduction in 'critical stenosis' due to the increased flow is clearly seen. ▲—▲ - before sympathectomy, ●—● - after sympathectomy. After May et al (65).

The suggestion that the term 'per-cent lumen reduction' should be abandoned in favour of absolute stenosis dimensions was made by Fiddian et al (66) in a study undertaken in an extra-corporeal circulation using a dog as a source of pulsatile blood flow. Here it was possible to adjust the peripheral resistance artificially (difficult to achieve in the typical in vivo dog experiment). By using a drilled internal stenosis, accurate dimensions were assured. The absolute value of the internal diameter of the stenosis was clearly very important no matter the size of the unstenosed vessel. The values of PR were, however, very unphysiological: in reality flow is tailored to size of unstenosed vessels and thus for any particular system per-cent area reduction remains a useful practical term.

The effect of increasing stenosis length was relatively less important, as predicted by Poiseuille's law, but a critical length could be calculated for each level of lumen reduction (67). Multiple stenoses produced additive effects, the major energy losses occurring at the tightest stenosis (68,69). The clinical importance of dealing with all significant stenoses or occlusions in a particular segment is obvious.

All this theoretical knowledge has led to a more rational approach to the surgery of arterial occlusive disease. One clinical problem, that of pulse assessment in patients

with arterial narrowing, was well demonstrated by Keitzer et al (70) in a dog model. Both the disappearing pulse beyond a stenosis (caused by exercise leading to increased flow and decreased distal pressure) and the strong pulse sometimes felt proximal to a more distal occlusion were explained in simple haemodynamic terms.

The importance of collateral flow has been investigated in animal carotid models by several workers (71,72). A critical level of internal carotid stenosis was reduced by ligating the vertebral vessels. This of course had the same effect as manipulating the peripheral resistance, and has important clinical consequences where multiple vessels supply the same organ (such as the brain or GI tract).

Haemodynamic effects of diseased and normal human aorto-iliac segments were investigated by Schultz et al (73) by excising cadaver specimens and placing them in a pulsatile pump circulation. The relationship between pressure and flow was essentially as predicted using artificial stenoses; only at very high and unphysiological flow rates was there a measureable aortofemoral pressure drop in the normals.

The effects of arterial stenoses have recently been placed on a sounder mathematical basis in a series of papers by DF Young and colleagues. In a systematic enquiry they started by looking at flow in vitro using pumps and tubes

with stenoses of various shapes and sizes both for steady (74) and unsteady flow using a harmonically oscillating flow superimposed on steady flow (75). They derived an expression for pressure drop and flow across a stenosis which may be simplified as follows:-

$$\Delta P = AU + BU|U| + CdU/dt$$

where A relates to viscous losses and is strongly dependent on geometry, B relates to turbulent losses and C inertial losses.

The validity of this relationship was confirmed in a series of animal experiments (76) and in a further study at elevated flow rates (77). The effect of multiple stenoses was also investigated (78) and found to be less simple than previous workers (68) had suggested; in particular, certain configurations of stenoses could interfere with each other leading to smaller than predicted energy losses.

Although this work has led to a better understanding of the effects of arterial stenoses in a rather artificial model, when dealing with patients we are more interested in the resistance of a particular segment of the arterial tree rather than a discrete stenotic area. It may well be that aortofemoral resistance can be predicted from these more basic studies: if so, then the diagnostic tests described in

the next section will have a more reliable basis. At present, however, we are left with a rather empirical estimation of what constitutes a 'significant' aortofemoral pressure drop. Undoubtedly measurements under conditions of augmented flow will be of value if the resistance comes close to that for a critical stenosis; on theoretical grounds at least, resting pressure measurements over this segment would be unlikely to be helpful unless a vessel is close to total occlusion.

B. HAEMODYNAMIC TESTS IN ARTERIAL DISEASE

Although there is little doubt about the usefulness of haemodynamic tests in the assessment of overall functional impairment in the ischaemic limb, their place in the detection and quantification of aortoiliac disease is less certain. In the following sections some of the methods have a role in more academic studies of limb blood flow but have not become established as tests of proximal narrowing. They are, however, included for the sake of completeness and as an example of the limitations of indirect testing for more specific problems.

(i) Isotope clearance studies

The clearance of radio-active isotopes such as xenon has

been used as an indicator of blood flow in many tissues (79); used in the leg in claudicant patients, however, such measurements are usually within normal limits at rest. Nicolaides' group (80) has employed the same principle using measurements at sites in the thigh and calf during hyperaemia. By plotting thigh and calf 'hyperaemic indices' against each other, arteriographically clear cut cases are separated into four groups: normals; iliac block with patent superficial femoral artery (SFA); patent iliac with blocked SFA; blocked iliac and SFA. The graphical separation of these groups is impressive and further use in patients with stenotic rather than occluded segments has shown separation into intermediate areas making it theoretically possible to decide which of either a proximal or a distal lesion is contributing the greatest haemodynamic disadvantage to a particular limb.

This technique has much to commend it. It measures flow at two separate points with a method which seems reproducible and could easily be transferred to a non-academic unit, and makes use of augmented flow to accentuate the very small differences in flow at rest. To date, however, it lacks confirmation by other workers and this is a necessary requirement before widespread adoption. One potential source of error, the danger of proximal thigh (especially profunda) disease being mistaken for a lesion in the aorto-iliac segment, has not been discussed and although such pat-

ients are relatively unusual, they have been identified as a cause of false positives by workers using indirect pressure techniques.

(ii) Plethysmography

This method of estimating blood flow has been widely evaluated in vascular laboratories, usually in conjunction with indirect pressure measurements (27). More recently an air filled plethysmograph, the pulse volume recorder (81,82) has been used. Although volume flow at a point in a limb can be measured accurately, and the changes in waveform shape allow a semi-quantitative assessment of proximal arterial narrowing, accurate localisation of disease is less easy. Flow augmentation by reactive hyperaemia is difficult as the leg must be kept still. For flow detection, or assessment of flow changes following reconstructive arterial surgery, these instruments have a place although they are expensive and rather clumsy to use. They have no place in the assessment of mild to moderate aortoiliac narrowing.

(iii) Oscillometry

This is a more old-fashioned device (83) similar to the air filled plethysmograph but using a direct reading aneroid system. It is still in frequent use in Scandinavia, particularly for assessing proximal disease. It shares the same

problems of other types of plethysmography, namely that it can only provide an approximate site for a significant lesion, - ie somewhere proximal to the measurement site. It therefore lacks the accuracy for the detection of moderate degrees of aortoiliac disease; however, a strongly positive mid-thigh value should exclude significant proximal disease.

(iv) Indirect pressure measurement

The origin of this method of exploiting pressure drop distal to arterial stenosis or occlusion is usually attributed to Winsor (84). In 1950, using a blood pressure cuff and a pneumo-plethysmograph to detect flow, he measured arterial pressure in the arm and at several sites in the leg both in normal controls and in patients with arterial disease. He confirmed previous findings that at equivalent sites, leg pressure tended to be slightly higher than arm pressure in the normals, and he was able to localise the sites of major narrowing or occlusion in his patient group. Some of his segmental limb gradients in normals were rather large and this can probably be explained by his use of a small cuff for all pressure measurements including the thigh, with the consequent large cuff artefact.

From this work has come an abundance of further studies using the method; more recently a Doppler device has been found more convenient for detecting flow. At times extra-

vagant claims have been made about the ability to localise significant lesions, but it has slowly been realised that inherent defects in the method do not allow these claims to be substantiated. Its major use must be in eliminating patients with no significant arterial disease, or in following up those with stenoses both before and after operative intervention.

Carter (85), in a large study which also included an analysis of changes in pulse waveform shape, appreciated the need for a wide cuff in measuring thigh pressure and also realised that calcified arteries would be relatively incompressible leading to the recording of higher than actual pressure values.

The use of a Doppler flow detector as described by Yao and colleagues (86) simplified the method of ankle pressure measurement by eliminating the rather clumsy plethysmographic equipment previously employed. It was possible to distinguish clearly between normals and patients with arterial disease and the use of exercise to increase discrimination was first recorded (87). Yao's definition of ankle/arm pressure index has become a widely accepted standard; he also suggested the usefulness of the method in assessing post-operative graft patency, particularly at an early stage when pulses are often hard to feel.

The extension of the method to attempt to define the effect of individual stenoses at different levels in the arterial tree was described by Cutajar et al in the UK (88) and by workers in the USA (89) at about the same time. Although it was possible to differentiate between normals and patients with an iliac occlusion by measuring thigh occlusion pressure, there was considerable overlap in cases of non-occlusive but angiographically significant aortoiliac disease (90). Even when combined with other non-invasive measurements such as the pulse volume recorder (91,92) these methods have not become a substitute for arteriography, nor have they been shown to influence clinical decision making. In spite of this, results from different centres continue to be reported in the literature (93-95).

What, then, can indirect pressure measurements provide which is of clinical value? Simple ankle pressure, with post-exercise recovery curves (96,97) can give some guide to the presence or absence of arterial disease and its severity and is undoubtedly useful in the post-operative period. More complex tests cannot provide the necessary localisation of disease or help to decide which of several lesions is the most significant in haemodynamic terms. They may be able to predict the likely success of, for example, aortofemoral grafts in relieving symptoms of claudication (98,99), but these results require confirmation by others. The major obstacle is the inherent inaccuracy of thigh occlusion pres-

sure measurements; Gundersen gives an excellent account of the values and deficiencies of the method in his thesis (100).

Looking specifically at the assessment of aortoiliac disease, Flanigan (101) has recently published his results comparing thigh pressure measured indirectly, direct femoral artery pressure and arteriography. The main problem was the high false positive rate (59%) due to superficial femoral artery disease which gave the indirect method consistently lower values than intra-arterial results. A normal high thigh pressure, however, was fairly reliable in excluding significant aortoiliac disease although there were 13% false negatives.

This is an important paper because data from direct pressure measurement is used as the standard for comparison and also because claims for the method are realistic. Hyperaemia was not employed so the full value of direct pressure measurements may not have been realised. Similar problems with the method had previously been reported from our unit (102,103) and in conclusion, indirect pressure measurement is inadequate for assessing anything less than total occlusion in the aortoiliac system; this is a situation unlikely to be missed on clinical examination.

(v) Direct pressure measurements

With their greater accuracy over the indirect method, it is rather surprising that direct pressure measurements have not been more widely used. Moore and Hall (1) were among the early workers to recognise the frequency of subclinical but nonetheless significant aortoiliac narrowing and they proposed a method of measuring femoral artery pressure at rest and during hyperaemia induced by exercise. A control needle was placed in the opposite, non-exercising limb. Their results gave a clear assessment of aortoiliac disease and enabled them to offer proximal reconstruction to several patients who might otherwise have undergone a femoropopliteal bypass, with good clinical results.

A similar technique had been described by Sako (104) but here the intra-arterial injection of papaverine, a potent vasodilator, was used to provide hyperaemia; flow was measured simultaneously (the test was employed per-operatively). This method was developed by Quin et al for use in the vascular laboratory (105). Very satisfactory recordings were obtained using a 19swg needle connected to a distant strain gauge manometer through plastic tubing. A dose response curve for papaverine was described, and it appeared that 20mg produced a maximal flow increase in all cases studied. Comparison with arteriography allowed the definition of a figure of 18% reduction in pressure as the division between the pat-

ients with a relatively 'normal' aortoiliac segment and those with more obvious disease. It is of course likely that by the use of a better gold standard it would be possible for this figure to be reduced so that lesser degrees of stenosis might be assessed. The simplified test, however, was unable to measure flow and its change with papaverine, although operative studies had suggested that an increase of 300% could be anticipated at least in claudicant patients.

A recent paper from Canada has confirmed the usefulness of the papaverine test (106). Of 32 patients in whom the test was positive, 3 had normal aortoiliac arteriography and 16 had only apparently mild disease. Clinical results following aortoiliac reconstruction were excellent in all cases and the authors recommend the test in patients with normal or equivocal proximal arteriograms in whom a vascular reconstruction is indicated.

Lorentsen et al (107) were able to achieve flow measurements using plethysmography after ischaemic reactive hyperaemia caused by cuff release - this enabled a more precise 'stenosis index' to be calculated, but their central pressure was measured indirectly in the arm, an obvious source of error. However, they were able to suggest with some confidence that a resting aortofemoral pressure gradient of >20 mmHg meant severe disease and a hyperaemic pressure drop of 10-20 mmHg indicated significant aortoiliac narrowing.

A further variation in technique was described by Brener et al (108). They measured femoral artery pressure at rest and after cuff release hyperaemia and considered that a fall of >10% was suggestive of significant aortoiliac disease. Pressures were measured at the time of transfemoral aortography, and they were able to show a fall of less than 10% in a 'normal' group having studies for reasons other than peripheral arterial disease - they also measured intra-operative flow in a small number of cases and found that cuff occlusion caused an increase in flow of 160-700% on release. Clinical outcome in those cases followed up post-grafting suggested that femoral artery pressure measurements had good predictive value and they felt that the test could be useful in any case where there was clinical or radiological doubt about the adequacy of the aortoiliac segment.

Why, then, are not more surgeons employing direct pressure measurements for aortoiliac assessment? The answer presumably lies in their invasive nature. To date, however, no reports of serious complications have been seen and in this unit several hundred femoral artery punctures have been performed without incident (over 100 by the author in the present study). The papaverine test was therefore included in the protocol for the patient investigations for this thesis and some minor modifications will be described later.

To keep the number of arterial punctures to a minimum,

the measurements can be combined with arteriography (49,51). Indeed, in a recent study on Doppler waveform analysis by Demorais and Johnston (109) direct aortic and femoral artery pressure measurements were taken as the 'gold standard' for comparison. The development of small catheter mounted pressure transducers has also opened up the field for simultaneous recording of pressure at two points in the arterial tree and a pilot study using this method is being performed in Leicester. Again ideally flow measurements are needed, but provided that a sizeable increase in flow can be guaranteed by causing hyperaemia, this drawback becomes less important. There is an obvious advantage in measuring the pressure of the same arterial pulse at two points in the circulation as beat to beat changes are eliminated.

CONCLUSIONS

Of the methods outlined, only direct arterial pressure measurement appears to have the necessary accuracy to provide the detailed information required for accurate aortoiliac assessment. Ideally, flow should be recorded as well and the use of hyperaemia is essential. Of the less direct methods, the most promising results so far come from differential isotope clearance rates, again using hyperaemia; however it is too early to be certain of this technique as it has not been widely studied. It should probably be tested

against direct pressure and flow measurements before it becomes accepted.

Chapter 4

DOPPLER METHODS IN THE ASSESSMENT OF AORTOILIAC DISEASE

The deficiencies of several of the methods outlined in the last chapter led to a search for more reliable yet preferably non-invasive techniques. The use of Doppler ultrasound as a flow detector and velocimeter goes back to 1959 (110,111) and clinical applications were first reported in 1966 (112). It was not until the development of directional capability by McLeod (113) that the full potential of continuous wave Doppler ultrasound could be realised. Subsequent work has concentrated on better signal processing and the detailed analysis of waveform shapes in an attempt to understand flow characteristics in both the venous and arterial sides of the circulation.

At the same time, the very nature of the Doppler ultrasound device - its safety, portability and non-invasiveness - has led to its application to problems which may demand too much of the instrument. There is a risk when assessing a new technique to search for applications and to be overenthusiastic about initial results rather than to analyse a particular problem and then determine the most appropriate

way of solving it.

A great deal of work has gone into the use of the Doppler velocimeter for the assessment of aortoiliac narrowing, but the majority of the studies have failed to be adequately controlled. In the first instance such a new technique must be checked against the most reliable haemodynamic methods available, even if these are invasive, rather than simply with arteriography; after all, it is just because of the accepted inadequacy of arteriographic imaging of aortoiliac disease that a better test is needed. Flow and pressure data, rather than arteriography, should be the 'gold standard' for comparison; this information did not exist at the start of this study.

A further important consideration for any new test must be its ability to influence clinical decisions. This factor is extremely difficult to quantify in any objective fashion for Doppler ultrasound even from the published results of centres which have pursued the method enthusiastically; anecdotal evidence would suggest, however, that most vascular surgeons are reluctant to accept Doppler results when there is already uncertainty about the adequacy of the aortoiliac segment on clinical and radiological grounds.

A. THE DOPPLER PRINCIPLE

The Doppler effect was first used by its originator to explain the different colours of stars according to whether they were moving away from or towards the observer. This turned out to be incorrect and the theory was much criticised by Buys Ballot who arranged the famous experiment using a railway engine as a moving source of sound (114). To his surprise, the Doppler effect clearly applied to sound waves!

It has subsequently been shown that the Doppler effect also applies to light but not in the way Doppler had thought (115). The change in frequency of audible sound waves in the Buys Ballot experiment was relatively small; if, however, an ultrasonic source is aimed at moving red corpuscles in a superficial blood vessel, the difference between the incident and reflected frequency happens to fall into the human auditory range. This Doppler shifted frequency is directly proportional to the velocity of the reflecting surface, and so the typical Doppler flow detector gives a signal easily comprehended by the ear. Using a variety of probes with frequencies in the 2-10 MHz range it is possible to insonate many human vessels transcutaneously providing there is no intervening zone of a non-transonic nature (such as bowel gas). Deep abdominal vessels are therefore difficult to reach with ultrasound, but superficial vessels in the limbs and the neck are easily examined.

The Doppler equation,

$$\Delta f = 2fv\cos\theta/c$$

applies provided that v, the velocity of the moving particles is small compared with c, the speed of ultrasound in the tissue. Δf, the change in frequency between incident (f) and reflected sound, is measured by the device; it follows that velocity can be calculated provided that θ, the angle between the beam and the direction of the reflecting particles, is known. This illustrates one of the limitations of the technique in that θ may in practice be quite hard to measure accurately. To get round this problem, methods of Doppler waveform interpretation have usually tried to be independent of θ.

Two applications of Doppler ultrasound are in general use. Continuous wave machines transmit and receive through separate crystals all of the time. The beam of ultrasound must be uniform and large enough to allow all parts of a particular vessel to be insonated; otherwise only a proportion of the erythrocytes will have their velocities measured. Pulsed Doppler, on the other hand, by 'gating' the reflected sound, will only process signals from a certain and usually variable depth. This allows the assessment of movement at a point of relatively small size; for example, it is possible to focus on blood in a superficial vessel at depths

changing by about a millimeter and therefore to observe the differing flow patterns as the vessel is crossed. Conversely, the same principle can be used to obtain visualisation of vessels from this range-gated information. Two such devices are currently available commercially, and both allow not only imaging but also waveform analysis at any point within the image (116,117). A B-mode real time ultrasound scanner interfaced with a pulsed Doppler for waveform analysis has also been developed and has gained wide use in cardiology: it is useful for assessing carotid disease (118).

For general vascular purposes, however, most work has been done using using the simpler continuous wave (cw) machine in such a way that the whole of a vessel is insonated, and the varying velocities of blood at different depths are either averaged or presented as a spectrum; this is the method which was selected for the present study.

B. SIGNAL PROCESSING

(a) Directional capability. Simple Doppler flow detectors have no ability to determine directional flow; if used for measuring ankle pressure, this is no disadvantage. However, if required to investigate more subtle changes in flow patterns, they should have directional resolution as in normal vessels both forward and reverse flow can coexist at

certain points of the pulse cycle (119). The absence of reverse flow in the femoral artery is a sensitive indicator of either proximal narrowing or peripheral vasodilatation; it is also useful to have directional capability in order to exclude venous signals when studying flow patterns in arteries.

McLeod (113) developed an early method of separation but for full spectral analysis more complex processing is needed. The methods which have been used are reviewed by Coghlan and Taylor (120). In the present study phase quadrature detection with additional processing (121) was employed.

(b) Zero crossing detection. In any application of Doppler ultrasound more complex than simple flow detection it is necessary to have a visual rather than simply an auditory record of the signal. The zero crossing detector is the simplest and most widely used method of achieving this. Both the method and its limitations are considered in a clearly written review by Lunt (122). Essentially a pulse is produced every time the audio signal goes from negative to positive and as the frequency of the audio signal increases, so does the frequency of these pulses enabling an analogue representation of the audio frequency to be produced. Problems of high noise levels occur, however, especially at low or zero flow rates, and it is difficult to exclude a venous contribution to the signal.

(c) Maximum frequency follower. This type of equipment provides the output which most workers in the field have used for further waveform analysis - the maximum frequency of the audio signal. The same information is available in the full spectrum analysed signal; however, the equipment described by Skidmore and Woodcock (123) is simpler and cheaper and its analogue output can easily be processed further. A similar electronic approach can produce a mean frequency output, but this has no obvious advantage.

The signal produced by the maximum frequency follower is clearly superior to that of the zero crossing detector. However, the equipment does demonstrate some noise and the elimination of venous components relies heavily on subjective assessment of the audio signal at the time of recording. The method has not been widely adopted by other workers; initial directional processing is of course still necessary.

(d) Spectrum analysis. This method arose from instruments previously used to analyse sound in the auditory range. A spectrum analyser, with the necessary initial processing, outputs a signal which represents the several frequencies present in the Doppler signal at any one time; it can also provide some additional amplitude information at particular times and frequencies (124). Forward and reverse flow can be demonstrated simultaneously and the equipment can operate

in real time. Three methods are currently in use (120); in the present work an analyser of the time compression type was employed.

The big advantages of spectrum analysis are (i) all the information from the Doppler signal is recorded and (ii) artefacts are usually obvious and can be ignored in any subsequent processing. The main disadvantage is the cost of the equipment; however recent technological advances mean that the instruments are improving and at the same time prices are falling. The method was therefore adopted in the subsequent studies in an attempt to get the maximum useful information from the Doppler signals.

C. FLOW PATTERNS BEYOND ARTERIAL NARROWINGS

As outlined in Chapter 3, a good deal is now known about the relationship between flow and pressure across arterial stenoses. However, there has been surprisingly little experimental work to investigate the changes occurring in the velocity profile. This is what Doppler is potentially able to measure, and one of the aims of this thesis is to try to define the effects of arterial disease on Doppler waveforms and, in particular, the effect of proximal narrowing. The mathematics of volume flow and pressure in vivo have been seen to be highly complex; changes in velocity profile might

be expected to be even more so and hence unlikely to be predictable in patients with arterial disease without a good deal of preliminary experimental work, both in pump/tube systems and subsequently in animal models.

From first principles, changes in velocity waveform shape might be expected with a high enough proximal resistance or if some type of flow disturbance was initiated by a stenotic segment. There is no doubt that a severe proximal stenosis will produce a damped waveform at all measurement sites downstream, the change in shape being due in part to a lowering of the peripheral resistance. However, such changes are only likely to occur if the stenosis is severe enough to cause a pressure drop and this is unlikely to happen until a critical level of narrowing is reached. There have been few quantitative investigations of velocity waveform changes beyond diseased arterial segments using Doppler ultrasound or indeed any other suitable measurement technique.

There has been some interest in the development of turbulence beyond stenoses; for example, Kim and Corcoran, using a hot film anemometer, measured 'turbulence spectra' at varying distances downstream from different stenotic segments in a tubular model (125). They concluded, not surprisingly, that in steady conditions flow becomes laminar disturbed and finally turbulent with increasing Reynolds number and with

decreasing stenosis diameter. Turbulence detectable close to the stenosed segment also disappeared within a relatively short distance downstream. Although their studies attempted to quantify turbulence, it is not easy to extrapolate to the clinical situation especially as only steady flow was investigated. However, they did suggest the possibility of detecting a stenosis in the diseased arterial system by measuring turbulence downstream.

Yongchareon and Young (126) extended this work to a model using pulsatile flow. They also realised the diagnostic possibilities of turbulent flow and they stressed the importance of stenosis geometry in the initiation of turbulence at a particular Reynolds number. Cassanova and Giddens (127) using a similar model, investigated the complex post-stenotic flow disturbances using both hot film anemometry and direct flow visualisation. They made the important point that, for given flow rates and stenoses, turbulence is more likely to develop with pulsatile rather than steady flow; they also noted the presence of flow disturbance with relatively mild lumen incursions, again strongly dependent on geometry.

Perhaps the most useful contribution has been the work of Clark (128) who, starting from the observation that Doppler waveforms can demonstrate turbulence distal to aortic valvular stenosis for a considerable distance downstream, has examined the propagation of turbulence in a pump/tube system

using both a dye visualisation method and the hot film anemometer. Single flow pulses through the stenosis were employed. Turbulence was found to be propagated downstream for a distance related to the severity of the stenosis and in some cases this was more than one stroke length. In other words, some of the blood flowing through the stenosis would be expected to travel much further downstream in the presence of turbulence than in the normal situation with no stenosis.

These experimental studies have certainly been of value in turbulent flow. However, turbulence is by no means always produced by significant arterial stenoses; its initiation is highly dependent on stenosis geometry. The question which needs to be answered is: what changes in Doppler waveform shape might be expected distal to diseased arterial segments in man? Most workers have, understandably, avoided attempting a mathematical solution but have simply looked at waveforms from patients with radiologically defined disease and correlated Doppler changes with X-rays on a visual basis. This leads back to the main problem: it was the deficiencies of radiological estimation of cross-sectional area reduction which led to the search for a new test.

An exception has been the work of Skidmore (129) who has employed transmission line theory to solve the problem and, in addition, has developed a method of waveform interpret-

ation based on his solution. Although the theory is attractive, his results lack confirmation by in vivo studies with careful control of all the parameters likely to affect waveform shape - this is not possible in patient studies.

Others, for example Reneman and Spencer (130) and Jonnart (131), have tried to explain Doppler waveform changes on a physical basis; however, such studies suffer from the inability, in patients, to define precisely the internal shapes of diseased arteries. It seemed likely that the only way to quantify Doppler changes produced by stenoses was to employ an animal model in which pressure and flow could be measured accurately and where a stenosis of known dimensions could be implanted; this approach was used for the experimental work to be described later in this thesis.

D. METHODS OF WAVEFORM ANALYSIS

Although full spectral information is clearly an advantage in Doppler signal processing, the quantity of information present in any single waveform is very large and further computation becomes involved. It is however possible to extract the maximum frequency envelope as described by Gosling (124) using a digitiser; this is the method we chose for further waveform analysis. It has the advantage that artefacts can be ignored, but is rather time consuming.

Current technology has advanced so that it is now possible to extract such information electronically; the waveform may be stored or, if necessary, analysed in real time.

Inevitably much information relating to blood flowing at less than maximal frequencies is lost; the eye itself is an excellent information processor and simple inspection of the fully analysed waveform allows a wealth of interpretation to be performed visually. However, if techniques from different units are to be compared, it is desirable to have a more objective system of waveform shape analysis; the maximum frequency envelope has been the most widely used and is the method adopted in all the present studies.

A typical example of a waveform recorded from a normal common femoral artery is illustrated in Fig 1(a). The outline is then digitised including both forward and reverse flow envelopes (1b). This data is processed electronically to give a summed curve (1c) which is the maximum frequency envelope used for subsequent calculations; it is also essentially the same curve produced by Skidmore and Woodcock in their maximum frequency follower device (123). A similar series for a damped waveform recorded from distal to an iliac occlusion is shown in Fig 2.

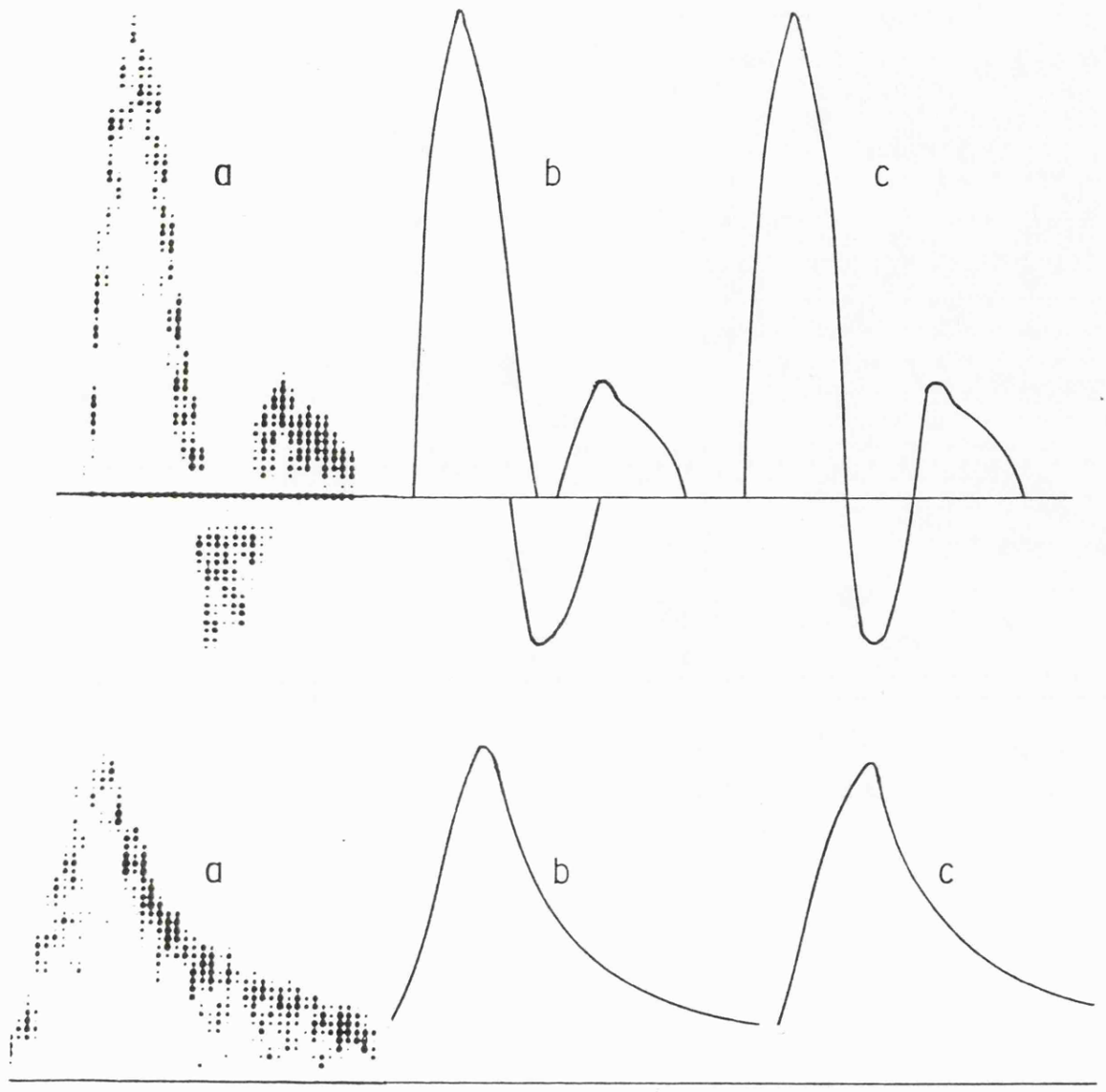


Figure 1. (a) Doppler waveform recorded from the common femoral artery of a fit young man; (b) the forward and reverse flow envelopes which were digitised; (c) the summed curve used for subsequent calculations. Figure 2. The same sequence for a waveform recorded from below a severe iliac stenosis with no reverse flow.

Objective methods of waveform analysis have been based on four main approaches: (i) a simple measurement of the waveform shape such as pulsatility index; (ii) a time related measurement using either time between points on the waveform itself, the time from the ECG R-wave to a fixed point on the waveform or a transit time using two recording probes; (iii) a complex interpretation of waveform shape using a Laplace transform and (iv) feature extraction or pattern recognition techniques. Time based methods are particularly attractive as they can be used without complex equipment, time being relatively easy to measure electronically; they are, however, probably the least suitable for assessing aortoiliac disease. The remainder of this section will attempt to review the large number of methods used to date.

(i) Pulsatility Index

Originally described by Gosling and his group (132) as a Fourier based parameter, subsequent work has shown that the peak to peak method (133) of obtaining the index is simpler and gives essentially the same information (134). Peak to peak PI is defined diagramatically in Fig 3 for waveforms both with and without reverse flow.

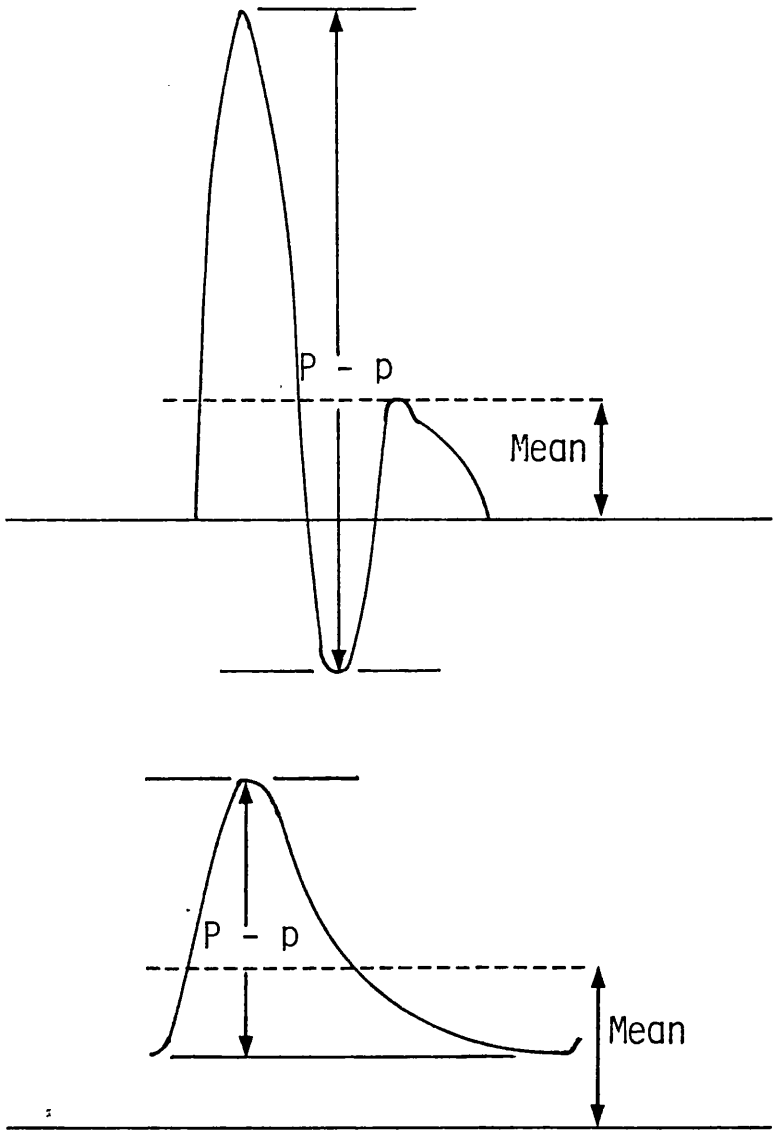


Figure 3. The definition of pulsatility index in the presence (a) and in the absence (b) of reverse flow. In each case PI is calculated by dividing the peak to peak excursion of the waveform by the mean frequency over one cardiac cycle.

Although Gosling himself has never claimed that common femoral PI by itself can quantify proximal narrowing, but defined it simply as a dimensionless expression related to pulse wave damping, several other groups have suggested that it is valuable in this respect. Charlesworth (135) showed that femoro-popliteal grafts were more likely to fail with a femoral PI of <4, and Johnston (136) found a good correlation between femoral PI and arteriography. More recently, Aukland and Hurlow (137), in a paper examining the use of Doppler at several levels in the lower limb, have also reported good agreement between PI and arteriographic grade in the aorto-femoral segment. They graded their X-rays into mild (<50% stenosis), severe (>50% stenosis) and occluded and found significantly different values of PI for these three groups. Unfortunately they did not present their results individually so that overlap of values between the groups could not be assessed adequately. Interestingly, they found only a small reduction in common femoral PI produced by disease in the superficial femoral artery.

The main criticism of all these studies is the inadequacy of the control investigation, namely arteriography. Ideally the accuracy of PI should be confirmed using flow and pressure data but, of course, this is necessarily invasive. Demorais and Johnston (109) have recently compared femoral PI with aortofemoral pressure drop measured at rest during arteriography. Flow measurements were not used; however

resting flow rates are relatively constant in all but the most severely diseased proximal segments. A pull back technique was also used which somewhat diminishes the accuracy of small pressure difference measurement because of beat to beat fluctuation in systemic arterial pressure. Despite these reservations this study provides the only attempt at haemodynamic correlation with PI in patients so far published.

The beauty of PI is its ease of measurement and its independence of probe angle. It clearly tells us something about the waveform shape, but uses only a small quantity of the potentially available data in the Doppler signal. It can easily be calculated in real time using a small dedicated microprocessor (138). It is unfortunately very sensitive to changes in peripheral resistance (139) and in addition may be affected by distal or local disease (this point will be illustrated in the patient studies in Chapter 9).

Nevertheless, the reliability and ease of PI calculation has made it a widely used parameter and it may have a place in defining disease in more distal arterial segments. A similar quantity (waveform index, RI) has been described by Nicolaides, but was derived using a zero crossing detector (140).

(ii) Damping factor

Again derived by Gosling and colleagues (141), this is the ratio of proximal to distal PI. The damping factor of several segments can be calculated and related to arteriography or other measurements. The problem with this method for aortoiliac assessment is that clear aortic waveforms are often difficult to obtain especially in obese patients. Damping factor may provide more reliable information in distal arterial segments (142); here, however, there is less need for additional clinical information as arteriographic assessment is very satisfactory.

(iii) Transit time

As used by Gosling's group (141), this parameter measures the time from the start of a pulse waveform at a proximal recording to the start of the same waveform at a downstream position. It is comparatively insensitive to disease less than total occlusion and is mainly related to arterial compliance (137,142,143). When used with damping factor, good correlation was found in a large series of cases using arteriograms as standard (124); however it was not possible to quantify non-occlusive stenoses. This type of transit time requires two probes working simultaneously and, ideally, two operators so adding to the complexity of the method.

(iv) Transit time ratios

To try to correct for idiosyncrasies in the patient's arterial wall and heart, various transit time ratios have been derived using the ECG R-wave as the origin (143,144). These methods clearly pick up severe disease but are not sufficiently sensitive to assess moderate degrees of stenosis. In addition, some of the methods use time to the arm as a reference - this may well be unreliable in patients with generalised arterial disease.

(v) Reactive hyperaemia recovery time

This test appears promising (143) but the results have not been confirmed by other workers. A zero crossing velocimeter is used to give the mean frequency at the common femoral artery. A thigh cuff is then inflated and deflated after 5 minutes. The resulting increase in mean frequency due to hyperaemia is recorded (the probe angle remaining constant) and the decay time to 50% of maximal hyperaemic velocity is measured. There appeared to be a good relationship with arteriography, but one must be wary of any report relying on external palpation of the iliac arteries for haemodynamic assessment! Furthermore the method may be rather painful; certainly our own experience with thigh cuffs would suggest that many vascular patients would not be able to tolerate the test.

(vi) Rise time

This quantity is defined in Fig 4 and is clearly influenced by proximal narrowing when used with common femoral waveforms. The original authors (142) described it for examining the femoro-popliteal segment as a ratio and were realistic about their claims, finding it to be about as sensitive as PI but rather easier to measure. A recent study (145) confirms that rise time is a fairly sensitive guide to proximal disease; however, in any time based measurement from the femoral artery, systolic time becomes important and allowance may need to be made for its lengthening in older patients.

Rise time was also used by Nicolaides (140) without in itself being useful; as a component of a multivariate analysis it seemed to do better. However a zero crossing detector was used and it is certain that for this type of analysis spectral analysis is essential.

(vii) Deceleration time

Also used by Nicolaides (140) this appears difficult to measure accurately (Fig 5). It may be helpful as part of a multivariate analysis but seems more likely to be affected by local and distal disease. It is mentioned for completeness; it has not been investigated by other workers.

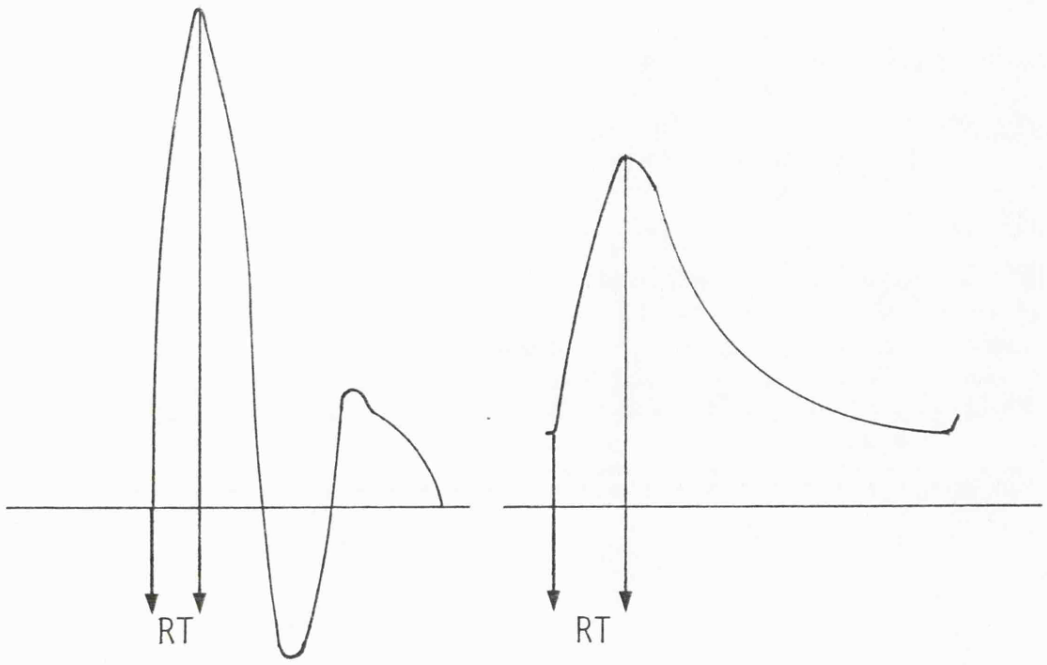


Figure 4. Rise time is defined as the time between the initial forward component of a Doppler waveform and its peak.

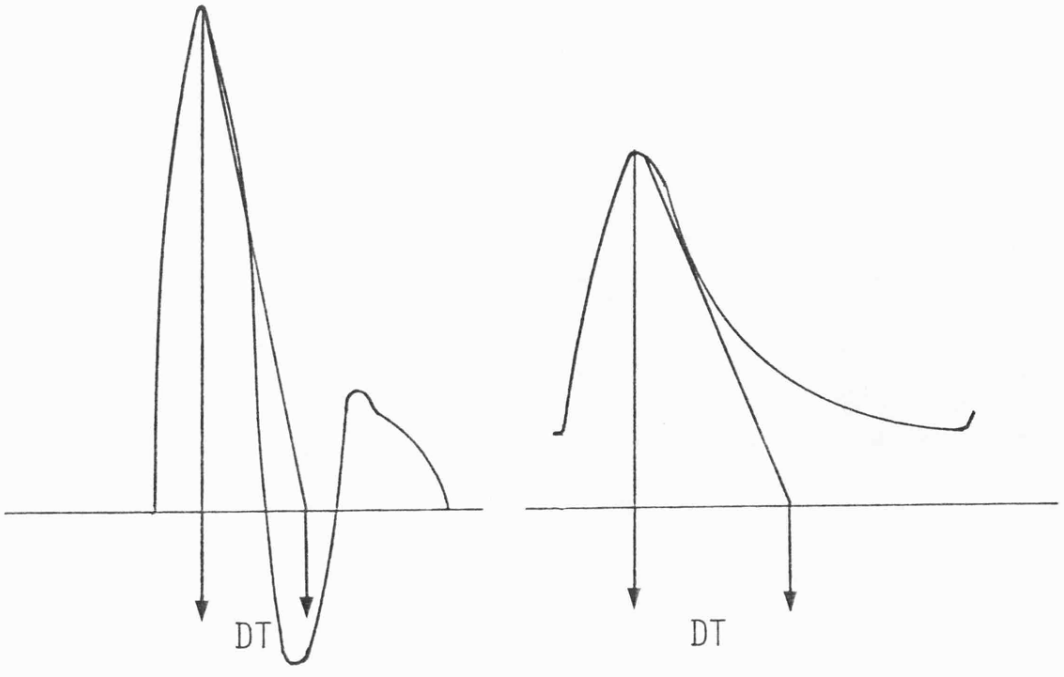


Figure 5. The definition of deceleration time.

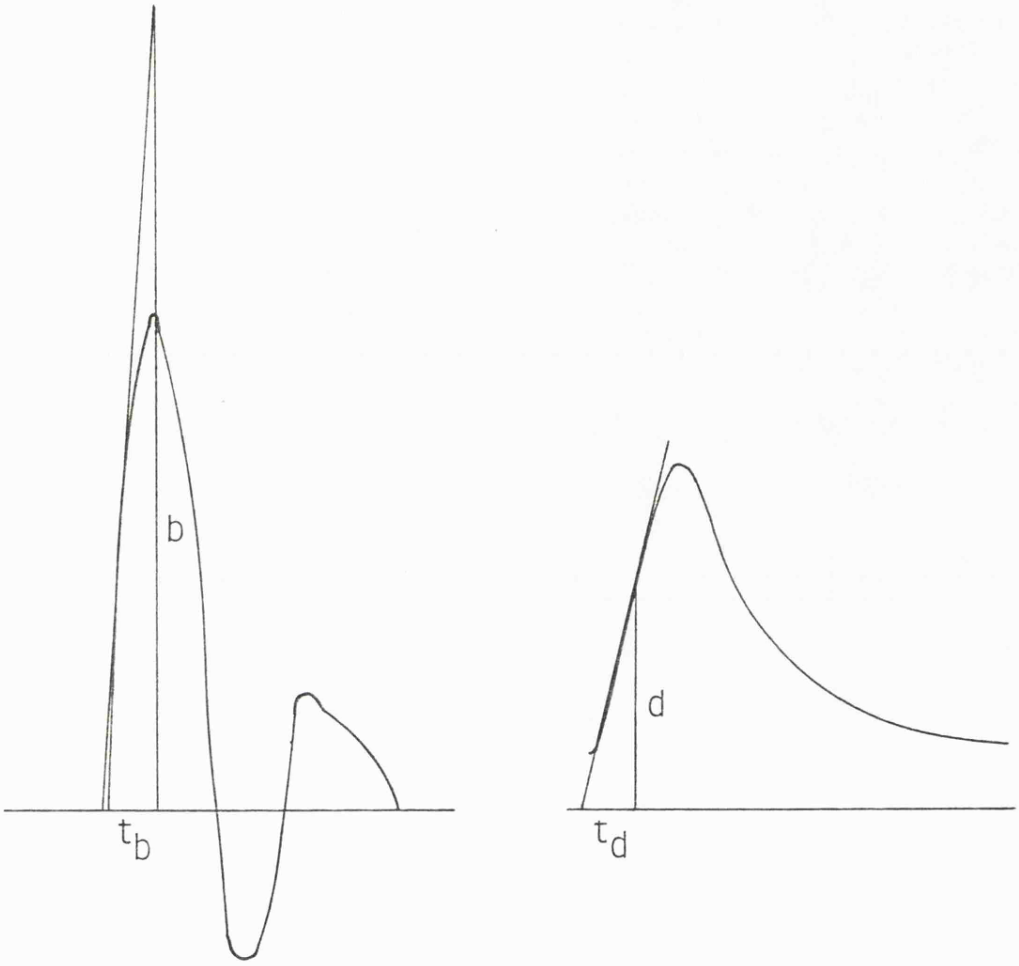
(viii) Peak and mean forward velocity

Although clearly affected by proximal disease (146) these parameters are obviously sensitive to probe angle. In practice this is difficult to apply constantly to different patients and the interpretation of the effects of mild and moderate degrees of proximal narrowing by these methods must be suspect as a result.

(ix) Acceleration ratio

An attempt to keep the probe angle constant by constructing a plastic rig at 45^{o} was made by Forsberg et al (147) and an acceleration ratio defined (Fig 6). This is basically a measure of the slope of the acceleration phase of a waveform below a diseased segment compared with a control site (the brachial artery).

Good separation was achieved with aortoiliac disease when compared with arteriography in the >90% stenosis group; the method made use, probably acceptably, of a zero crossing unit and the idea of maintaining probe angle constant was original. However the use of the brachial artery as control leads to difficulties if there is any disease in the proximal arm vessels and the method has not been assessed by others.



When $t_b = t_d$, AR = d/b

Figure 6. Acceleration ratio is defined as the slope of the test waveform divided by the slope of the brachial artery waveform, using a 45^{o} rig to maintain a constant probe angle.

(x) Proximal damping quotient

This seemingly arbitrary quantity has been shown to be related to proximal disease (148) and is defined in Fig 7. It attempts to relate waveform shape to transit time and acceleration time; a zero crossing detector was used and the same criticism of variation in systolic time between patients can be made as for other R-wave dependent time measurements. Clearcut aortoiliac disease was picked up but the method did not help in those with multilevel disease.

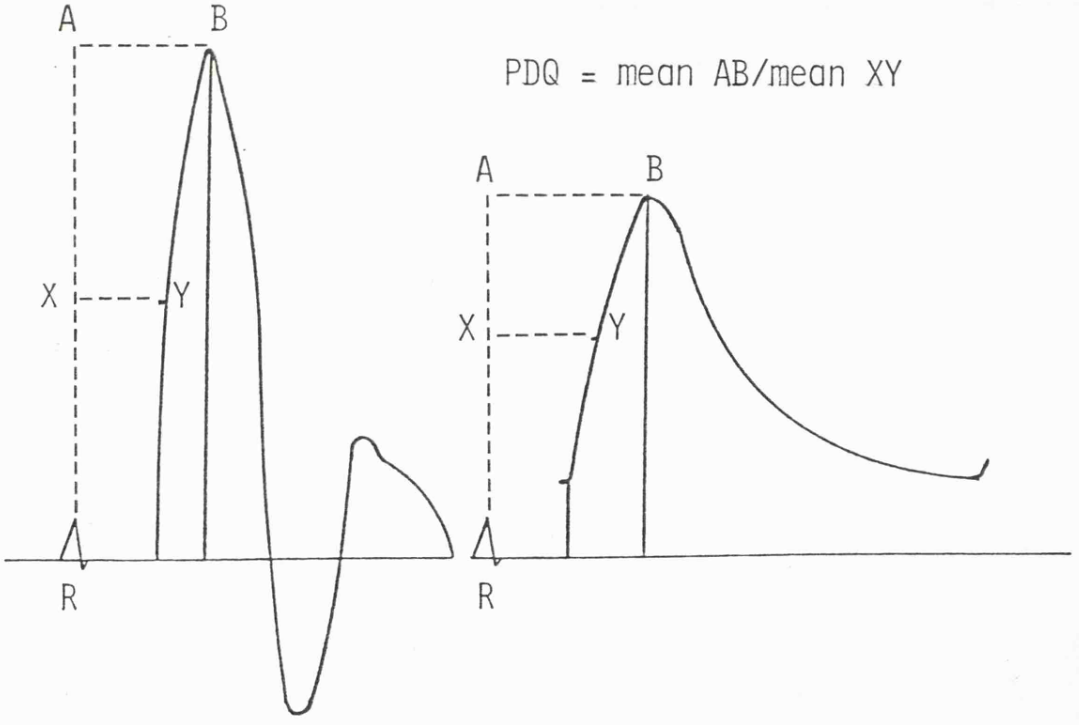


Figure 7. The definition of proximal damping quotient. R represents the ECG R-wave and Y is the point half way up the initial forward component of the Doppler waveform.

(xi) Laplace transform damping

Also known as transfer function analysis, Skidmore (129, 149) has developed this method from his transmission line model of the peripheral circulation. Basically a third order curve is fitted to the Doppler waveform (transformed into the frequency domain) and the roots obtained are thought to vary independently with proximal disease (δ), peripheral resistance (γ) and elasticity of the vessel wall (ω). Preliminary studies in normals appear to confirm that the values of the roots change as predicted by the model (123). The theoretical advantage of being able to separate out these effects on waveform shape is considerable; the main drawback of PI is its sensitivity to changes in peripheral resistance.

Unfortunately, so far all the reports of the test in patients have simply used arteriography as the control, and this remains a major criticism of the method (150,151). Furthermore, no use has been made of animal or in vitro experiments to confirm the theoretical predictions of the model. Because of the sound basis of the method and its reputed ability to separate proximal and distal effects on waveform shape it was included in both the animal and patient studies to be described later.

So far, most interest has been expressed in the first of these roots, (δ) or Laplace transform damping (LTD). A

recent paper from the Bristol group (152) has investigated the elasticity factor (ω) as a ratio of values between the femoral and posterior tibial arteries, and this ratio appears to be related to occlusive disease in this segment. It also seems to be superior to Gosling's damping factor (141). The usefulness of this new ratio must be confirmed and its full evaluation should ideally include comparison with pressure and flow data.

(xii) Principal component analysis

Objective methods of feature extraction or pattern recognition have only recently been applied to Doppler waveforms. Martin et al (153) used this method to compare the outlines of Doppler waveforms from normal and diseased common carotid arteries, using just the maximum frequency envelope. Subsequent work by the same group (154) has used the full spectral information to look at lesser degrees of carotid disease with most encouraging results.

The method can be likened to Fourier analysis, but instead of sine and cosine waves, a particular Doppler signal is broken down into simpler component curves which have been derived from a known population of waveforms. This reference population should include examples of the whole range of abnormalities likely to be encountered. The test waveform can then be defined by giving coefficients or weighting

factors to each of the component parts and the original can be reconstructed by adding together each principal component multiplied by its coefficient. By specifying the type of waveform concerned (eg common femoral Doppler waveforms) the principal components are chosen in a non-arbitrary fashion, unlike Fourier components; in other words, they are customised to the broad pattern of waveform shape found at any site. It follows that a waveform, when related to the reference population, can be described accurately by a small number of components (each weighted by a coefficient). The method is described further in the next chapter.

In practice the outline of a femoral artery Doppler waveform can be reconstructed using only the first two components; each waveform can therefore be adequately described by two numbers, the coefficients of the first two principal components. In Fourier analysis the same degree of accuracy would entail analysing the first four or five harmonics.

E. THE ROLE OF DOPPLER IN AORTOILIAC DISEASE

From this review it seemed that most of the tests described were able to confirm the presence of obvious severe disease, but this is not usually a problem as such patients will be identified on clinical grounds in all cases. They are not a substitute for arteriography, nor can they help to

decide which patients should be referred for arteriography; this remains a clinical decision. What is needed is an accurate way of assessing lesser degrees of narrowing in the range of 50-80% area reduction. Such patients will usually have a normal femoral pulse at rest but may have some disease apparent on arteriography. It is important to identify this group because (i) they may benefit from proximal reconstruction and (ii) if a distal operation is performed its outcome may be prejudiced by the poor inflow.

It was therefore decided to assess the three most promising methods of waveform analysis using data from a single site. Pulsatility index (PI), Laplace transform damping (LTD) and principal component analysis (PCA) were chosen because they seemed the most likely to give the necessary answers. In addition to comparison with arteriography the patient studies would include direct pressure measurement (the papaverine test, Chapter 3) and animal studies would be performed so that waveform changes could be analysed with full knowledge of the dimensions of a narrowed arterial segment and with accurate flow and pressure data.

Chapter 5

MATERIALS AND METHODS

The measurement equipment and techniques employed in the following animal and patient studies will be described in this section. In the animal work they included direct intra-arterial pressure measurement, electromagnetic flowmetry and cw Doppler velocimetry. In addition to clinical assessment of the femoral pulse and arteriography, the patients were studied with cw Doppler and both direct and indirect pressure measurements were made.

A. PALPATION OF THE FEMORAL PULSE

This subject has received surprisingly little attention in the literature despite its central role in decision making in vascular surgery. Eastcott (155) simply suggests a classification into present or absent and mentions, almost in passing, the possibility that a pulse might be diminished. Quin (156), when comparing pulses with arteriography in his thesis, uses a similar three point system. Kinmonth et al (157) in their textbook suggest a five point system from 0

(absent) to ++++ (normal). More recently, Kester and Leveson (158) suggest a scheme very like that of Eastcott.

The standard practice in Leicester at the outset of this study appeared to be a four point system as follows:

Clinical symbol	Definition	Grade (used in thesis)
+	normal	1
$\underline{+}$	diminished	2
$\overline{+}$	just palpable	3
-	absent	4

to which may be added ++ when the vessel is aneurysmal. This number of divisions seemed the most that could reasonably be expected of even experienced clinicians and was therefore adopted for the palpation of all pulses although it is mainly in the context of the femoral pulse that it is used in this thesis. It was also possible to correlate this system fairly easily with the method used for grading arteriograms.

B. ARTERIOGRAM ASSESSMENT

In view of the accepted difficulty of estimating arterial narrowing on single plane films, it was felt once again that a relatively simple system would be (a) more accurate and (b) easier to compare with other methods. Quin (156) used a four point scale for the assessment of aortoiliac disease, like that used by Morton et al (159) in more distal arterial segments, and a similar method was used in the present study. The precise grouping was a little different and it was hoped that the divisions chosen would relate to the clinical, Doppler and direct pressure assessments of the aortoiliac segment. The method also reflected standard reporting practice in the local X-ray departments and was as follows:

Grade 1 : Normal or minor irregularity
Grade 2 : Stenosis <50% diameter reduction
Grade 3 : Stenosis >50% diameter reduction
Grade 4 : Total occlusion.

The femoropopliteal segment was graded in the same manner, but in the subsequent analysis this was simplified to two groups:

Grade 1 : Normal or stenosis <50% diameter reduction
Grade 0 : Occlusion or stenosis >50% diameter reduction

In each case a particular arterial segment received the appropriate grading for the most severe lesion in that segment. Examples of standard forms used for acquiring the clinical and radiological data will be found in appendix A. Although all arterial segments visualised in the arteriograms were classified, only the aortofemoral and femoropopliteal segments were used in the subsequent analysis.

The reporting of the arteriograms was done at a different time from the pressure and Doppler tests by an independent assessor who was unaware of the results of the other investigations. A single experienced radiologist was used throughout, so eliminating inter-observer variation which can be quite pronounced in arteriogram reporting (160).

C. DOPPLER EQUIPMENT

The velocimeter used throughout was a Sonicaid BV380 with a 7.6MHz transducer (Fig 1). The tissue penetration and beam shape of this instrument make it suitable for examining the common femoral artery; it was also used to examine the popliteal and pedal arteries. The velocimeter was modified by including a heterodyne board for further signal processing prior to spectral analysis (121).

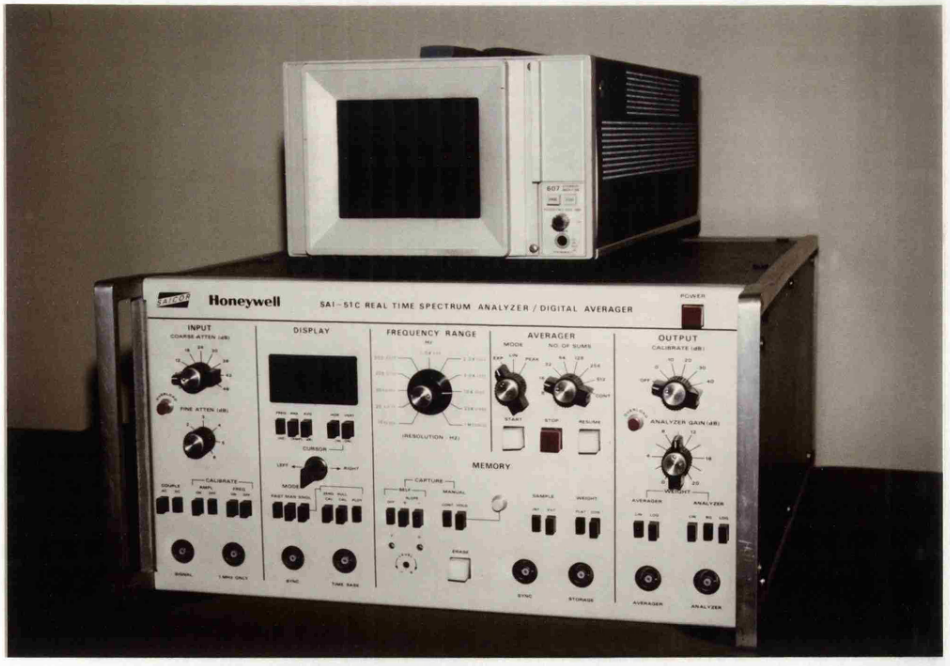


Figure 1. The Sonicaid Doppler unit used throughout the work described in the thesis. Figure 2. The spectrum analyser.

In some of the animal work, Doppler signals from the Sonicaid were recorded on a two channel AM tape recorder (UHER 4400 IC) and replayed through the spectrum analyser at a later stage. This allowed the analyser settings to be optimised, a procedure which takes valuable time if performed during an experiment. Occasionally patient studies were similarly recorded if, for example, the patient was too frail to be taken to the vascular laboratory.

The spectrum analyser used was a SAICOR SAI 51C manufactured by Honeywell (Fig 2). In order to speed up its operation it had been modified to sweep the first 100 frequency bins every 20 msec. Output from the analyser was recorded on light sensitive paper using an ultraviolet recorder (Medelec For-4); this was the only permanent means of storing the whole waveform. Frequency was represented on the ordinate, time on the abscissa and amplitude as a grey scaling of the frequency/time points. Typical waveforms recorded in humans were seen in the last chapter.

In the patient studies PI was calculated in real time using a small dedicated microprocessor (138) and also recorded on the Medelec. In practice this meant that only alternate waveforms were recorded, the time between being used to calculate and write the results of PI. An additional uninterrupted sequence of waveforms was also recorded and these were subsequently digitised and used for the calcul-

ation of PI, LTD and PCA coefficients: it is these values of PI which are found in the results sections, although very similar values were obtained by the microprocessor.

The spectrum analysed Doppler signal was displayed in real time on a Tektronix 607 variable persistence oscilloscope as well as being played through the loudspeaker of the Doppler unit. The operator was therefore able to adjust the probe to give the clearest signal using both visual and auditory information and it was usually possible to avoid both venous noise and vessel wall thump.

In both the animal and patient studies the hard copy of the Doppler signals recorded on the Medelec was stored and the maximum frequency envelope subsequently digitised on a Ferranti table digitiser interfaced with the University Cyber CDC 73 main frame computer. At least five waveforms for each measurement series were digitised in this way and stored on disk for further processing. Only those waveforms used in subsequent calculations were digitised as it is an extremely time consuming procedure. These included all waveforms in the first series of dog experiments and the resting common femoral waveforms in the patient studies.

Following digitisation of the maximum frequency envelope, this information was processed by two series of programs; in the first, PI and Laplace transform roots were

calculated and in the second, using data from the total population of waveforms, either animal or human, PCA coefficients were found. The exact details of the programs are beyond the scope of this thesis; however, they may be summarised as follows:

PI and Laplace transform Program

1) Read in the waveform
2) Calculate PI (peak to peak/mean)
3) Find the Fourier transform of the waveform
4) Fit a third order polynomial to the transform
5) Find the roots of the polynomial
6) Calculate LTD from these roots.

PCA Program

1) Read in waveforms and adjust their lengths to 600msec either by truncation or extrapolation
2) Adjust mean height of each waveform to unity
3) Determine the population sample mean record (SMR)
4) Subtract the SMR from each sample waveform
5) Calculate the covariance matrix of the new set of waveforms
6) Find the eigen-values and eigen-vectors of the covariance matrix. (The eigen-vector corresponding to the largest eigen-value is then the first principal component and so on)
7) Use the SMR and principal components to find the coefficients of the first few principal components for each sample waveform.

Examples of the output of each waveform analysed in the patient studies are found in Appendix D as well as the summarised results. In order to save space, the results of the analysis of the dog waveforms are not included individually but only in summarised form (Appendix B).

D. ARTERIAL BLOOD PRESSURE MEASUREMENT

The measurement of arterial pressure has rightly assumed a key position in patient management and it is remarkable that it was not until 1905 that Korotkoff described the present indirect method for systolic and diastolic pressures (161). The first semi-quantitative method of assessing pulse strength (and by implication blood pressure) was described by Struthius in 1555 (162); he observed the transmission of pulsation to an object overlying a peripheral artery and the gradual obliteration of pulsation by increasing this weight. Exactly the same concept was used in the various 19th century sphygmographs (163).

The technique of indirect pressure measurement as we know it today is derived from that of Riva-Rocci who used a 5cm cuff encircling the whole of the upper arm to measure systolic pressure (164). The cuff size was subsequently enlarged to 12cm for the average adult arm, and the same method and cuff were used in the present patient studies for

ankle pressure measurement. A Doppler flow detector was employed to assess the return of pulsation on cuff release as described by Yao (86). Although included in the patient protocol these measurements were not of much practical use for assessing aortoiliac disease for the reasons outlined in Chapter 3.

The historic intra-arterial measurements of Rev Stephen Hales are widely known and he is rightly given credit for initiating an important area of physiological research, although little further work was done until the apparatus had reached more manageable proportions. Hales found the arterial pressure of the horse to be 8'3" of blood (185mm Hg), but the rather small pulse pressure of 2-4" presumably indicated excessive damping in his system (165). Continued bleeding from the animal resulted in a gradual lowering of the arterial pressure although initially there was an attempt at compensation, and stimulation would usually produce a transient elevation. The animal became faint and sweaty when the arterial pressure had fallen to about 2'6" (56mm Hg) and expired soon afterwards. Hales is at pains to point out that he confined his experiments to horses which were disabled in some way and due for slaughter, presumably to avoid criticism from animal lovers!

In the last 50 years rapid developments have taken place and small transducers with excellent frequency response are

available which are both reliable and easy to use. A useful review of current methods can be found in McDonald's text book (166).

The system for all direct pressure measurements employed an intra-arterial cannula or needle connected by manometer tubing (Portex type 200/490/100) one meter in length to a strain gauge type transducer. In the animal experiments the proximal (aortic) pressure was monitored through a side hole cannula (modified Medicut 18 swg) to eliminate end pressure artefact (166). The distal pressure was measured with an unmodified 18 swg Medicut inserted in a side branch. The transducers used were Elcomatic EM 751. The signals were fed to Hewlett-Paçkard 8805C pressure pre-amplifiers and recorded on a Gould Brush Accuchart chart recorder and a Tandberg FM tape recorder.

For the patient studies a 21 swg hypodermic needle was employed attached by similar manometer tubing to Elema Schonander transducers (type EMT 746). Waveforms were recorded on a Mingograf 800 ink writing chart recorder but no further record was needed as each study took a comparatively short time compared with the animal work.

The results of the pressure studies in patients were expressed as a gradient in mm Hg between the test femoral vessel and a central control which was usually a needle in

the contralateral femoral artery. In a few cases of severe bilateral aortoiliac disease or where the contralateral femoral artery could not be needled, indirect brachial artery pressure was used as control; this was accepted only if the result was completely unequivocal. Two gradients were available for each femoral artery tested: a resting gradient and a hyperaemic gradient measured at the point of maximal flow increase after papaverine. The test is described more fully in Chapter 8.

A four point grading system was again used for comparison with other methods of assessment:

Grade 1 : Resting gradient <10mm Hg and hyperaemic gradient 0-14mm Hg

Grade 2 : Resting gradient <10mm Hg and hyperaemic gradient 15-19mm Hg

Grade 3 : Resting gradient <10mm Hg and hyperaemic gradient 20-24mm Hg

Grade 4 : Resting gradient >10mm Hg or hyperaemic gradient >25mm Hg.

Although it was possible simply to plot the pressure gradient itself against other parameters, it was felt that the papaverine test as presently used was not sufficiently reliable to allow such fine discrimination, especially in patients with rest pain where flow increases may be less than expected

(156). The limits of the grading system are somewhat arbitrary but were derived from the few available guidelines in the literature (107,108,109).

Static calibration of the manometer systems was performed before each series of measurements in both the animal and patient studies using a standard mercury column. The frequency and phase response of the systems had previously been investigated by Dr DH Evans (167) and found to be satisfactory for systolic pressure determination; problems with damping from small air bubbles, which are very hard to remove completely in fluid filled manometers, may cause significant changes to the shape of the pressure waveform and great care was taken to eliminate these as far as possible.

Because the pressure difference between the proximal and distal transducers was small in parts of the animal work, it was calculated electronically and written to the chart recorder; in addition, this signal was meaned by passing through a low pass filter so providing a guide to the stability of the preparation and an early indication of any clotting.

E. ELECTROMAGNETIC FLOWMETRY

The concept of induced current when particles move in a magnetic field has now reached sophisticated levels in the

current generation of electromagnetic flowmeters. Faraday himself attempted to measure flow in the Thames at Waterloo bridge, but was unable to do so (168); he employed the earth's own magnetic field, but the current so produced was too small for his measuring equipment. In the twentieth century the same idea was applied to physiology and, in particular, to haemodynamics initially using large external magnets and more recently using small electromagnets mounted in a cuff to go round a vessel or on a catheter to pass inside a vessel. The technique has many attendant problems, and is well summarised in a review by DG Wyatt (169).

One of the main problems with the cuff type probe is the difficulty in obtaining good electrical contact with the vessel. This problem could be overcome in the animal experiments by using a cannulating probe, but this requires a large opening to be made in the artery which is not practical in patients.

The instrument used throughout this study was the Statham SP2201 flowmeter (Fig 3). It employs an interrupted rectangular wave excitation which allows non-occlusive zeros to be checked during a measurement run. Occlusive zeros must also be used, but the necessary interruption of flow means that no useful measurement is subsequently possible until the period of reactive hyperaemia has passed.

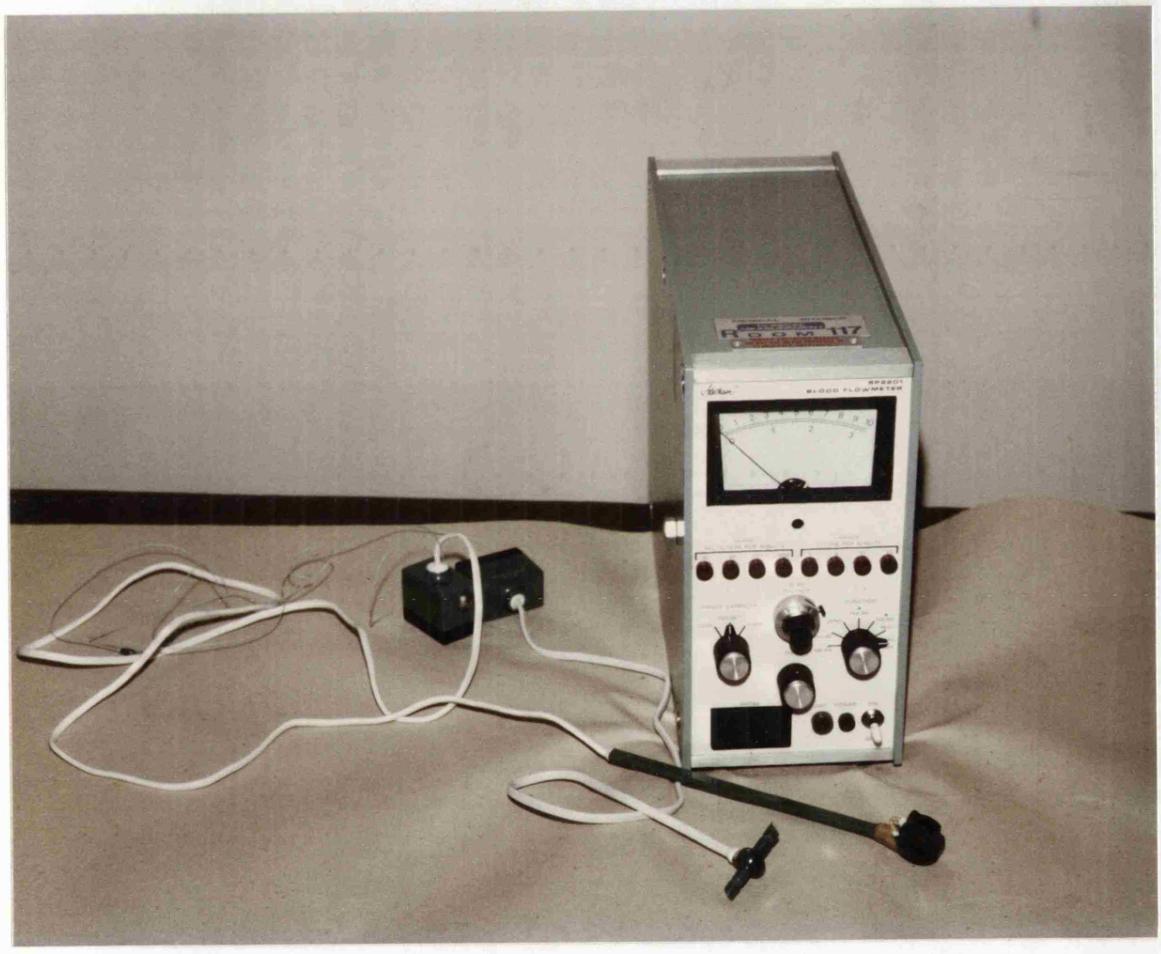


Figure 3. The Statham electromagnetic flowmeter with examples of the cuff type and cannulating flow probes.

The probes are pre-calibrated; however, if accurate data on absolute flow are needed it is necessary to perform a further calibration using a standard flow rate. This was not possible during an experiment without exsanguinating the animal, and it was felt that change in flow (and hence change in peripheral resistance) was the more important factor. For the same reason, haematocrit was not routinely monitored, the assumption being that this would change little during a series of measurements in a particular dog.

Pulsatile electromagnetic flow was displayed on the chart recorder during the animal experiments and also recorded on FM tape. Mean flow was calculated and displayed and, together with mean pressure difference, enabled a ready check to be made on the stability of the animal preparation. Examples of recordings of pressure and flow made during the animal experiments will be found in the next chapter.

Chapter 6

THE EFFECT OF PROXIMAL STENOSIS ON DOPPLER WAVEFORMS IN A CANINE MODEL

For the reasons outlined in the introductory chapters, it was decided to assess the three methods of Doppler waveform analysis used for the patient studies in an animal model. The aim of the first series of experiments was to quantify changes in Doppler waveforms occurring distal to a stenosis of known dimensions in a situation where both flow through and pressure across the stenosed segment could be measured accurately.

A. METHOD

A preliminary study from this department (139) had already examined changes in PI with varying proximal stenosis in the anaesthetised dog. The model was, therefore, well developed before the start of the present work although changes in the anaesthetic technique have led to much improved stability of the preparation. In particular, cardiac rate was maintained relatively constant and closer to physio-

logical resting rates by using intermittent positive pressure ventilation and a neuroleptic technique. Five greyhounds were used in this work (Table 1).

TABLE I: DOGS USED IN THE STUDY

Dog no.	Sex	Weight
22	M	27 Kg
23	M	30 Kg
24	M	23 Kg
25	M	26 Kg
26	F	22 Kg

(i) Anaesthesia

The animals were fasted overnight having been kept in kennels in the University on a good diet for at least two weeks prior to surgery. No premedication was given. Anaesthesia was induced with thiopentone (20mg per Kg) given intravenously. A reliable intravenous line was established and an infusion of normal (0.9%) saline commenced. A cuffed endotracheal tube of suitable size was introduced and the cuff inflated. The animals were ventilated with a mixture of 50% oxygen and 50% nitrous oxide initially supplemented with halothane. The ventilator used was a Manley pulmovent and was set to provide approximately 6 l/min. Arterial

blood gas estimations were not performed during this series of experiments.

Anaesthesia was maintained with a fentanyl/fluanisone preparation (Hypnorm, Janssen) given by continuous intravenous infusion at the rate of 2-3 ml per hour. The use of this agent made further barbiturates unnecessary and allowed the halothane to be turned off soon afterwards. Depth of anaesthesia was assessed from time to time by Dr. D. Morton, keeper of animal houses in the University, and was always found to be satisfactory. No neuromuscular relaxants were used, so it was possible to assess reflex activity throughout. By avoiding barbiturates and halothane, and by using adequate ventilation, it was possible to eliminate tachycardias of up to 160-180/min which had caused difficulties with waveform assessment in the previous experiments (139).

(ii) Animal Preparation

The dogs lay supine on the operating table once adequate anaesthesia had been achieved. The anus was sutured, and ECG electrodes fixed appropriately after shaving and cleaning a small area of skin. A warming blanket, thermostatically controlled by an intra-rectal probe, maintained the animal at normal temperature (ca 38^{o}C) throughout the experiment. A passive diathermy electrode was positioned under the animal after shaving.

The abdomen was opened through a mid-line incision after shaving the necessary area, and this was extended into the right thigh through the inguinal ligament. Intestines were packed away with moist packs and a self retaining retractor allowed excellent visualisation of the arterial tree from the distal aorta to the mid-femoral artery. A catheter was placed in the bladder through the vault; urine output was not monitored.

Before mobilisation, the diameter of the right external iliac artery at the point where the stenosis would be inserted was calculated by measuring the circumference using a ligature passed three times round the vessel (Table III). The artery was then mobilised from the aorta to the groin. All the small branches at the level of the inguinal ligament were ligated and divided, leaving one small side branch just proximal to the inguinal ligament for a pressure line. Further mobilisation of the femoral artery in the thigh was carried out until the vessel went deep to the thigh muscles, again ligating and dividing all branches.

Heparin (3000u iv) was then given. The proximal pressure line (Medicut 18 swg) was placed at the level of the aortic trifurcation through the right internal iliac artery which was also ligated distally. The cannula was modified by blocking off the end hole and making a side hole of approximately equal size to eliminate end pressure artefact (see

Chapter 5). The distal pressure cannula (unmodified Medicut 18 swg) was placed in a side branch and advanced so that its orifice was at the edge of the main vessel. The branch was firmly tied around the cannula. Both cannulae were connected by manometer tubing to the pressure transducers, placed at the height of the stenosis, taking great care to eliminate all air bubbles. The transducers were in turn connected to pressure pre-amplifiers and the chart recorder, and their signals were also recorded on magnetic tape.

The stenosis assembly (seen in longitudinal section in Fig 1) had previously been devised by Dr. David Evans and consisted of adaptors permanently fixed into the proximal iliac artery with an interchangeable middle section which allowed the insertion of a tubular axi-symmetric stenosis with ends cut at right angles to the direction of flow. The unstenosed internal diameter was 5 mm in all the animals studied; this was found to correspond very closely to the size of the vessel in all cases. The stenosis dimensions available are shown in Table II.

One slight disadvantage of the stenosis was the need to interrupt limb blood flow each time the stenosed segment was changed. Although only taking about 15 seconds to perform, the ensuing period of hyperaemia lasted for several minutes depending on the tightness of stenosis inserted.

TABLE II: DIMENSIONS OF STENOSIS INSERTS

Length (mm)	Internal diameter (mm)	Area reduction (%)
-	5	0
8.7	3.5	51
8.5	2.95	65
9.0	2.38	77
9.1	1.95	85
9.2	1.7	88
9.0	1.4	92
8.8	1.1	95

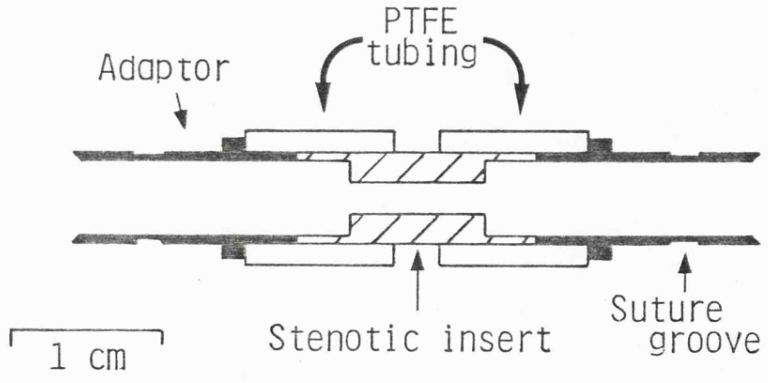


Figure 1. The stenosis assembly in longitudinal section: the unstenosed diameter was 5mm and the length (L) of the stenosed segment 9mm.

Figure 2. The stenosis in its component parts.

The stenosis (seen in Fig 2 in component form) was inserted into the proximal iliac artery having controlled the vessel above and below with clamps. The adaptors were introduced by making two transverse slits in the front of the vessel and inserting each end piece before applying an encircling ligature. The ligatures round the adaptors were left long and could be clamped together, so preventing the assembly from springing apart once flow had been restored.

The cannulating EM flow probe was then placed below the stenosis just beyond the distal pressure line. It was introduced in precisely the same manner as the adaptors for the stenosis assembly. Calibration, including an occlusive zero, was carried out at this time. Doppler signals were recorded from further downstream near the point where the femoral artery goes deep in the thigh. The preparation is summarised diagramatically in Fig 3 and photographically in Fig 4.

With a zero stenosis inserted into the assembly, flow was restored and the preparation allowed to stabilise for at least 30 minutes. During this period the spatial relationships of the pressure lines, stenosis, flow probe and Doppler position were noted (Table III). Saline was infused at a rate to compensate for the minimal blood loss and estimated insensible and urinary losses; the rate of infusion was approximately 500 ml/hour throughout the experiments. Proximal

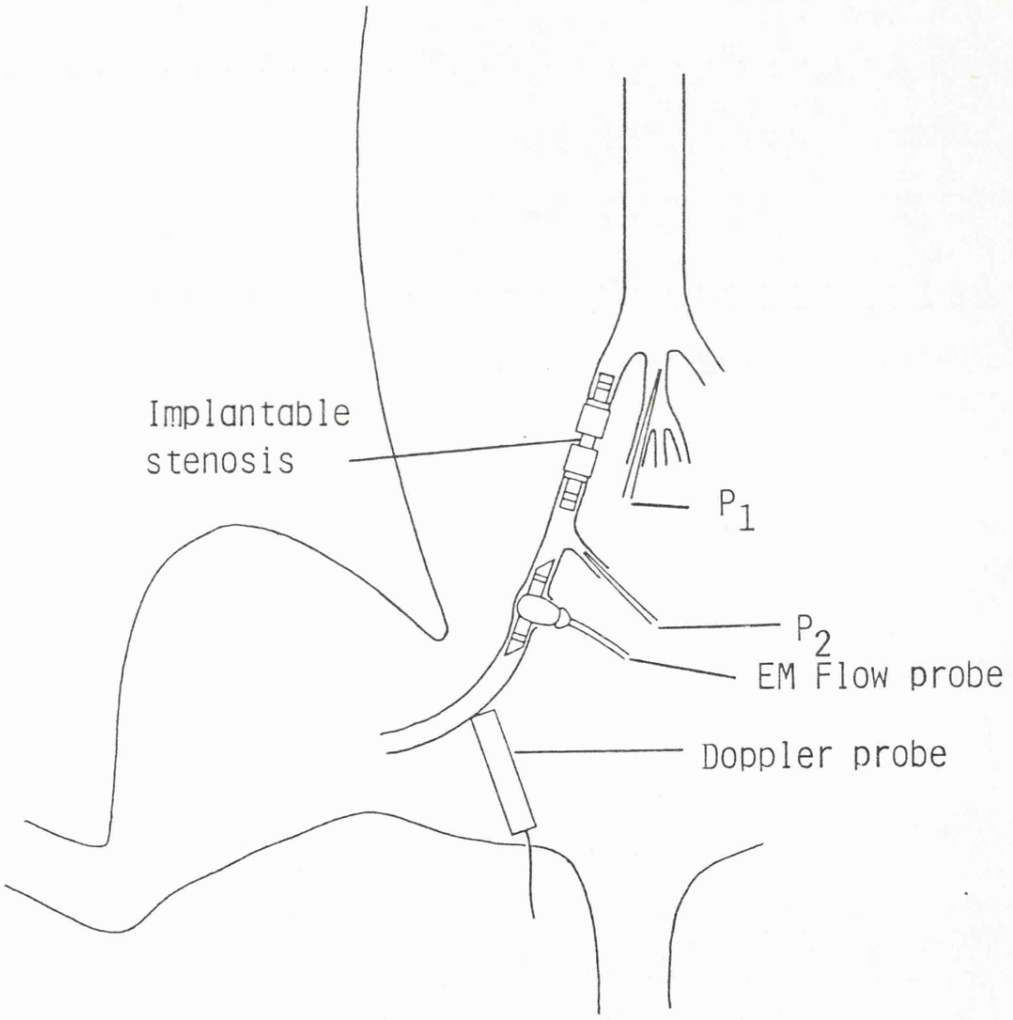


Figure 3. The animal model.

and distal pressures, EM flow and ECG were monitored continuously on the chart recorder. A general view of the experimental set-up is seen in Fig 5.

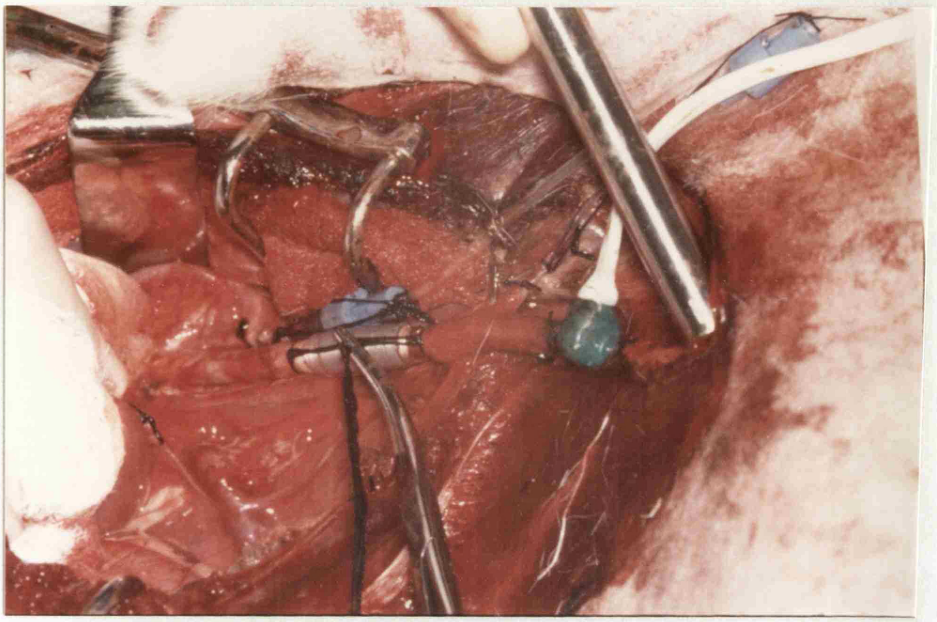
TABLE III: IMPORTANT DIMENSIONS

DOG NUMBER:	22	23	24	25	26
ED[+] of iliac artery (mm)	6.3	6.0	6.6	7.3	5.7
Aorta to stenosis (mm)	41.5	46.5	44.5	51.5	48.0
Stenosis to P_2[*] (mm)	31.5	31.0	30.0	31.0	30.0
P_2 to EM flow probe (mm)	30.5	29.0	22.0	30.0	32.5
EM flow to Doppler (mm)	49.5	43.0	31.0	40.0	33.0

[+] ED = external diameter
[*] P_2 is the site of the distal pressure line

(iii) Measurement Protocol

Once the preparation appeared completely stable with steady pressure and flow signals, the stenosis insert was changed to one of the seven lumen reducing sizes. Pressure and flow were monitored continuously and also recorded on tape at the time of a measurement run. Five minutes and ten minutes after changing the stenosis a series of Doppler signals was recorded on AM tape; by this time, flow and pressure had once more returned to a steady state. When all stenoses had been used (in random order) the zero stenosis was once more inserted. Examples of typical Doppler waveforms recor-



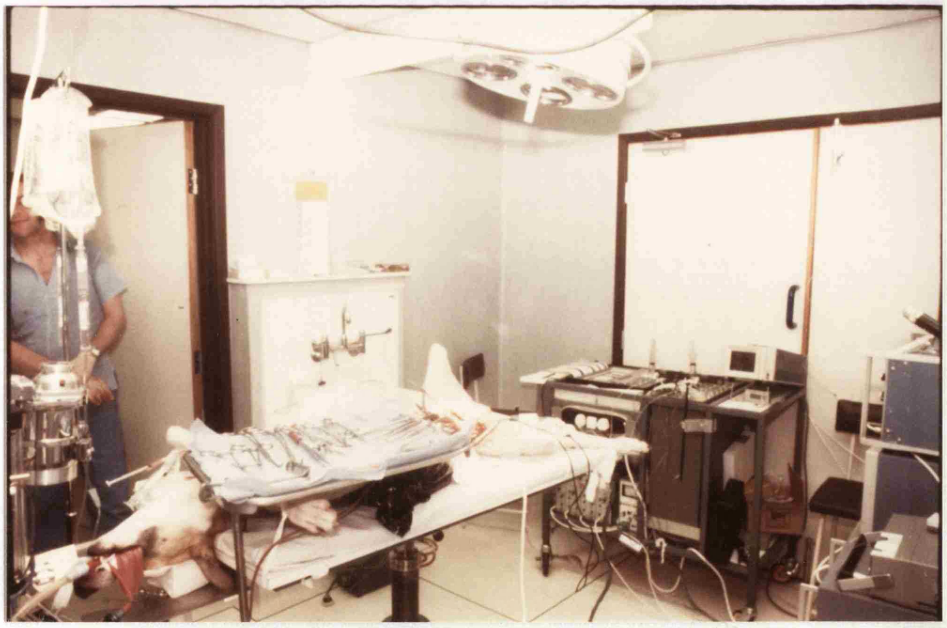


Figure 4. View of the animal preparation. The stenosis, EM flow probe and Doppler probe are clearly seen. Figure 5. A general view of the experimental set-up.

ded from below mild, moderate and severe stenoses are shown in Fig 6.

During the measurement runs it was found that the very tight stenoses (92 and 95% area reduction) had a tendency to clot, and if this happened it was immediately obvious from the flow recordings. Such measurements were not used in subsequent calculations; if clotting started to happen often more heparin was given; regular clotting times were not, however, performed.

The preparation was found to remain stable and it was possible to make measurements for about three hours. In total 150 complete sets of pressure, flow and Doppler data were recorded from the five experiments and subsequently analysed. Synchronisation signals were used to link the AM and FM tape recorders so precise flow and pressure data were available for each individual series of Doppler waveforms.

B. CALCULATION OF RESULTS

Following the experiments, the AM tapes were played back through the spectrum analyser and the Doppler waveforms digitised as described in the previous chapter; PI, the Laplace transform roots and PCA coefficients were then calculated.

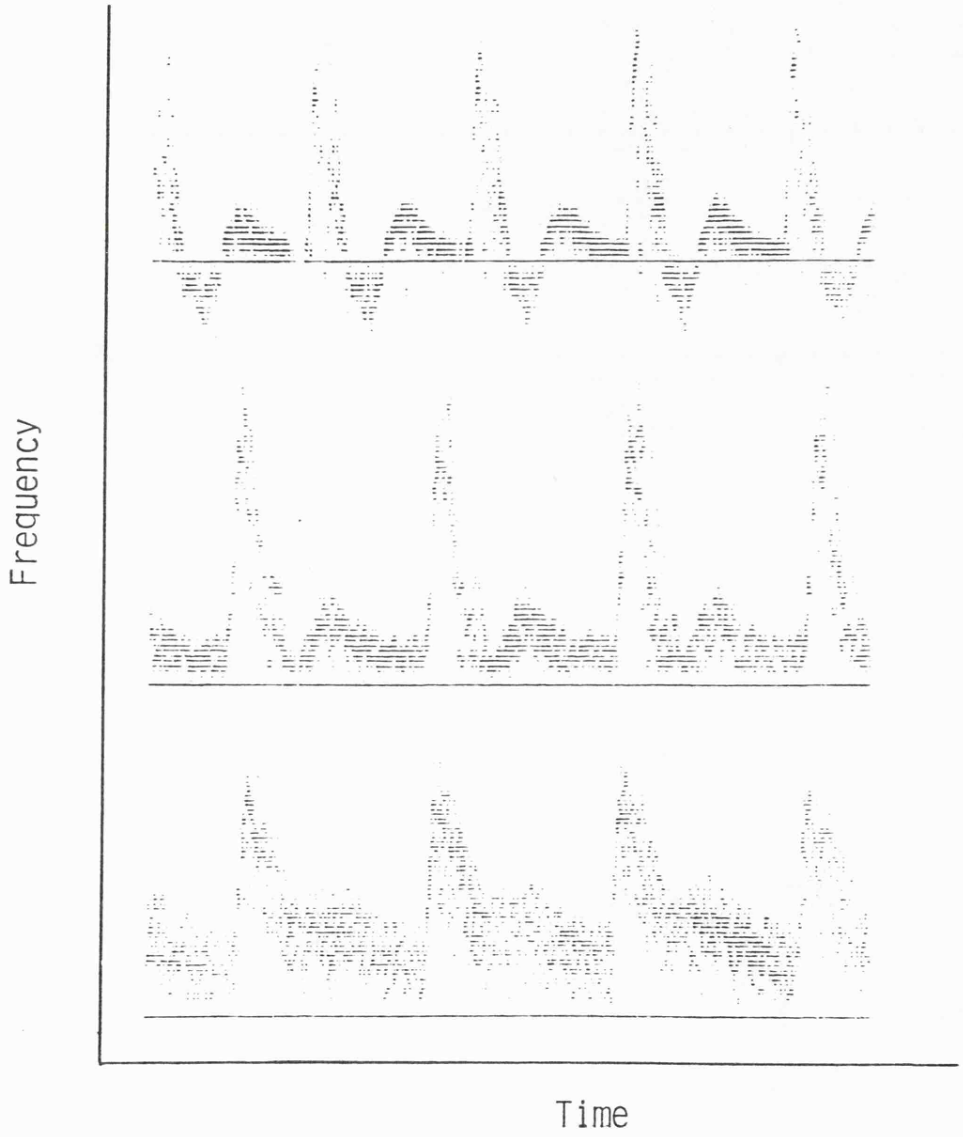


Figure 6. Examples of Doppler waveforms recorded from below stenoses of 0%, 77% and 92% area reduction.

Five waveforms were available for each measurement sequence (ie a total of 750 waveforms) but 91 were lost during the analysis, either because the Doppler waveform itself was of inadequate quality, or due to a fault in digitisation. A further 19 waveforms were discarded during processing because an adequate curve fit could not be achieved, and 17 waveforms were excluded from the Laplace transform analysis alone because of markedly inappropriate values of LTD when compared with the other waveforms in the same sequence.

It was necessary (because of the need for truncation or extrapolation discussed in Chapter 5) to impose some limitations on waveform length for principal component analysis to be carried out. The limits chosen excluded heart rates of greater than 100 or less than 50 beats per minute, and a total of 64 waveforms were lost from the analysis for this reason. The values of PI, LTD and PCA coefficients, together with sample standard deviations, for each measurement run are found in Appendix B.

The FM tapes were also replayed and pressure waveforms proximal and distal to the stenosis and pressure difference across the stenosis were then meaned by passing through a low pass filter; mean EM flow was similarly calculated. An example of the replayed flow and pressure data is shown in Fig 7. The main purpose of the accurate flow and pressure data was to enable the calculation of peripheral resistance.

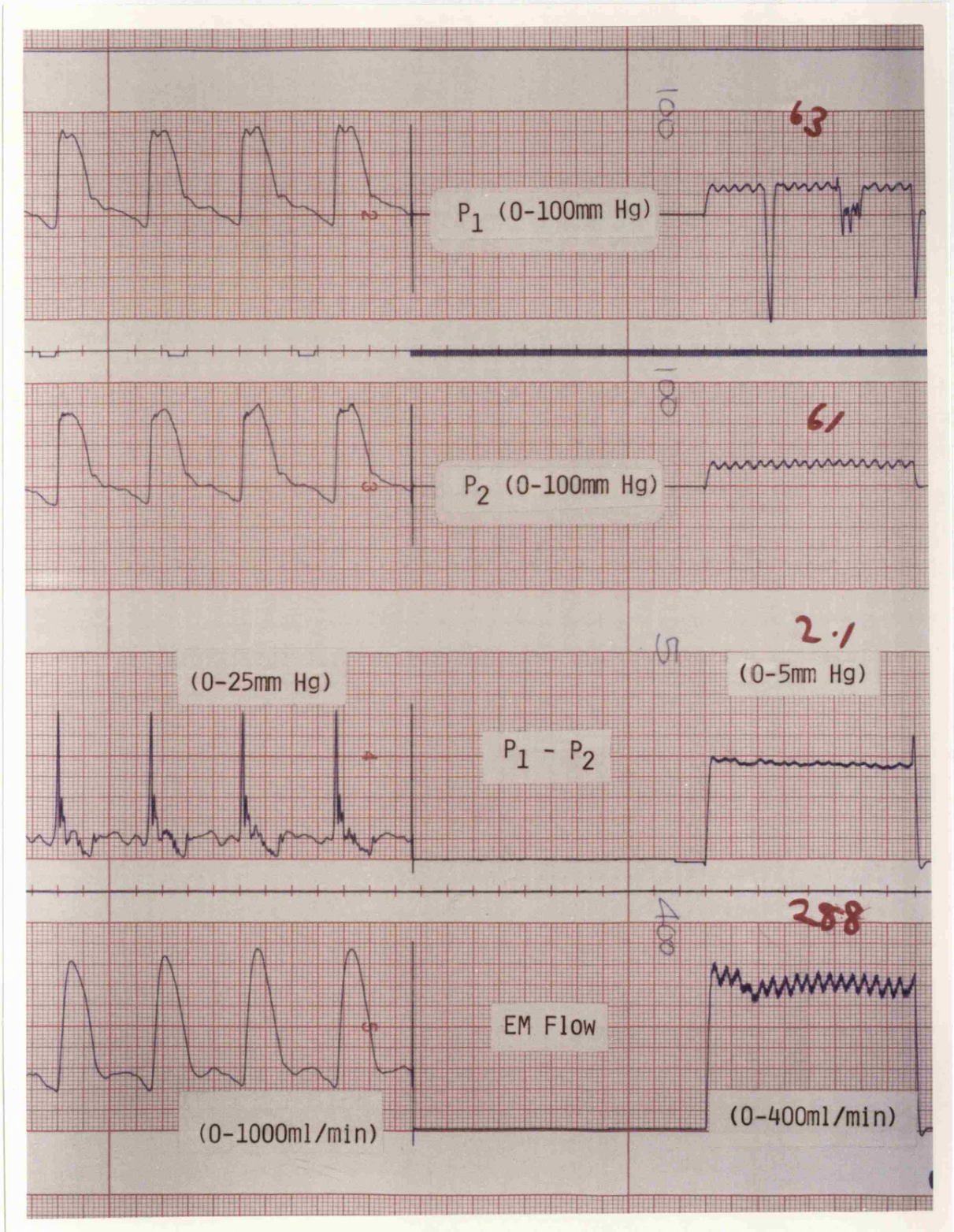


Figure 7. An example of the replayed pressure and flow signals; raw results are on the left and means on the right.

Although when considering pressure and flow relationships affecting the whole limb it is important to take into account collateral flow, in this series of experiments all collateral vessels between the aorta and the Doppler probe had been ligated. The important peripheral resistance was therefore the resistance beyond the Doppler measurement point; this is given by

$$R_p = P_2/Q$$

where P_2 is the pressure in the artery downstream from the stenosis and Q the EM flow through the stenosis. Venous pressure was assumed to be small and approximated to zero. When dealing with a pulsatile system the mathematics, as we have seen, become very complex and peripheral resistance was therefore derived from mean flow and mean distal pressure. It was similarly possible to calculate the resistance of the stenosis R_s (= $[P_1-P_2]/Q$) using mean values once more.

C. RESULTS

For each series of Doppler waveforms recorded from each stenosis change, the following results were available for comparison: mean pressure above and below and mean flow through the stenosis; electronically calculated mean pressure difference; and stenosis and peripheral resistances. The

detailed results of pressure, flow and resistance measurements, and Doppler indices, are found in Appendix B. These tables also provide a chronological record of each of the five experiments. In order to show that stenosis resistance changes predictably with stenosis severity these have been plotted in Fig 8; a few wayward points for the tight stenoses may indicate some partial occlusion with thrombus.

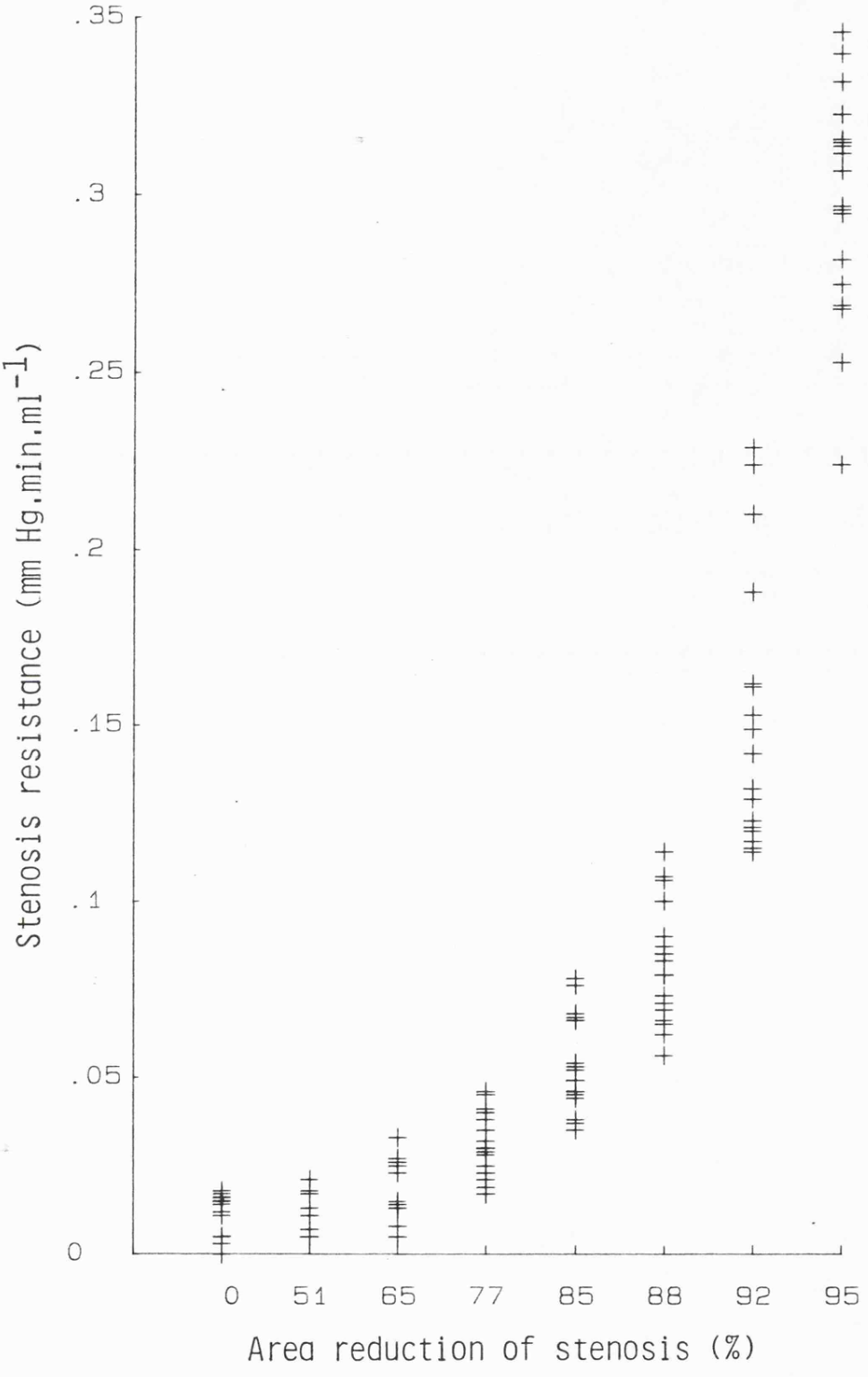


Figure 8. Calculated stenosis resistance for each stenosis.

(i) Pulsatility Index

The results of pulsatility index for each stenosis and each dog are listed in Table IV. Each value represents the mean (± standard deviation) for all (n) observations in a particular experiment. This usually included several measurement runs at different times during the experiment. For example, for stenosis 0 and dog 22, 28 waveforms were analysed: these were obtained from six measurement runs of five waveforms each, a total of 2 waveforms being lost during processing.

PI is plotted against stenosis severity for all the dogs in Fig 9. Each point represents a single measurement run and is usually the mean of 5 waveforms. The mean value of PI for all the runs is also shown, and the error bars indicate one sample standard deviation from the mean. It can be seen that, although there is a tendency for PI to decrease with increasing stenosis severity, the overlap between the groups is considerable and only very tight (88% area reduction or greater) stenoses are always clearly differentiated.

PI is similarly plotted using the results from individual experiments in Fig 10. Although there is a slightly better separation there is again marked overlap with the less severe stenoses.

TABLE IV: VALUES OF PI FOR EACH STENOSIS IN THE FIVE DOGS

Stenosis:	0	51	65	77	85	88	92	95
Dog:								
22	3.77	--	--	2.84	1.55	1.46	1.19	0.72
	(.89)			(.33)	(.09)	(.09)	(.26)	(.09)
	n=28			n=6	n=9	n=19	n=20	n=20
23	3.56	--	3.50	3.56	2.49	2.03	1.58	0.96
	(.62)		(.24)	(.36)	(.61)	(.14)	(.13)	(.15)
	n=24		n=9	n=20	n=19	n=14	n=19	n=19
24	3.49	4.06	3.10	2.92	1.99	1.49	1.39	0.83
	(.96)	(.08)	(1.1)	(.85)	(.50)	(.32)	(.17)	(.09)
	n=34	n=10	n=18	n=20	n=20	n=19	n=18	n=15
25	4.67	--	3.69	3.42	2.37	1.86	--	1.09
	(.86)		(.33)	(.93)	(.41)	(.05)		(.07)
	n=31		n=15	n=10	n=19	n=4		n=19
26	2.63	3.22	3.35	2.07	1.47	1.46	0.99	0.58
	(.58)	(.68)	(.50)	(.34)	(.09)	(.23)	(.10)	(.10)
	n=25	n=20	n=20	n=20	n=19	n=19	n=19	n=20

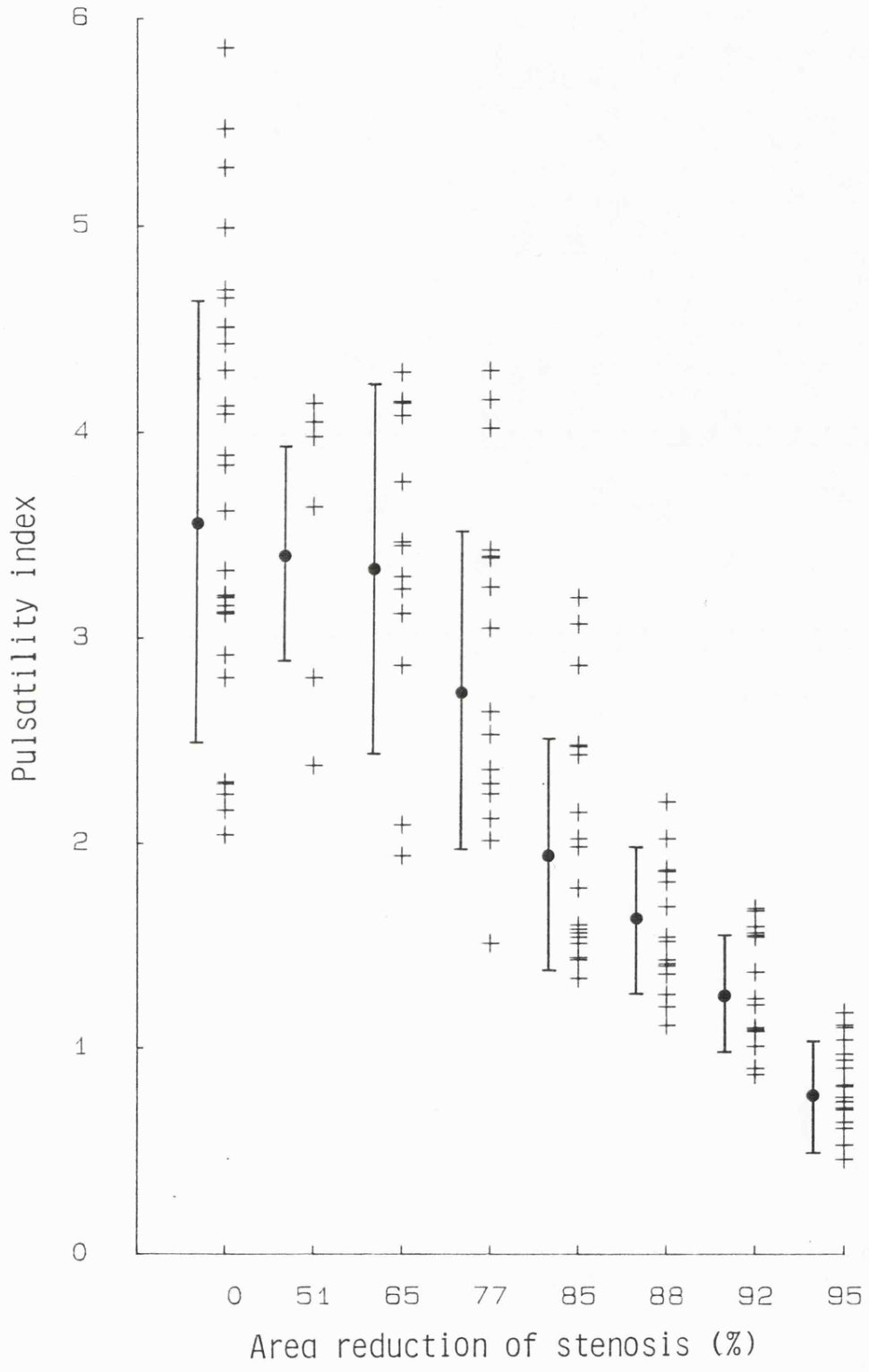


Figure 9. PI plotted against stenosis severity for all five dogs. Individual values are given together with means and standard deviations for each group.

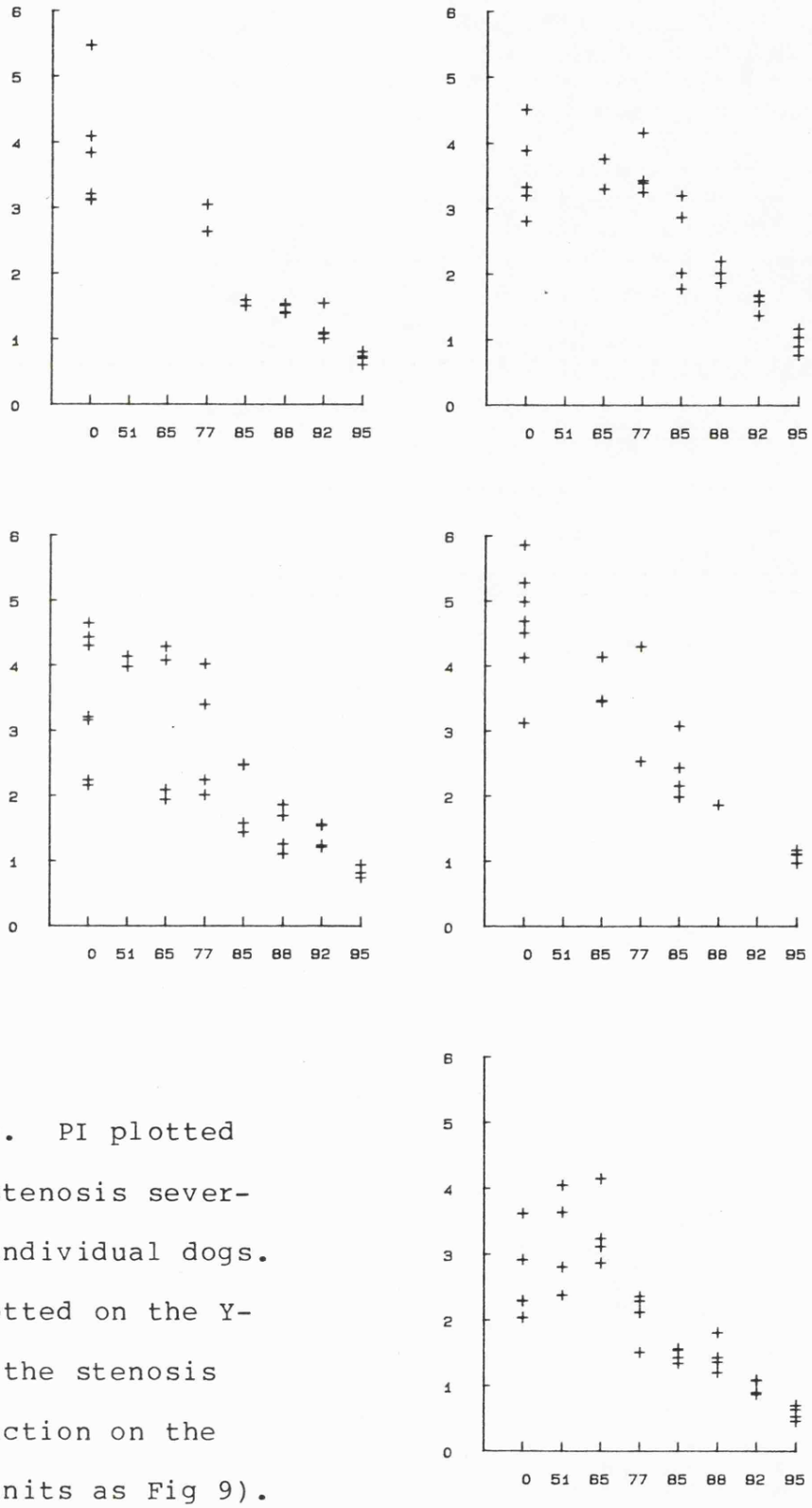


Figure 10. PI plotted against stenosis severity for individual dogs. PI is plotted on the Y-axis and the stenosis area reduction on the X-axis (units as Fig 9).

The effect of peripheral resistance is illustrated for a zero stenosis and a moderately severe stenosis in Fig 11. Although if taken by individual dogs the results tend to show higher values of PI with greater peripheral resistances, there is no clear relationship, especially when all the dogs are taken together. This is in contrast to the previous study from this department (139). The only conclusion must be that although PI is undoubtedly affected by PR this effect is unpredictable in the dog and other unmeasured factors such as elasticity of the vessel may be changing simultaneously.

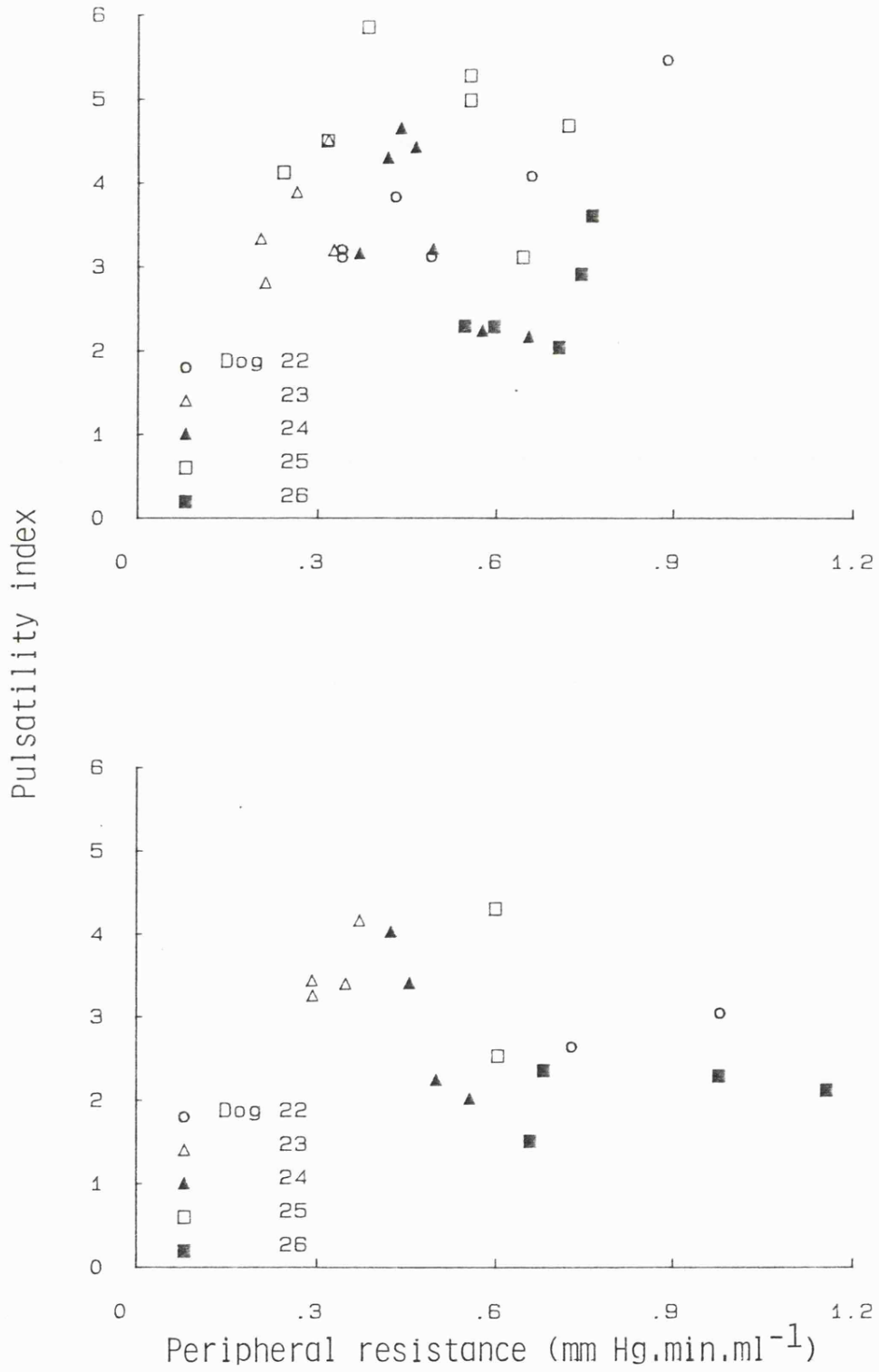


Figure 11. PI plotted against peripheral resistance for a 0% (top) and a 77% (bottom) area reduction stenosis.

(ii) Laplace transform damping

The results of LTD are similarly recorded in Table V. Once more each value represents the mean (± SD) for all waveforms recorded from below each individual stenosis in each of the five dogs; n is the number of waveforms analysed for each observation. LTD is also plotted against stenosis severity in Fig 12 for all the dogs. The results show the same trend as with PI except in the opposite direction: high values of LTD are associated with marked proximal stenosis. Unfortunately there is a similar, but probably slightly more pronounced, overlap between the values for each stenosis and those in adjacent groups.

Again results are better for individual dogs (Fig 13). However when looking for a measurement which might be applied to patients in differing circumstances, it is important that such a method should be able to allow for some subject to subject variation. LTD would appear, taken on its own, to be a rather poor determinator of proximal stenosis, at least in this model.

TABLE V: VALUES OF LTD FOR EACH STENOSIS IN THE FIVE DOGS

Stenosis:	0	51	65	77	85	88	92	95
Dog:								
22	.34	--	--	.34	.83	.39	.71	.95
	(.16)			(.07)	(.04)	(.06)	(.07)	(.07)
	n=28			n=6	n=8	n=19	n=20	n=20
23	.37	--	.37	.52	.57	.69	.98	.98
	(.09)		(.03)	(.11)	(.06)	(.09)	(.02)	(.02)
	n=24		n=9	n=20	n=19	n=14	n=19	n=19
24	.30	.34	.20	.25	.32	.68	.89	.95
	(.14)	(.07)	(.08)	(.02)	(.03)	(.12)	(.08)	(.05)
	n=34	n=10	n=18	n=15	n=20	n=15	n=18	n=15
25	.38	--	.44	.29	.46	.45	--	.97
	(.17)		(.31)	(.01)	(.19)	(.10)		(.03)
	n=31		n=14	n=10	n=18	n=4		n=18
26	.11	.11	.11	.12	.22	.30	.81	.85
	(.02)	(.00)	(.01)	(.01)	(.05)	(.04)	(.13)	(.18)
	n=25	n=20	n=20	n=20	n=19	n=19	n=15	n=20

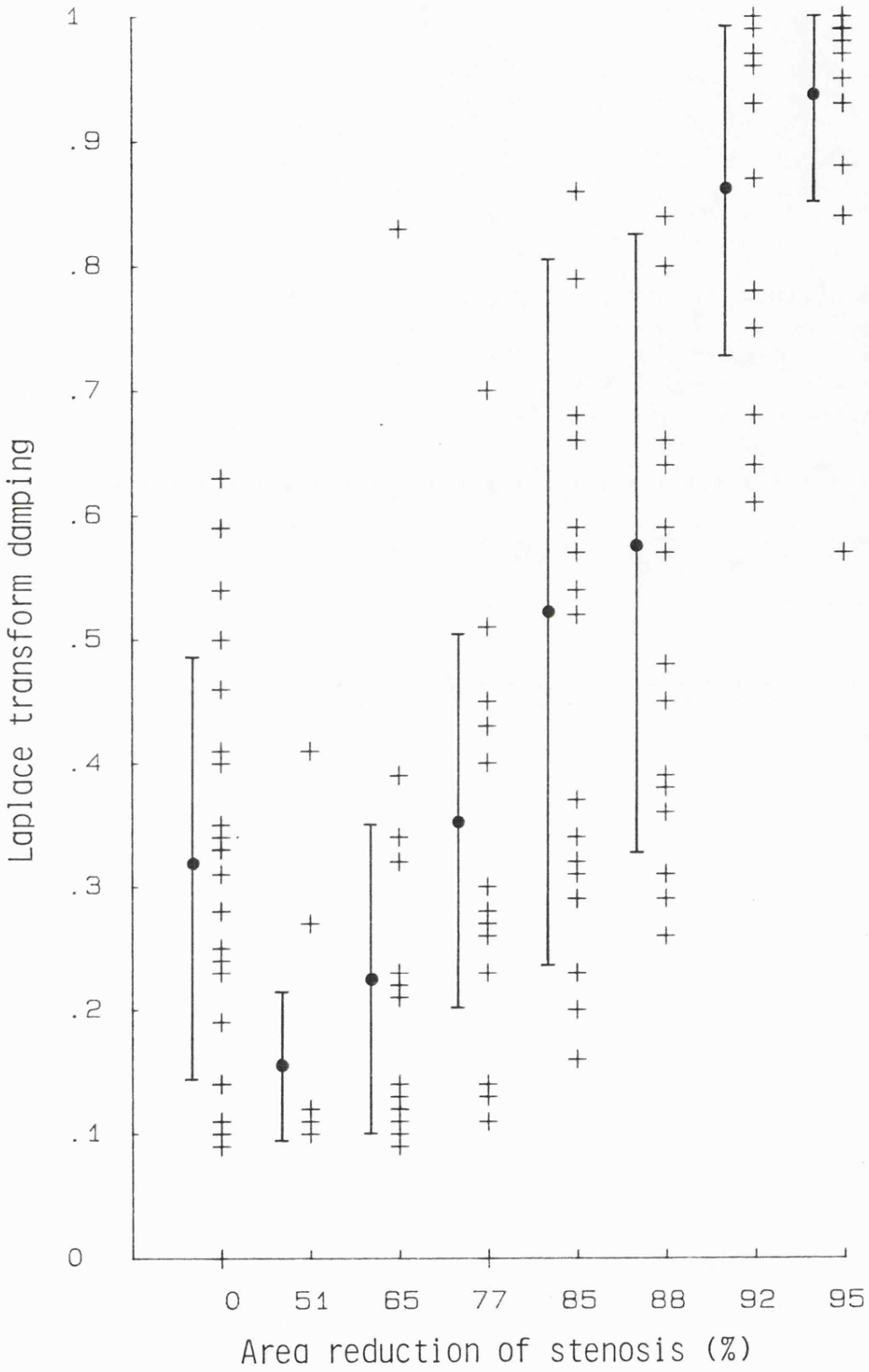
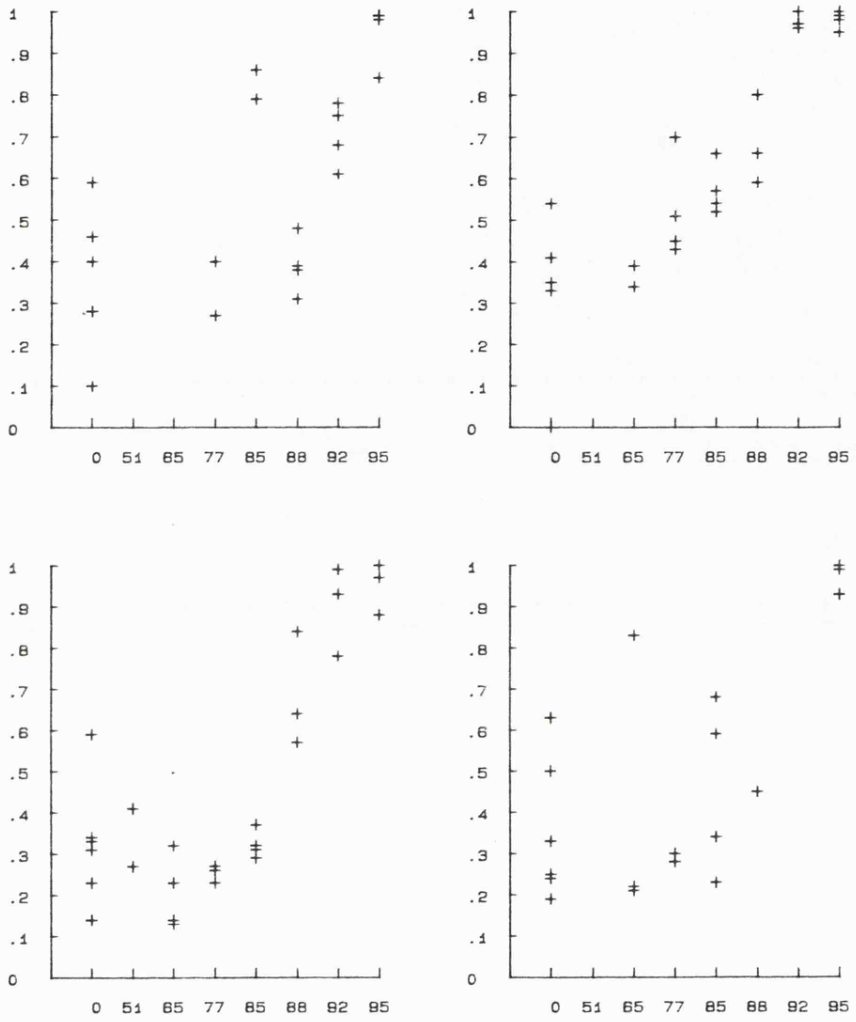


Figure 12. LTD plotted against stenosis severity for all five dogs. Individual values are given together with means and standard deviations for each group.



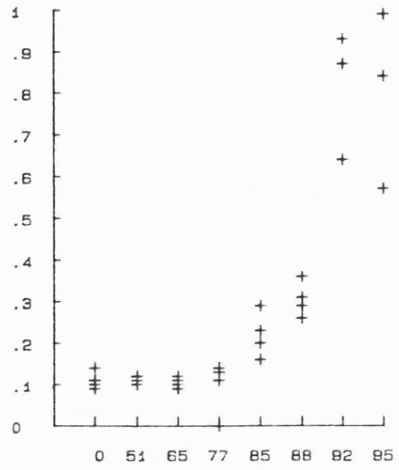


Figure 13. LTD plotted against stenosis severity for individual dogs. LTD is plotted on the Y-axis and the stenosis area reduction on the X-axis (units as Fig 12).

The advantage of LTD claimed by its originators is its independence of peripheral resistance. Looking at the less severe stenoses in all the dogs, this is clearly not the case; indeed there appears to be a highly significant relationship in this study (Fig 14).

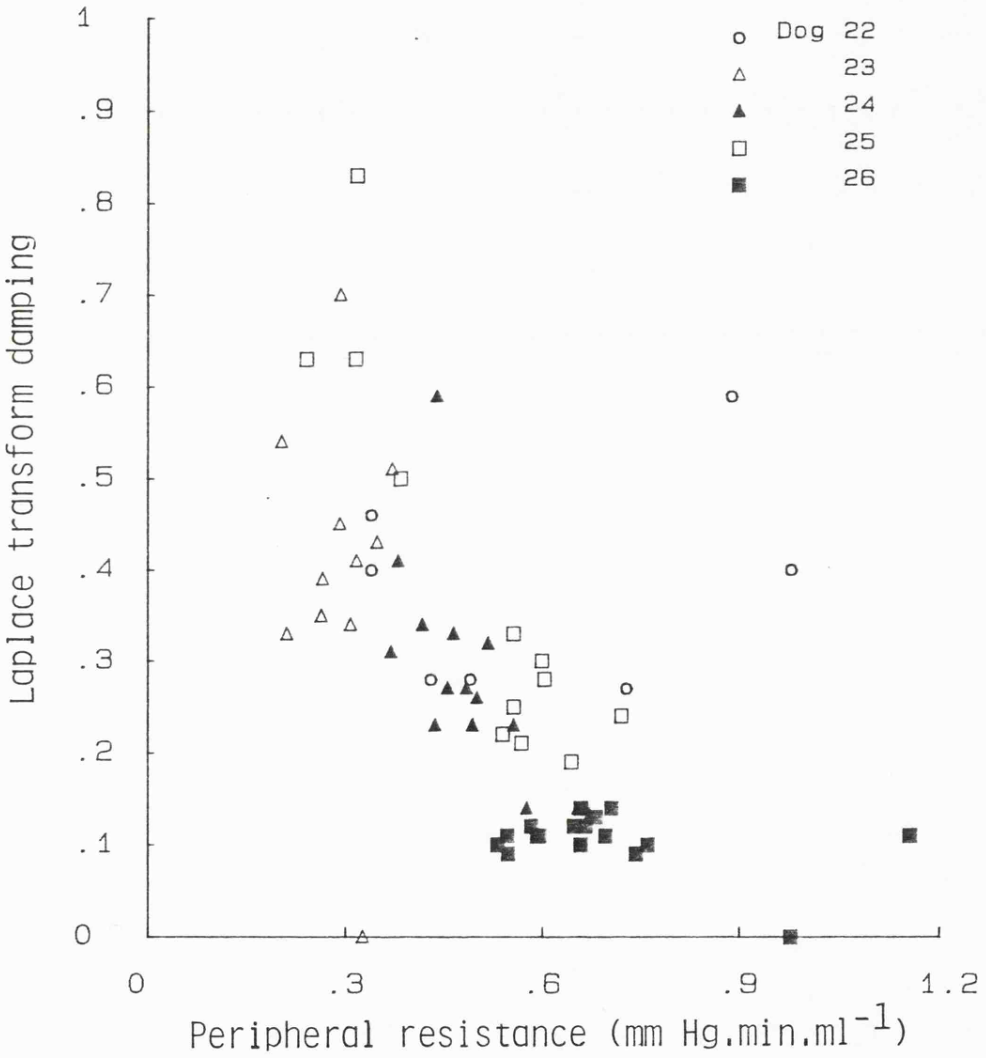


Figure 14. LTD plotted against peripheral resistance R_p for the less severe stenoses (0 - 77% area reduction).

Finally, the reciprocal relationship between PI and LTD is examined in Fig 15. Although derived in entirely different manners, there does appear to be a close relationship between these values; these results come from one dog, but the findings were similar in the other dogs examined.

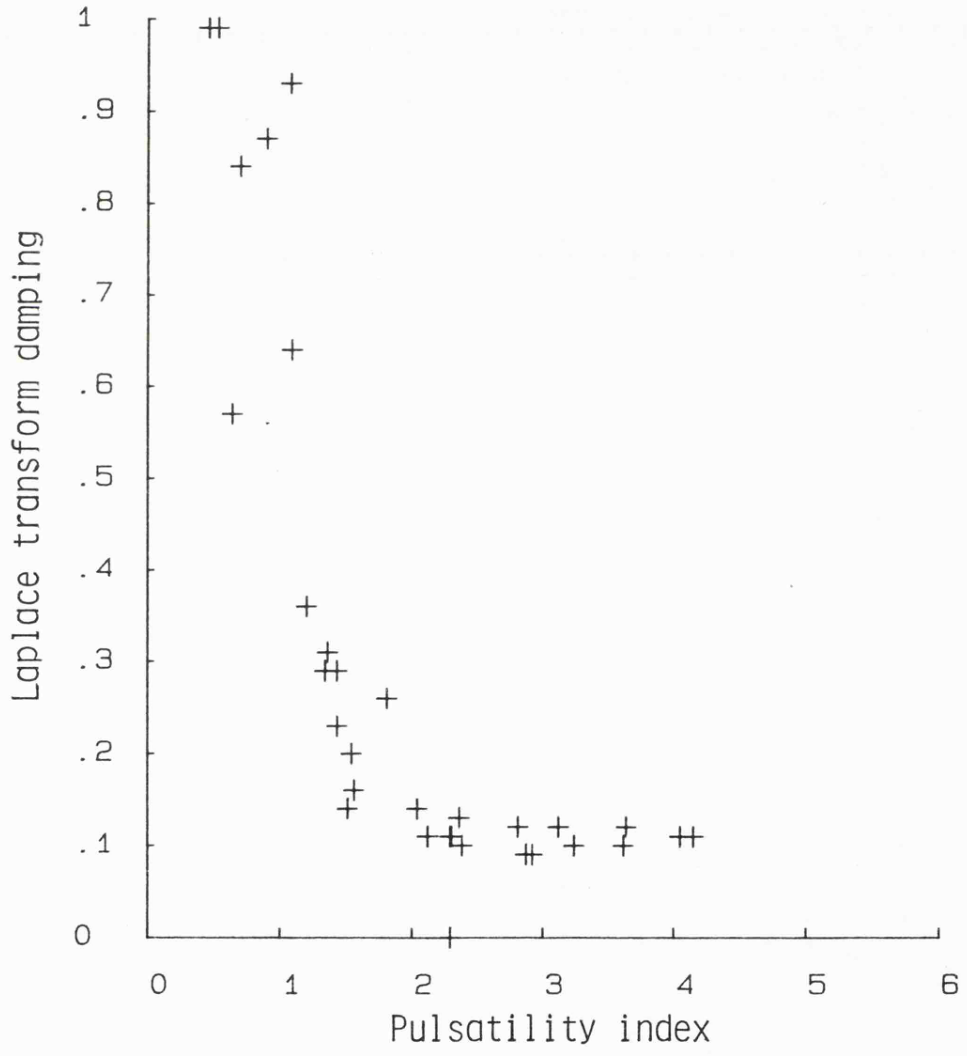


Figure 15. The relationship between PI and LTD for dog 26.

(iii) Principal component analysis

This method, as described in chapter 4, compares a test waveform with a population of similar waveforms already available. The test waveform is then described in terms of the principal components of the whole population; the amount by which each component must be weighted to reproduce the test waveform is known as a coefficient. Potentially each test waveform can be described in terms of all 32 components used in our version of the method; in other words, each component multiplied by its own unique coefficient (or weighting factor) and added to all the rest will reproduce the original waveform. In practice, the method enables a satisfactory reconstruction using only a small number of components; for simplicity in these studies, only the first two were used. An excellent reconstruction was possible with this method; Fig 16 illustrates two waveforms from the series together with a reconstruction using the first two principal components. It was possible, therefore, to define accurately a particular waveform by these two numbers plotted against each other.

A similar reconstruction of the original waveforms is possible with the Laplace transform method and examples (using the same waveforms as for Fig 16) are seen in Fig 17. The curve fit is not quite as good, and one of the constraints of the Laplace method, that the fitted curve must

always go through the origin, is demonstrated.

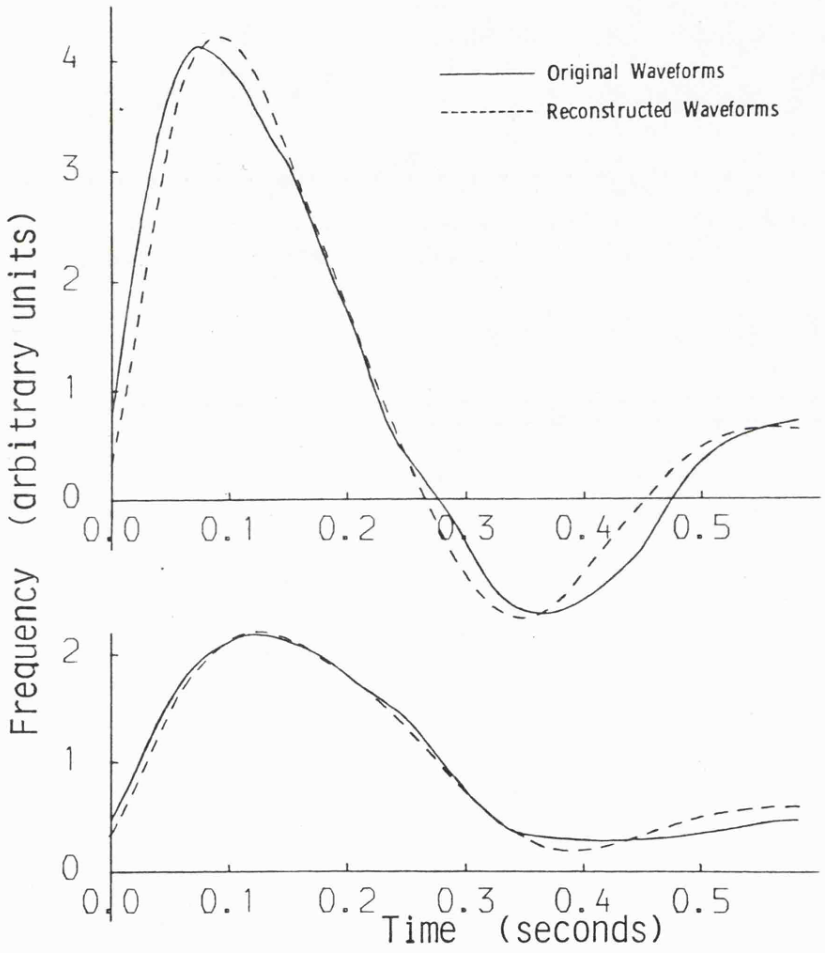


Figure 16. Original and reconstructed waveforms using PCA.

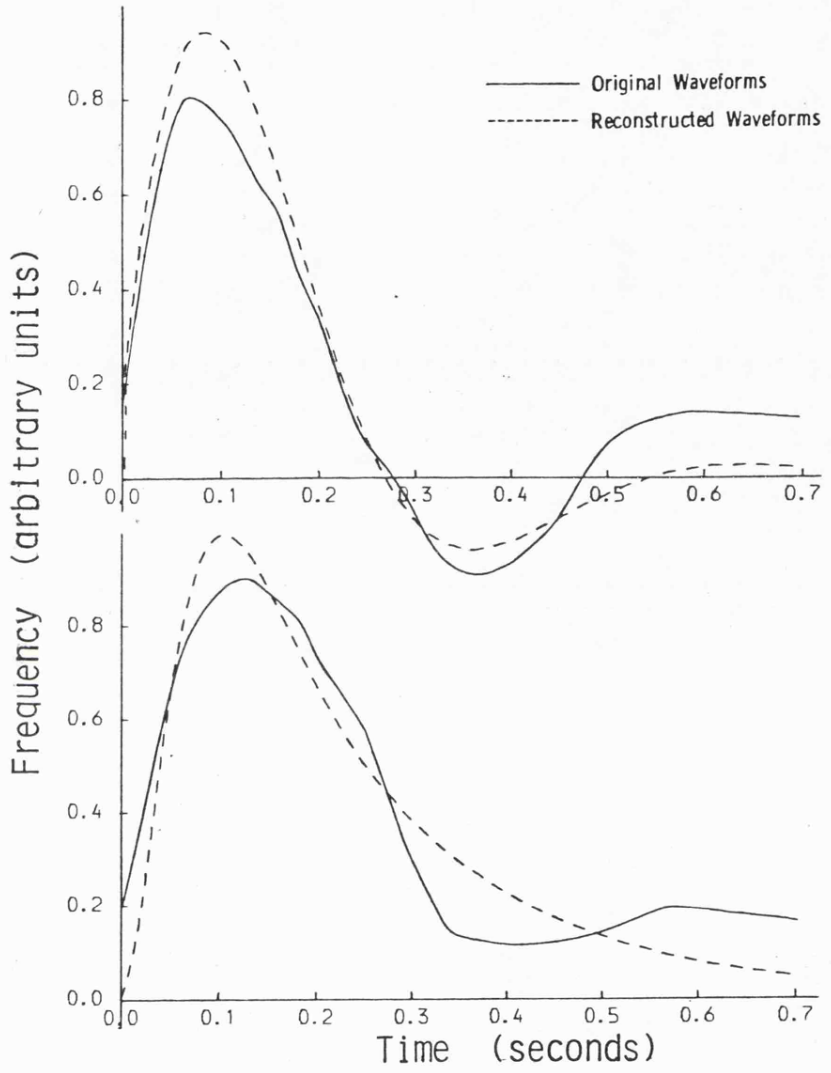
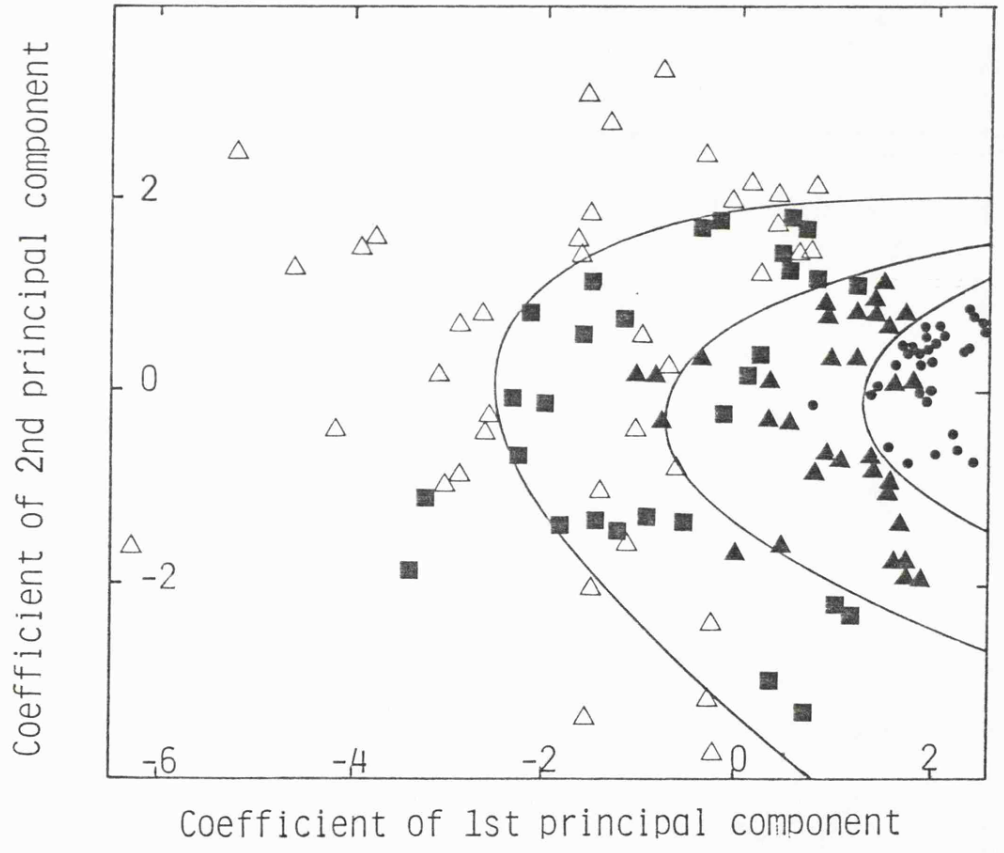


Figure 17. The same waveforms reconstructed using LTD. Note that the reconstruction always goes through the origin even when the original does not.

The results of PCA are shown for all dogs and all stenoses in Fig 18. It is clear that clustering of points has occurred with the severe stenoses; for convenience these have been classified as one group. Less severe stenoses occupy positions in 'feature space' further from this area. Although mathematical methods may be employed to draw a plane to give optimal separation of the groups it was found that parabolae drawn as shown by eye gave an excellent separation into four main groups.



(Area reduction: △= 0 or 51%, ■= 65 or 77%, ▲= 85 or 88%, •= 92 or 95%)

Figure 18. The coefficients of the first two principal components plotted against each other.

Individual dogs occupied differing segments (Fig 19), again emphasising that dogs and experimental conditions were subject to variation. However, only this method came near to an adequate separation according to stenosis severity when looking at all the waveforms in all five dogs.

In the patient studies described in Chapter 9 a good correlation was found between clinical assessment of the femoral pulse and the coefficient of the first principal component alone. A similar relationship was found in the dog experiments, although there was no greater separation than with either PI or LTD (Fig 20). There was, however, a striking relationship between PI and PC1, as shown in Fig 21, and it is clear that these parameters contain very similar information in most cases. To get the most out of PCA, it appears that use must be made of at least the first two principal components, but the very availability of more components represents an advantage for PCA.

(iv) Comparison of the three methods

Although PI and LTD are easily compared with each other, it is more difficult to compare them with PCA. For this purpose, an attempt was made to define a normal range of values of PCA, LTD and PI for four groups (as had been used for plotting the PCA results) i.e. 0 and 51% stenosis, 65 and 77% stenosis, 85 and 88% stenosis, 92 and 95% stenosis. This

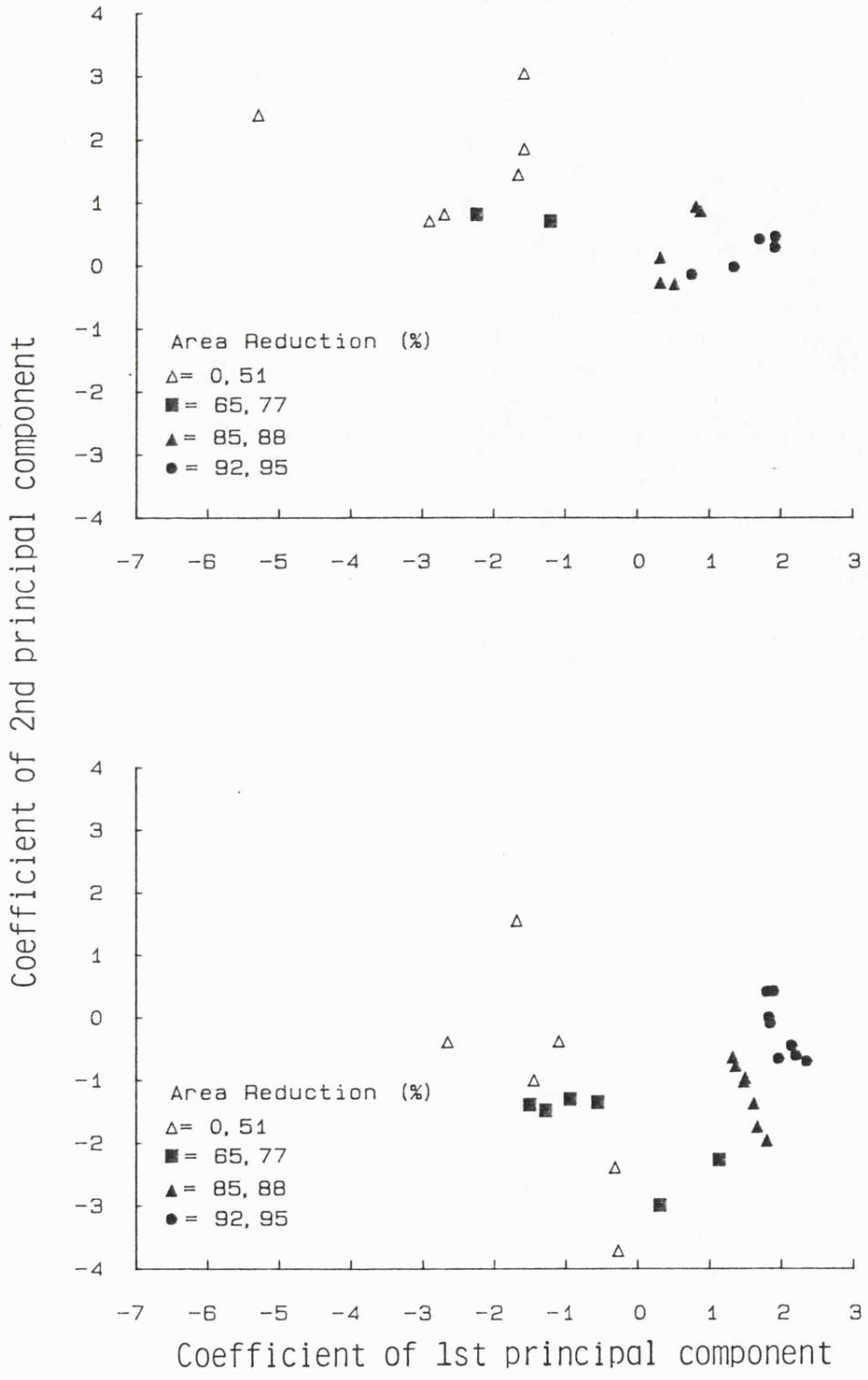


Figure 19. PC1 and PC2 for dogs 22 and 23, showing that they lie in different areas of 'feature space'.

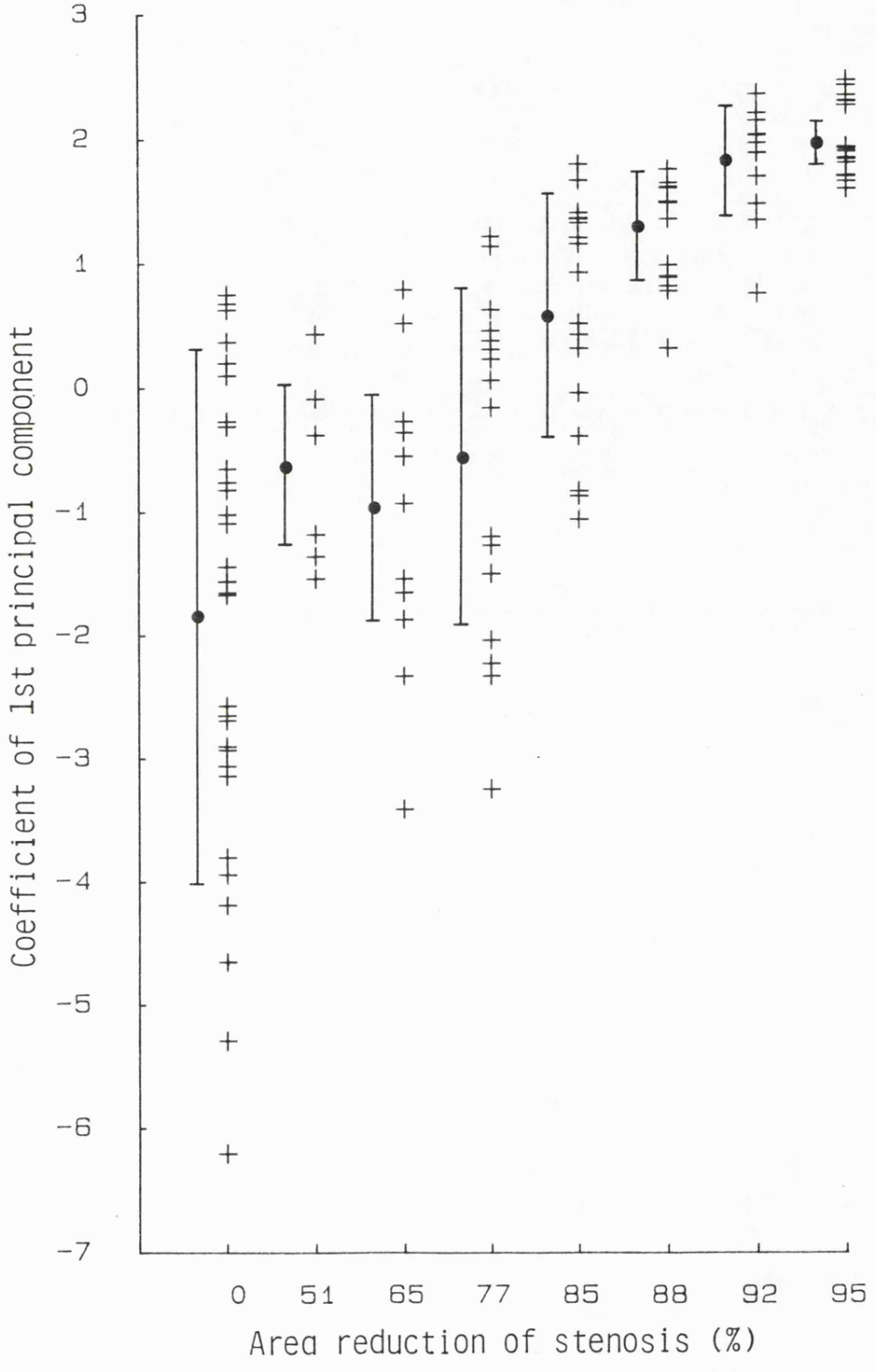


Figure 20. The coefficient of the first principal component plotted against stenosis severity.

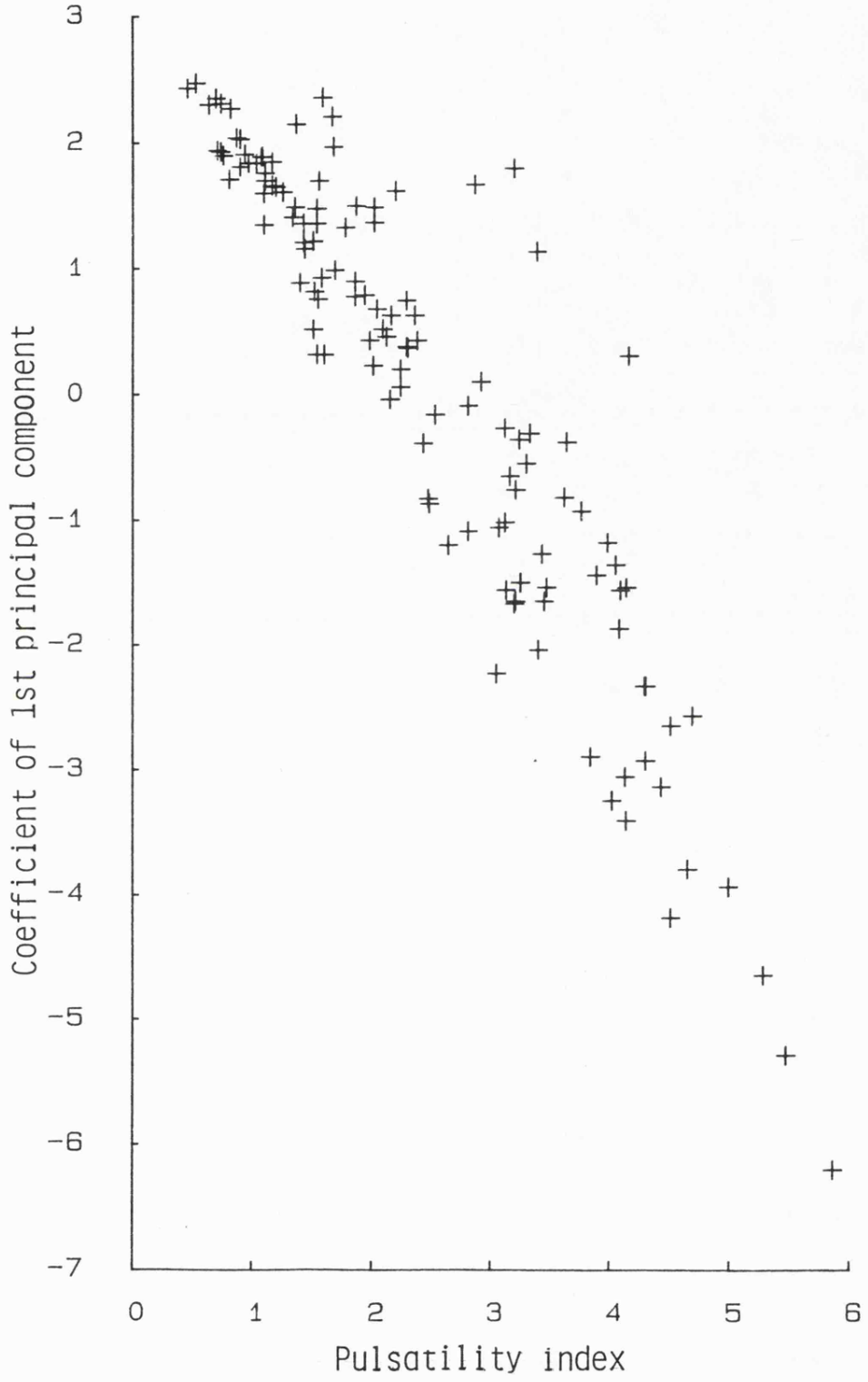


Figure 21. The relationship between PI and the coefficient of the first principal component.

was achieved by drawing horizontal dividing lines in such a way as to misclassify the smallest number of waveforms in each of the four groups using the data in Figs 9 and 12. In other words, divisions were made so as to create the fewest false positive and false negative misclassifications for PI and LTD. This was essentially what had been done when the parabolic divisions had been chosen for Fig 18. It was then possible to compare actual and predicted results for each set of waveforms (Table VI). PCA is clearly the most sensitive and LTD the least, mainly because of a marked lack of sensitivity in the moderately stenosed group.

Subjective assessment was also performed to see if the author could predict a stenosis from simply looking at the waveform. For this study the entire spectrum-analysed signal was used. All waveforms were shown randomly and blindly on two occasions and a mean value of these observations used for comparison with the actual results. It can be seen that subjective assessment is certainly no better than PI or LTD and is clearly less accurate than PCA.

(v) Direct pressure measurements

Pressure gradient is plotted against stenosis severity in Fig 22. It is interesting to compare the separation of values of pressure gradient according to stenosis severity for all the dogs with that obtained by either PI or LTD.

TABLE VI COMPARISON OF PI, LTD, PCA AND SUBJECTIVE ASSESSMENT

(Underlined values indicate a correct classification)

		Actual stenosis:			
		0 or 51%	65 or 77%	85 or 88%	92 or 95%
Classified by PI as: (n=133)	0 or 51%	<u>19</u>	8	0	0
	65 or 77%	16	<u>18</u>	8	0
	85 or 88%	1	3	<u>24</u>	6
	92 or 95%	0	0	2	<u>28</u>
Classified by LTD as: (n=130)	0 or 51%	<u>26</u>	21	15	0
	65 or 77%	4	<u>4</u>	3	0
	85 or 88%	6	2	<u>13</u>	7
	92 or 95%	0	0	2	<u>27</u>
Classified by PCA as: (n=132)	0 or 51%	<u>28</u>	2	0	0
	65 or 77%	11	<u>23</u>	4	0
	85 or 88%	0	4	<u>27</u>	1
	92 or 95%	0	0	2	<u>30</u>
Subjective assessment: (n=148)	0 or 51%	<u>15</u>	11	0	0
	65 or 77%	25	<u>9</u>	3	1
	85 or 88%	3	9	<u>28</u>	5
	92 or 95%	0	1	7	<u>31</u>

Although such comparison is not strictly fair to the Doppler methods, the accuracy of pressure gradient even without flow measurements bears comparison with the results of the subsequent patient studies.

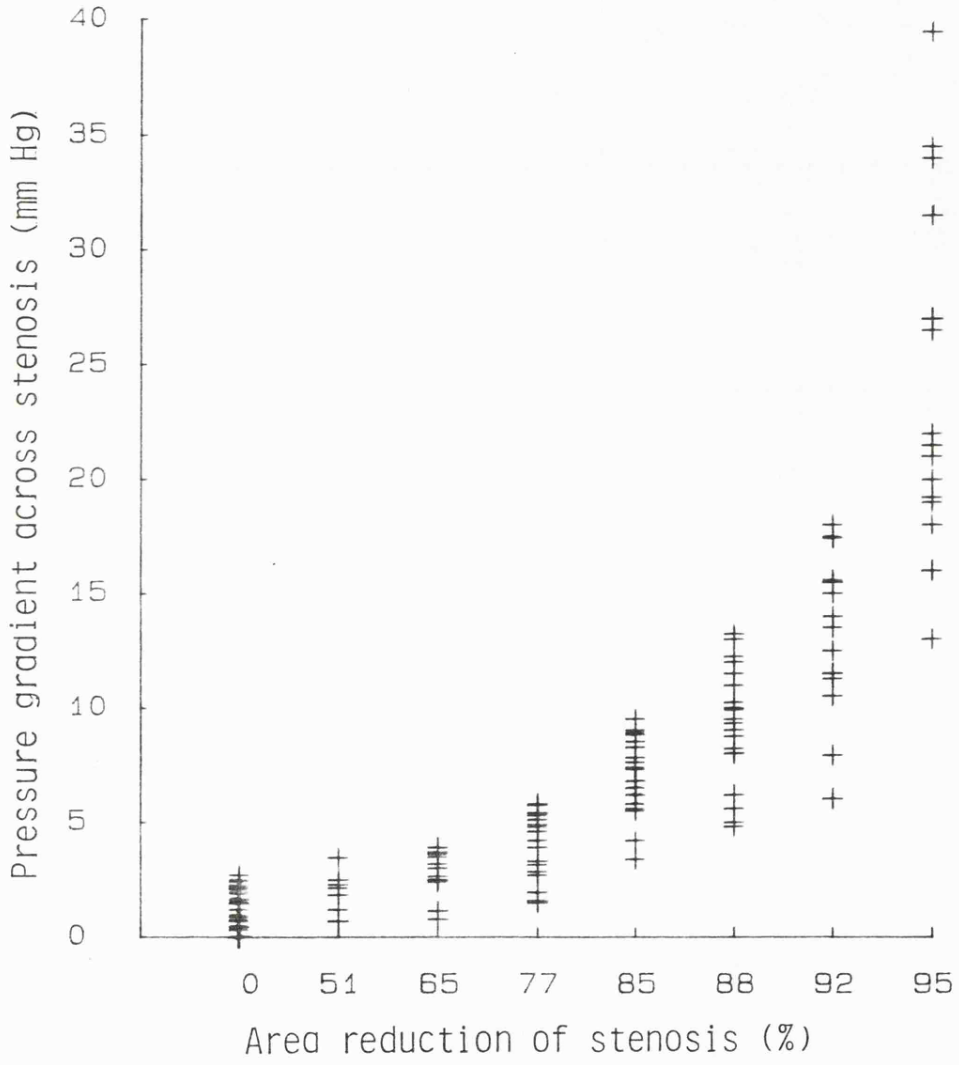


Figure 22. Pressure gradient across the stenosis plotted against stenosis severity. There is a striking relationship in spite of considerable variation in flow rates during the five experiments.

D. DISCUSSION

Is the use of such a canine model justified? Criticism may certainly be made of the use of general anaesthesia and a long experiment with the inevitable problem of maintaining a stable preparation. The use of healthy arteries in a relatively small species and a highly artificial type of stenosis is also far from ideal. However the advantage of direct comparison with pressure and flow measurements surely outweighs such criticism. It would be impossible to obtain similar data in humans without taking measurements during operations; even then, some information, such as that obtained using the cuff type EM flow probe, might well be inadequate and an anaesthetic would still be necessary. The problem of assessing the physical size of any stenosed segment at operation would also have to be overcome. The use of in vitro methods for investigating the complex changes occurring in the diseased cardiovascular system is probably a non-starter.

Do the results help in possible clinical applications of Doppler ultrasound? PI is shown to be only very broadly related to stenosis severity with considerable overlap especially with the intermediate stenoses. LTD appears to offer no advantage over PI in this model; although the Bristol group have not tested LTD in animals, there appears to be nothing in their method (129) which would make such an app-

roach unacceptable. The effect of peripheral resistance on LTD remains to be confirmed, but a recent study in patients from King's College Hospital (Law et al, unpublished) would suggest that LTD is not independent of PR. It may be that the model on which the Laplace transform method is based is not able to make allowance for the full range of changes taking place within the diseased arterial system and our own studies in patients tend to bear this out (see Chapter 9).

Of the three methods investigated, PCA seems the most likely to be of use in patients, given the need for separating the effects of proximal, distal and, if possible, local effects on Doppler waveform shape; it may not be justified to compare these methods with each other because of the different ways of estimating normality; however, in a further study (170) to investigate the possibility of microprocessor use of PCA, it was found that the new data fell closely within the limits defined in the present series of experiments, even with a few minor changes in anaesthetic technique (Fig 23).

Subjective assessment is clearly unreliable, and this underlines the need for objectivity if waveform analysis is to be of any real value in patients. The problem is that waveform shapes are altered by several factors other than proximal narrowing. One of these, flow disturbance near a stenosis, will be examined in the next chapter. However, in the present series of dogs, Doppler waveforms were recorded

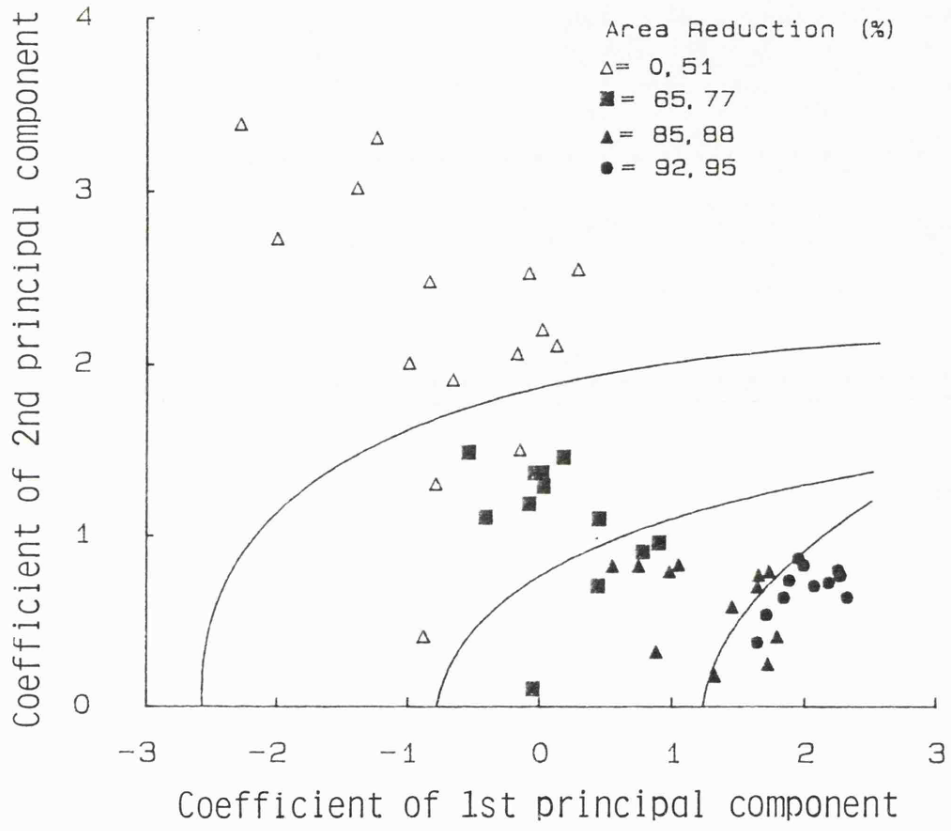


Figure 23. The coefficients of the first and second principal components obtained in a further completely separate series of experiments (Prytherch et al (170)), demonstrating the reproducibility of PCA with new data.

from 83-112mm (41-56 unstenosed diameters) downstream which should be adequate for the damping out of most turbulence; indeed, very little evidence of flow disturbance was found in the waveforms.

The influence of peripheral resistance on Doppler waveform shape is clear from its effect on both PI and LTD. This was a disappointing finding of the study: if the effect of peripheral resistance could be eliminated (as the Laplace transform method was supposed to achieve) lesser degrees of proximal stenosis could almost certainly be recognised.

One interesting ancillary finding, that pressure drop over a stenosis is clearly related and sensitive to degree of stenosis despite widely varying flow rates, is also potentially useful. The difficulty of measuring flow accurately in patients has prevented attempts to define proximal disease in terms of flow and pressure; however, if pressure drop can be defined for a fair range of flow rates in terms of stenosis severity, then perhaps this is the method we should be using.

E. CONCLUSIONS

Despite its deficiencies, an animal model seems justified in an attempt to test which of several methods of waveform analysis is best; the clear answer from this study is that PCA is superior to both PI and LTD, when two principal components are used. Although peripheral resistance changed unpredictably and elasticicity probably likewise, PCA managed to define lesser degrees of stenosis in the majority of cases.

Chapter 7

CHANGES IN DOPPLER WAVEFORMS AT VARYING DISTANCES FROM STENOSES

Changes occurring in velocity patterns distal to stenoses were discussed briefly in Chapter 4. Although some work had been done in vitro (Clark, 128), most other studies were empirical and uncontrolled. In particular, such effects on Doppler waveform shape had not been studied either in man or in animal models. From Clark's work it might be expected that flow disturbances caused by stenoses would propagate downstream for varying distances according to the severity of the stenosis and the size of the stroke volume.

It was therefore decided to investigate such changes in a modification of the animal model described in the last chapter. The object was to assess the type of flow disturbance produced by stenoses of varying severity at different distances downstream. It was hoped that such a study might shed light on some of the more unusual waveforms recorded in humans; Fig 1 illustrates such a waveform which, while appearing pulsatile with some reverse flow, has an outline which is difficult to define accurately. Almost certainly the

artery from which this waveform was recorded was diseased either locally or proximally, and the irregular outline probably indicates disturbed flow.

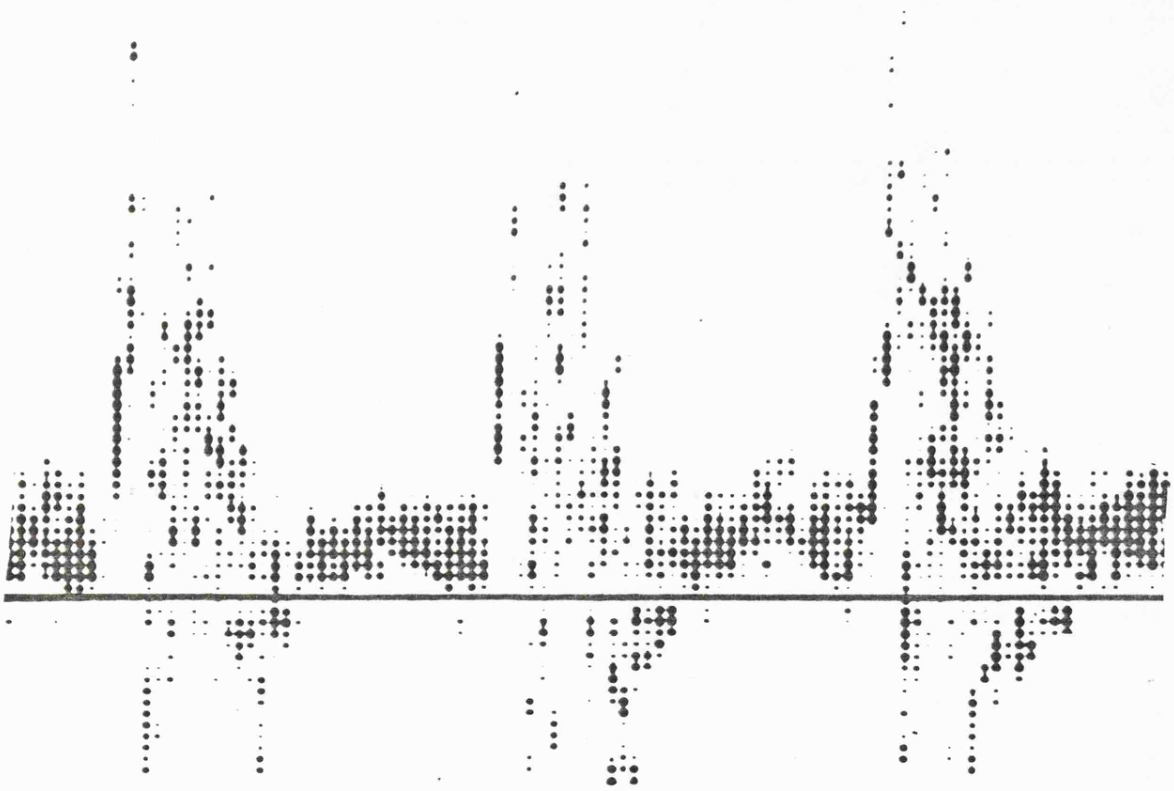


Figure 1. Doppler waveforms recorded from a pulsatile common femoral artery exhibiting probable disturbed flow.

METHOD

In order to examine waveforms at varying distances below a particular stenosis, it was more important than ever to try to obtain stability of the preparation. Furthermore, the period of reactive hyperaemia found in the previous animal studies following a stenosis change precluded a large number of recordings on one particular dog. Both the anaesthetic technique and stenosis assembly were therefore slightly modified.

(i) Anaesthesia

Five dogs were fasted and anaesthetised as described in Chapter 6 (Table I). Once again a fentanyl/fluanisone mixture was used to maintain anaesthesia, and blood gas estimations were performed and the ventilator adjusted to produce a physiological pCO_2 of about 4.5 kPa. Observations of pulse and systemic blood pressure remained remarkably constant during the series of measurements. Rectal temperature was also monitored and maintained close to normal (ca $38^{o}C$).

(ii) Animal preparation

The preparation was basically similar to that used in the previous experiments. Pressure lines and monitoring technique were identical. The EM flow probe, however, was

TABLE I: DOGS USED IN THE STUDY

Dog no.	Sex	Weight
27	F	24 Kg
28	F	20 Kg
31	M	25 Kg
32	M	27 Kg
33	M	30 Kg

positioned distally in the thigh to give a long stretch of iliac and femoral artery from which to record Doppler waveforms (Fig 2). The pressure and flow data was used to assess stability of the preparation and to determine when clotting was taking place in the tighter stenoses and also for the calculation of stroke volume.

The main difference was in the stenosis assembly itself. In order to eliminate the problem of hyperaemia following temporary arterial occlusion, the author designed a revolving mechanism which allowed one of eight possible inserts to be brought into the arterial blood stream. Fig 3 illustrates this both in complete and component form. The whole assembly was tied into the proximal iliac artery and it was then possible to rotate individual stenosed segments ranging from 0 to 95 % area reduction rather like the rotating cylinder of a revolver. It was easy to change from one insert to the

next during a single diastole, so there was effectively no interruption of flow when the stenosis was changed.

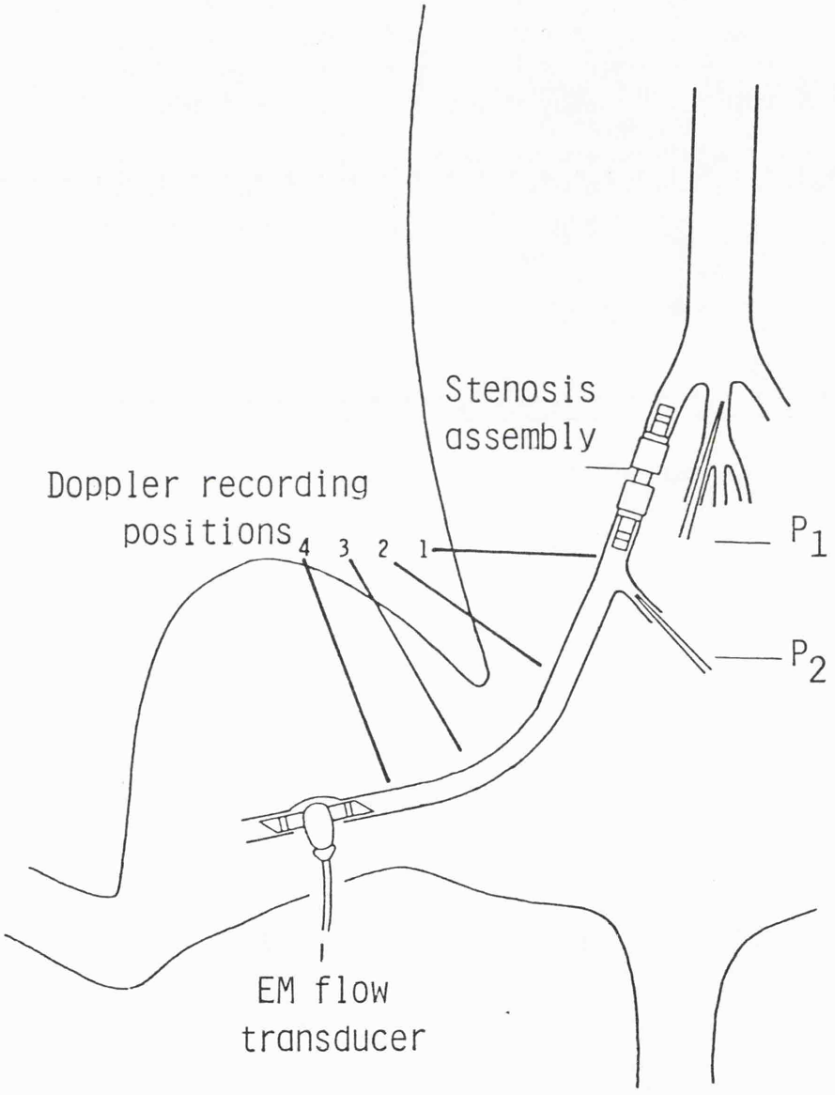


Figure 2. The animal preparation showing the main positions for recording the Doppler waveforms.

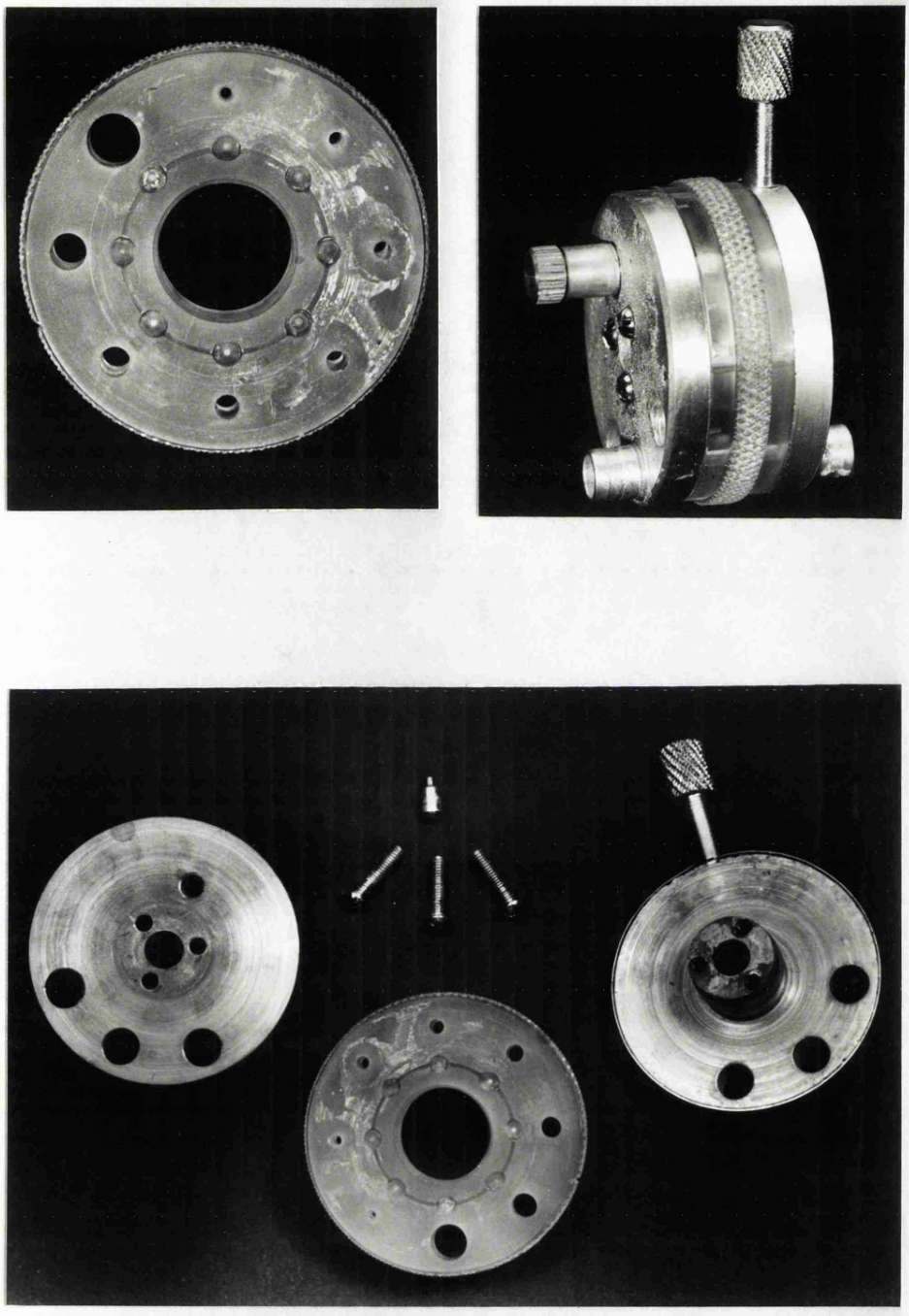


Figure 3. The variable stenosis in complete and component form. The adaptors with their suture grooves for tying into the artery are visible at the base of the complete version.

The assembly consisted of a central perspex disc rotating tightly within two alloy flanges; holes were available to irrigate the adjacent stenosed segments before insertion to ensure freedom from clots. The length of the stenosed segment was 10 mm. Individual diameters are recorded in Table II. The unstenosed internal diameter of the assembly was very slightly smaller than in the previous experiments.

TABLE II: DIMENSIONS OF STENOSED SEGMENT

Length (mm)	Internal diameter (mm)	Area reduction (%)
-	4.9	0
10	3.2	57
10	2.8	67
10	2.2	80
10	1.9	85
10	1.6	90
10	1.3	93
10	1.1	95

(iii) Measurement protocol

The preparation was left for 30 minutes with a zero stenosis in position. Once pressure and flow appeared stable, a series of Doppler waveforms was recorded from each of the four measurement sites shown in Fig 2. These were iden-

tified in individual dogs by the placing of artery clips attached to tissue adjacent to the artery. The absolute length between individual measurement sites varied slightly from dog to dog, but was about 20-30 mm, starting with a recording from close to the distal edge of the stenosis. If there appeared to be a large variation in waveform shape between two positions, then recordings were also made from intermediate sites. The distances between the stenosis and the main recording sites are shown in Table III.

TABLE III: IMPORTANT DIMENSIONS

DOG NUMBER:	27	28	31	32	33
ED+ of iliac artery (mm)	7.9	5.8	5.7	7.4	7.4
Stenosis to P_1 (mm)	22	33	26	24	24
Stenosis to P_2 (mm)	45	63	50	50	50
Stenosis to P_3 (mm)	68	88	73	75	75
Stenosis to P_4 (mm)	84	112	95	117	110

+ = external diameter

Although for safety waveforms were again recorded on AM tape, the timing of the recordings was less critical in these experiments and it was possible to use Doppler waveforms played through the spectrum analyser and recorded on ultraviolet paper in real time for subsequent analysis. A series

of at least five waveforms was recorded from each measurement site for each stenosis insert.

Once a full series of waveforms had been recorded at all the downstream sites, the stenosed segment was changed, stability quickly regained and a further series of measurements recorded at the same downstream sites. With the tight (93 & 95% area reduction) stenoses, clotting was a problem and if this occurred, waveforms were discarded. In all, 345 sets of Doppler waveforms were recorded from 79 changes of stenosis in the five dogs.

B. CALCULATION OF RESULTS

(i) Waveform classification

The majority of the waveforms recorded from close to the stenosis showed such marked flow disturbance that objective analysis was not possible. It was therefore decided to classify a set of waveforms into one of five possible groups according to a subjective assessment of the degree of disturbance. The major selection criterion was the smoothness or otherwise of the outline of the waveform. The groups were as follows: A-sharp, B-minor irregularity, C-disturbed, D-very disturbed and E-without structure. The classification was performed blindly by the author and an associate. Examples of sonagrams for each class are shown in Fig. 4.

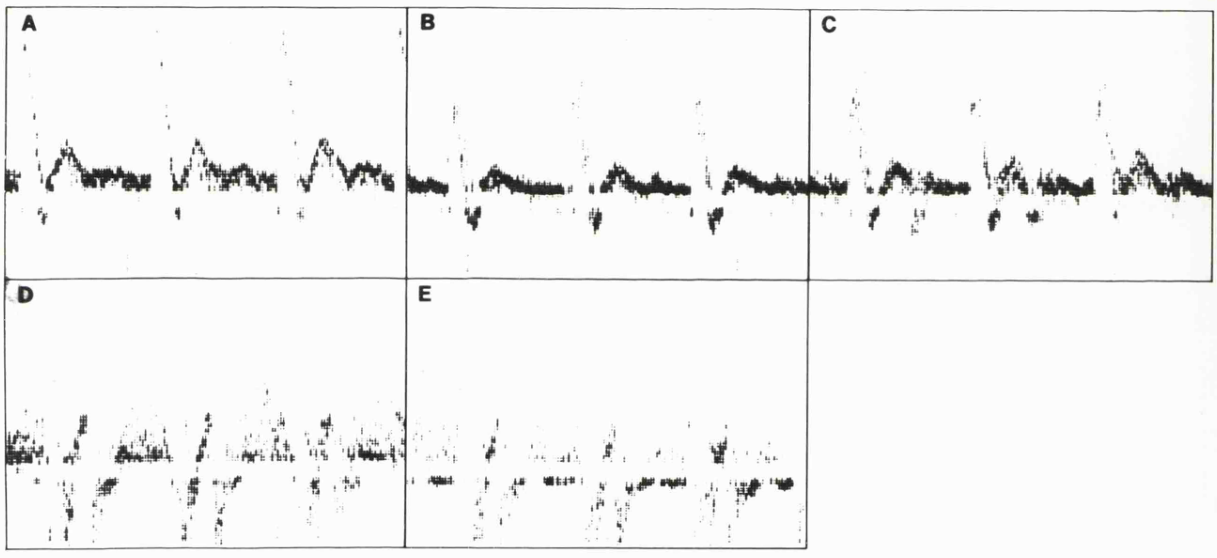


Figure 4. Examples of sonagrams in each class A - E.

(ii) Calculation of stroke length

It was possible to calculate stroke volume (V_s) by dividing mean flow through the stenosis (i.e. the flow measured by the EM flow meter) by heart rate at the time of measurement. Stroke length (L_s), the quantity used by Clark (128) for comparison with turbulence extent, could then be calculated:-

$$Ls = 4V_s/\pi D^2$$

where D is the unstenosed diameter of the vessel. This can be converted from millimeters to unstenosed diameters by dividing by D:-

$$Ls \text{ (unstenosed diameters)} = 4V_s/\pi D^3$$

Although the use of D rather than the true measurement of the undisturbed inflow portion of the iliac artery represents a slight approximation, it is the true size of the tube immediately before the stenosis and, when compared with d, the stenosis diameter, is large enough for the approximation to have a minimal effect on the results.

(iii) Extent of turbulence

In Clark's work this was determined by an indicator dye and high speed photography. In the present study it was decided simply to choose the point downstream at which a

Doppler waveform reverted from class C to class B. Although rather arbitrary this seemed the only method applicable to such an in vivo study, and when carrying out the waveform classification it was always possible to decide to which of these groups a particular waveform belonged. The method is clearly less accurate than Clark's, if only because we took measurements at a limited number of sites downstream. If there was any doubt at the time of the experiments, further intermediate recording sites were sometimes used. In practice the method of subjective classification gave consistent results as can be seen from the details in Appendix C where there is almost always a regular transition from disturbed to less disturbed classes with increasing distances downstream. Class B waveforms, although described as irregular, did not in fact usually show much sign of flow disturbance but lacked the perfect outline which identified waveforms in class A.

C. RESULTS

The full results of this series of experiments will be found in Appendix C. This represents a chronological record of each measurement run and is complete apart from a total of 21 waveforms (almost all from the 95% area reduction stenosis) in which clotting was obviously occurring.

Examples of waveforms at varying distances below the

stenoses are shown in Fig 5. A trend can be seen in this visual representation with waveforms recorded from below a zero stenosis all being clearcut and those below a tight stenosis all being disturbed until a long way downstream. These changes can be seen more clearly in Fig 6 where each value represents the number of waveforms for a particular stenosis and recording site belonging to each of the classes A-E. For the zero stenosis, nearly all waveforms, apart from those recorded from adjacent to the stenosis, are class A or B. With tighter stenoses more points appear in the more disturbed categories, particularly when recorded close to the stenosis, but the waveforms usually revert to A by 22 diameters downstream.

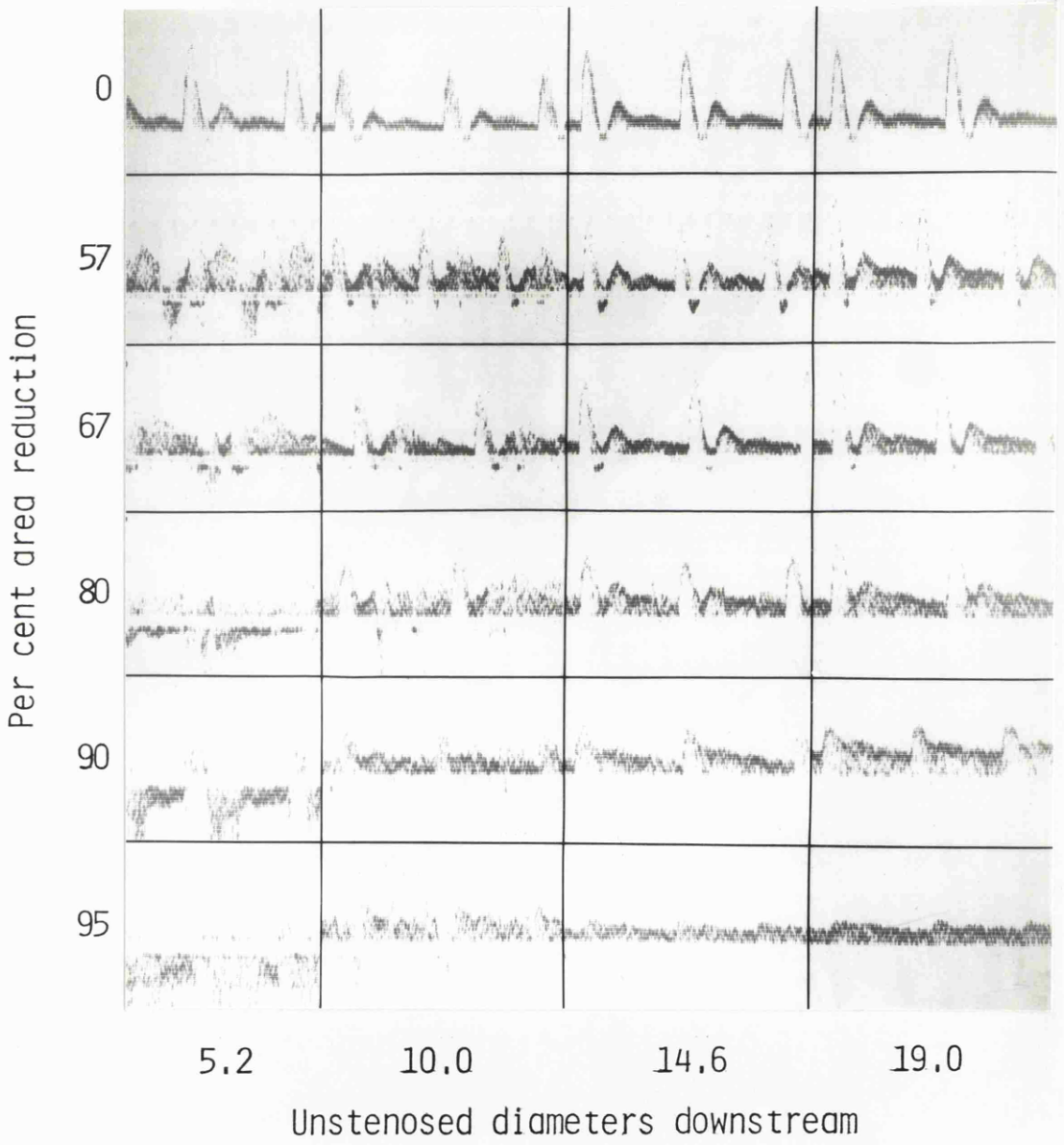


Figure 5. Examples of waveforms recorded from varying distances downstream from different stenoses.

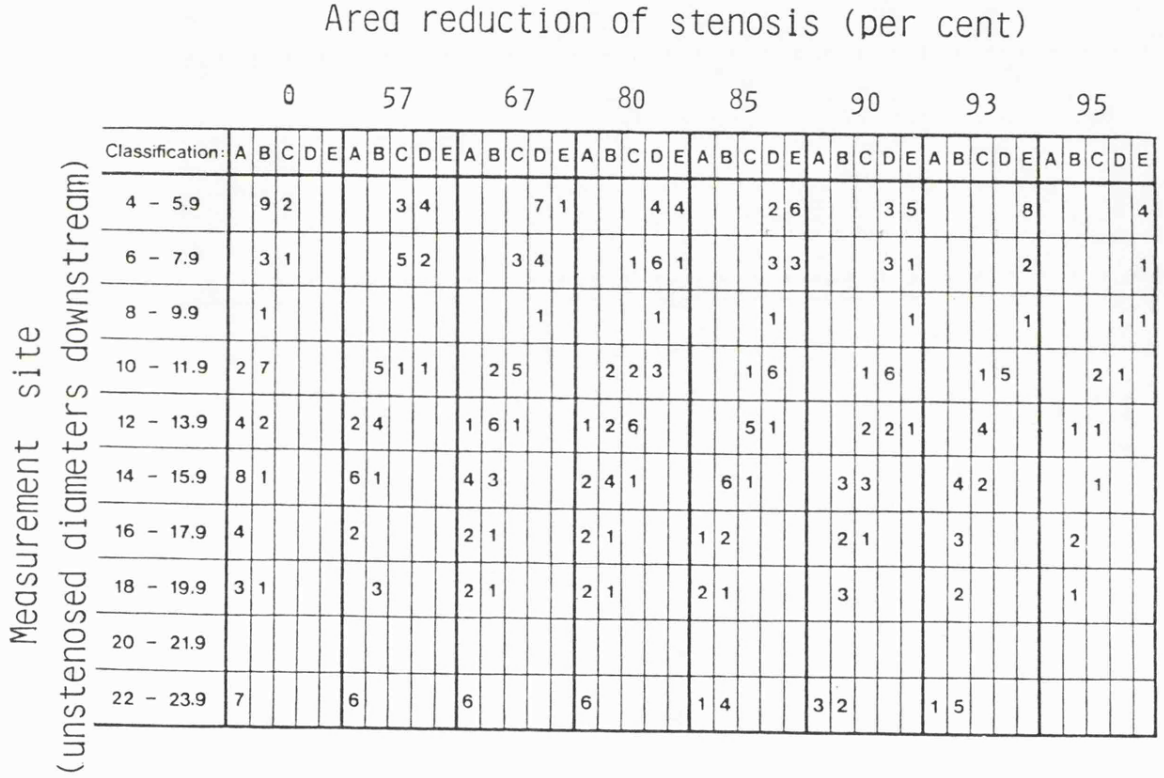


Figure 6. Classification of individual sets of waveforms according to stenosis severity and distance downstream of the recording site. The figures represent the actual number of observations in each category at a particular site.

This information is presented in a rather simpler form in Table IV. Here the average value for the classification of all waveforms recorded from the various recording sites is shown. The trend of greater propagation of turbulence with the tighter stenoses is clearly seen.

TABLE IV: AVERAGE WAVEFORM CLASSIFICATION FOR EACH RECORDING SITE IN THE FIVE DOGS.

STENOSIS: (% area reduction)	0	57	67	80	85	90	93	95
POSITION:								
1	B	C/D	D	D	E	E	E	E
1.5		C	C	D	D	D		
2	B	B	B/C	B/C	D	D	D	
2.5		A/B	B	B	C	C	C	
3	A	A	A	A/B	B	B	B	
4	A	A	A	A/B	B	B	B	

The extent of the turbulence should also increase with stroke length. Using the point where most waveforms revert to B from C, it is possible, with rather wide confidence limits, to construct a series of values for each of the stenoses from 57 to 93% area reduction (Fig 7). From Clark's work a gradual increase in length of disturbance propagation would be expected with increasing stroke lengths; this was not found in this study, probably because of (i) the inaccuracy in determining the end point and (ii) the limited range of stroke lengths produced by an in vivo model. The range

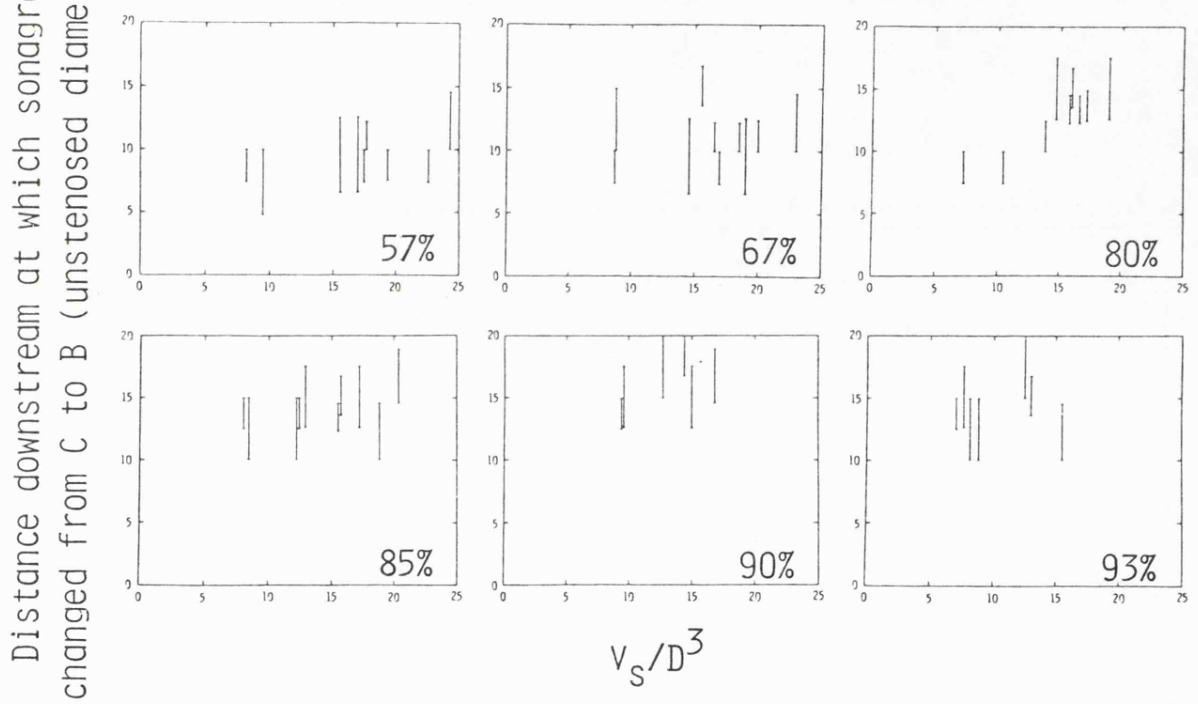


Figure 7. The effect of stroke length on disturbance propagation. The error bars indicate considerable variability of the results; the range of stroke lengths is limited.

of stroke length in all the dog experiments was from 8 to 36 unstenosed diameters, but the majority of points were in the rather narrower range of 12 to 24 unstenosed diameters, so limiting the range of values available for assessment.

D. DISCUSSION

Although of necessity subjective, this study is useful in that in vitro results are confirmed, at least with regard to the increasing distances which disturbed flow is propagated by increasing stenosis. The effect of stroke length would probably have been clearer given a wider range of values and a better method of assessing the extent of turbulence propagation.

Extrapolating to diseased human arteries must be done with caution, but the following points can be made. First, moderate degrees of stenosis (50 - 80% area reduction) will probably not be detected by Doppler at normal flow rates unless the probe is within 8 - 10 unstenosed diameters of the lesion. For example a 75% stenosis at the common iliac origin is unlikely to be recognised by a probe at the common femoral artery by the detection of disturbed flow. It is possible that such a stenosis may cause changes in the overall shape of the waveform but the outline will be smooth. Secondly, local flow disturbances can certainly be detected

but they may be caused by relatively small lumen incursions which are not responsible for much disability. If it is possible to make recordings from several points at varying distances from a diseased segment, a good deal more may be learned than from a single site: this may be particularly relevant to the carotid artery, but is not likely to be useful in the aortoiliac region as good recordings can only be obtained from a relatively short segment of the vessel. Finally, the difficulty of recognising flow disturbance subjectively, and the absence of objective methods which might quantify it, make it unlikely that it will be possible to exploit it diagnostically unless combined with other techniques such as imaging of the vessel.

E. CONCLUSIONS

Flow disturbance due to arterial stenoses can be assessed qualitatively by cw Doppler: such disturbances are transmitted further downstream the tighter the stenosis. This study does not show a clear relationship with stroke length, but this is probably due to inadequacies of the method. In any event, any such relationship is unlikely to be useful diagnostically as stroke length is hard to alter in clinical practice. Although the findings of this study may well be relevant to other arteries such as the carotid, it is unlikely that the presence of disturbed flow in common femoral waveforms will improve the assessment of aortoiliac disease.

Chapter 8

THE METHOD OF PATIENT ASSESSMENT

At the outset of the study it was not clear which test would be of most value in detecting aortoiliac disease; in consequence, more data was collected on each patient than was subsequently utilised. Because of previous experience in the department it was possible to devise a test protocol which, hopefully, would include adequate information; this was adhered to in the majority of cases although by the end of the study it had become clear that some of the procedures were of little value.

A. PATIENT REFERRAL

An attempt was made to include a broad spectrum of patients with varying patterns of arterial disease rather than to concentrate on those, for example, with predominantly distal or proximal lesions. Selection was biased towards those patients in whom surgery was a definite possibility in order that arteriography would be performed, but patients did not undergo arteriography merely because they were included

in the study. The only invasive part of the test protocol, direct pressure measurement, was already well established in the department as a test of aortoiliac disease and it was therefore not felt necessary to take the protocol to the ethical committee for its approval.

The referring clinician was asked to fill out a simple form in which the peripheral pulses were assesssed according to the method described in Chapter 5. This was done before arteriography although in some cases a previous arteriogram was available. The clinician was also asked to suggest which operation, in his opinion, should be performed on the basis of this initial assessment. An example of such a form may be found in Appendix A.

The majority of patients attended the vascular laboratory as out-patients as part of their pre-operative work-up. Most of these were claudicants; patients with more severely ischaemic limbs were usually admitted and studied as in-patients. All but two patients had clear evidence of degenerative occlusive arterial disease. One of the exceptions was a 20 year old female with Raynaud's disease and the other an 11 year old boy with a previous traumatic occlusion of his superficial femoral artery. Neither of these patients, nor four of the arteriopaths, underwent arteriography. Three healthy young subjects were also included in the Doppler study, but a large group of normals was not thought to be

necessary as controls; it was felt that the asymptomatic limbs of the patients would be more valuable in this respect.

B. THE TEST PROTOCOL

Patients were brought to the vascular laboratory at a convenient time: the tests were not, therefore, all conducted at the same time of day but this was not thought to be a serious defect. The temperature of the room was monitored and kept in the range $22\pm2^{o}C$. The patients reclined on a standard examination couch with one or two pillows according to their comfort, and rested there for at least 20 minutes before the start of the test. During this time, basic clinical information was acquired including a brief outline of the presenting complaint, relevant past history, drug therapy and associated problems such as diabetes or smoking. An explanation of the tests was also provided. Peripheral pulses were palpated and bruits noted: pulses were assessed on the same basis as that used by the referring clinicians. A series of leg measurements was also obtained: the object was to be able to determine absolute blood flow per ml of tissue, having calculated leg volume from the measurements. ECG electrodes were attached in order to trigger a microprocessor through an R-wave detector for the on-line calculation of PI.

Following the 20 minute rest period, Doppler signals were recorded from the right and left common femoral arteries in turn. The clearest sounding and looking signal was chosen, no attempt being made to keep the probe at the same angle for all patients. While the author was positioning the probe a technician adjusted the controls of the spectrum analyser until a satisfactory waveform was obtained. A series of waveforms in which PI was calculated in real time was followed by a continuous run of at least five waveforms without PI calculation which were used subsequently for digitisation. Doppler waveforms were then recorded from the popliteal and pedal arteries on each leg with on-line calculation of PI.

Resting ankle pressure was then measured in each leg using a standard 12cm cuff and the method described by Yao (86). The cuff was placed around the lower calf just high enough to allow insonation with the Doppler probe of the posterior tibial artery behind the medial malleolus. Values were obtained for both dorsalis pedis and posterior tibial vessels, but occasionally the peroneal was used if a good signal could not be obtained.

Those patients who were able to walk were then exercised on a treadmill. The speed was adjusted to suit the individual patient and was normally about 3 km/hr. The patients exercised on the level for 5 minutes or until their claudi-

cation prevented them going further. The exercise time and speed were then recorded. They were then transferred back to the examination couch and Doppler waveforms were again recorded from each femoral artery in turn at time 0, 5 and 15 minutes after completion of exercise.

Once the patients were fully recovered the direct pressure studies were performed. The manometer system had already been calibrated; pressure lines were attached to 21 gauge needles and to the pressure transducers and the whole system flushed with saline. Local anaesthetic, approximately 5 ml of 1% lignocaine, was infiltrated subcutaneously in each groin. The needles were then inserted into each femoral artery immediately below the inguinal ligament. This was usually simple to perform but occasionally, especially in obese patients or when the femoral pulse was rather weak, it was not possible to find the artery with the needle. The chart recorder was in operation and an assistant was able to indicate whether the waveform recorded by the system was satisfactory. He was also able to notice the appearance of any damping of the waveform which usually meant that the needle had become displaced or that clotting was taking place. The needle could then be repositioned or the system flushed with more saline. Towards the end of the study no attempt was made to record from femoral arteries with obviously diminished pulses. A record of the pressure studies carried out in patients, including any difficulties with the

method, will be found in Table VI of Appendix D.

When satisfactory pressure waveforms were obtained from both sides, 20 mg papaverine sulphate was injected through one of the pressure lines. The hyperaemic response was recorded continuously on the chart recorder until a steady state was reached. Maximal flow (and hence pressure drop) was usually found to occur about 15 sec after the injection of papaverine and recovery took from 1-3 minutes. Papaverine was then injected down the other pressure line to study the opposite leg. In a small number of cases when an adequate control needle could not be inserted, central systolic pressure was recorded indirectly using an arm cuff. From the recordings it was possible to derive a value for any resting pressure gradient and also the maximal hyperaemic gradient for each limb. The method for grading the response to papaverine was described in Chapter 5. Examples of the pressure recordings during papaverine tests on patients with normal and significantly diseased proximal vessels are seen in Figs 1 and 2.

No local or embolic complications were noted in approximately 100 arterial puncture attempts. One patient became markedly hypotensive following the injection of papaverine, but he recovered quickly and was able to go straight home from the vascular laboratory. The standard Doppler and pressure test described above took about 2 hours to perform.

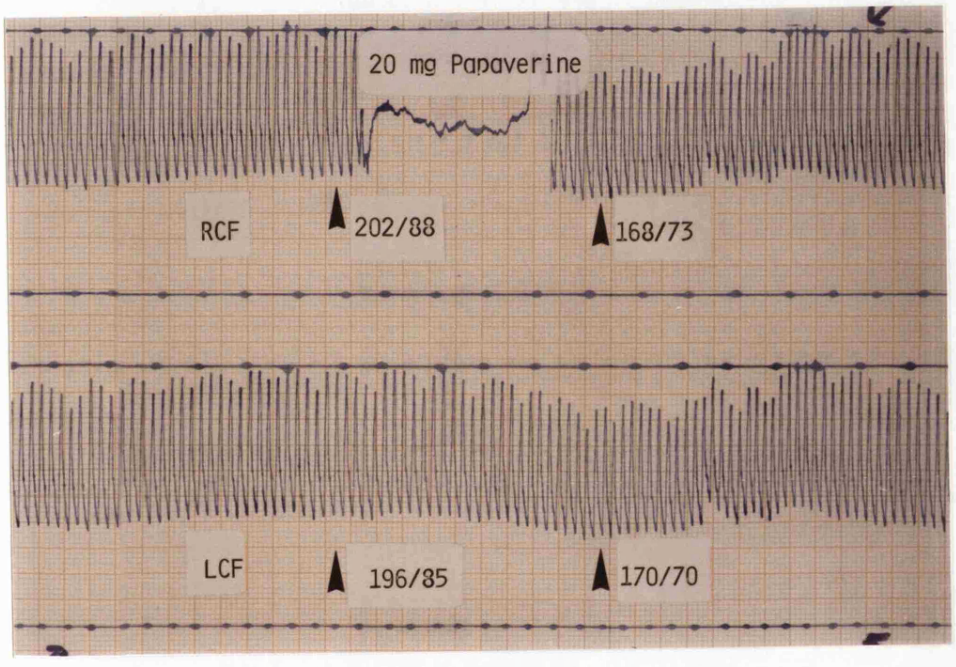


Figure 1. Pressure waveforms recorded from the left and right common femoral arteries and the effect of the intra-arterial injection of papaverine. There is no significant pressure gradient either before or after, although there is a marked fall in systemic pressure which quickly returns to normal.

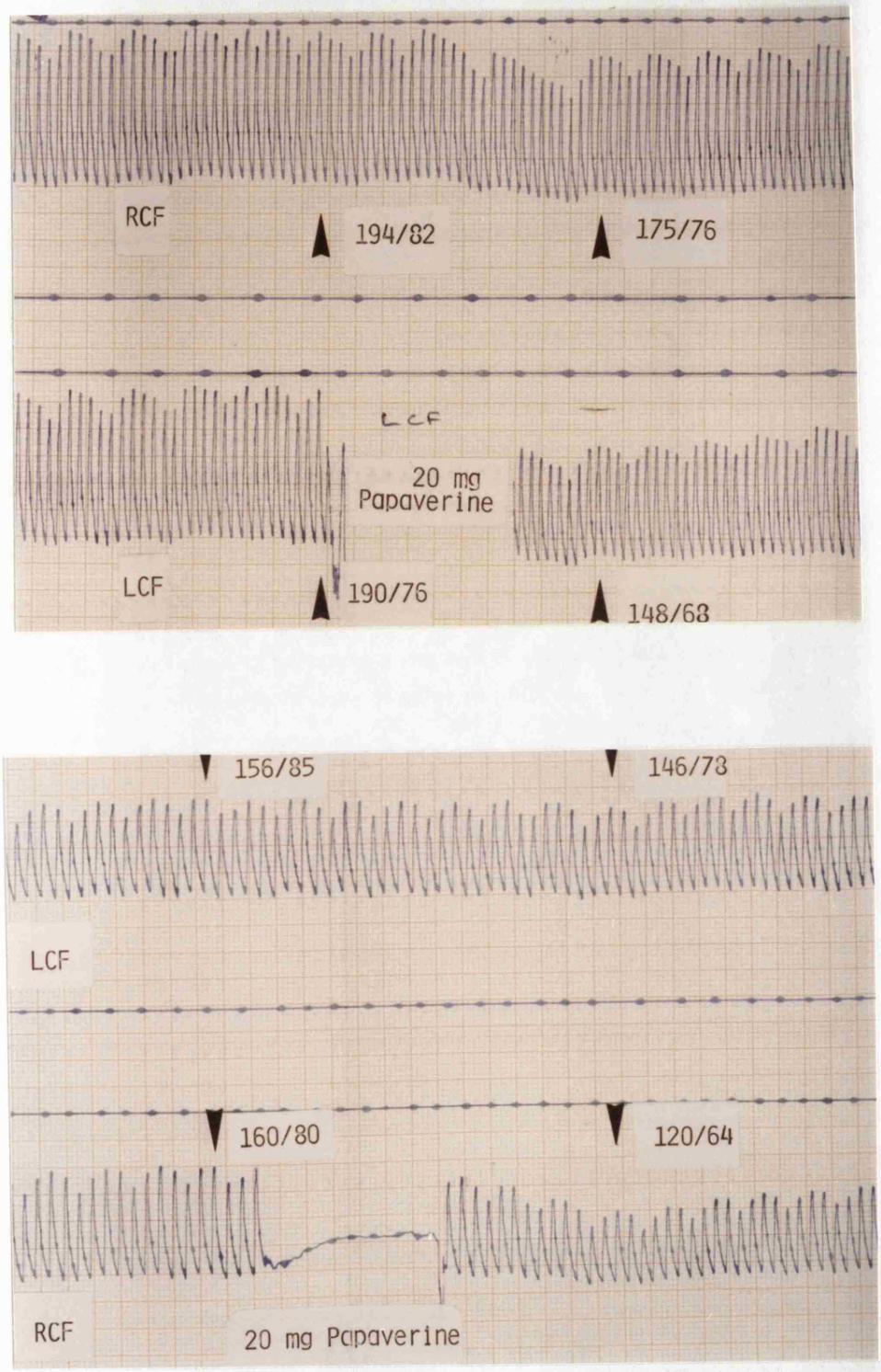


Figure 2. Pressure waveforms recorded from the left and right common femoral arteries: two examples of 'significant' pressure gradients after papaverine.

Most patients underwent a single assessment. In a small number of cases a further assessment was performed 6-12 months later, usually when there was a genuine clinical problem, and this interesting sub-group will be described with the results in the next chapter. A few patients had pressure and/or flow studies performed at operation within a few days of their assessment and this data was used for comparison with the Doppler results if for any reason the laboratory pressure study was inadequate.

C. PATIENT FOLLOW-UP

No further formal testing was done in the majority of patients. However, between 2 and 3 years after the study their case notes were reviewed and their clinical course documented. Although this method has obvious disadvantages, it was felt unreasonable to submit a group of patients, often elderly and infirm, to another rigorous test when there was no longer an active management problem. Many of the patients were, however, seen by the author himself in the follow-up clinic. This information was not used as part of the comparative study whose results will be found in the next chapter; however in a few cases useful clinical information was extracted. For example, the persistence of a femoral pulse thought to be weak at the initial assessment but still palpable 3 years later, or the survival or otherwise of a

vascular graft, allowed a further chance for comparison with the results of the clinical tests; some of this information will be referred to briefly in the discussion in Chapter 9.

Chapter 9

RESULTS OF THE PATIENT STUDIES

Of the data recorded from the protocol outlined in the last chapter, the analysis of common femoral Doppler waveforms was the central component and was available in all patients. Comparison was then possible with the clinical assessment of the femoral pulse, direct femoral artery pressure measurements and with arteriography. It was clear that, while usefully excluding limbs with serious overall vascular disease, neither ankle pressure nor pressure index was going to contribute toward the assessment of proximal narrowing, although they remained useful clinical parameters particularly in those patients undergoing reconstructive surgery.

Similarly, the Doppler waveforms recorded from the femoral artery after exercise were not utilised further. The main reason for this was the tendency of the hyperaemic waveforms to have irregular outlines possibly due to turbulence, making objective analysis difficult. It is possible that with a faster analyser such irregularities could be smoothed out and, in theory at least, hyperaemic Doppler signals, or

perhaps the time taken for them to return to normal following exercise, might form the basis of a useful test of proximal narrowing. Again, because of the obvious difficulties of measuring volume flow with cw Doppler, the leg dimension measurements were not in fact used in the manner suggested in the last chapter.

The patient results are found in Appendix D. The raw results of Doppler waveform analysis are presented in Table D-I (PI and LTD) and Table D-III (PCA). Mean values of PI, LTD and the first two PC coefficients have been extracted and can be found in Tables D-II and IV; the latter table also includes the information content of the 32 principal components. Tables D-I to D-IV are derived directly from the original computer print-outs in order to eliminate errors in transcription. The summarised results are also found in Table D-V together with the results of femoral pulse palpation, arteriography and the pressure tests. A further parameter, standard clinical assessment, is also listed: its derivation will be described later in this chapter. The direct pressure results are listed separately in Table D-VI together with explanatory notes and reasons for exclusion from this part of the study. The comparisons of data found in the tables and figures in the remainder of this chapter are derived from these results.

A. STANDARD METHODS

(i) Comparison of arteriography with femoral pulse palpation

The results of this comparison in 92 limbs are shown in Table 1. There is a broad agreement between the two methods and roughly the same numbers of limbs are classified above and below the diagonal of agreement, suggesting that the scoring system has achieved its aim of comparability. There is disagreement by more than one classification in only 5 limbs, one where the pulse felt very weak but arteriography was normal, and four where palpation was normal but arteriography showed a greater than 50% stenosis. It is unlikely that those graded by palpation and arteriography in either groups 3 or 4 will be missed - clearly such patients require proximal reconstruction. Of more interest are those five patients already mentioned who had marked disagreement between the two methods, and also all patients in either clinical or arteriographic grade 2 - a total of 49 limbs (53%).

Without further assistance from other tests, the clinician is faced with a difficult decision; very often this will be simply to wait and see, although if forced into an operation some will believe their fingers, and others the arteriogram. One can conclude, from this simple examination of basic data, that there is a genuine need for objective tests in this diagnostic area.

TABLE I: COMPARISON OF FEMORAL PULSE WITH ARTERIOGRAPHY

(Figures represent numbers of limbs in each category; those underlined indicate agreement between the two methods.)

		FEMORAL PULSE GRADE:			
		1	2	3	4
ARTERIOGRAPHIC GRADE:	1	23	11	1	0
	2	17	9	4	0
	3	4	3	4	3
	4	0	0	5	8

(ii) Comparison of arteriography and femoral pulse palpation with direct pressure measurements

It was similarly possible to evaluate direct pressure measurement using the results of the papaverine test. The limbs were graded as described in Chapter 5, and the results are presented in Tables II and III. If the limits of the pressure gradients chosen are justified (and on theoretical grounds they are) then it is clear that direct pressure gradient measurement provides a much more sensitive assessment of aortoiliac disease than either palpation or arteriography.

TABLE II: COMPARISON OF FEMORAL PULSE WITH DIRECT PRESSURE

(Figures represent numbers of limbs in each category; those underlined indicate agreement between the two methods.)

		PRESSURE ASSESSMENT:			
		1	2	3	4
FEMORAL PULSE					
GRADE:	1	<u>26</u>	7	8	8
	2	7	<u>5</u>	2	9
	3	0	0	<u>1</u>	9
	4	0	0	0	<u>7</u>

TABLE III: COMPARISON OF ARTERIOGRAPHY WITH DIRECT PRESSURE

(Figures represent numbers of limbs in each category; those underlined indicate agreement between the two methods.)

		PRESSURE ASSESSMENT:			
		1	2	3	4
ARTERIOGRAPHIC					
GRADE:	1	<u>17</u>	4	3	3
	2	8	<u>5</u>	6	7
	3	0	0	<u>1</u>	10
	4	0	0	0	<u>4</u>

<u>(iii) Definition of standard clinical assessment</u>

It was possible to compare the Doppler results with individual standard assessments using either arteriography or

the direct pressure measurements. However, it is known that occasionally the papaverine test can be misleading, usually because the flow increase is inadequate, and it may be unrealistic to rely on the pressure test alone as the gold standard in all cases. A further combined assessment, that of standard clinical assessment (SCA) was therefore proposed and a similar grading system utilised.

SCA was defined by what the referring clinician actually decided to do with the patient after pulse palpation, arteriography and direct pressure measurements. In some cases there was conflict between the various assessments: if, for example, pulse palpation and arteriography were normal but the pressure study showed a significant drop, the latter test was usually ignored. If there was disagreement between palpation and arteriography, then an unequivocal pressure study could swing the decision appropriately. The Doppler results were not used as part of this assessment.

Limbs were graded into one of five categories. The first group included all those with unequivocal severe aorto-iliac disease. The second group consisted of patients with significant superficial femoral artery disease as defined radiologically but with a relatively normal proximal segment. If surgery were contemplated in this group, then a primary femoro-distal operation would be performed. A third group of patients included those with relatively normal proximal

and distal vessels. Such limbs were usually found in patients who had disease on the opposite side, and were thus not true normals. A fourth group of limbs was made up of those with genuine uncertainty about the status of the proximal vessels. Some members of this group had superficial femoral artery disease and others did not. A final small group of true normals was also included. The classification is summarised in Table IV.

TABLE IV: DEFINITION OF STANDARD CLINICAL ASSESSMENT

Grade	Definition
1	Unequivocal aortoiliac disease
2	Severe SFA disease; AI segment probably normal
3	Relatively normal proximal and distal vessels
4	Clinical uncertainty about proximal vessels
5	True normals

It was felt that this system of classification was justified because it reflected the standard practice in the unit at the outset of the study. The criteria for inclusion of a particular limb in either of the first three clear cut clinical groups were sufficiently strict to make it very unlikely that such limbs would be classified incorrectly; the method should, therefore, provide a sound basis for comparison with the Doppler results. The separation of the limbs with superficial femoral artery disease became necessary when soon

after the start of the study it was obvious that such distal disease had a significant effect on common femoral artery waveform shape. The reasons for classifying 24 limbs in the fourth group, those with clinical uncertainty, are summarised in Table D-VII in Appendix D.

B. DOPPLER METHODS (I)

In this section the results of the various Doppler methods will be compared with standard clinical assessment as defined above.

(i) PI compared with SCA

The results are shown in Fig 1. Each point represents one limb and is the mean of five waveforms. There is a good separation between the normals (Groups 3 and 5) and those limbs with severe aortoiliac disease. It is possible to draw a dividing line between these two groups so that only 7 limbs are misclassified. Three limbs with severe aortoiliac disease are, however, clearly wrong and will be discussed later. They were also incorrectly classified by the other Doppler methods. Those patients with a diseased superficial femoral artery but relatively normal proximal vessels have a range of values intermediate between the normals and the limbs with severe proximal disease. PI therefore appears to

be lowered by SFA disease. This has been noted previously by Baird et al (151) although other workers (Aukland et al (137)) did not find a statistically significant difference. In this study there is unequivocal evidence of a reduction of PI caused by SFA disease.

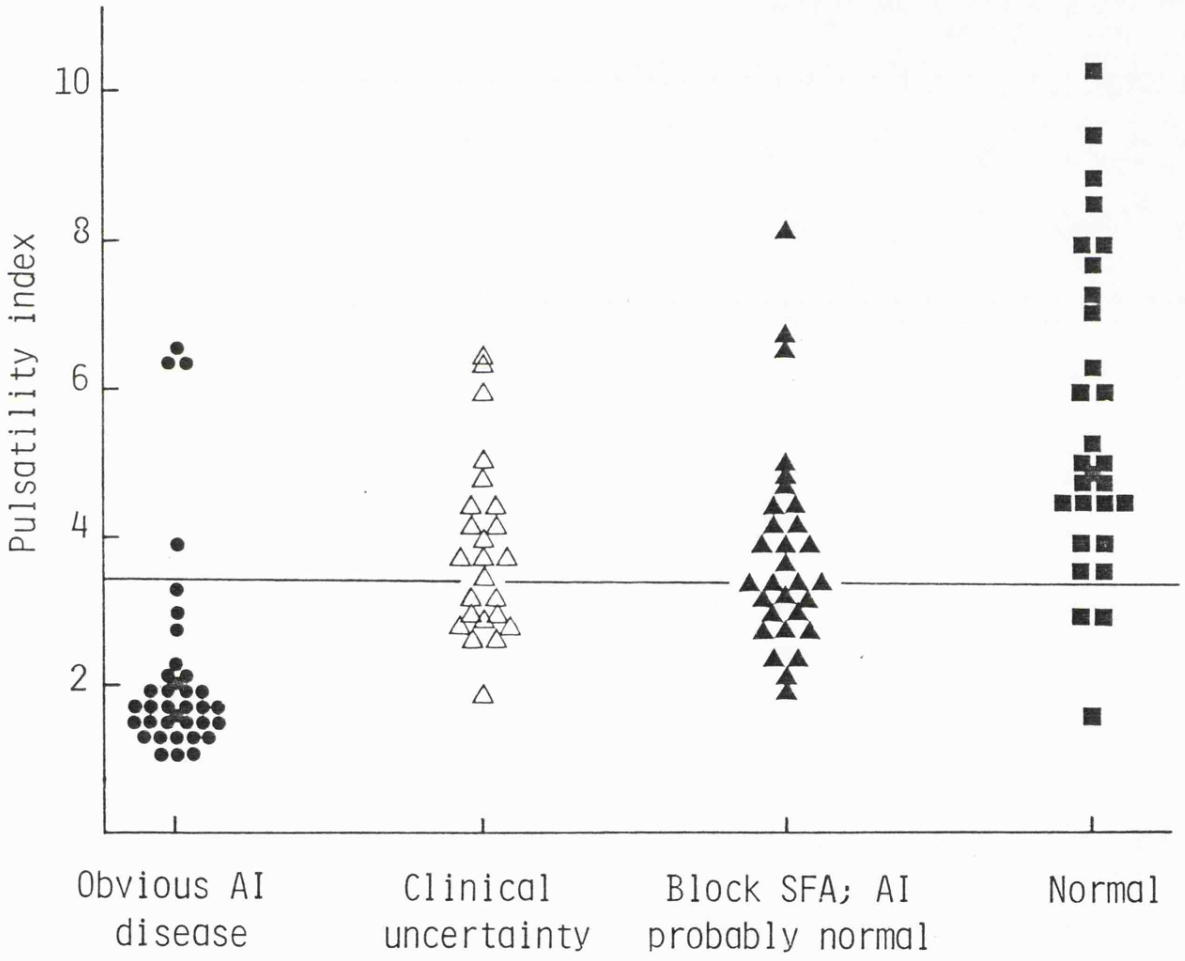


Figure 1. PI compared with standard clinical assessment for each limb in the study. The division has been drawn so that the smallest number of limbs in the extreme groups are misclassified (normals and those with severe proximal disease).

Although each of these clear cut groups is statistically distinguishable from the others, there is marked overlap of results especially in the range of values of PI between 2 and 4. A single normal limb has a very low PI; again this limb was misclassified by all Doppler methods because of a localised lesion in the common femoral artery.

Looking now at the limbs where clinical uncertainty remained after standard assessment, it can be seen that values of PI are predominantly in the 2-5 range and overlap all the clear cut groups. The value of PI in this difficult group of patients would thus appear to be limited.

By excluding the 3 limbs with aortoiliac disease and a high PI, and 1 limb with no aortoiliac disease and a low PI, there is excellent separation between the extreme groups. It is only by including the intermediate group with SFA disease that it becomes clear that PI is not going to add significantly to discrimination.

(ii) LTD compared with SCA

The results are presented in Fig 2. There is broad comparability with the results for PI although there appears to be more overlap between the clear cut groups. Those patients where there was clinical uncertainty (Group 4) are scattered over a wide range of values of LTD and overlap

almost completely with the ranges for the three clinically distinct groups. LTD would appear to offer no advantage in this respect over PI.

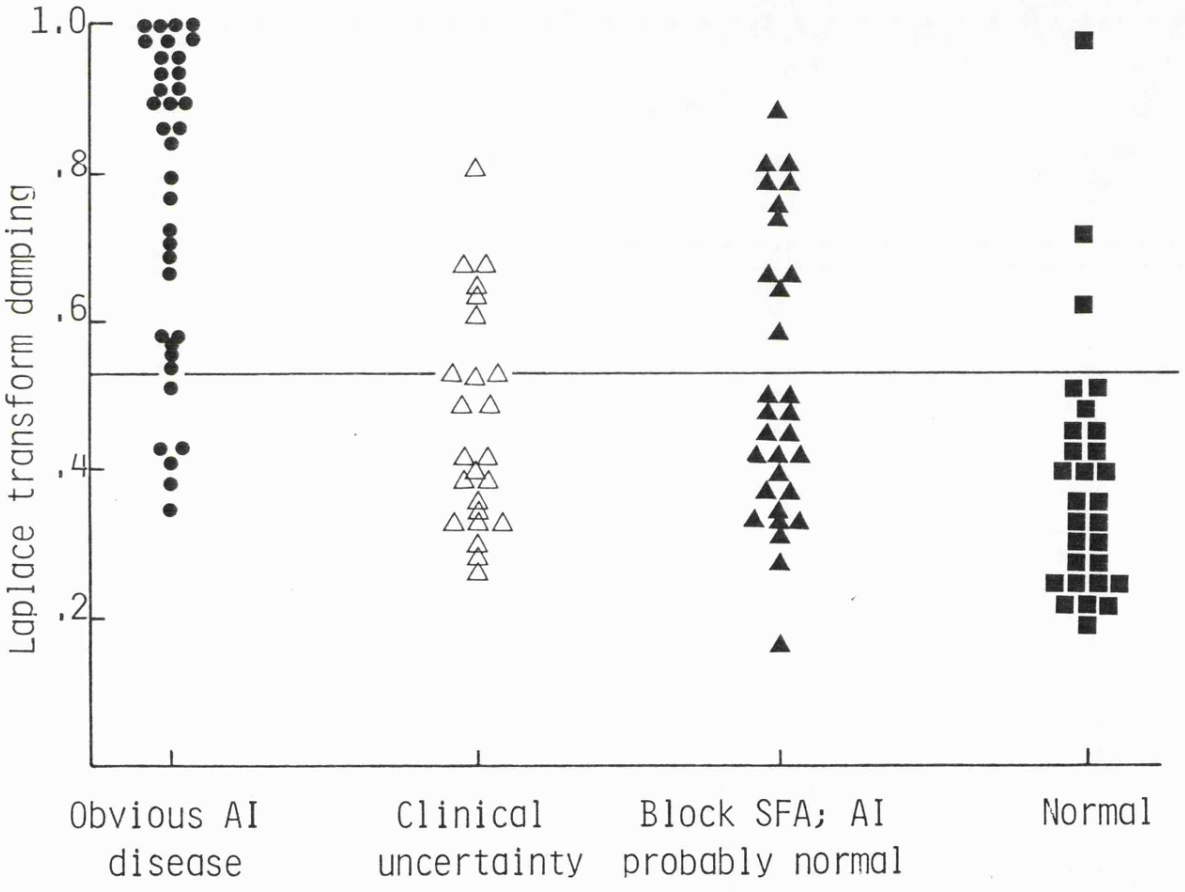


Figure 2. LTD compared with standard clinical assessment. The division has been drawn using the same criteria as in Fig 1.

(iii) The relationship between PI and LTD

Although calculated in an entirely different fashion, both these parameters are clearly affected by proximal narrowing and in the animal work (Fig 16, Chapter 6) had been shown to be related. In the patient study, those limbs with obvious aortoiliac disease tended to be clustered at low values of PI and high values of LTD, but there was otherwise no discernible relationship between the two values (Fig 3).

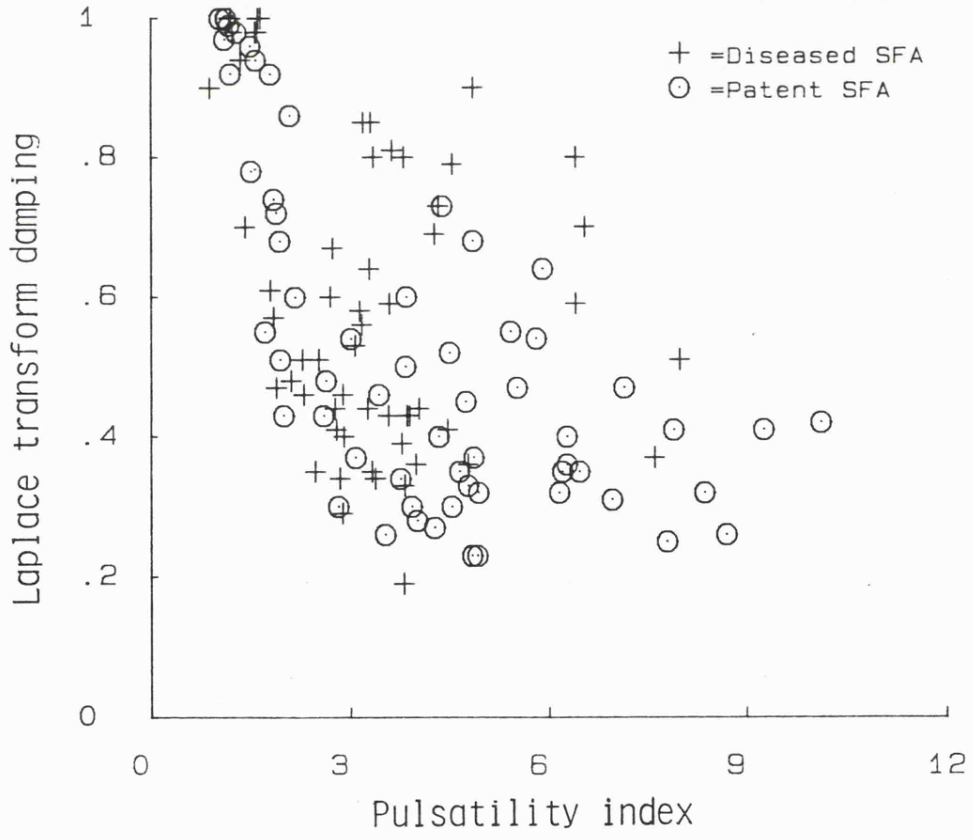


Figure 3. The relationship between PI and LTD for each limb.

(iv) PCA compared with SCA

The method as originally applied to Doppler waveforms and as subsequently used for the present work has made use of the first two principal components. The coefficients for the limbs in the clinically clear cut groups are plotted in Fig 4 and it is possible to identify three areas where the points are clustered. This method therefore appears to be able to distinguish the three important groups with very little overlap between them.

It is possible to separate these groups by a variety of methods but the one which gives the best results is the Bayes classifier technique which assumes that each class has a bivariate normal distribution (171). The dividing lines in Fig 4 have been constructed using this method, and applying it to the clinically clear cut patients, 77 out of 92 limbs (84%) are correctly classified. When the doubtful limbs are added (Fig 5) they are spread over the three main areas; however it is possible, using the Bayes method, to ascribe a probability that a particular point is in fact correctly classified. These probabilities are listed in Table V: the patient identifying number is followed by the coefficients of the first two principal components and the classification of each of the uncertain points by the method. P(1), P(2) and P(3) are the probabilities that a particular limb belongs to clinical groups 1, 2 and 3 respectively. Seven of the 23

limbs in Group 4 are classified with a probability of >.9 into one of the three clear groups. It is not possible to achieve this kind of separation with either PI or LTD because of the marked overlap between the groups; this difficulty is mainly due to the influence of superficial femoral artery disease on these parameters. PCA appears to be able to allow for this and the method seems to come closest to clinical usefulness.

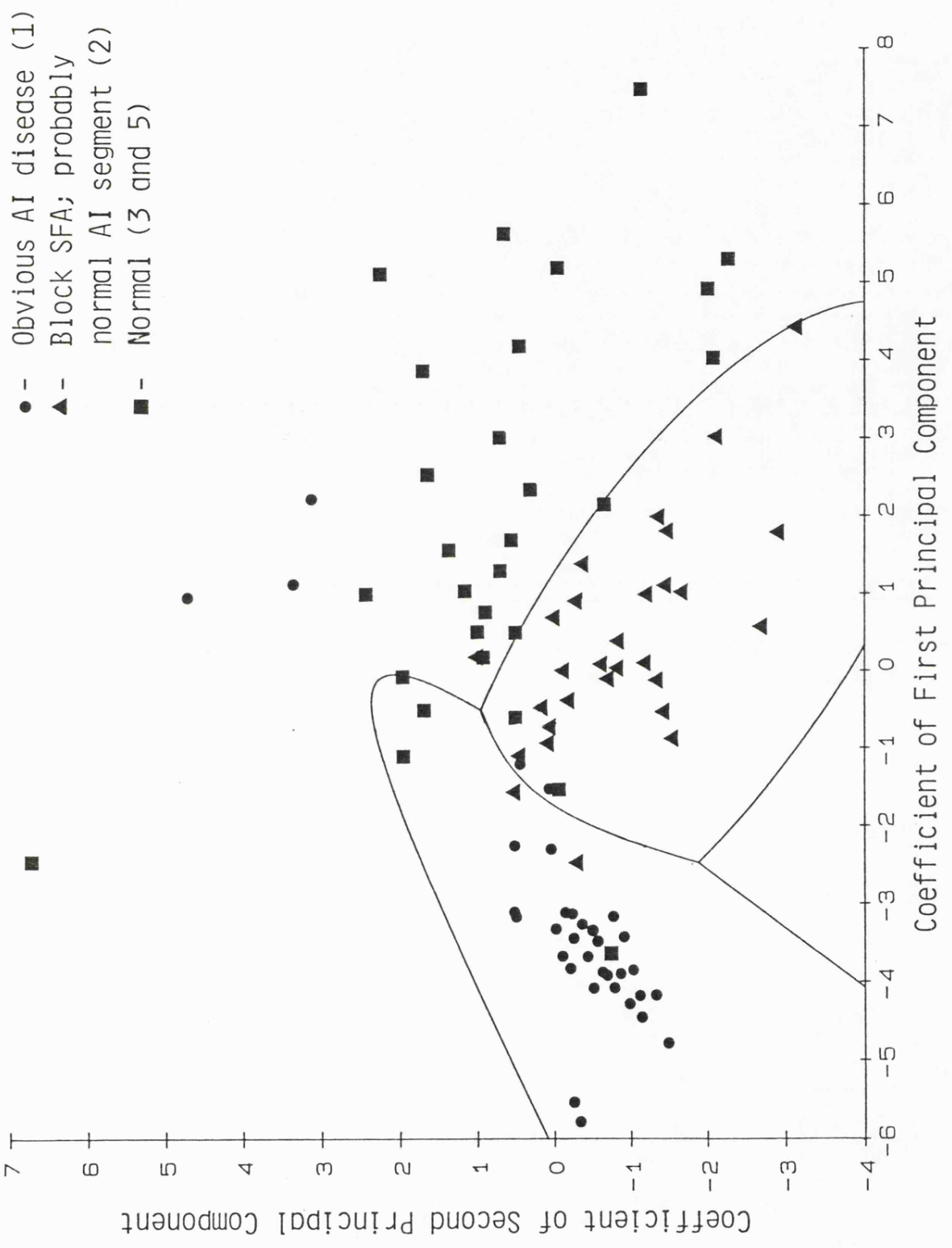


Figure 4. The coefficients of the first and second principal components for clinical groups 1,2,3 and 5. The dividing lines have been drawn using the Bayes classifier technique.

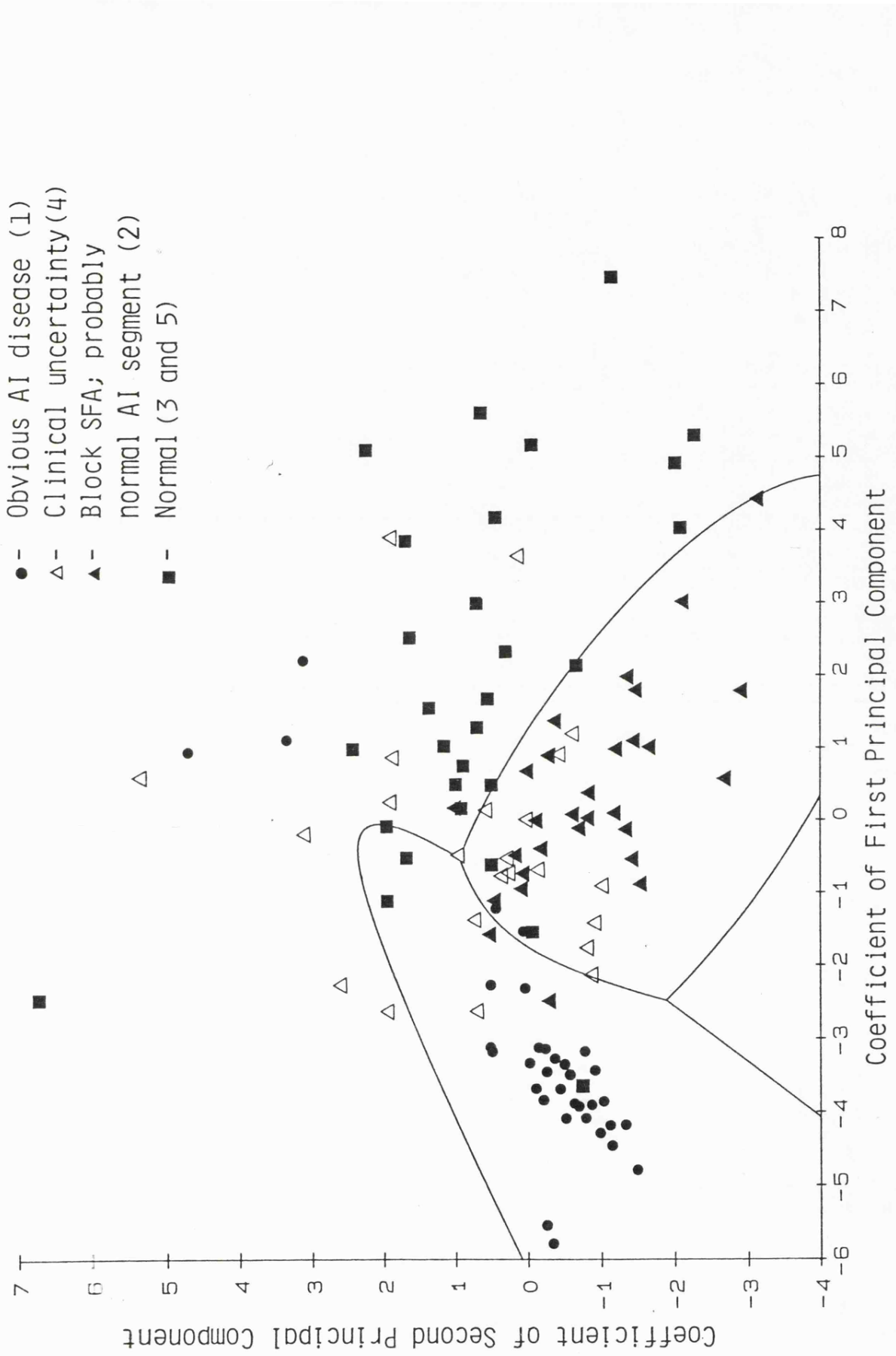


Figure 5. The same data as in Fig 4, but now including limbs with clinical uncertainty about proximal disease (Group 4).

TABLE V: THE MOST PROBABLE CLASSIFICATION FOR EACH OF THE WAVEFORMS IN GROUP 4 (THOSE WITH CLINICAL UNCERTAINTY) TOGETHER WITH A MEASURE OF THIS PROBABILITY.

PATIENT IDENTITY	PC1	PC2	CLASSED IN GROUP:	P(1)	P(2)	P(3)	SFA CLASS
1854	3.65	0.12	3	.000	.001	.999	1
1864	1.23	-0.60	2	.000	.823	.177	1
1904	0.16	0.55	2	.009	.558	.433	0
1944	-2.40	1.95	3	.236	.176	.589	1
2024	0.27	1.88	3	.338	.005	.656	0
2034	-2.62	0.66	1	.873	.098	.028	---
2091	-0.68	-0.16	2	.006	.914	.081	0
2094	-0.75	0.31	2	.073	.786	.141	0
2121	0.70	1.90	3	.152	.002	.847	1
2171	-2.25	2.58	3	.018	.032	.950	1
2194	3.90	1.89	3	.000	.000	1.000	1
2204	0.01	-0.02	2	.000	.855	.144	0
2211	-1.39	0.61	1	.560	.357	.083	---
2241	-0.52	0.25	2	.024	.823	.153	0
2254	-0.19	3.10	3	.186	.000	.814	1
2264	-0.89	-1.04	2	.000	.952	.047	0
2271	0.92	-0.45	2	.000	.838	.162	0
2274	-2.11	-0.90	2	.391	.536	.073	0
2281	-1.74	-0.81	2	.091	.836	.073	1
2314	0.76	5.44	3	.000	.000	1.000	1
2344	-0.41	0.92	3	.257	.365	.378	1
2371	-1.43	-0.96	2	.008	.927	.064	0
2374	-0.72	0.24	2	.049	.819	.132	1

Although we cannot confirm the results of this classification of the clinically doubtful limbs as far as the aortoiliac segment is concerned, for lack of an ideal test, it is interesting to look at those limbs classified into Groups 2 and 3 in whom the aortoiliac segment should be adequate. The state of the superficial femoral artery (SFA) is known from arteriography and is listed in the final column of Table V, but this information was not known by the method. Of 21 limbs in Group 4 placed in either Groups 2 or 3, PCA has correctly identified the presence or absence of SFA disease in 17 cases (81%) (those limbs underlined in Table V).

A possible criticism of PCA as used in this study is that the principal components were chosen by looking at the whole population of waveforms in the study and then each test waveform was individually compared with the total. To test the system adequately would necessitate a further prospective study comparing new waveforms with the original population. Such a study is at present under way in Leicester, but preliminary results using the common femoral principal components from another unit (Bristol) and the patient data from the present series show a very similar classification. These results are seen in Fig 6. Good comparability was also found in a further series of dog experiments used to test a PCA on line microprocessor in which the reference population consisted of the principal components derived from the first dog experiments described in Chapter 6 (170).

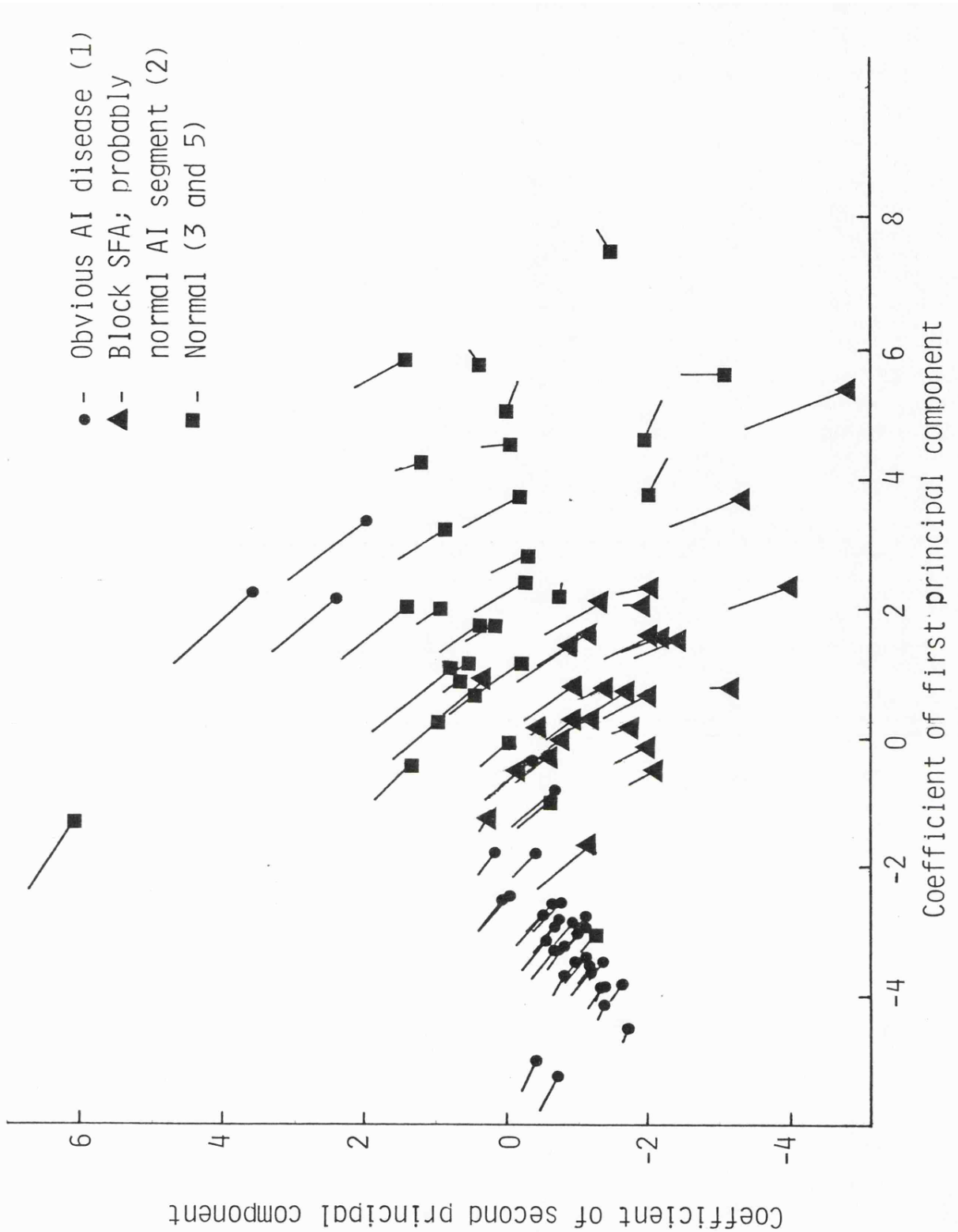


Figure 6. The patient data from the present series classified using the principal components derived from an entirely different patient population. The figure shows that each point has moved in a comparatively constant direction for a short distance along the lines indicated; new divisions would be required to go with these new components.

The use of two principal components for PCA makes comparison with LTD and PI difficult. PCA, however, concentrates most information in the first component and it was therefore decided to plot the coefficient of only the first component against SCA. This is shown in Fig 7 and it is clear that there is a good overall separation between the extreme groups. In addition, however, those patients with SFA disease are classified in the same range as the normals with little overlap with patients with severe aortoiliac disease. This represents a major advantage over both PI and LTD. It would now appear possible to ascribe a meaningful probability that a particular limb about which there is clinical uncertainty belongs to one of two categories. If the coefficient of the first principal component is less than -2 there is a 95% probability that there is severe proximal disease. If greater than -1, there is a 90% probability that the limb has a normal aortoiliac segment. The range of values where there is overlap between the groups is much smaller with PC1 than with either PI or LTD.

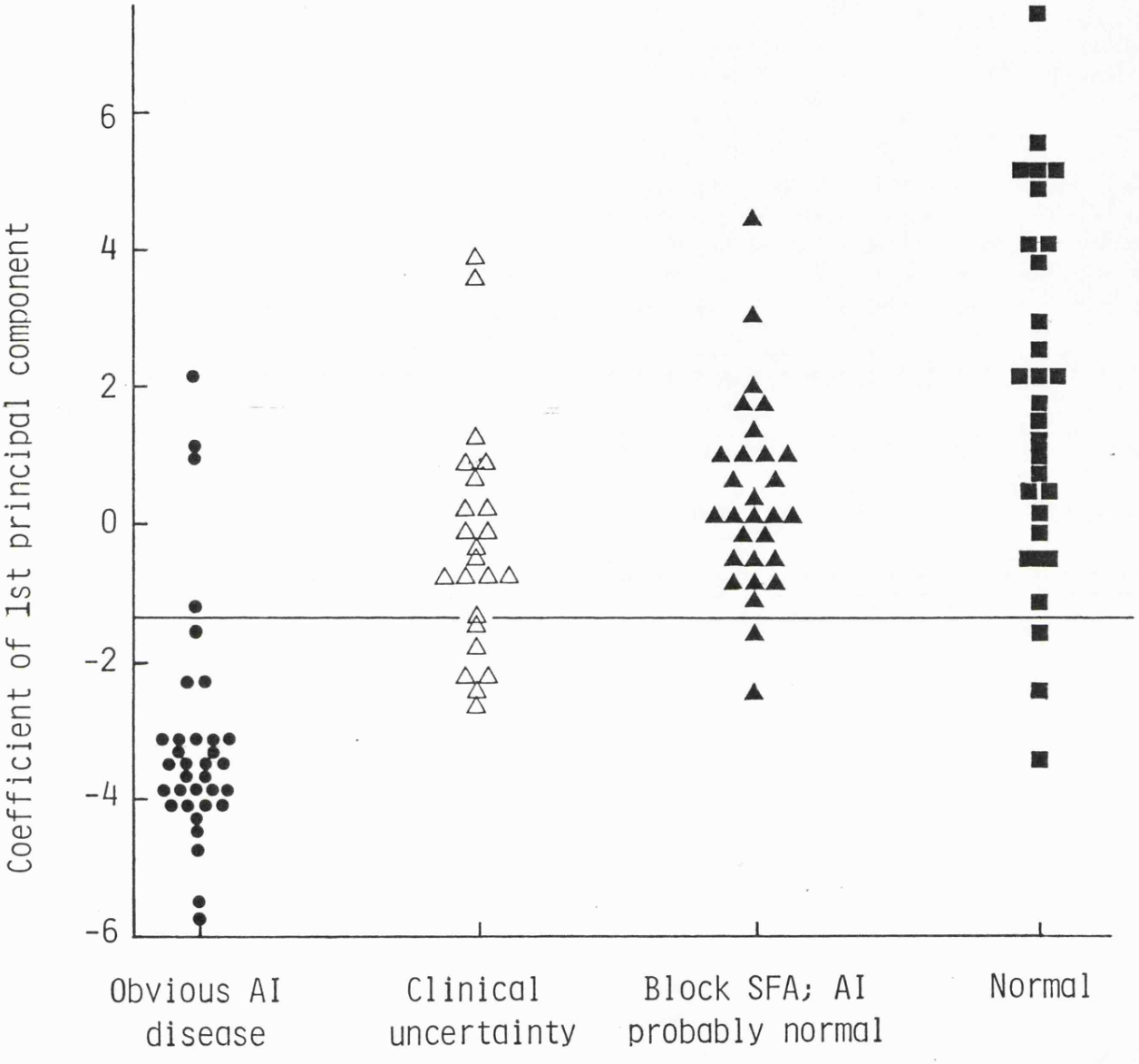


Figure 7. The coefficient of the first principal component compared with standard clinical assessment. The division has been drawn using the same criteria as in Figs 1 and 2.

(v) Comparision of PI, LTD and PCA

In an attempt to achieve the greatest specificity and sensitivity, lines have been drawn so as to misclassify the smallest numbers of patients in the extreme groups (normals and those with severe aortoiliac disease) and these can be seen in Figs 1, 2 and 7. It is then possible to assess the total numbers of correctly and incorrectly classified limbs in all the clear cut groups (i.e. including those with SFA disease) and compare the overall accuracy of the three methods. This is set out in Table VI. It is clear that the first principal component performs better than PI and LTD particularly in the group of patients with severe femoral artery disease.

TABLE VI: COMPARISON OF PI, LTD AND 1ST PRINCIPAL COMPONENT

CLINICAL GROUP:		1 Severe AI Disease	2 Severe SFA Disease	3&5 Normal
PI:	Correct	32	16	26
	Incorrect	4	14	3
LTD:	Correct	30	19	26
	Incorrect	6	11	3
PC1:	Correct	30	27	26
	Incorrect	4	2	3

(vi) The relationship between PI and PC1

PI is plotted against the coefficient of the first principal component in Fig 8. There is an excellent straight line relationship between them with only a small number of aberrant points. This is perhaps surprising in view of the very different methods used to obtain these values, but it must be remembered that principal component analysis by definition includes the majority of information in the first few components. A very similar relationship was found in the animal experiments. It appears that the coefficient of the first principal component is providing basically similar information to PI although, as we have seen in the last section, it is slightly less influenced by the presence or absence of superficial femoral disease. It is only with the inclusion of the second principal component that the full advantage of the method becomes clear.

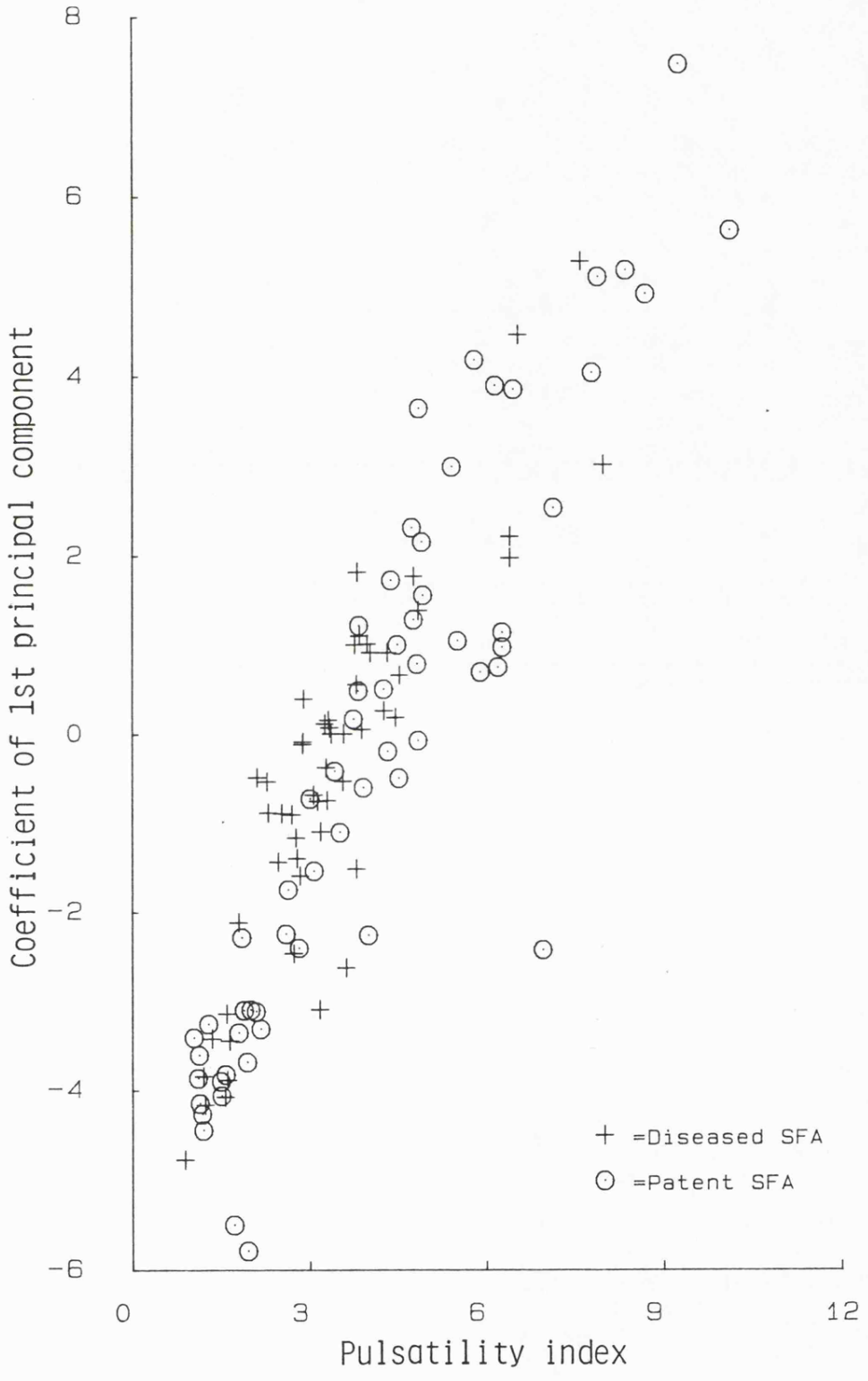


Figure 8. The relationship between PI and the coefficient of the first PC coefficient.

C. DOPPLER METHODS (II)

It can be argued that standard clinical assessment represents a rather 'soft' method of summarising clinical data, even though it is actually what is used in day to day patient management. Other workers have compared Doppler results with arteriography but the criticism of using this method in isolation has been argued in the introductory chapters.

It was therefore decided to perform the same series of comparisons as in B above, but this time to use only the hard results of the papaverine test to compare with the Doppler methods. It should be noted that the pressure assessment was carried out on only three quarters of the total patient population: the reasons for the exclusions are outlined in Table D-VI in Appendix D.

(i) PI compared with direct pressure measurement

The results are shown in Fig 9. In order to simplify the analysis, the pressure results have been grouped as mild, (Groups 1,2 and 3 as defined in Chapter 5) and severe (Group 4). In addition, the radiological status of the superficial femoral artery is included to demonstrate once more the effect of distal disease on femoral waveforms. A horizontal dividing line has been drawn as a cut off to give the smallest total number of misclassified points. The effect of

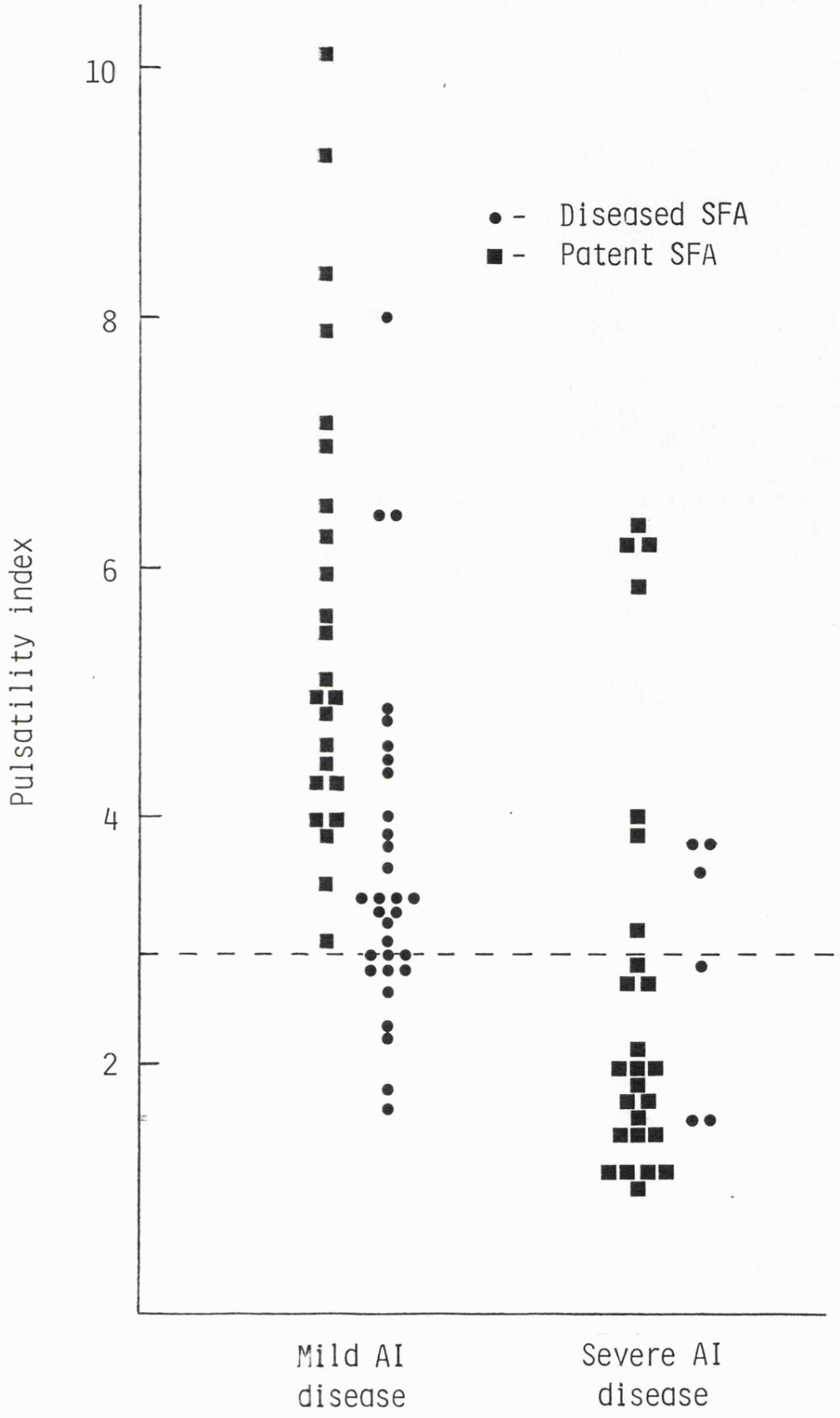


Figure 9. PI compared with direct pressure assessment. The groups are as defined in Chapter 5.

superficial femoral disease, by lowering the value of PI in those patients with relatively mild aortoiliac disease according to the pressure study, is again clear. The effect of superficial femoral disease on PI in the six patients with severe proximal disease as well is, understandably, less marked.

The group of four limbs with severe AI disease on the pressure test and values of PI greater than 5 is again of interest. Three of these limbs are those which were misclassified by all the Doppler methods and there is little doubt that the waveform changes induced by proximal stenosis were too small to be seen, at least in the waveform outline. It must be remembered that in the dog study, PI and LTD could only reliably pick up stenoses of greater than 88% area reduction. It is also possible to plot absolute hyperaemic pressure gradient against PI (Fig 10) for all the limbs. Different symbols have been used to represent limbs with and without severe superficial femoral disease. Those with open circles (minimal SFA disease) produce a curve very similar to that of Demorais and Johnston (109) who employed pressure measurements made at the time of arteriography for comparison with PI. Patients with diseased superficial femoral arteries have lower PI's for the same aortofemoral pressure gradient, but this is only apparent when the gradient is small.

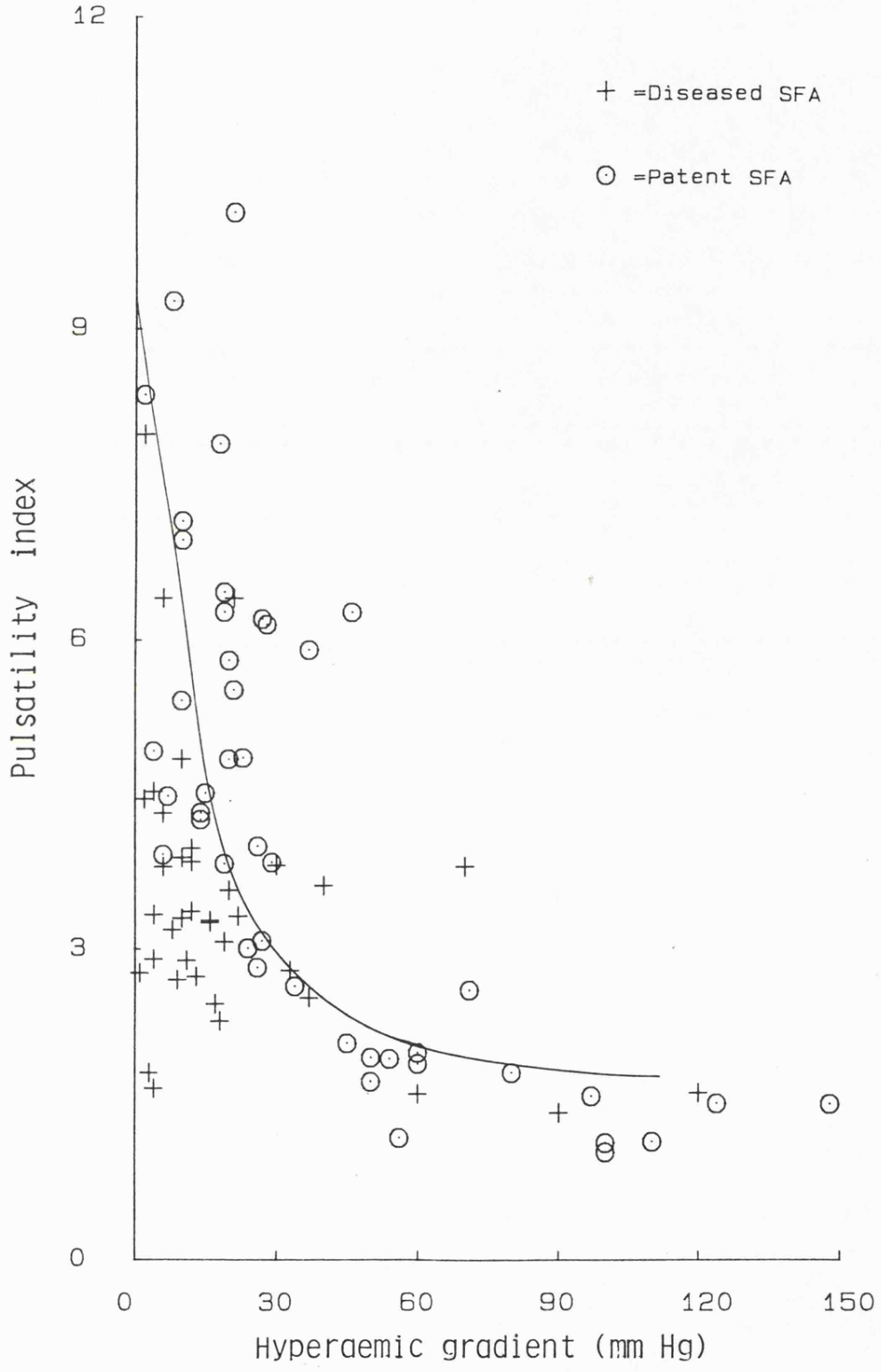


Figure 10. PI plotted against hyperaemic pressure gradient. The solid line represents the relationship found by Demorais and Johnston (109).

In conclusion, these results support the value of PI as a measure of proximal disease in the presence of a relatively normal femoropopliteal segment. The difficulty lies in those patients with SFA disease and a query about the proximal vessels. This is the group, after all, with arguably the greatest need for further objective assessment. In this group PI does not appear to add any useful discrimination.

(ii) LTD compared with direct pressure measurement

The results are similar plotted in Figs 11 and 12. There is considerable overlap between patients with mild and severe aortoiliac disease as defined by the pressure test. Once more this is especially so in those patients with superficial femoral artery disease. When LTD is plotted against hyperaemic pressure gradient there appears little correlation except for those limbs with obvious severe aortoiliac disease (those with a large gradient and a high value of LTD).

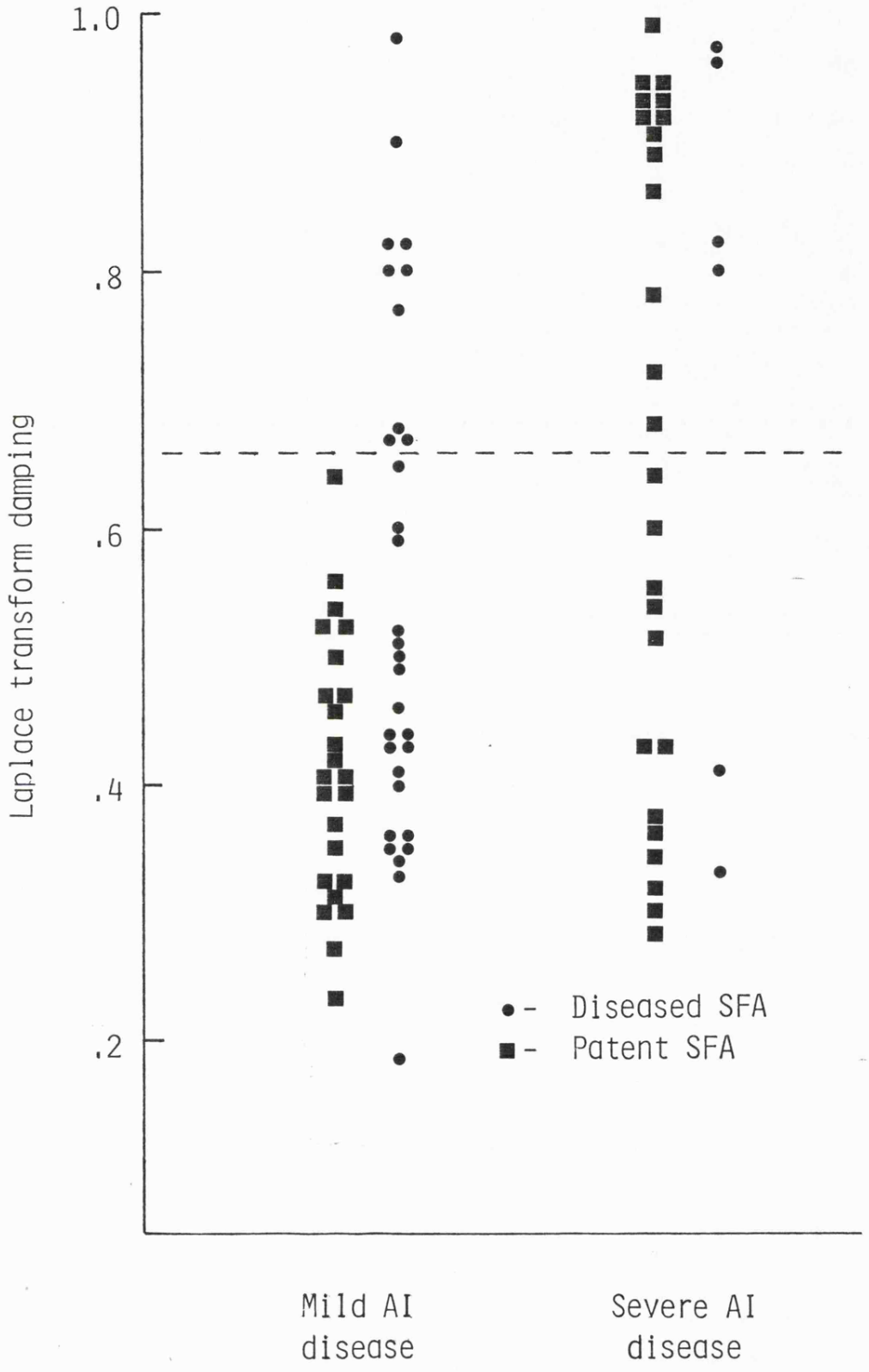


Figure 11. LTD compared with the direct pressure assessment.

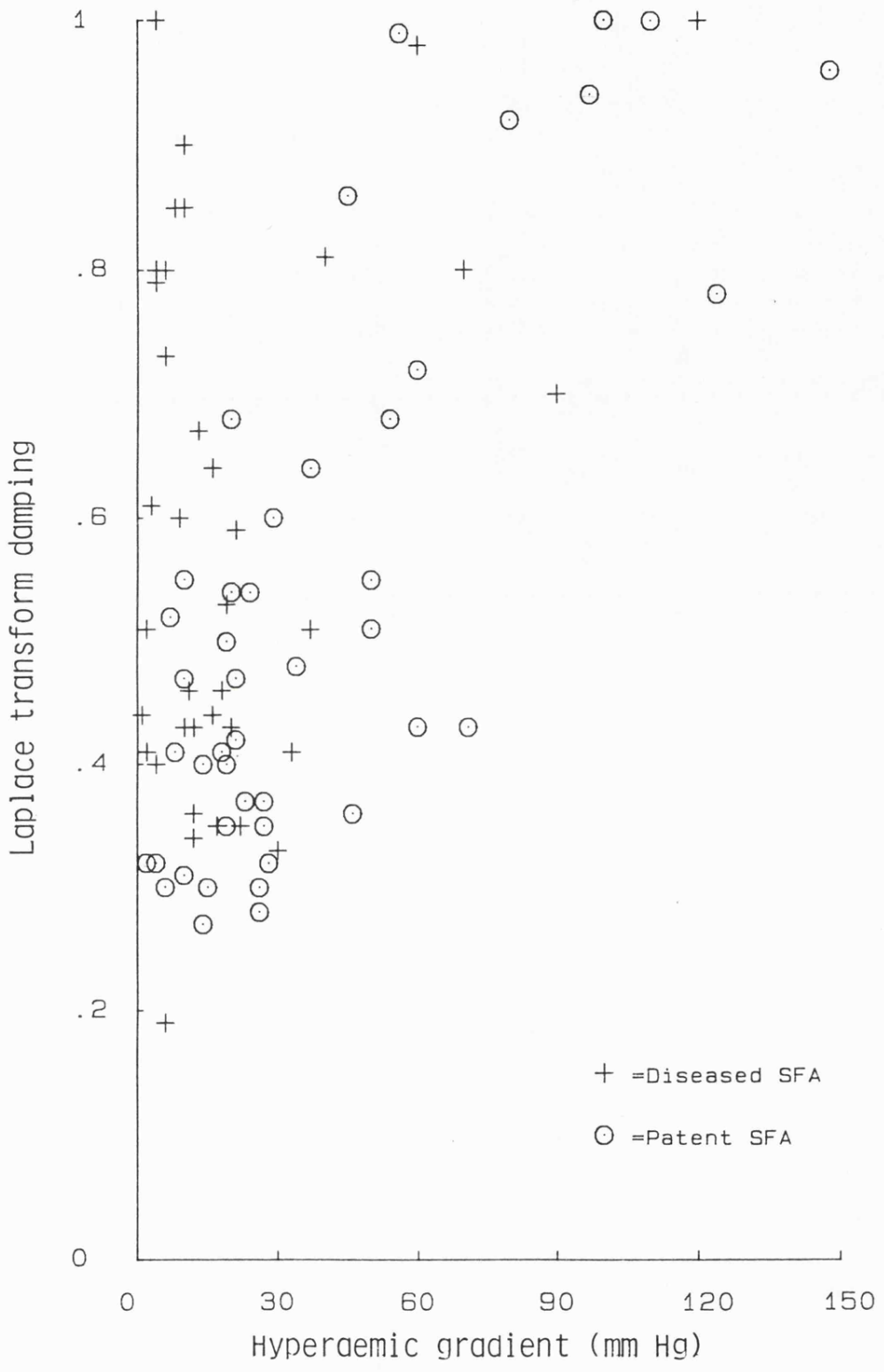


Figure 12. LTD compared with hyperaemic pressure gradient.

(iii) PCA compared with direct pressure measurement

The coefficients of the first and second principal components are plotted against the direct pressure assessment in Fig 13. For simplicity, those limbs with severe aortoiliac disease have not been separated according to the status of the superficial femoral artery. The results are markedly similar to those found with standard clinical assessment, although there are a few more points which appear to be misclassified. The Bayes technique has again been used to draw divisions between areas of feature space where a particular result in one class is most likely to occur.

Comparing only the first principal component with the pressure assessment, it is again apparent that the effect of superficial femoral artery disease is less marked in patients with relatively mild proximal narrowing than with either PI or LTD (Fig 14). The best horizontal cut off line producing the smallest number of false positive and false negative results misclassifies only 12 limbs as opposed to 19 with PI and 25 with LTD (Table VII). The first principal component is significantly better than LTD using the X^2 test ($X^2=5.8$, $p<0.2$); the difference between the first principal component and PI just fails to reach significance.

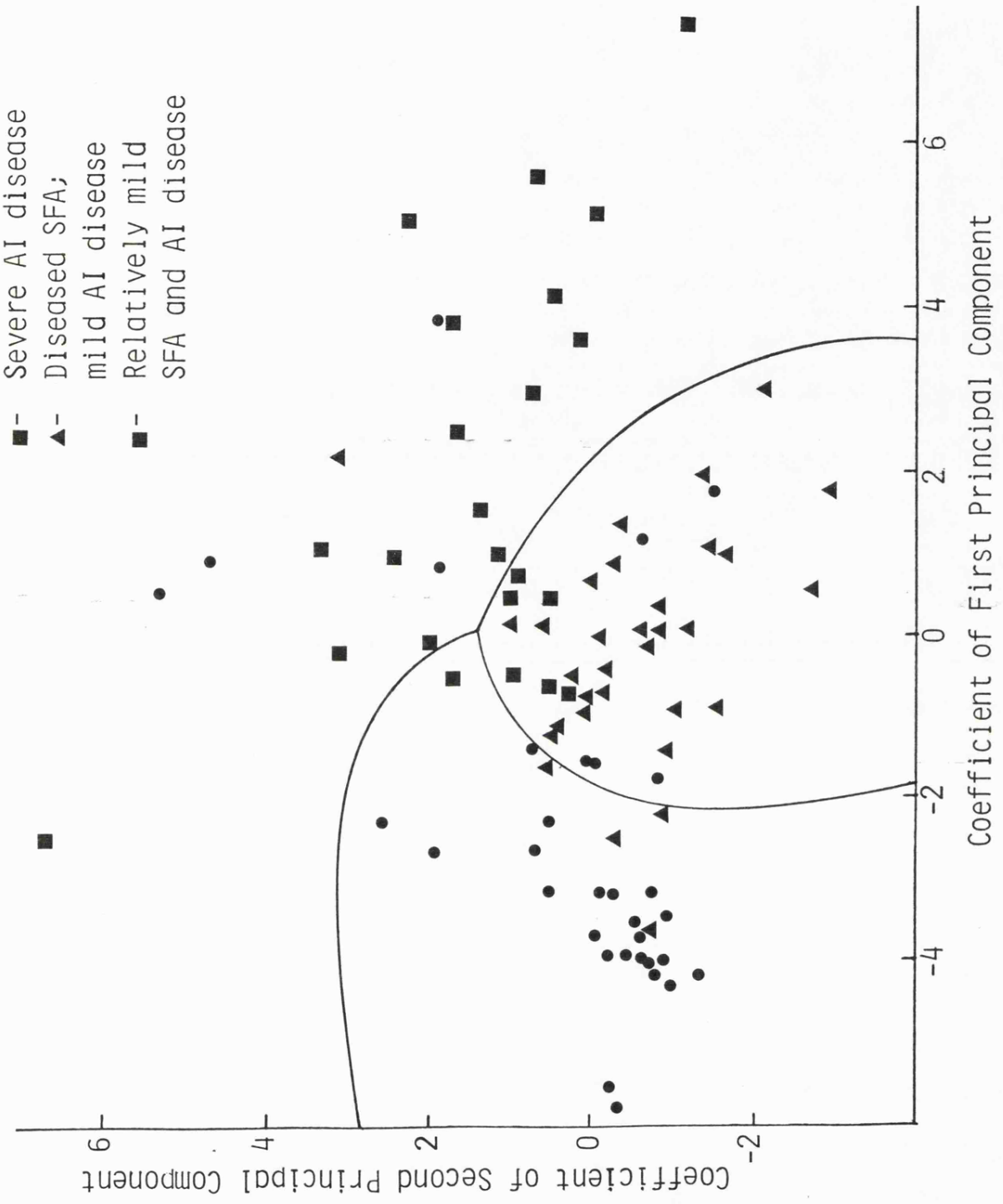


Figure 13. The coefficients of the first and second principal components using the direct pressure assessment as the standard for comparison. The dividing curves have been drawn using the Bayes technique. 75% of limbs are correctly classified.

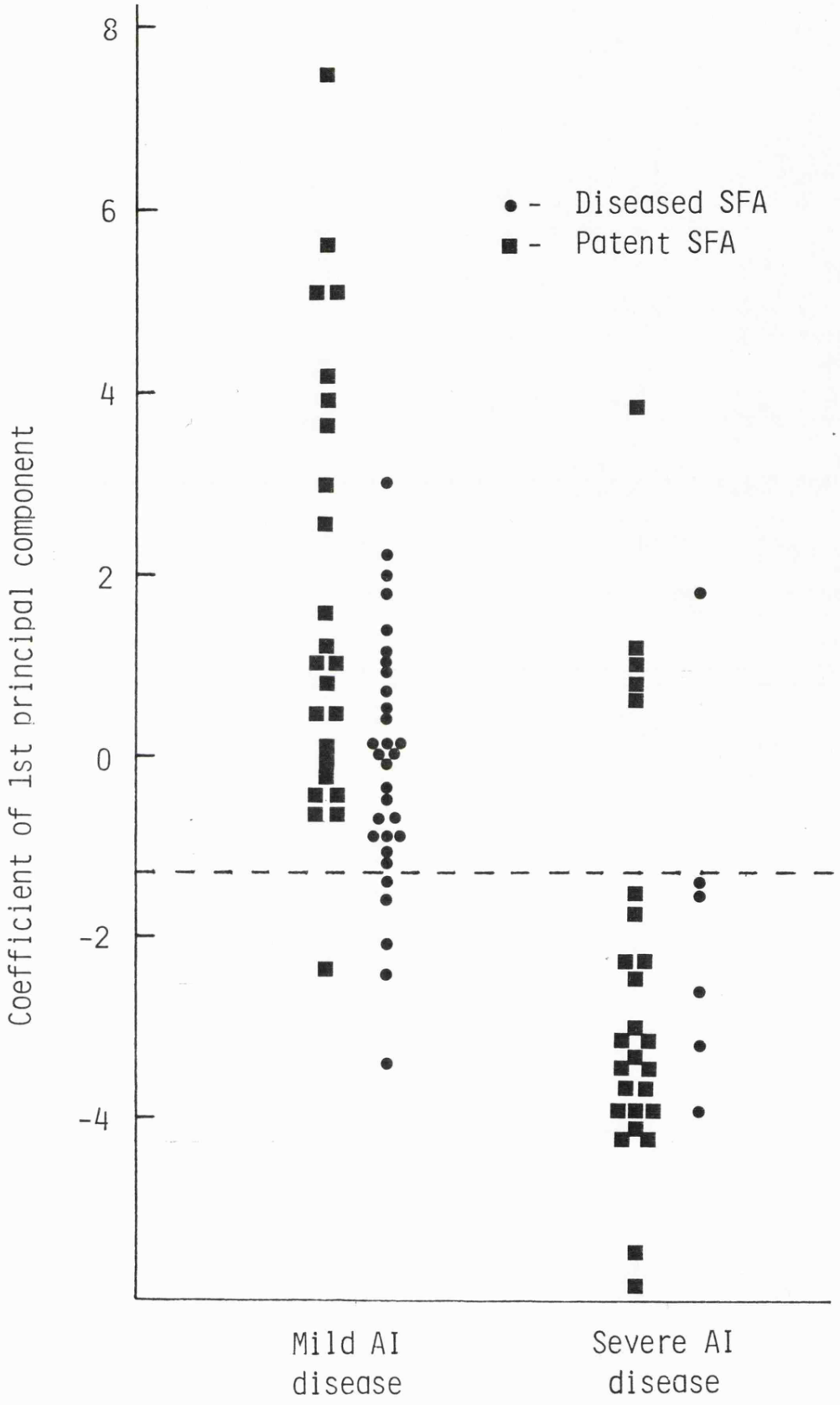


Figure 14. The coefficient of the first principal component compared with direct pressure measurement.

TABLE VII: LIMBS CORRECTLY AND INCORRECTLY CLASSIFIED BY PI, LTD AND THE COEFFICIENT OF THE FIRST PRINCIPAL COMPONENT.

	PRESSURE CLASSIFICATION OF LIMBS:	
	severe AI disease (Group 4: n=32)	mild AI disease (Groups 1,2&3: n=55)
PI		
Correct	22	46
Incorrect	10	9
LTD		
Correct	17	45
Incorrect	15	10
1st PC		
Correct	26	49
Incorrect	6	6

The coefficient of the first principal component is plotted against hyperaemic gradient for all limbs in Fig 15. A relationship very similar to that with PI is found, but with apparently less effect of superficial femoral artery disease at lower pressure gradients.

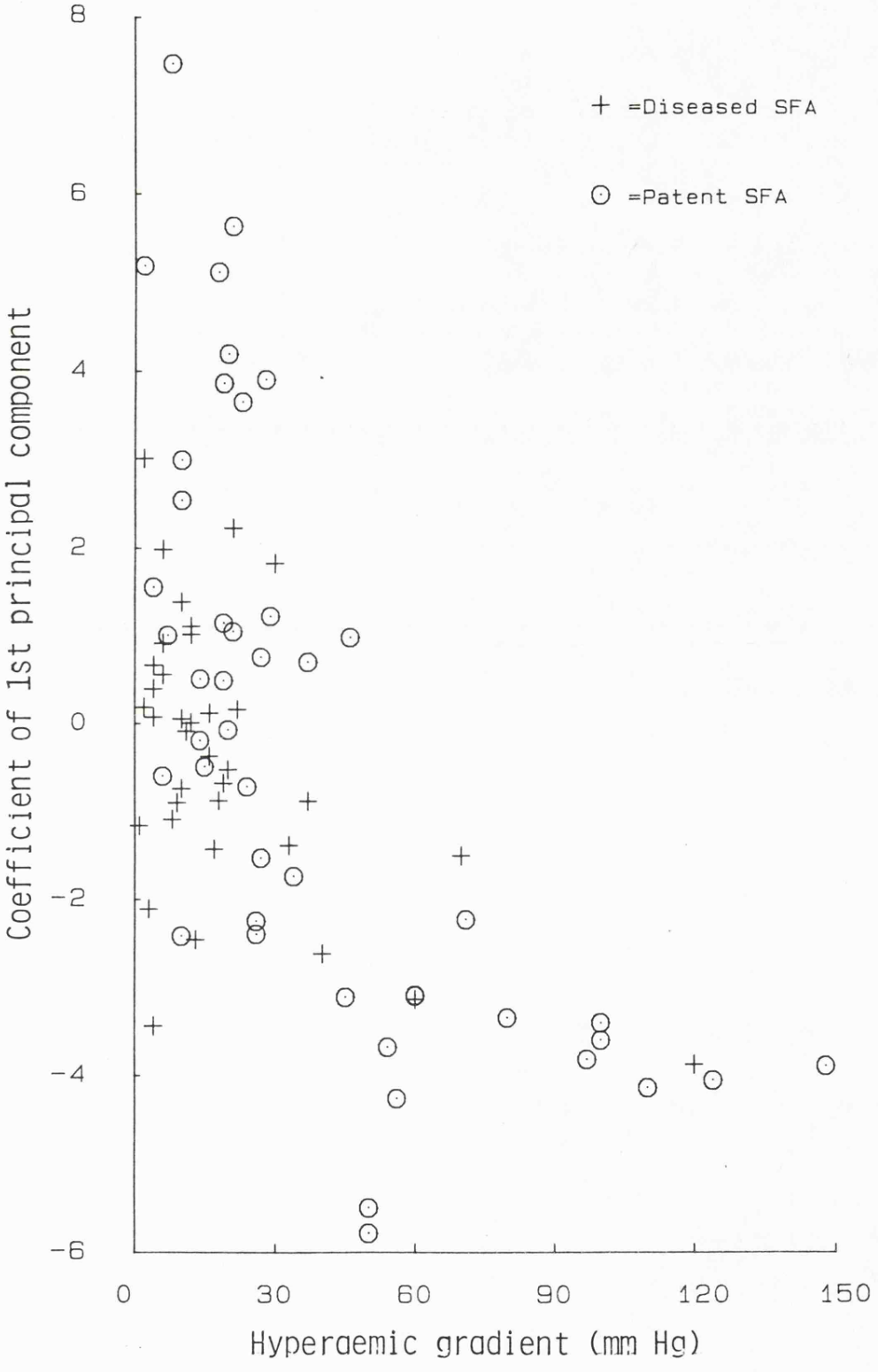


Figure 15. The coefficient of the first principal component plotted against hyperaemic pressure gradient.

D. DISCUSSION

This comparison of methods of Doppler waveform analysis gives broadly similar results using either standard clinical assessment or the direct pressure test alone. It is clear that both PI and LTD can, in the majority of cases, identify severe AI disease when the superficial femoral artery is relatively disease free. When SFA disease exists, values of PI are lower and LTD greater, and there is considerable overlap with values obtained from patients with severe AI disease. For the patient with a blocked SFA in whom a femoro-popliteal reconstruction is contemplated, measurement of PI or LTD is unlikely to be able to confirm that the aortoiliac segment is adequate. PCA appears to be able to identify those patients with relatively normal AI segments and disease in the femoro-popliteal region, and is therefore potentially more useful. This advantage is still present when use is made of only the coefficient of the first principal component although it must be emphasised that this study would recommend the use of at least two components.

Certain waveforms were misclassified by all the Doppler methods: an example is shown in Fig 16, together with values of PI, LTD and the first two PC coefficients. This patient (2174) had a diminished femoral pulse, a proximal iliac stenosis on arteriography and a 21mm Hg pressure gradient. A further series of waveforms was obtained 6 months later and

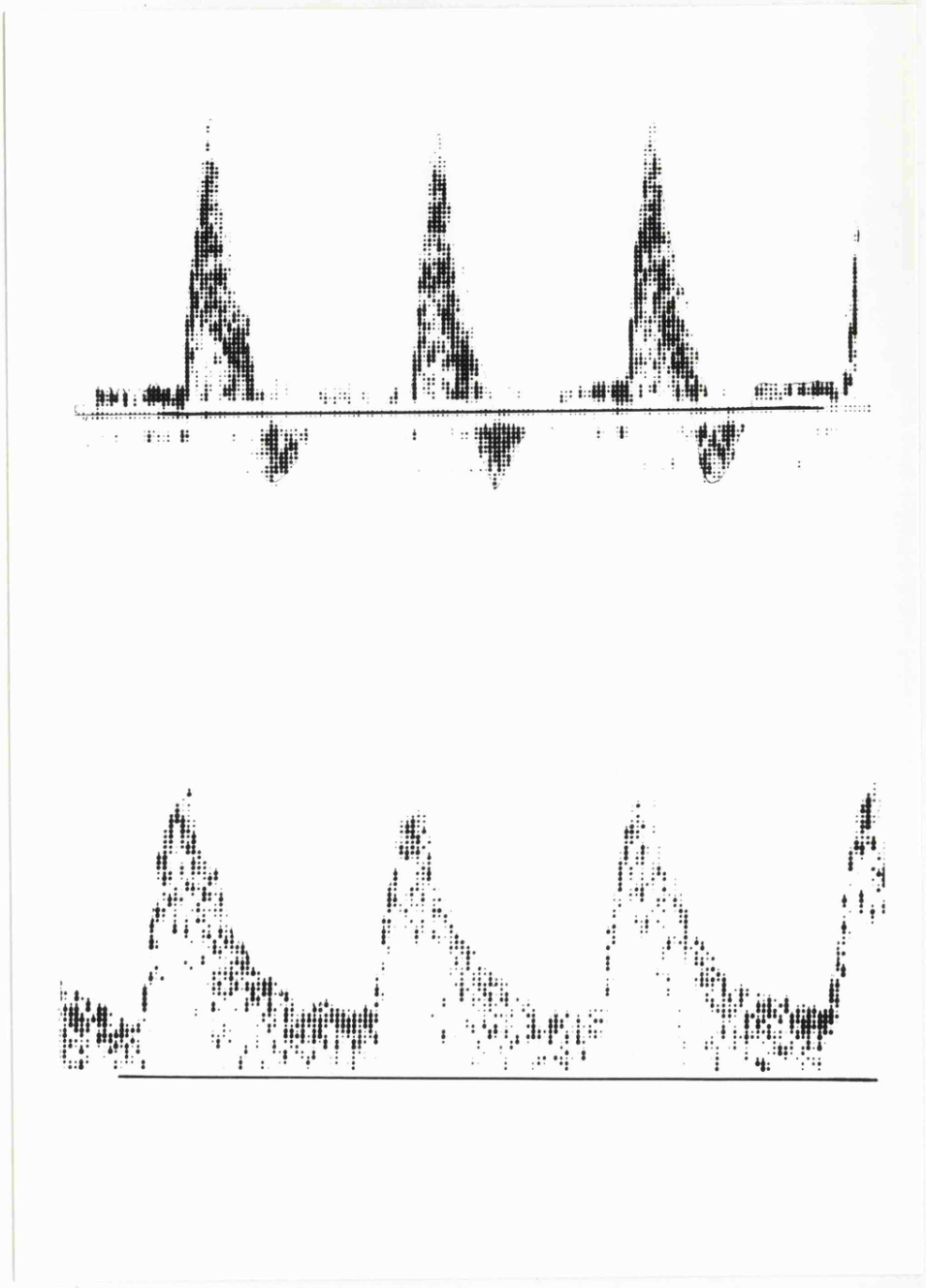


Figure 16. Example of Doppler waveform recorded from the common femoral artery of a patient with clear evidence of proximal disease: (upper) the initial recording, PI = 6.41, LTD = .59, PC1 = 2.22, PC2 = 3.15; (lower) a subsequent recording made 6 months later.

there is now little doubt about the presence of proximal disease from these damped Doppler signals. Presumably the stenosis had become 'critical' in the intervening period, at least as far as the Doppler methods were concerned. The initial waveforms from this patient are not strictly normal although the outline was so classified: there is a greater proportion of lower frequencies than in the typical normal shape (see Fig 1, Chapter 4) and it is possible that by including some measurement of this 'spectral broadening' such patients might be correctly classified.

Why does the Laplace transform method not perform better? One reason may be that the model on which it is based is concerned primarily with the normal arterial system and it may not be able to take account of various disease states. A small investigation on normal subjects may support this view. Table VIII shows the values of PI and LTD in two normal subjects on whom several manoeuvres were performed while making recordings from their common femoral arteries. Most of these were designed to alter the peripheral resistance. PI is seen to be very variable while LTD stays much more constant, suggesting that in normal subjects it is able to allow for such changes. The full results of this study are found at the end of the patient results in Table D-I (Appendix D).

TABLE VIII: VALUES OF PI AND LAPLACE TRANSFORM ROOTS IN TWO NORMAL SUBJECTS WHILE MANIPULATING PERIPHERAL RESISTANCE

SUBJECT IDENTITY	PI	LTD	GAMMA	OMEGA	MANOEUVRE
801	7.8	.25	9.7	21.2	Resting
802	15.3	.22	31.0	19.8	Thigh cuff inflated
803	2.8	.24	3.1	18.8	Cuff release
804	6.0	.24	7.5	19.9	Cuff release (+15 sec)
805	8.7	.26	11.2	20.8	Resting
806	22.8	.17	33.8	15.3	Thigh cuff inflated high
807	1.3	.57	2.7	35.8	Cuff release
808	2.6	.24	2.6	22.0	Cuff release (+15 sec)
809	5.0	.16	3.9	50.4	Cuff release (+25 sec)
810	11.6	.27	22.6	18.2	Cuff release (+120 sec)
811	12.0	.29	40.6	17.6	Cuff release (+5 min)
700	2.9	.23	3.6	25.1	Resting
701	2.8	.22	3.1	22.2	After further rest
702	4.2	.46	11.2	14.5	Thigh cuff inflated
703	1.8	.39	3.3	24.1	Cuff release
704	2.3	.29	3.2	22.7	Cuff release (+5 min)

It is also interesting that γ, the Laplace root related to peripheral resistance, varies exactly as one would expect during these changes while ω, the elasticity factor, is relatively constant. Values of these roots, especially γ, found in our patients tended to be much more variable than in the few normals in the study.

Did the follow-up data help in deciding on the correct classification of any of the limbs? Most of those limbs in the clear cut groups as defined by standard clinical assessment in whom further information was available had the initial decision confirmed. Details of the group with clinical uncertainty are included in Table D-VII in Appendix D. A few interesting points emerge. Four patients eventually had inflow procedures (2204, 2254, 2281 and 2371) but continued to have significant symptoms; the first two subsequently underwent distal reconstruction as well. Limb no. 2034 had inflow disease suggested by PI (3.5), LTD (.82) and PCA, but the femoral pulse remained fairly good over the next three years without any operation. Four patients had bifurcation grafts performed because of severe disease on the opposite side, so the outcome of the limb in question cannot be assessed. Two patients eventually underwent femoro-popliteal bypass with a good result (2091 and 2271) so presumably the inflow was adequate as suggested by PCA (see Table V above). One patient had a failed femoro-popliteal bypass and subsequently required proximal reconstruction prior to an eventual amputation (1834) in spite of relatively normal Doppler indices (PI 4.6, LTD .35, no PCA). Most of the remainder of the patients in this group were treated conservatively. These examples serve to confirm the initial problems with correctly assessing this difficult group of patients, and on the whole the Doppler results did not help in any consistent way.

The results of the pressure test must be interpreted with caution, and several such tests were excluded because of inadequacies (see Table VI, Appendix D). However, an unequivocal pressure test, such as the examples in Chapter 8, provides very convincing evidence of proximal narrowing. It may be possible to tighten up this test by providing information on flow or flow change after papaverine, and such a method using Doppler ultrasound for flow estimation is at present under trial in Leicester.

One of the requirements for a better pressure test would be reliable knowledge of the aorto-femoral pressure gradient to be found in normals and in patients with varying degrees of aortoiliac disease. Although flow is also important it is known that it remains fairly constant in a particular subject under resting conditions. It is probable that a normal range of aorto-femoral pressure gradient for the general population can be defined in the same way as the range of normal values for systolic and diastolic arterial pressure, but at the present time such information is not available. The limit accepted in this study for hyperaemic gradient (>25mm Hg) almost certainly represents severe AI disease, but it may well be that lesser pressure gradients are still important and should be corrected before distal reconstruction. With the coming of transluminal angioplasty, such knowledge becomes even more important both for

the correct identification of significant lesions and, equally, for the identification of areas of no haemodynamic significance in the arterial tree.

E. CONCLUSIONS

From this study, Doppler ultrasound does not provide a reliable assessment of proximal narrowing in the majority of cases where there is clinical uncertainty, particularly if there is disease in the superficial femoral artery. Of the indices tested, PCA appears the most promising but it still gives some anomalous results. Two avenues for further study are identified: (i) the use of hyperaemia may cause changes in common femoral artery Doppler waveform shape which might be more useful in defining proximal narrowing, and (ii) more subtle changes in the Doppler spectrum, especially at the time of maximum forward flow, might be better guides to proximal disease than the simple outline of the waveform. Direct pressure studies provide easily comprehended data which can usually be seen to be adequate or not at the time of the test, and such tests or a modification using flow in addition provide, in the author's opinion, the best current method of assessing proximal disease.

Chapter 10

SUMMARY AND CONCLUSIONS

The use of Doppler ultrasound as a diagnostic tool in patients with arterial disease remains attractive because of the basic simplicity of the method and its non-invasive nature. If it provided the necessary accuracy for the assessment of significant degrees of proximal arterial narrowing, it would find a routine place in every department of vascular surgery. Unfortunately this has not been shown by this study, mainly because of the effect of other factors on waveforms recorded from the common femoral artery. These effects have been identified both in the animal and the patient work.

Animal studies (i)

The animal model described in Chapter 6 provides near ideal conditions for assessing the effect of proximal stenosis on flow, pressure and waveform shape, both because the stenosis size is accurately known and also because it is possible to calculate peripheral resistance. Such studies had not been used previously for the investigation of either

LTD or PCA, and the information provided would suggest that the analysis of the Doppler waveform outline is unlikely to give us the necessary information when the method is applied to patients.

The problem with all the methods of waveform analysis investigated is the overlap between groups with large standard deviations. The animal preparation remained stable throughout most of the duration of the experiments as can be seen from the arterial blood pressure recordings in Appendix B. Peripheral resistance changed rather unpredictably, tending to increase with time. None of the methods gave the ideal smooth curve, similar to that found for stenosis resistance with increasing stenosis (Fig 8, chapter 6), which might have been anticipated on theoretical grounds. Changes in peripheral resistance and possibly vessel elasticity are presumably contributing to the labile nature of waveform shape.

Of the methods examined in the animal model, PCA appeared the most promising because of its ability to recognise stenoses of moderate severity in most cases (those of 65-85% area reduction). All the methods are clearly able to distinguish the very severe group (>88% area reduction) from the normals, but such obvious disease is unlikely to be overlooked in clinical practice.

LTD in theory should be able to separate the effects of proximal narrowing, peripheral resistance and elasticity, and hence should perform better than PI. This was not found in the animal investigations; indeed there seemed to be a significant relationship between LTD and peripheral resistance. It may be that the method cannot be easily translated to an animal model, but there seems no reason on theoretical grounds why this should not be possible.

Animal studies (ii)

One of the factors which might affect waveform shape other than proximal narrowing itself is flow disturbance produced by such a narrowing and propagated downstream; the experiments described in Chapter 7 set out to investigate this. The conclusions from this study, while confirming in vitro observations of increased propagation of disturbance with increasing stenosis, do nothing to support the use of Doppler ultrasound in the detection of proximal narrowing because of the impossibility of knowing accurately the spatial relationship between the major stenosis and the Doppler probe. Waveforms which show flow disturbance in clinical practice almost certainly come from diseased arteries, but marked changes can be expected from relatively minor lumen incursions if the probe is close to the lesion.

Patient studies

This study set out to investigate Doppler ultrasound as a method which, by itself, might lead to better diagnosis of disease proximal to the femoral artery. Although there are clear trends seen in the indices examined, none provides the discrimination necessary to influence clinical decision making. For example, does a patient with a relatively normal femoral pulse and proximal arteriography but a PI of less than 4 need an inflow procedure, as suggested by Charlesworth (135), before proceeding to femoro-popliteal reconstruction? The pressure test used as the gold standard in the present work would suggest that the majority (65%) of patients with SFA occlusions have a PI of less than 4 even in the presence of mild proximal disease, and presumably do not need a proximal operation first.

Peripheral resistance clearly affects Doppler waveforms recorded from the common femoral artery; this is well illustrated by the small study of normal subjects in the discussion in Chapter 9. A decreased PR tends to lower PI, but LTD seems much less affected at least in normals. What is certain is that disease in the superficial femoral artery changes both PI and LTD, tending to classify such limbs in the same range as those with significant proximal disease; this is the major factor which has been identified as the cause of the marked overlap found between the clinical

groups. It is probably not simply PR which is changing, but more likely that the common femoral waveform shape is in some way altered by the distal block, possibly due to a reflection effect.

Would the greater use of statistical analysis provide a more encouraging conclusion from the data? It is possible to show that the clear cut clinical groups do belong to significantly different populations using the Mann Whitney U test on the PI and LTD results (Figs 1 and 2, Chapter 9). Unfortunately, because of the wide spread of these results, and the overlap of the three main groups with the uncertain limbs, this does not help much when assessing the chances of an unknown limb belonging to a particular group: in clinical work we are concerned not so much with how a particular group of patients behaves but how we can best help an individual, and the overlap between groups, especially taking into account the effect of SFA disease, precludes meaningful conclusions being made except for extreme values (for example, a PI of >6.5 or <2).

Are these results confirmed by other workers? There is as yet little data on the use of LTD and PCA, but a recent unpublished study by Junger et al (172) suggested that LTD was able to confirm the presence of arteriographically significant aortoiliac disease, though it was not superior to PI in this respect. Furthermore, LTD was affected by distal

impedance, a finding which confirms results in the present study. The King's group (145) has reported similar findings with LTD, and has also used PCA in a small patient study whose results are remarkably similar to our own.

KW Johnston has always been an enthusiastic proponent of Doppler methods in proximal disease, and his use of pressure gradient for comparison with PI has already been mentioned (109). In a recent paper he examines this further and includes in his study patients with and without distal disease (173). Interestingly, he does not find as much influence of distal disease upon common femoral PI as in the present study, although the trend is still present.

He also introduces the concept of receiver operator characteristic (ROC) curves for assessing the method (174). Basically these curves examine the results at different levels of specificity and sensitivity and allow a cut off to be decided at the appropriate level desired. Although possibly more scientific than the simpler method of line drawing used in this thesis, the end results are very similar. Johnston has shown that the smallest number of false positive and false negative results is obtained using a cut off value of common femoral PI (max) of 5.5. When patients with and without distal disease are analysed separately, the best ROC curves are obtained from those with no distal disease, again confirming our own results.

Although clearly encouraging, can these results from one unit be extrapolated to the average vascular department with perhaps a smaller number of cases and less adequate technical assistance? In particular, can arteriography be avoided in some or all cases? The answer to both these questions at the present time is probably not. The majority of patients require arteriography before surgery and the data obtained from simultaneous pressure studies probably provides the best source of additional information in the small number of cases where there is genuine doubt about the extent of proximal disease. If Doppler waveform analysis is to be of value, objective methods are essential and of those examined, PCA looks the most promising.

Does the vascular laboratory have any role to play in the assessment of patients with arterial disease? Undoubtedly simple ankle pressure measurement with or without stress testing is widely used and considered valuable. The investment of resources to assess proximal disease by Doppler methods cannot be recommended by this study although further research should be encouraged. With slightly improved accuracy it might, for example, be possible to assess patients using a combination of Doppler methods and intravenous arteriography without resorting to aortography at all. However, at present it must be concluded that the Doppler methods examined in this thesis are not sufficiently accurate in most cases to provide the desired extra information,

especially when both proximal and distal disease co-exist.

CONCLUSIONS

The preliminary animal experiments suggested a level of 'critical' stenosis of about 88% area reduction before changes in Doppler waveforms could be reliably detected downstream. The patient studies have confirmed that in most cases where there is genuine uncertainty, particularly if patients have distal disease, Doppler studies are not adequate for assessing the aortoiliac segment. PCA is the most attractive method because of its ability to recognise disease in the superficial femoral artery from common femoral recordings. When there is doubt about the adequacy of the aortoiliac segment, the author would recommend the use of pressure gradient measurement before and during hyperaemia as the most reliable currently available test of proximal narrowing.

APPENDIX A

The following pages contain reproductions of the original forms used for collecting the data in the patient studies. Although some of the material collected was not further analysed for the reasons mentioned in Chapter 9, the forms were found to be adequate for the task and were used throughout the clinical study. The original referral form containing initial clinical details is followed by the form used for the vascular assessment study and finally the form for collection of the arteriographic data.

PERIPHERAL VASCULAR DISEASE

Clinical Form

1. Presenting Complaint: Severe claudication <100m
   Specify site, and Moderate claudication 100-300m
   (L) or (R). Mild claudication >300m
   Rest pain
   Gangrene

2. Clinical Findings:

Score: 0 Absent
- + Just palpable
+ - Diminished
+ Normal
++ Aneurysmal

	R	L	Bruit(Specify site)
Carotids			
Radials			
Aortic			
Femoral			
Popliteal			
Ant.Tibial			
Post Tibial			

3. Is the inflow acceptable ? Yes ☐ No ☐

4. Is the run-off acceptable ? Yes ☐ No ☐

5. Is amputation inevitable in the near near future if reconstruction fails? Yes ☐ No ☐

6. Do you think there is carotid stenosis ? Yes ☐ No ☐

7. Do you think the patient should have an operation - and if so which ? Yes ☐ No ☐

8. If you do not think he should have an operation, say why not ?

9. Do you think he will do well ? Yes ☐ No ☐

Sign .....

Date.....

PERIPHERAL VASCULAR DISEASE

Assessment

1. Clinical Information

Date:

Weight: I.P.: Diabetic: Yes

Height O.P.: No

Room Temperature: Drugs:

Smoking: Never

(specify details) in past

now

2. Clinical Findings:

Score: 0 Absent

$\frac{-}{+}$ Just palpable

$\frac{+}{-}$ Diminished

\+ Normal

++ Aneurysmal

	R	L	Bruit(Specify site)
Carotids			
Radials			
Aortic			
Femoral			
Popliteal			
Ant.Tibial			
Post Tibial			

3. Leg dimensions:

	R	L
Inside leg lenth		
Mid thigh circumference		
Knee "		
Calf "		

4. Treadmill: Speed:

	Time	Distance
Onset of pain		
Stopping machine		

5. Pulsatility Index:

	At rest	After Exercise 1 min	5 min	15 min
R.C.F.				
L.C.F.				
R.Pop.				
L.Pop.				
R.D.P.				
R.P.T.				
R.Per.				
L.D.P.				
L.P.T.				
L.Per.				

Comments on Doppler Tracing:-

6. Ankle Pressure Index (At Rest)

Brachial B.P. < R / L

	Systolic	Pressure Index
R. D.P.		
R. P.T.		
L. D.P.		
L. P.T.		

7. Pressure Studies

Site	Probe	Measurement	Change	Measurement	Δ%	Comment

PERIPHERAL VASCULAR DISEASE

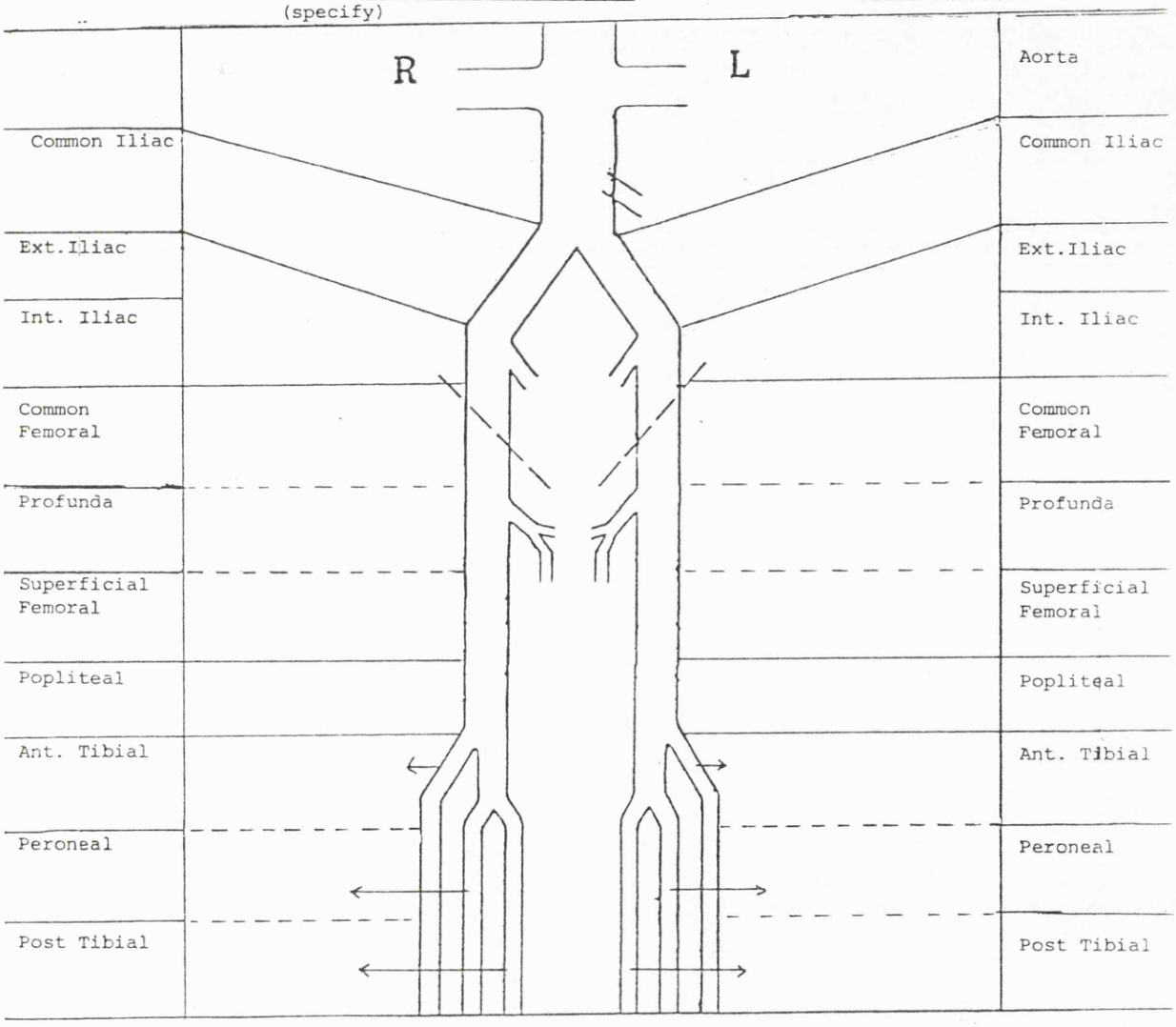
Arteriography

1. Type: Translumbar ☐ Femoral R ☐
Seldinger R ☐ L ☐
L ☐ Other (Specify) _____

2. Complications None ☐
Yes _____
(specify)

3. Assessment

Score: 0 - +++, Draw main stenoses and write comments



Score: 0 - vessel occluded
+ - vessel more than 50% stenosed
++ - vessel less than 50% stenosed
+++ - vessel normal or slightly uneven.

APPENDIX B

The results of the five dog experiments described in Chapter 6 will be found on the following pages. In order to save space, the raw results are not reproduced; print-outs very similar to those included in the patient results in Appendix D were available, but were even more lengthy, and it was not thought necessary to include them. The results are summarised by dog below: each series represents a chronological record of each of the five experiments. The key to the abbreviations is as follows:

AR	Area reduction of stenosis (%)
P_1	Proximal mean arterial pressure (mm Hg)
P_2	Distal mean arterial pressure (mm Hg)
ΔP	Mean pressure drop across stenosis (mm Hg)
Q	Mean electro-magnetic flow through stenosis (ml/min)
R_s	Stenosis resistance (mm Hg.min.ml^{-1})
R_p	Peripheral resistance (mm Hg.min.ml^{-1})
N	Number of waveforms analysed
PI	Pulsatility index ($\pm$ standard deviation)
LTD	Laplace transform damping ($\pm$ standard deviation)
PC_1	Coefficient of 1st principal component ($\pm$ SD)
PC_2	Coefficient of 2nd principal component ($\pm$ SD)

AR	P1	P2	ΔP	Q	Rs	Rp	N	PI	LTD	PC1	PC2
0	66	66	0	100	0	0.66	5	4.09 +/- .75	0.10 +/- .04	-1.56 +/- .26	3.04 +/- .97
88	64	59	5.6	100	0.056	0.59	5	1.52 +/- .12	0.31 +/- .05	0.82 +/- .14	0.93 +/- .22
88	66	59	6.2	100	0.062	0.59	5	1.40 +/- .03	0.38 +/- .06	0.89 +/- .12	0.86 +/- .32
95	64	42	22.0	78	0.282	0.54	5	0.61 +/- .03	0.98 +/- .01		
95	57	42	16.0	54	0.296	0.78	5	0.81 +/- .01	0.84 +/- .16	1.71 +/- .11	0.43 +/- .11
0	56	56	0	165	0	0.34	4	3.21 +/- .10	0.40 +/- .08	-1.65 +/- .21	1.44 +/- .44
0	60	60	0	122	0	0.49	5	3.13 +/- .01	0.28 +/- .09	-1.56 +/- .14	1.85 +/- .23
92	60	49	10.5	85.5	0.123	0.57	5	1.08 +/- .14	0.68 +/- .13		
92	63	51	11.5	100.5	0.114	0.51	5	1.01 +/- .07	0.75 +/- .22		
85	52	48	4.2	95	0.044	0.51	4	1.60 +/- .06	0.79 +/- .16	0.32 +/- .12	-0.28 +/- .13
85	54	51	3.4	96	0.035	0.53	5	1.51 +/- .09	0.86 +/- .08	0.52 +/- .16	-0.30 +/- .22
0	52	52	0	155	0	0.34	5	3.12 +/- .18	0.46 +/- .05		
0	51	51	0	80	0	0.64	5			-2.69 +/- .46	0.81 +/- .69
77	50	49	1.6	50	0.032	0.98	3	3.05 +/- .35	0.40 +/- .02	-2.23 +/- .63	0.82 +/- .53
77	52	51	1.5	70	0.021	0.73	3	2.64 +/- .14	0.27 +/- .06	-1.20 +/- .11	0.71 +/- .37
88	50	44	4.8	55	0.087	0.80	4	1.54 +/- .05	0.39 +/- .14	0.32 +/- .10	0.12 +/- .12
88	54	48	5.0	59	0.085	0.81	5	1.41 +/- .02	0.48 +/- .26		
95	58	42	16.0	47.25	0.275	0.89	5	0.71 +/- .06	0.99 +/- .01	1.94 +/- .09	0.47 +/- .17
95	55	42	13.0	47.25	0.224	0.89	5	0.74 +/- .08	0.99 +/- .01	1.93 +/- .11	0.30 +/- .15
0	50	50	0.3	115	0	0.43	5	3.84 +/- .16	0.28 +/- .03	-2.90 +/- .28	0.70 +/- .24
0	50	49	0.9	55	0	0.89	4	5.47 +/- .67	0.59 +/- .21	-5.29 +/- .72	2.38 +/- .89
92	48	40	7.9	35.25	0.224	1.13	5	1.10 +/- .04	0.78 +/- .16	1.35 +/- .12	-0.01 +/- .15
92	46	40	6.0	26.25	0.229	1.52	5	1.55 +/- .27	0.61 +/- .24	0.76 +/- .21	-0.13 +/- .22

AR	P1	P2	ΔP	Q	Rs	Rp	N	PI	LTD	PC1	PC2
0	77	75	1.5	230	0	0.326	5	3.2 +/- .30	0.27 +/- .05	-1.67 +/- .16	1.54 +/- .40
88	82	68	13.25	200	0.066	0.340					
88	80	67	13.0	164	0.079	0.408					
95	71	44.5	27	88	0.307	0.506	5	0.76 +/- .04	0.95 +/- .05	1.90 +/- .09	0.42 +/- .16
95	71	42	27	91	0.297	0.462	5	0.90 +/- .03	1.00 +/- .00	1.81 +/- .05	0.41 +/- .13
0	63	61	2.1	288	0	0.212	5	2.81 +/- .19	0.33 +/- .03	-1.09 +/- .17	-0.39 +/- .21
0	60	57	2.0	180	0	0.317	5	4.51 +/- .26	0.41 +/- .09	-2.65 +/- .13	-0.40 +/- .48
88	60	48.5	11.5	146	0.079	0.332	4	2.02 +/- .06	0.66 +/- .12	1.49 +/- .17	-1.04 +/- .17
88	58	49	9.0	114	0.079	0.430	5	1.87 +/- .11	0.59 +/- .10	1.50 +/- .35	-0.98 +/- .13
65	53	50	2.65	188	0.014	0.266	5	3.30 +/- .11	0.39 +/- .08	-0.55 +/- .36	-1.35 +/- .49
65	56	53	2.4	172	0.014	0.308	4	3.76 +/- .48	0.34 +/- .05	-0.93 +/- .25	-1.30 +/- .25
92	55	40	15.6	118	0.132	0.339	5	1.37 +/- .09	0.97 +/- .07	2.15 +/- .16	-0.45 +/- .11
92	59	44	15	114	0.132	0.386	4	1.59 +/- .04	0.97 +/- .05	2.36 +/- .11	-0.70 +/- .11
0	53	52	1.5	320	0	0.163					
0	59	58	1.6	220	0	0.264	5	3.89 +/- .45	0.35 +/- .03	-1.44 +/- .39	-1.01 +/- .14
85	58	50	8.25	180	0.046	0.278	4	2.02 +/- .18	0.57 +/- .16	1.37 +/- .25	-0.79 +/- .20
85	64	55	9.5	184	0.052	0.299	5	1.78 +/- .11	0.66 +/- .18	1.33 +/- .17	-0.65 +/- .22
77	58	52	5.4	178	0.030	0.292	5	3.43 +/- .15	0.45 +/- .10	-1.27 +/- .39	-1.48 +/- .62
77	53	48	4.9	164	0.030	0.293	5	3.25 +/- .18	0.70 +/- .08	-1.50 +/- .27	-1.39 +/- .20
95	54	32	21	83	0.253	0.386	5	1.04 +/- .06	0.99 +/- .01	1.84 +/- .09	0.00 +/- .16
95	54	33	21.5	68	0.316	0.485	4	1.17 +/- .05	0.98 +/- .04	1.85 +/- .12	-0.09 +/- .20
88	48	38.5	9.5	120	0.079	0.321	5	2.20 +/- .07	0.80 +/- .14	1.62 +/- .24	-1.39 +/- .10
88	50	40	10.0	120	0.083	0.333					
0	46	44	0.9	216	0	0.204	5	3.33 +/- .33	0.54 +/- .08	-0.31 +/- .66	-2.40 +/- .24
0	50	48	0.8	168	0	0.286	3			-0.27 +/- .50	-3.72 +/- .22
92	46	34	11.5	95	0.121	0.358	5	1.68 +/- .05	1.00 +/- .00	1.97 +/- .16	-0.66 +/- .09
92	47	36	11.25	94	0.120	0.383	5	1.67 +/- .08	0.96 +/- .07	2.21 +/- .16	-0.61 +/- .08
85	46	40	5.6	114	0.049	0.351	5	2.87 +/- .33	0.54 +/- .05	1.67 +/- .31	-1.76 +/- .15
85	47	42	5.5	112	0.049	0.375	5	3.20 +/- .16	0.52 +/- .11	1.80 +/- .27	-1.98 +/- .14
77	46	43	3.3	116	0.028	0.371	5	4.16 +/- .28	0.51 +/- .07	0.31 +/- .43	-2.99 +/- .24
77	50	46	3.9	132	0.030	0.348	5	3.39 +/- .23	0.43 +/- .03	1.14 +/- .19	-2.27 +/- .17
0	48	46	0.4	172	0	0.267					
0	47	45	1.0	136	0	0.331					

AR	P1	P2	ΔP	Q	Rs	Rp	N	PI	LTD	PC1	PC2
0	74	72	2.4	164	0.015	0.439	5	4.65 +/- .40	0.59 +/- .12	-3.80 +/- .58	1.61 +/- .34
92	79	62	18	96	0.188	0.646	5	1.24 +/- .03	0.78 +/- .24		
92	76	58	17.4	83	0.210	0.699	4	1.21 +/- .05			
77	63	56	5.4	132	0.041	0.424	5	4.02 +/- .17		-3.25 +/- .35	-1.11 +/- .47
77	68	61	5.3	134	0.040	0.455	5	3.40 +/- .07	0.27 +/- .02	-2.04 +/- .12	-0.07 +/- .42
85	70	62	9	116	0.078	0.534	5	2.47 +/- .09	0.29 +/- .01	-0.83 +/- .25	-0.33 +/- .56
85	74	66	8.8	116	0.076	0.569	5	2.48 +/- .13	0.31 +/- .04	-0.87 +/- .13	0.19 +/- .32
95	68	47.5	20	62	0.323	0.766	5	0.94 +/- .05	0.88 +/- .15	1.91 +/- .13	0.00 +/- .11
0	65	65	2.2	156	0.014	0.417	5	4.30 +/- .35	0.34 +/- .07	-2.93 +/- .49	-0.88 +/- .59
0	67	65	2.1	140	0.015	0.464	5	4.43 +/- .20	0.33 +/- .09	-3.14 +/- .42	0.18 +/- .43
88	67	57	10.25	96	0.107	0.594	5	1.86 +/- .07	0.57 +/- .22	0.78 +/- .14	-0.82 +/- .11
88	67	57	10	88	0.114	0.648	5	1.69 +/- .03	0.64 +/- .21	0.99 +/- .15	-0.67 +/- .20
65	65	61	3.5	140	0.025	0.436	5	4.08 +/- .22	0.23 +/- .03	-1.87 +/- .46	-1.43 +/- .61
65	65	62	3.2	120	0.027	0.517	4	4.29 +/- .05	0.32 +/- .12	-2.33 +/- .31	-0.68 +/- .58
92	64	51	12.5	77	0.162	0.662	4	1.54 +/- .07	0.99 +/- .03	1.48 +/- .09	-0.56 +/- .08
92	62	50	11.5	77	0.149	0.649	5	1.56 +/- .09	0.93 +/- .14	1.70 +/- .08	-0.75 +/- .17
51	59	57	2.5	150	0.017	0.380	5	4.14 +/- .13	0.41 +/- .16	-1.54 +/- .55	-2.02 +/- .53
51	65	62	2.3	128	0.018	0.484	5	3.98 +/- .17	0.27 +/- .07	-1.18 +/- .47	-1.54 +/- .61
0	67	65	1.9	176	0.011	0.369	5	3.16 +/- .23	0.31 +/- .04	-0.65 +/- .35	-0.78 +/- .50
0	78	75	2.7	152	0.018	0.493	5	3.21 +/- .35	0.23 +/- .06	-0.76 +/- .36	0.25 +/- .40
77	81	76	5.75	152	0.038	0.500	5	2.24 +/- .09	0.26 +/- .03	0.06 +/- .11	0.17 +/- .31
77	85	80	5.1	144	0.035	0.556	5	2.01 +/- .08	0.23 +/- .03	0.23 +/- .18	0.34 +/- .31
85	93	84	8.9	132	0.067	0.636	5	1.58 +/- .06	0.32 +/- .05	0.93 +/- .17	0.33 +/- .20
85	95	86	8.5	124	0.068	0.694	5	1.44 +/- .08	0.37 +/- .04	1.16 +/- .11	0.36 +/- .21
95	98	69	26.5	78	0.340	0.885	5	0.82 +/- .03	1.00 +/- .00	2.27 +/- .13	0.42 +/- .08
95	99	70	27	78	0.346	0.897	5	0.74 +/- .06	0.97 +/- .06	2.31 +/- .12	0.45 +/- .12
88	100	86	12	113	0.106	0.761	4	1.26 +/- .08		1.61 +/- .14	0.17 +/- .22
88	103	89	11	110	0.100	0.809	5	1.11 +/- .03	0.84 +/- .15	1.76 +/- .10	0.20 +/- .11
65	100	94	3.6	140	0.026	0.671	5	2.09 +/- .06	0.13 +/- .06	0.52 +/- .12	1.26 +/- .30
65	101	95	3.7	142	0.026	0.669	4	1.94 +/- .11	0.14 +/- .06	0.79 +/- .18	1.13 +/- .23
0	96	91	2.5	158	0.016	0.576	5	2.24 +/- .11	0.14 +/- .03	0.20 +/- .20	1.20 +/- .24
0	101	97	2.25	148	0.015	0.655	4	2.16 +/- .01	0.14 +/- .02	0.63 +/- .17	1.42 +/- .26

AR	P1	P2	ΔP	Q	Rs	Rp	N	PI	LTD	PC1	PC2
0	56	56	0.7	146	0.005	0.384	5	5.86 +/- .50	0.50 +/- .02	-6.20 +/- .40	-1.72 +/- .21
85	60	52	7.6	144	0.053	0.361	5	2.15 +/- .06	0.68 +/- .13	-0.04 +/- .29	-1.62 +/- .28
85	60	52	7.8	156	0.054	0.333	5	1.98 +/- .07	0.59 +/- .07	0.43 +/- .27	-1.60 +/- .35
65	57	54	2.5	170	0.015	0.318	5	4.14 +/- .29	0.83 +/- .12	-3.41 +/- .48	-1.83 +/- .53
0	60	58	1.2	240	0.005	0.242	3	4.13 +/- .43	0.63 +/- .11	-3.06 +/- .64	-0.95 +/- .27
0	63	62	0.5	196	0.003	0.316	4	4.51 +/- .19	0.63 +/- .12	-4.19 +/- .18	-0.42 +/- .36
95	65	45.5	19	71	0.268	0.641	5	1.10 +/- .03	0.99 +/- .01	1.60 +/- .06	0.24 +/- .10
95	66	45	21.5	73	0.295	0.616	4	0.97 +/- .04	0.93 +/- .12	1.84 +/- .03	0.29 +/- .14
77	64	60	4.2	170	0.025	0.353					
77	67	60	5.8	146	0.040	0.411					
88	66	54	9.3	110	0.085	0.491					
88	70	58	9.9	116	0.085	0.500					
51	67	65	2.15	164	0.013	0.396					
51	73	70	3.45	168	0.021	0.417					
92	74	58.5	15.5	101	0.153	0.579					
92	73	58	15.5	96	0.161	0.604					
0	70	70	1.5	126	0.012	0.556	4	5.28 +/- .78	0.33 +/- .10	-4.65 +/- .82	1.27 +/- .57
0	70	69	2.1	124	0.017	0.556	5	4.99 +/- .12	0.25 +/- .04	-3.94 +/- .23	1.48 +/- .71
85	70	62	7.4	112	0.066	0.554	4	3.07 +/- .78	0.34 +/- .04	-1.06 +/- .61	0.18 +/- .26
85	71	65	7.3	110	0.066	0.591	5	2.43 +/- .10	0.23 +/- .05	-0.39 +/- .12	0.40 +/- .25
65	71	69	3.0	128	0.023	0.539	5	3.45 +/- .15	0.22 +/- .01	-1.65 +/- .19	0.62 +/- .40
65	70	67	3.9	118	0.033	0.568	5	3.47 +/- .12	0.21 +/- .03	-1.54 +/- .16	1.13 +/- .40
95	67	50	18	67	0.269	0.746	5	1.17 +/- .06	1.00 +/- .00	1.66 +/- .06	0.44 +/- .13
95	70	52	19.2	61	0.315	0.852	5	1.11 +/- .07	0.93 +/- .14	1.70 +/- .06	0.40 +/- .13
77	64	60	4.6	100	0.046	0.600	5	4.30 +/- .05	0.30 +/- .04	-2.33 +/- .10	-0.04 +/- .53
77	68	64	4.8	106	0.045	0.604	5	2.53 +/- .11	0.28 +/- .04	-0.16 +/- .12	-0.21 +/- .27
88	68	60	8.2	91	0.090	0.659	4	1.86 +/- .05	0.45 +/- .10	0.90 +/- .07	-0.66 +/- .21
0	66	65	1.45	90	0.016	0.722	5	4.69 +/- .46	0.24 +/- .02	-2.57 +/- .44	-0.26 +/- .34
0	72	71	1.65	110	0.015	0.645	5	3.12 +/- .12	0.19 +/- .02	-1.02 +/- .16	0.58 +/- .25

AR	P1	P2	ΔP	Q	Rs	Rp	N	PI	LTD	PC1	PC2
0	108	106	0.7	178	0	0.596	5	2.29 +/- .29	0.11 +/- .03	0.75 +/- .27	2.13 +/- .23
85	100	94	6.8	148	0.046	0.635	5	1.54 +/- .14	0.20 +/- .03	1.36 +/- .00	0.90 +/- .00
85	104	98	6.5	144	0.045	0.667	5	1.56 +/- .12	0.16 +/- .02		
95	100	64	34.5	110	0.314	0.582	5	0.64 +/- .06	0.57 +/- .10	2.30 +/- .00	0.86 +/- .01
95	104	69	34	109	0.312	0.633	5	0.70 +/- .04	0.84 +/- .11	2.35 +/- .00	0.80 +/- .00
65	106	102	2.45	192	0.013	0.531	5	3.24 +/- .20	0.10 +/- .03	-0.36 +/- .00	1.74 +/- .00
65	108	104	2.5	190	0.013	0.547	5	2.87 +/- .20	0.09 +/- .02		
88	116	100	12.25	168	0.073	0.595	4	1.20 +/- .07	0.36 +/- .12	1.65 +/- .10	0.80 +/- .21
88	106	98	8.75	135	0.065	0.711	5	1.36 +/- .11	0.31 +/- .08	1.49 +/- .07	0.70 +/- .18
51	112	108	1.85	162	0.011	0.667	5	3.64 +/- .28	0.12 +/- .04	-0.38 +/- .20	2.45 +/- .49
51	110	108	1.2	164	0.007	0.659	5	2.38 +/- .24	0.10 +/- .05	0.43 +/- .25	1.72 +/- .06
92	110	94	15.5	120	0.129	0.783	5	1.09 +/- .07	0.64 +/- .23	1.89 +/- .04	0.66 +/- .11
92	114	97	17.5	123	0.142	0.789	5	0.90 +/- .14	0.87 +/- .18	2.03 +/- .09	0.63 +/- .17
77	120	116	3.15	170	0.019	0.682	5	2.36 +/- .19	0.13 +/- .02	0.63 +/- .35	1.70 +/- .24
77	116	112	2.85	170	0.017	0.659	5	1.51 +/- .12	0.14 +/- .08	1.22 +/- .10	1.08 +/- .33
0	120	119	0.5	160	0	0.744	5	2.92 +/- .18	0.09 +/- .03	0.10 +/- .24	2.17 +/- .28
0	120	120	0	170	0	0.706	5	2.04 +/- .19	0.14 +/- .01	0.68 +/- .11	1.43 +/- .11
85	122	114	6.2	164	0.038	0.695	5	1.43 +/- .08	0.23 +/- .02	1.21 +/- .16	0.82 +/- .06
85	119	112	5.8	158	0.037	0.709	4	1.34 +/- .11	0.29 +/- .13	1.41 +/- .17	1.10 +/- .09
95	116	86	31.5	100	0.315	0.860	5	0.53 +/- .05	0.99 +/- .00	2.47 +/- .11	0.63 +/- .02
95	116	77	39.5	119	0.332	0.647	5	0.46 +/- .03	0.99 +/- .01	2.43 +/- .09	0.68 +/- .09
65	92	91	0.8	156	0.005	0.583	5	3.12 +/- .12	0.12 +/- .02	-0.27 +/- .00	1.76 +/- .00
65	86	84	1.15	142	0.008	0.592	5	4.15 +/- .31	0.11 +/- .02		
88	90	82	8.0	113	0.071	0.726	5	1.81 +/- .10	0.26 +/- .02		
88	97	89	8	116	0.069	0.767	5	1.43 +/- .09	0.29 +/- .05	1.36 +/- .12	0.88 +/- .03
51	100	99	0.7	142	0.005	0.697	5	4.05 +/- .19	0.11 +/- .01	-1.36 +/- .17	2.78 +/- .31
51	97	96	0.7	148	0.005	0.649	5	2.81 +/- .25	0.12 +/- .01	-0.09 +/- .33	1.98 +/- .30
92	108	94	14	120	0.117	0.783	4	0.87 +/- .05		2.04 +/- .11	0.61 +/- .15
92	98	82	13.5	117	0.115	0.701	5	1.08 +/- .04	0.93 +/- .17	1.89 +/- .13	0.57 +/- .19
77	94	90	2.7	92	0.029	0.978	5	2.29 +/- .14	0.11 +/- .07	0.38 +/- .24	1.43 +/- .35
77	100	96	1.95	83	0.023	1.157	5	2.12 +/- .17	0.11 +/- .05	0.46 +/- .17	1.74 +/- .16
0	96	96	0	126	0	0.762	5	3.62 +/- .19	0.10 +/- .01	-0.82 +/- .43	3.32 +/- .37
0	82	83	0	152	0	0.546	5	2.30 +/- .11	0.11 +/- .04	0.37 +/- .23	2.04 +/- .26

APPENDIX C

The results of the five experiments described in Chapter 7 are found on the following pages. Each dog is individually listed and the results provide a chronological record of each experiment. A total of 21 sets of waveforms were excluded from the analysis because clotting was clearly taking place: these were nearly all from the 95% area reduction stenosis. Symbols and units are defined as follows:

SYMBOL	DEFINITION	UNITS AND NOTES
AR	Area reduction	Per cent
HR	Heart rate	Beats per minute
p	Recording position	See Fig 2, Chapter 7
DD	Distance downstream of P	Unstenosed diameters
DC	Doppler waveform class	A - E (see Chapter 7)
P_2	Pressure below stenosis	mm Hg
DP	Pressure gradient	mm Hg across stenosis
Q	EM flow	ml per minute
R_s	Stenosis resistance	mm Hg.min.ml^{-1}
R_p	Peripheral resistance	mm Hg.min.ml^{-1}
V_s	Stroke volume	ml (Q / HR)
L_s	Stroke length	Unstenosed diameters

DD and L_s are expressed in unstenosed diameters to facilitate comparison with Clark's paper (128).

RESULTS OF DOPPLER CLASSIFICATION, PRESSURE, FLOW AND RESISTANCE MEASUREMENTS AND CALCULATED STROKE VOLUME AND LENGTH FOR THE EXPERIMENTS DESCRIBED IN CHAPTER 7

DOG 27

AR	HR	P	DD	DC	P_2	DP	Q	R_s	R_p	V_s	L_s
0	65	1	4.4	B	76	2.1	160	.013	.475	2.46	25.1
		3	13.6	A	78	2.1	160	.013	.488	2.46	25.1
		4	16.8	A	79	2.0	160	.013	.494	2.46	25.1
95	64	2	9.0	E	49	33.5	84	.399	.583	1.31	13.4
		3	13.6	C	48	33.5	82	.409	.585	1.28	13.1
		4	16.8	B	49	33.0	82	.402	.598	1.28	13.1
93	64	1	4.4	E	62	19.5	105	.187	.593	1.63	16.6
		2	9.0	E	62	20.0	106	.189	.585	1.66	16.9
		3	13.6	C	61	20.5	104	.197	.587	1.63	16.6
		4	16.8	B	61	21.0	103	.204	.592	1.61	16.4
90	64	2	9.0	E	68	11.0	117	.098	.581	1.83	18.6
		3	13.6	E	68	11.5	114	.101	.596	1.78	18.2
		4	16.8	C	68	11.0	116	.095	.589	1.80	18.4
85	63	1	4.4	D	70	7.8	127	.062	.553	2.01	20.5
		2	9.0	D	71	8.2	125	.066	.568	1.98	20.2
		3	13.6	C	71	7.7	124	.062	.575	1.96	20.0
		4	16.8	A	71	7.9	122	.065	.584	1.93	19.7
80	63	1	4.4	D	72	5.2	130	.040	.554	2.06	21.0
		2	9.0	D	74	5.2	130	.040	.569	2.06	21.0
		3	13.6	C	72	5.0	125	.040	.576	1.98	20.2
		4	16.8	A	71	5.0	120	.042	.592	1.90	19.4
67	63	1	4.4	D	74	3.3	130	.025	.569	2.06	21.0
		2	9.0	D	74	3.2	130	.025	.569	2.06	21.0
		3	13.6	C	74	3.2	130	.025	.569	2.06	21.0
		4	16.8	B	73	3.1	125	.025	.584	1.98	20.2
0	63	1	4.4	B	73	1.3	130	.010	.562	2.06	21.0
		2	9.0	B	73	1.3	130	.010	.562	2.06	21.0
		3	13.6	B	73	1.3	125	.010	.584	1.98	20.2
		4	16.8	A	75	1.3	132	.010	.568	2.10	21.4
95	62	1	4.4	E	-	-	-	-	-	-	-
		2	9.0	D	-	-	-	-	-	-	-
		3	13.6	B	43	32.5	63	.516	.683	1.02	10.4
		4	16.8	B	41	32.0	63	.508	.651	1.02	10.4

DOG 28

AR	HR	P	DD	DC	P_2	DP	Q	R_s	R_p	V_s	L_s
0	81	1	6.6	B	96	1.7	137	.012	.701	1.69	17.2
		2	12.6	B	95	1.6	140	.011	.679	1.73	17.6
		3	17.6	A	96	1.6	145	.011	.662	1.79	18.2
		4	22.4	A	95	1.6	145	.011	.655	1.79	18.2
95		1	6.6	E	-	-	-	-	-	-	-
93	75	1	6.6	E	65	27.0	95	.285	.686	1.26	12.9
		2	12.6	C	61	34.0	85	.396	.711	1.14	11.7
		3	17.6	B	52	38.0	73	.523	.715	0.97	9.9
		4	22.4	B	49	45.0	73	.619	.674	0.97	9.9
90	66	1	6.6	D	77	13.5	127	.107	.609	1.92	19.5
		2	12.6	D	76	14.5	123	.118	.616	1.77	19.0
		3	17.6	B	75	16.0	121	.137	.641	1.77	18.1
		4	22.4	A	72	16.5	117	.141	.615	1.77	18.1
85	65	1	6.6	E	83	8.1	140	.058	.593	2.15	21.9
		2	12.6	C	82	8.0	140	.057	.586	2.15	21.9
		3	17.6	B	82	8.1	137	.059	.599	2.11	21.5
		4	22.4	A	80	8.0	133	.060	.602	2.05	20.9
80	65	1	6.6	E	97	5.6	177	.032	.548	2.72	27.7
		2	12.6	C	88	5.2	155	.034	.568	2.38	24.3
		3	17.6	A	86	5.3	150	.035	.573	2.31	23.5
		4	22.4	A	81	5.1	140	.036	.579	2.15	21.9
67	68	1	6.6	D	90	2.6	162	.016	.556	2.38	24.3
		2	12.6	B	85	2.4	153	.016	.556	2.25	22.9
		3	17.6	A	83	2.4	149	.016	.557	2.19	22.3
		4	22.4	A	83	2.5	145	.017	.572	2.13	21.7
57	71	1	6.6	C	87	2.2	150	.015	.580	2.11	21.5
		2	12.6	B	85	2.2	145	.015	.586	2.04	20.8
		3	17.6	A	87	2.2	150	.015	.580	2.11	21.5
		4	22.4	A	84	2.2	147	.015	.571	2.07	21.1
0	77	1	6.6	B	92	1.5	165	.009	.558	2.14	21.8
		2	12.6	A	86	1.4	155	.009	.555	2.01	20.5
		3	17.6	A	84	1.4	150	.009	.560	1.95	19.9
		4	22.4	A	88	1.4	157	.009	.561	2.04	20.8
93	70	1	6.6	E	50	30.0	66	.452	.753	0.95	9.7
		2	12.6	C	52	32.0	66	.483	.785	0.95	9.6
		3	17.6	B	48	33.0	63	.524	.762	0.90	9.3
		4	22.4	B	46	34.0	57	.596	.807	0.81	8.3
90	70	1	6.6	E	67	15.0	89	.169	.757	1.26	12.9
		2	12.6	D	65	17.0	84	.203	.776	1.20	12.2

		3	17.6	B	65	15.0	87	.172	.747	1.24	12.7
		4	22.4	A	65	16.0	85	.187	.761	1.22	12.4
85	66	1	6.6	E	75	10.5	109	.096	.688	1.65	16.8
		2	12.6	C	72	11.5	106	.108	.679	1.61	16.4
		3	17.6	B	71	12.0	101	.119	.703	1.53	15.6
		4	22.4	B	69	12.5	96	.130	.719	1.45	14.8
80	68	1	6.6	D	77	6.3	125	.050	.616	1.84	18.7
		2	12.6	C	77	6.4	125	.051	.616	1.84	18.7
		3	17.6	B	78	6.4	120	.053	.650	1.76	18.0
		4	22.4	A	77	6.4	123	.052	.626	1.81	18.4
67	73	1	6.6	D	81	2.9	132	.022	.614	1.81	18.4
		2	12.6	B	79	3.0	122	.025	.648	1.84	17.0
		3	17.6	A	82	3.3	134	.025	.612	1.84	18.7
		4	22.4	A	82	3.4	131	.026	.626	1.79	18.3
57	81	1	6.6	D	87	2.1	157	.013	.554	1.94	19.8
		2	12.6	B	90	2.2	173	.013	.520	2.14	21.8
		3	17.6	A	91	2.2	175	.013	.520	2.16	22.0
		4	22.4	A	85	2.2	162	.014	.525	2.00	20.4

DOG 31

AR	HR	P	DD	DC	P_2	DP	Q	R_s	R_p	V_s	L_s
0	59	1	5.2	B	92	0.3	205	.001	.449	3.47	35.4
		2	10.0	A	90	0.2	200	.001	.450	3.39	34.5
		3	14.6	A	88	0.1	185	.001	.476	3.14	32.0
		4	19.0	B	82	0.1	175	.001	.469	2.97	30.2
95	52	1	5.2	E	49	37.0	79	.468	.620	1.52	15.5
		2	10.0	C	-	-	-	-	-	-	-
		3	14.6	C	-	-	-	-	-	-	-
		4	19.0	B	-	-	-	-	-	-	-
93	49	1	5.2	E	66	21.0	133	.158	.496	2.71	27.7
		2	10.0	D	65	22.0	130	.169	.500	2.65	27.0
		3	14.6	C	-	-	-	-	-	-	-
		4	19.0	B	-	-	-	-	-	-	-
90	46	1	5.2	D	63	11.0	114	.096	.553	2.48	25.3
		2	10.0	D	-	-	-	-	-	-	-
		3	14.6	C	-	-	-	-	-	-	-
		4	19.0	B	-	-	-	-	-	-	-

85	47	1	5.2	E	75	7.4	125	.059	.600	2.66	27.1
		2	10.0	D	75	8.0	120	.067	.625	2.55	26.0
		3	14.6	C	75	8.4	120	.070	.625	2.55	26.0
		4	19.0	B	75	9.2	120	.080	.652	2.45	24.9
80	46	1	5.2	E	75	4.0	125	.032	.600	2.72	27.7
		2	10.0	D	76	4.3	128	.034	.596	2.77	28.2
		3	14.6	C	78	5.0	130	.038	.600	2.83	28.8
		4	19.0	B	79	5.5	130	.042	.608	2.83	28.8
67	47	1	5.2	D	82	1.1	140	.008	.586	2.98	30.4
		2	10.0	C	81	1.1	135	.008	.600	2.87	29.3
		3	14.6	B	80	1.1	135	.008	.593	2.87	29.3
		4	19.0	B	81	1.3	137	.009	.591	2.91	29.7
57	56	1	5.2	D	100	0.4	185	.002	.541	3.30	33.7
		2	10.0	D	98	0.4	170	.002	.576	3.04	30.9
		3	14.6	B	80	0.3	155	.002	.516	2.77	28.2
		4	19.0	B	80	0.4	155	.003	.516	2.77	28.2
0	49	1	5.2	B	82	0	162	0	.506	3.31	33.7
		2	10.0	B	83	0	158	0	.525	3.22	32.9
		3	14.6	A	82	0	155	0	.529	3.16	32.2
		4	19.0	A	82	0	150	0	.547	3.06	31.2
95		1	5.2	E	-	-	-	-	-	-	-
		2	10.0	D	-	-	-	-	-	-	-
93	48	1	5.2	E	64	18.0	101	.178	.634	2.10	21.4
		2	10.0	D	62	19.0	93	.204	.667	1.94	19.7
		3	14.6	B	57	25.0	106	.236	.538	2.21	22.5
		4	19.0	B	58	25.0	90	.278	.644	1.88	19.1
90	58	1	5.2	D	77	15.0	131	.115	.588	2.26	23.0
		2	10.0	D	75	17.0	125	.136	.600	2.16	22.0
		3	14.6	C	74	18.0	122	.148	.607	2.10	21.4
		4	19.0	B	69	19.0	111	.171	.622	1.91	19.5
85	51	1	5.2	E	76	8.5	120	.071	.633	2.35	24.0
		2	10.0	D	77	9.5	120	.079	.642	2.35	24.0
		3	14.6	B	77	11.0	120	.092	.642	2.35	24.0
		4	19.0	A	76	12.0	120	.100	.633	2.35	24.0
80	58	1	5.2	E	80	7.8	120	.065	.667	2.07	21.1
		1.5	7.6	D	-	-	-	-	-	-	-
		2	10.0	D	79	8.7	119	.073	.664	2.05	20.9
		2.5	12.3	C	-	-	-	-	-	-	-
		3	14.6	B	80	10.0	122	.082	.656	2.10	21.4
		4	19.0	B	81	10.0	122	.082	.664	2.10	21.4

67	54	1	5.2	D	80	3.4	120	.028	.667	2.22	22.6
		1.5	7.6	D	-	-	-	-	-	-	-
		2	10.0	C	82	3.6	125	.029	.656	2.31	23.6
		2.5	12.3	B	-	-	-	-	-	-	-
		3	14.6	B	83	3.9	125	.031	.664	2.31	23.6
		4	19.0	A	83	3.9	122	.032	.680	2.26	23.0
57	54	1	5.2	C	88	1.5	130	.012	.667	2.41	24.5
		1.5	7.6	C	-	-	-	-	-	-	-
		2	10.0	B	87	1.4	130	.011	.669	2.41	24.5
		2.5	12.3	A	-	-	-	-	-	-	-
		3	14.6	A	87	1.5	130	.012	.669	2.41	24.5
		4	19.0	B	86	1.4	130	.011	.662	2.41	24.5
0	54	1	5.2	B	85	0.8	145	.006	.586	2.69	27.4
		1.5	7.6	B	-	-	-	-	-	-	-
		2	10.0	B	88	0.8	142	.006	.620	2.63	26.8
		2.5	12.3	A	-	-	-	-	-	-	-
		3	14.6	A	89	0.8	140	.006	.636	2.59	26.4
		4	19.0	A	89	0.8	138	.006	.645	2.56	26.0
93		1	5.2	E	-	-	-	-	-	-	-
90	51	1	5.2	E	73	14.5	98	.148	.745	1.92	19.6
		2	10.0	D	-	-	-	-	-	-	-
		3	14.6	B	-	-	-	-	-	-	-
		4	19.0	B	-	-	-	-	-	-	-
85	56	1	5.2	E	83	7.5	108	.069	.769	1.93	19.7
		1.5	7.6	E	-	-	-	-	-	-	-
		2	10.0	D	86	9.5	114	.083	.754	2.04	20.7
		2.5	12.3	D	-	-	-	-	-	-	-
		3	14.6	B	82	9.0	103	.087	.796	1.84	18.7
		4	19.0	A	79	9.0	101	.089	.782	1.80	18.4
80	53	1	5.2	E	80	4.0	105	.038	.762	1.98	20.2
		1.5	7.6	D	-	-	-	-	-	-	-
		2	10.0	D	83	4.7	105	.045	.790	1.98	20.2
		2.5	12.3	C	-	-	-	-	-	-	-
		3	14.6	B	84	5.1	105	.049	.800	1.98	20.2
		4	19.0	A	83	5.3	105	.050	.790	1.98	20.2
67	52	1	5.2	E	83	2.4	105	.023	.790	2.02	20.6
		1.5	7.6	D	-	-	-	-	-	-	-
		2	10.0	C	85	2.5	108	.023	.787	2.08	21.2
		2.5	12.3	B	-	-	-	-	-	-	-
		3	14.6	A	84	2.5	105	.024	.800	2.02	20.6
		4	19.0	A	84	2.6	105	.025	.800	2.02	20.6

57	50	1	5.2	D	100	0.3	130	.002	.769	2.60	26.5
		1.5	7.6	D	-	-	-	-	-	-	-
		2	10.0	C	94	0.2	110	.002	.855	2.20	22.4
		2.5	12.3	B	-	-	-	-	-	-	-
		3	14.6	A	91	0.1	105	.001	.867	2.10	21.4
		4	19.0	B	90	0.2	105	.002	.857	2.10	21.4
0	53	1	5.2	C	83	1.1	105	.010	.790	1.98	20.2
		1.5	7.6	C	-	-	-	-	-	-	-
		2	10.0	B	83	1.0	110	.009	.755	2.08	21.1
		2.5	12.3	A	-	-	-	-	-	-	-
		3	14.6	A	82	0.9	110	.008	.745	2.08	21.1
		4	19.0	A	83	0.9	115	.008	.722	2.17	22.1

DOG 32

AR	HR	P	DD	DC	P_2	DP	Q	R_s	R_p	V_s	L_s
0	84	1	4.8	B	78	0.5	105	.005	.743	1.25	12.7
		2	10.0	A	77	0.5	102	.005	.755	1.21	12.4
		3	15.0	B	78	0.6	102	.005	.765	1.21	12.4
		4	23.4	A	77	0.7	100	.007	.770	1.19	12.1
95	80	1	4.8	E	58	34.0	57	.598	1.019	0.71	7.2
		2	10.0	C	48	38.0	55	.695	.868	0.68	7.0
93	77	1	4.8	E	61	14.5	85	.170	.714	1.11	11.3
		2	10.0	D	62	14.0	78	.181	.800	1.01	10.3
		3	15.0	B	65	13.5	81	.166	.800	1.06	10.8
		4	23.4	A	64	14.0	78	.181	.826	1.01	10.3
90	86	1	4.8	E	66	10.7	77	.139	.857	0.90	9.1
		1.5	7.4	D	-	-	-	-	-	-	-
		2	10.0	D	62	13.5	72	.188	.861	0.84	8.5
		2.5	12.5	C	-	-	-	-	-	-	-
85	84	1	4.8	D	72	7.3	88	.083	.818	1.05	10.7
		1.5	7.4	D	-	-	-	-	-	-	-
		2	10.0	D	72	8.5	86	.099	.837	1.02	10.4
		2.5	12.5	C	-	-	-	-	-	-	-
		3	15.0	B	70	9.8	82	.120	.854	0.98	9.9
		4	23.4	B	68	10.8	81	.133	.840	0.96	9.8
80	75	1	4.8	E	87	13.3	113	.118	.770	1.51	15.4
		1.5	7.4	C	-	-	-	-	-	-	-
		2	10.0	B	67	12.4	82	.151	.817	1.09	11.1
		2.5	12.5	A	-	-	-	-	-	-	-
		3	15.0	A	69	13.5	92	.147	.750	1.23	12.5
		4	23.4	B	66	13.0	85	.153	.776	1.13	11.5

67	84	1	4.8	D	68	3.5	90	.039	.756	1.07	10.9
		1.5	7.4	C	-	-	-	-	-	-	-
		2	10.0	B	69	3.6	90	.040	.767	1.07	10.9
		2.5	12.5	A	-	-	-	-	-	-	-
		3	15.0	A	71	3.7	88	.042	.807	1.05	10.7
		4	23.4	A	71	3.6	87	.041	.816	1.04	10.6
57	81	1	4.8	D	69	1.2	82	.015	.841	1.01	10.3
		1.5	7.4	C	-	-	-	-	-	-	-
		2	10.0	B	69	1.2	82	.015	.841	1.01	10.3
		2.5	12.5	A	-	-	-	-	-	-	-
		3	15.0	A	71	1.3	82	.016	.866	1.01	10.3
		4	23.4	A	72	1.4	82	.017	.878	1.01	10.3
0	78	1	4.8	B	72	0.5	140	.004	.514	1.79	18.3
		2	10.0	B	71	0.5	120	.004	.592	1.54	15.7
		3	15.0	A	71	0.5	110	.005	.645	1.41	14.4
		4	23.4	A	72	0.5	105	.005	.686	1.35	13.7
93	82	1	4.8	E	53	23.0	98	.235	.541	1.20	12.2
		2	10.0	D	53	22.0	89	.247	.596	1.09	11.1
		3	15.0	B	53	21.0	90	.233	.589	1.10	11.2
		4	23.4	B	55	18.0	82	.220	.671	1.00	10.2
90	95	1	4.8	E	49	15.0	75	.200	.653	0.79	8.0
85	82	1	4.8	E	68	7.4	90	.082	.756	1.10	11.3
		1.5	7.4	D	-	-	-	-	-	-	-
		2	10.0	C	67	8.3	86	.097	.779	1.05	10.7
		3	15.0	B	67	9.2	84	.110	.798	1.02	10.4
		4	23.4	B	67	9.2	83	.111	.807	1.01	10.3
90	86	1	4.8	E	62	12.5	60	.208	1.033	0.70	7.1
		2	10.0	D	-	-	-	-	-	-	-
		3	15.0	B	-	-	-	-	-	-	-
		4	23.4	B	-	-	-	-	-	-	-
80	106	1	4.8	D	70	3.6	94	.038	.745	0.89	9.0
		1.5	7.4	D	-	-	-	-	-	-	-
		2	10.0	B	70	3.8	96	.040	.729	0.91	9.2
		2.5	12.5	B	-	-	-	-	-	-	-
		3	15.0	A	73	4.0	105	.038	.695	0.99	10.1
		4	23.4	B	72	3.9	99	.039	.727	0.93	9.5
67	96	1	4.8	D	71	3.4	106	.032	.670	1.10	11.3
		2	10.0	C	71	3.4	105	.032	.676	1.09	11.1
		3	15.0	B	70	3.5	105	.033	.667	1.09	11.1
		4	23.4	A	70	3.6	106	.034	.660	1.10	11.3
57	95	1	4.8	C	71	2.3	112	.021	.634	1.18	12.0
		2	10.0	B	71	2.3	115	.020	.617	1.21	12.3
		3	15.0	A	72	2.4	117	.021	.615	1.23	12.5
		4	23.4	A	73	2.4	120	.020	.608	1.26	12.9

0	107	1	4.8	C	72	1.5	150	.010	.480	1.40	14.3
		2	10.0	B	75	1.5	150	.010	.500	1.40	14.3
		3	15.0	A	77	1.5	150	.010	.513	1.40	14.3
		4	23.4	A	77	1.5	150	.010	.513	1.40	14.3

DOG 33

AR	HR	P	DD	DC	P_2	DP	Q	R_s	R_p	V_s	L_s
0	81	1	4.8	B	71	0.6	180	.003	.394	2.22	22.6
		2	10.0	B	74	0.6	180	.003	.411	2.22	22.6
		3	15.0	A	73	0.5	178	.003	.410	2.20	22.4
		4	22.0	A	73	0.5	168	.003	.435	2.07	21.1
57	70	1	4.8	D	70	0.9	155	.006	.452	2.21	22.6
		1.5	7.4	C	-	-	-	-	-	-	-
		2	10.0	B	69	0.9	150	.006	.460	2.14	21.8
		3	15.0	A	67	0.9	147	.006	.456	2.10	21.1
		4	22.0	A	66	0.9	145	.006	.455	2.07	21.1
67	70	1	4.8	D	65	1.8	145	.012	.448	2.07	21.1
		1.5	7.4	C	-	-	-	-	-	-	-
		2	10.0	B	67	2.0	150	.013	.447	2.14	21.8
		2.5	12.5	B	-	-	-	-	-	-	-
		3	15.0	A	66	2.1	145	.014	.455	2.07	21.1
		4	22.0	A	67	2.2	145	.015	.462	2.07	21.1
80	75	1	4.8	D	63	3.6	125	.029	.504	1.67	17.0
		1.5	7.4	D	-	-	-	-	-	-	-
		2	10.0	C	65	4.1	130	.032	.500	1.73	17.7
		2.5	12.5	B	-	-	-	-	-	-	-
		3	15.0	B	66	4.6	130	.035	.508	1.73	17.7
		4	22.0	A	63	4.8	120	.040	.525	1.60	16.3
85	82	1	4.8	E	64	6.1	122	.050	.525	1.49	15.2
		2	10.0	D	66	6.6	125	.053	.528	1.52	15.5
		3	15.0	B	66	7.0	122	.057	.541	1.49	15.2
		4	22.0	B	65	7.2	118	.061	.551	1.44	14.7
90	74	1	4.8	E	64	3.7	122	.030	.525	1.65	16.8
		2	10.0	D	63	3.7	118	.031	.534	1.59	16.2
		3	15.0	C	62	3.8	118	.032	.525	1.59	16.2
		4	22.0	B	62	4.0	116	.034	.534	1.57	16.0
93	65	1	4.8	E	58	15.0	106	.142	.548	1.63	16.6
		2	10.0	D	59	16.0	108	.149	.549	1.65	16.9
		3	15.0	C	57	16.5	101	.163	.563	1.56	15.9
		4	22.0	B	55	18.0	96	.187	.571	1.48	15.1

0	77	1	4.8	B	91	1.4	230	.006	.396	2.99	30.4
		2	10.0	B	91	1.3	225	.006	.404	2.92	29.8
		3	15.0	A	92	1.3	225	.006	.409	2.92	29.8
		4	22.0	A	93	1.3	225	.006	.413	2.92	29.8
57	71	1	4.8	C	96	2.8	200	.014	.480	2.82	28.7
		1.5	7.4	C	-	-	-	-	-	-	-
		2	10.0	B	95	2.9	200	.015	.475	2.82	28.7
		2.5	12.5	B	-	-	-	-	-	-	-
		3	15.0	A	92	2.9	195	.015	.472	2.75	28.0
		4	22.0	A	90	3.0	190	.016	.474	2.68	27.3
67	74	1	4.8	D	89	4.3	190	.023	.468	2.57	26.2
		1.5	7.4	C	-	-	-	-	-	-	-
		2	10.0	C	89	4.3	185	.023	.481	2.50	25.5
		2.5	12.5	B	-	-	-	-	-	-	-
		3	15.0	A	84	4.3	168	.026	.500	2.27	23.1
		4	22.0	A	85	4.6	170	.027	.500	2.30	23.4
80	78	1	4.8	D	80	6.4	170	.038	.471	2.18	22.2
		1.5	7.4	D	-	-	-	-	-	-	-
		2	10.0	C	80	6.9	170	.041	.471	2.18	22.2
		2.5	12.5	C	-	-	-	-	-	-	-
		3	15.0	B	79	7.0	165	.042	.479	2.12	21.6
		4	22.0	A	79	7.5	170	.044	.465	2.18	22.2
85	90	1	4.8	E	77	10.0	153	.065	.503	1.70	17.3
		1.5	7.4	D	-	-	-	-	-	-	-
		2	10.0	D	75	10.5	143	.073	.524	1.59	16.2
		2.5	12.5	C	-	-	-	-	-	-	-
		3	15.0	B	73	13.0	137	.095	.533	1.52	15.5
90	104	1	4.8	E	67	10.5	122	.086	.549	1.17	12.0
		2	10.0	D	69	12.0	125	.096	.552	1.20	12.2
		2.5	12.5	C	-	-	-	-	-	-	-
		3	15.0	B	67	14.0	119	.118	.563	1.14	11.7
		4	22.0	B	63	16.0	115	.139	.548	1.11	11.3
93	94	1	4.8	E	56	23.0	89	.258	.629	0.95	9.6
		2	10.0	C	53	26.5	85	.312	.624	0.90	9.2
		2.5	12.5	C	-	-	-	-	-	-	-
		3	15.0	B	49	29.0	79	.367	.620	0.84	8.6
		4	22.0	B	48	30.0	95	.316	.505	1.01	10.3

APPENDIX D

The results of the patient studies will be found on the following pages. Table D-I contains the raw results of PI and Laplace transform analysis for each waveform in the study. The waveforms are usually in groups of five, all from a single measurement site. The fourth figure in the patient identity code indicates the measurement site: 1 is from the right common femoral artery and 4 from the left. The following figures are codes for the month and year of the observation.

Table D-II contains the summarised results for each patient including mean and sample standard deviation of PI and LTD for each group of waveforms.

Table D-III contains the raw results of principal component analysis, again for each waveform in the series. Waveforms with heart rates of greater than 100 or less than 50 were not analysed. Values for each of the first five PC coefficients are given. The summarised results of PCA are found in Table D-IV with means and sample standard deviations for the first three principal components; at the end of this table will be found the cumulative information content of the

various principal components. The raw results of PCA, LT and PI calculations are reproduced directly from the original computer printouts to eliminate possible errors in transcription.

The results of clinical, pressure, arteriographic and 'standard clinical' assessments will be found in Table D-V. For convenience, the summarised Doppler results are again included. Table D-VI contains details of the papaverine test on all the patients on whom it was performed. Finally in Table D-VII those patients whose aortoiliac segments were classified as uncertain after standard clinical assessment are described in more detail.

TABLE D-I

RESULTS OF PULSATILITY INDEX AND LAPLACE TRANSFORM ANALYSIS FOR THE PATIENTS (178-238) AND NORMAL SUBJECTS (700-811)

(HR = heart rate, RMSE = error in LT curve fitting)

PATIENT IDENTITY	HR	PI	LTD	GAMMA	OMEGA	RMSE
1781039	80.	6.18	.59	38.8	15.7	.08
1781039	80.	5.25	.60	14.8	18.6	.08
1781039	80.	5.20	.51	11.4	19.7	.08
1781039	78.	5.03	.51	11.1	19.3	.11
1784039	71.	3.09	1.00	91.7	28.1	.09
1784039	72.	3.37	.88	5.8	42.0	.10
1784039	71.	3.21	.66	5.2	27.8	.10
1784039	71.	3.43	1.00	55.7	22.2	.09
1784039	73.	3.42	.71	5.6	34.8	.10
1801049	72.	1.33	.92	123.0	5.3	.06
1801049	87.	1.20	1.00	126.6	10.9	.11
1801049	70.	1.22	1.00	-143.6	11.6	.09
1801049	83.	1.12	1.00	150.0	8.7	.10
1801049	67.	1.27	1.00	145.5	8.7	.09
1804049	71.	1.60	1.00	102.2	20.0	.06
1804049	76.	1.65	.90	3.4	37.2	.08
1804049	67.	1.58	1.00	156.9	22.5	.06
1804049	76.	1.61	1.00	77.5	15.6	.05
1804049	75.	1.54	1.00	58.5	19.6	.08
1811049	75.	8.38	.48	53.2	18.1	.06
1811049	74.	7.18	.47	20.9	18.6	.06
1811049	74.	8.29	.41	21.1	18.5	.04
1811049	75.	10.10	.36	26.9	18.6	.05
1811049	77.	10.03	.35	29.6	17.3	.06
1811049	75.	11.63	.36	61.3	17.9	.05
1814049	68.	7.78	.40	9.7	25.8	.05
1814049	67.	7.09	.46	9.4	29.9	.06
1814049	67.	7.25	.59	11.9	30.8	.04
1814049	67.	8.89	.54	19.6	28.6	.06
1814049	68.	8.95	.56	16.0	26.6	.05
1821049	80.	8.41	.40	39.2	14.8	.08
1821049	82.	7.47	.44	27.2	15.7	.06
1821049	78.	7.50	.40	19.1	17.8	.05
1821049	75.	6.96	.43	17.7	15.6	.06
1821049	74.	9.20	.38	25.2	15.8	.08

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1824049	79.	4.71	1.00	12.3	27.8	.06
1824049	79.	4.62	.93	34.4	16.2	.06
1824049	81.	4.41	.41	6.9	25.2	.07
1824049	78.	4.47	1.00	41.1	28.7	.06
1824049	78.	4.42	.61	8.5	22.0	.04
1831059	97.	2.03	.49	5.0	34.3	.10
1831059	96.	2.36	.45	5.1	32.2	.08
1831059	96.	2.36	.75	5.6	45.9	.06
1831059	99.	2.19	.43	5.0	38.9	.08
1831059	97.	2.47	.41	5.4	27.4	.09
1834059	116.	4.57	.33	12.6	17.7	.06
1834059	106.	4.50	.32	11.0	16.6	.07
1834059	109.	5.39	.38	21.6	15.8	.07
1834059	106.	4.11	.32	9.8	17.7	.07
1834059	108.	4.61	.38	15.1	17.3	.09
1841059	93.	3.64	.28	6.2	23.6	.09
1841059	94.	3.30	.29	6.2	25.8	.07
1841059	96.	3.61	.29	6.7	23.4	.06
1841059	97.	5.00	.32	9.2	22.3	.05
1841059	99.	3.52	.45	8.0	29.7	.09
1844059	89.	2.72	.45	6.1	29.6	.09
1844059	93.	3.43	.31	6.4	25.1	.08
1844059	90.	2.75	.44	5.7	27.3	.08
1844059	91.	2.71	.43	5.8	24.6	.05
1844059	93.	2.89	.37	5.5	24.1	.06
1851059	95.	1.38	.99	166.6	7.9	.07
1851059	94.	1.40	.92	112.0	7.2	.07
1851059	90.	1.38	.98	76.7	7.4	.08
1851059	93.	1.35	.98	85.6	7.7	.08
1851059	93.	1.30	.86	419.2	6.6	.07
1851059	96.	1.29	.91	155.5	7.4	.06
1854059	96.	5.18	.42	14.6	19.5	.07
1854059	98.	4.65	.32	9.3	18.7	.05
1854059	101.	4.35	.29	7.9	18.8	.04
1854059	97.	4.54	.33	9.8	20.5	.06
1854059	91.	5.56	.48	17.1	19.8	.07
1861059	83.	2.20	.38	3.8	40.8	.08
1861059	82.	2.30	.42	4.1	35.7	.06
1861059	88.	2.10	.58	4.7	38.5	.08
1861059	82.	2.58	.44	4.6	42.9	.09
1864059	76.	4.01	.47	6.8	27.3	.07
1864059	87.	3.60	.50	8.0	26.7	.08
1864059	90.	3.61	.45	7.3	22.3	.05
1864059	79.	4.22	.85	10.0	39.5	.05
1864059	85.	3.78	.74	9.1	33.8	.07

TABLE D-I

1871059	72.	4.72	.72	57.7	10.6	.08
1871059	73.	4.65	.76	58.2	11.6	.09
1871059	73.	4.89	.76	84.1	12.3	.07
1871059	77.	4.80	.67	660.5	10.8	.08
1871059	75.	5.18	.47	12.4	14.3	.07
1874059	77.	3.42	.57	6.2	23.0	.10
1874059	75.	2.89	1.00	78.9	22.1	.10
1874059	75.	3.36	.84	5.9	34.1	.11
1874059	73.	3.07	1.00	2008.3	18.6	.08
1881059	64.	12.22	.28	25.6	16.4	.07
1881059	65.	8.92	.36	18.6	19.0	.07
1881059	67.	9.28	.34	17.8	18.7	.06
1881059	65.	5.14	.30	6.5	19.3	.05
1881059	70.	6.31	.30	9.9	19.7	.10
1884059	66.	3.99	.26	4.0	21.8	.11
1884059	66.	4.43	.31	4.7	18.9	.07
1884059	61.	3.21	.34	3.6	20.2	.08
1884059	63.	3.97	.30	4.4	19.5	.08
1884059	60.	4.00	.28	3.9	17.5	.08
1891059	81.	3.00	.43	5.4	26.2	.11
1891059	87.	3.08	.44	5.9	31.2	.13
1891059	71.	3.03	.37	4.2	21.5	.08
1891059	70.	2.83	.24	3.5	23.6	.08
1891059	95.	2.53	.83	6.7	37.4	.09
1894059	69.	4.95	.25	5.3	18.5	.09
1894059	67.	3.95	.34	5.3	19.1	.07
1894059	65.	4.67	.21	4.3	19.3	.11
1894059	69.	4.04	.24	4.3	20.1	.11
1894059	80.	3.67	.30	5.4	18.1	.09
1901059	80.	5.38	.35	8.9	18.3	.07
1901059	81.	4.50	.32	7.4	19.9	.07
1901059	80.	4.76	.30	7.2	19.4	.09
1901059	78.	5.66	.30	9.0	17.2	.04
1901059	78.	4.35	.31	6.6	18.8	.06
1904059	82.	3.49	.37	6.1	21.5	.11
1904059	81.	3.30	.38	5.6	21.3	.09
1904059	80.	3.10	.36	5.0	20.0	.07
1904059	79.	3.29	.32	5.2	19.7	.09
1904059	83.	3.44	.34	5.7	20.6	.09
1911059	85.	3.59	.45	6.6	32.1	.08
1911059	84.	3.68	.35	6.0	26.2	.07
1911059	87.	3.75	.39	6.6	27.8	.08
1911059	88.	4.13	.38	6.6	26.4	.07
1911059	86.	3.71	.39	6.0	29.1	.07

TABLE D-I

1914059	83.	5.82	.60	20.1	20.5	.07
1914059	81.	4.63	.33	6.9	19.6	.05
1914059	85.	4.33	.50	9.6	22.6	.08
1914059	84.	4.23	.36	6.8	21.0	.05
1914059	86.	4.71	.47	10.3	21.9	.06
1924059	80.	8.00	.34	14.2	22.2	.04
1924059	80.	9.50	.38	21.4	20.4	.04
1924059	103.	7.02	.41	21.8	20.7	.04
1924059	89.	5.91	.42	12.7	25.0	.09
1924059	81.	8.27	.37	16.3	23.2	.04
1924059	83.	6.94	.29	10.8	24.4	.04
1931059	81.	1.64	.63	4.7	10.4	.08
1931059	75.	1.67	.61	4.0	12.6	.06
1931059	71.	1.80	.55	3.5	12.2	.07
1931059	69.	1.67	.52	3.3	11.3	.08
1931059	67.	1.80	.45	3.1	12.0	.06
1934059	67.	2.20	.50	3.6	10.7	.05
1934059	68.	1.83	.50	3.3	10.8	.06
1934059	67.	1.97	.54	3.6	10.6	.05
1934059	70.	1.84	.56	3.8	11.1	.06
1934059	68.	1.90	.47	3.3	11.7	.06
1941059	77.	3.10	.32	4.0	19.3	.05
1941059	76.	3.14	.29	3.7	19.7	.07
1941059	75.	2.58	.36	3.7	18.1	.06
1941059	77.	2.67	.39	4.2	24.6	.05
1941059	77.	2.70	.35	3.9	20.0	.04
1944059	78.	3.25	.29	4.5	16.8	.05
1944059	78.	2.86	.29	4.0	15.2	.05
1944059	77.	2.75	.30	3.8	15.7	.05
1944059	79.	2.61	.29	4.0	16.2	.05
1944059	78.	2.63	.31	3.9	16.6	.04
1951069	86.	1.24	1.00	37.6	19.7	.11
1951069	88.	1.05	1.00	133.7	15.9	.12
1951069	90.	1.11	1.00	45.6	16.9	.11
1951069	90.	1.05	1.00	109.8	11.3	.10
1951069	90.	1.11	1.00	87.6	14.6	.11
1951069	83.	1.21	.98	4.2	23.7	.12
1954069	92.	1.08	1.00	73.3	18.4	.12
1954069	90.	1.06	1.00	121.7	22.3	.12
1954069	92.	1.07	1.00	181.2	12.7	.12
1954069	88.	1.01	1.00	71.5	11.0	.13
1954069	87.	.98	1.00	109.4	13.0	.13
1961069	76.	6.12	.71	826.3	18.2	.05
1961069	67.	7.46	.86	63.4	23.7	.05
1961069	80.	6.08	.53	13.4	34.0	.06

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1964069	69.	4.81	.29	6.4	32.2	.08
1964069	69.	4.90	.28	8.7	41.4	.18
1964069	67.	5.26	.50	10.2	58.8	.12
1964069	68.	4.81	.56	9.4	45.4	.10
1964069	63.	4.05	.17	4.0	29.9	.11
1971069	81.	4.49	.96	101.6	14.7	.06
1971069	80.	5.22	.87	-385.6	16.2	.07
1971069	81.	4.94	.93	952.6	16.4	.07
1971069	77.	4.39	.86	171.6	13.2	.05
1971069	79.	5.22	.90	323.1	16.0	.07
1974069	80.	7.59	.31	12.9	11.7	.11
1974069	75.	8.16	.31	11.7	12.4	.09
1974069	82.	7.16	.30	13.7	11.4	.10
1974069	82.	5.59	.30	8.0	12.4	.09
1974069	79.	6.34	.31	8.5	12.7	.09
1981069	67.	1.23	1.00	-220.7	10.2	.06
1981069	66.	1.21	1.00	-207.3	10.1	.06
1981069	70.	1.18	1.00	3781.6	11.2	.06
1981069	71.	1.21	1.00	538.5	15.2	.07
1981069	70.	1.19	1.00	-150.5	10.3	.06
1984069	66.	.96	.89	-352.5	4.4	.07
1984069	71.	.83	.87	-175.1	4.5	.07
1984069	70.	.87	.88	-114.0	4.5	.07
1984069	69.	.87	.90	-142.5	4.6	.07
1984069	68.	.93	.92	-136.0	4.6	.07
1991069	60.	10.44	.45	88.2	16.5	.10
1991069	58.	10.18	.41	25.8	15.8	.08
1991069	57.	10.37	.41	28.8	17.0	.09
1991069	57.	10.61	.39	295.4	13.7	.08
1991069	56.	9.07	.43	18.7	15.9	.10
1994069	57.	6.86	.79	19.4	28.7	.11
1994069	59.	6.60	.93	60.3	20.6	.10
1994069	56.	6.10	.49	9.7	26.8	.11
1994069	58.	6.08	.98	-2681.0	18.7	.10
2001069	59.	1.88	.86	3.1	30.2	.06
2001069	56.	1.93	.81	3.0	27.4	.07
2001069	59.	1.69	1.00	89.0	24.3	.06
2001069	59.	1.73	1.00	62.6	17.8	.07
2004069	62.	1.94	.60	3.1	20.9	.06
2004069	61.	1.82	1.00	69.6	20.8	.07
2004069	61.	1.96	.81	3.3	31.7	.07
2004069	65.	1.79	.66	3.1	28.8	.08
2004069	62.	1.96	.54	3.1	17.7	.06

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2011069	96.	1.02	1.00	159.8	10.6	.10
2011069	90.	1.08	.88	100.7	6.2	.09
2011069	83.	1.16	1.00	54.1	14.4	.11
2011069	84.	1.18	1.00	39.8	15.0	.10
2014069	88.	1.41	.88	4.5	22.8	.09
2014069	92.	1.22	1.00	49.0	16.0	.10
2014069	89.	1.30	1.00	90.2	13.3	.09
2014069	88.	1.25	1.00	238.4	10.7	.09
2014069	90.	1.28	1.00	148.9	10.4	.10
2021069	82.	5.11	.64	43.9	14.2	.06
2021069	82.	4.73	.69	153.0	14.1	.07
2021069	85.	4.04	.76	240.2	13.2	.08
2021069	83.	4.04	.79	117.7	13.0	.07
2021069	85.	3.97	.79	363.8	12.5	.07
2024069	80.	4.42	.67	67.4	11.6	.05
2024069	81.	4.12	.69	34.2	12.0	.06
2024069	79.	4.15	.73	13.2	17.7	.05
2024069	80.	4.42	.67	44.0	12.2	.06
2024069	80.	4.19	.69	51.8	11.6	.05
2031079	57.	3.78	.78	-72.6	8.8	.02
2031079	61.	3.79	.85	-63.5	9.8	.02
2031079	57.	3.44	.88	-171.0	8.6	.02
2031079	56.	4.33	.71	-57.5	8.7	.02
2031079	58.	3.66	.80	-46.6	8.7	.02
2034079	57.	3.51	.82	747.2	8.1	.06
2034079	56.	3.57	.81	147.5	8.3	.07
2034079	58.	3.71	.82	61.2	8.8	.07
2034079	57.	3.75	.81	79.9	8.9	.07
2034079	57.	3.58	.81	597.6	8.1	.06
2041079	76.	5.76	.55	29.2	15.9	.10
2041079	77.	5.82	.52	-613.9	13.3	.11
2041079	76.	5.86	.53	3101.8	13.7	.09
2041079	76.	5.80	.55	-180.8	13.5	.09
2044079	75.	3.73	.50	6.6	40.0	.06
2044079	75.	4.50	.38	6.7	26.9	.06
2044079	75.	3.32	.42	5.7	35.1	.07
2044079	75.	3.84	.43	6.5	29.7	.06
2051079	71.	1.50	.89	3.6	20.0	.08
2051079	72.	1.42	1.00	152.8	11.8	.07
2051079	71.	1.52	1.00	26.7	21.4	.07
2054079	75.	6.02	.29	9.2	18.0	.08
2054079	76.	6.39	.29	9.8	18.5	.08
2054079	75.	6.79	.37	17.1	17.1	.10
2054079	74.	6.47	.33	11.5	16.8	.08
2054079	74.	6.66	.45	20.3	16.1	.10

TABLE D-I

2064089	107.	1.41	.73	4.2	60.8	.07
2064089	110.	1.42	.71	4.2	102.9	.07
2064089	103.	1.39	1.00	160.2	36.4	.06
2064089	106.	1.59	.42	4.8	67.3	.10
2064089	109.	1.29	.62	4.6	59.4	.08
2071079	71.	2.71	.29	3.4	18.4	.06
2071079	71.	5.59	.23	5.6	18.4	.11
2071079	71.	4.99	.20	4.8	18.0	.09
2071079	72.	4.29	.23	4.6	19.6	.13
2071079	71.	5.63	.24	5.7	18.6	.11
2071079	71.	5.02	.21	4.8	18.5	.12
2071079	73.	5.44	.25	6.3	18.7	.14
2071079	73.	5.00	.21	5.2	18.1	.14
2074079	76.	2.54	.38	4.0	18.9	.04
2074079	74.	3.04	.48	4.6	17.6	.04
2074079	72.	2.25	.43	3.8	18.2	.06
2074079	74.	2.28	.48	3.8	22.8	.06
2074079	71.	2.90	.38	3.9	18.5	.05
2081079	68.	1.17	1.00	-138.3	9.7	.08
2081079	67.	1.22	1.00	263.1	8.5	.08
2081079	68.	1.29	1.00	97.5	9.3	.09
2081079	72.	1.13	.99	-240.1	5.5	.09
2081079	72.	1.11	.97	-133.8	5.4	.08
2081079	71.	1.15	1.00	106.6	8.5	.09
2084079	71.	1.83	.44	3.3	18.0	.09
2084079	67.	1.93	.45	3.2	17.6	.08
2084079	65.	2.13	.42	3.3	16.7	.06
2084079	63.	2.11	.41	3.3	17.1	.08
2091089	71.	2.95	.62	4.9	28.0	.06
2091089	70.	3.03	.47	4.7	22.7	.06
2091089	71.	3.41	.52	5.1	30.5	.08
2091089	70.	2.89	.50	4.6	27.9	.08
2094089	74.	3.24	.83	6.3	40.8	.08
2094089	72.	3.00	.41	4.4	21.1	.08
2094089	73.	3.17	.50	5.5	20.8	.07
2101089	64.	1.64	1.00	2417.9	16.8	.08
2101089	65.	1.65	1.00	126.6	15.1	.08
2101089	61.	1.62	1.00	2528.2	12.3	.07
2101089	64.	1.61	1.00	114.8	35.5	.10
2101089	63.	1.65	1.00	430.3	17.4	.07
2101089	62.	1.77	1.00	6458.7	13.2	.09
2104089	64.	7.75	.46	18.9	14.7	.05
2104089	66.	6.92	.40	10.4	19.0	.07
2104089	64.	7.33	.45	12.5	18.4	.07
2104089	62.	7.08	.44	11.9	17.3	.07
2104089	64.	6.65	.58	15.2	20.4	.08

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2114089	99.	2.11	.49	6.1	22.3	.09
2114089	100.	2.26	.36	5.4	20.3	.07
2114089	103.	2.06	.52	6.5	24.7	.12
2114089	102.	2.01	.54	6.3	21.2	.08
2121089	57.	6.18	.65	63.6	10.8	.07
2121089	59.	6.10	.65	51.1	11.4	.05
2121089	60.	5.83	.64	58.4	11.1	.05
2121089	62.	5.80	.66	51.6	13.3	.05
2121089	64.	5.62	.61	237.7	11.3	.05
2124089	62.	1.60	1.00	154.4	14.9	.06
2124089	60.	1.58	1.00	2368.1	9.8	.06
2124089	60.	1.61	1.00	265.3	10.2	.06
2124089	58.	1.71	1.00	3966.8	16.1	.07
2124089	60.	1.53	1.00	255.4	15.6	.07
2131089	75.	4.23	.45	5.4	33.7	.08
2131089	71.	4.21	.36	4.4	23.4	.10
2131089	72.	3.66	.48	5.2	41.6	.08
2131089	70.	3.47	.42	5.0	40.7	.08
2134089	72.	3.28	.68	5.5	34.5	.06
2134089	72.	3.14	.65	5.6	32.6	.06
2134089	72.	3.35	.44	5.0	23.3	.07
2134089	68.	3.35	.79	5.4	45.4	.07
2141089	57.	5.36	.35	6.2	20.5	.14
2141089	55.	5.09	.45	6.3	21.1	.10
2141089	56.	5.76	.58	9.3	20.6	.11
2141089	59.	4.96	.47	7.2	24.1	.09
2141089	54.	6.44	.48	10.6	16.4	.07
2144089	59.	1.86	.57	2.8	19.4	.06
2144089	57.	2.13	.48	2.9	14.9	.05
2144089	59.	1.90	.70	2.9	21.0	.06
2144089	57.	1.91	1.00	40.0	25.9	.08
2144089	59.	1.88	.67	2.9	22.4	.09
2151089	94.	3.15	.48	6.2	39.5	.08
2151089	97.	3.19	.54	6.3	35.6	.08
2151089	92.	2.97	.38	5.2	24.1	.06
2151089	79.	3.68	.29	4.7	26.6	.07
2151089	88.	3.32	.51	5.7	35.3	.09
2154089	84.	3.82	.37	5.6	26.4	.07
2154089	85.	3.97	.34	6.3	28.2	.08
2154089	88.	3.99	.38	6.6	30.0	.08
2154089	83.	4.17	.35	6.4	31.1	.09
2154089	86.	3.94	.37	6.0	30.6	.10

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2161089	87.	3.30	.64	6.6	27.8	.09
2161089	85.	3.55	.76	7.4	31.9	.11
2161089	89.	3.21	.95	7.2	66.1	.09
2161089	86.	3.31	.83	6.7	41.5	.10
2164089	86.	4.00	.97	11.8	27.1	.06
2164089	86.	3.62	.46	6.1	22.8	.07
2164089	84.	5.30	.40	8.9	22.3	.09
2164089	87.	4.39	.82	9.3	44.9	.07
2164089	85.	4.29	1.00	125.3	19.6	.06
2171089	59.	3.92	.27	4.5	13.8	.09
2171089	60.	4.11	.30	5.0	13.7	.10
2171089	63.	3.72	.24	3.9	15.6	.12
2171089	58.	4.24	.31	5.2	14.2	.10
2174089	63.	6.45	.60	173.6	11.6	.10
2174089	61.	6.19	.61	56.1	11.6	.10
2174089	62.	6.43	.59	59.9	11.5	.09
2174089	65.	7.02	.55	40.3	13.2	.08
2174089	65.	5.98	.61	27.4	13.3	.09
2181089	68.	5.12	.27	5.8	18.8	.07
2181089	66.	4.83	.29	5.8	19.8	.09
2181089	63.	4.95	.42	6.9	22.9	.09
2181089	68.	4.70	.35	6.1	21.1	.10
2181089	69.	4.23	.34	5.5	20.8	.09
2184089	72.	4.22	.35	6.1	20.9	.08
2184089	74.	3.57	.33	5.1	19.7	.07
2184089	70.	3.71	.32	4.9	19.1	.07
2184089	74.	3.78	.37	5.5	20.2	.07
2184089	79.	3.45	.33	5.0	19.2	.06
2191099	79.	3.41	.23	3.9	23.1	.08
2191099	82.	3.76	.16	4.4	28.7	.16
2191099	82.	4.00	.16	4.6	27.3	.16
2191099	82.	3.95	.20	4.8	26.6	.12
2191099	81.	3.90	.21	4.8	25.2	.12
2194099	85.	6.87	.37	18.4	18.2	.05
2194099	81.	6.02	.29	10.5	17.6	.05
2194099	82.	5.94	.35	13.5	17.5	.07
2194099	81.	5.87	.28	9.5	17.1	.04
2194099	81.	6.12	.31	11.0	17.3	.05
2201109	83.	4.66	.44	11.1	16.5	.04
2201109	85.	4.25	.50	11.1	16.7	.07
2201109	83.	4.37	.53	10.8	16.4	.08
2201109	81.	4.77	.49	11.0	16.2	.07
2201109	83.	4.41	.64	16.2	17.0	.06

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2204109	78.	3.75	.67	7.1	28.6	.07
2204109	80.	3.86	.57	7.1	27.7	.07
2204109	79.	3.49	.48	5.9	26.5	.06
2204109	79.	3.53	.56	5.8	27.5	.07
2204109	79.	3.27	.65	6.1	28.7	.07
2211109	75.	2.57	.40	4.2	20.7	.06
2211109	74.	2.90	.41	4.3	19.6	.08
2211109	73.	3.25	.37	4.3	20.0	.08
2211109	75.	2.70	.42	4.5	20.3	.06
2211109	76.	2.52	.44	4.6	20.7	.06
2214109	77.	2.89	.49	5.3	24.3	.10
2214109	75.	2.90	.46	4.9	21.4	.08
2214109	76.	2.75	.40	4.5	20.1	.07
2214109	76.	2.54	.41	4.2	20.1	.06
2221109	51.	1.61	.78	2.4	26.8	.07
2221109	52.	1.38	1.00	40.3	20.5	.08
2221109	53.	1.49	.71	2.5	27.1	.09
2221109	51.	1.55	.77	2.5	25.3	.09
2221109	52.	1.50	.64	2.4	25.6	.10
2224109	51.	1.54	.95	2.2	29.4	.07
2224109	51.	1.53	.85	2.4	32.6	.09
2224109	54.	1.52	1.00	174.5	14.4	.08
2224109	50.	1.44	1.00	4154.8	15.4	.07
2224109	52.	1.49	1.00	2123.5	18.0	.07
2231109	80.	2.99	.59	5.5	29.6	.10
2231109	80.	2.97	.60	5.5	29.1	.09
2231109	80.	2.40	.52	5.2	21.4	.08
2231109	79.	2.44	.53	5.1	22.2	.06
2231109	82.	2.50	.74	5.8	32.7	.08
2231109	83.	2.87	.61	5.6	28.4	.09
2234109	77.	4.06	.44	6.8	19.9	.07
2234109	78.	3.92	.40	6.5	19.6	.07
2234109	85.	3.42	.53	7.4	24.9	.08
2234109	76.	3.75	.39	5.7	21.2	.07
2234109	80.	4.01	.74	8.4	31.8	.07
2241119	70.	3.25	.41	4.2	21.9	.05
2241119	68.	3.48	.41	5.1	20.8	.07
2241119	70.	4.14	.44	5.5	22.5	.07
2241119	70.	3.35	.40	4.5	23.1	.07
2241119	69.	3.65	.49	5.5	26.7	.08
2244119	64.	1.61	1.00	28.2	16.5	.07
2244119	66.	1.46	1.00	508.7	10.0	.07
2244119	65.	1.66	.92	3.3	21.4	.06
2244119	66.	1.56	1.00	29.6	17.2	.06

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2251010	71.	1.29	.97	150.9	5.3	.09
2251010	75.	1.18	.95	-126.5	5.4	.08
2251010	75.	1.21	.91	95.8	5.1	.09
2251010	81.	1.17	.88	226.6	5.3	.11
2251010	77.	1.16	.90	-572.3	5.3	.09
2254010	77.	4.36	.45	9.5	14.8	.07
2254010	82.	4.84	.41	11.0	15.1	.07
2254010	83.	3.98	.39	8.1	16.6	.06
2254010	78.	4.14	.36	7.0	15.7	.06
2261020	84.	1.80	1.00	62.3	19.8	.05
2261020	85.	1.78	.85	4.7	25.4	.05
2261020	83.	1.80	.63	4.2	24.0	.05
2261020	81.	1.87	.59	4.2	22.4	.06
2261020	83.	1.98	.63	4.8	25.0	.07
2264020	84.	2.81	.52	4.9	37.9	.06
2264020	88.	2.22	.52	4.5	35.6	.06
2264020	81.	2.61	.60	5.1	31.6	.07
2264020	83.	2.48	.38	3.9	26.5	.09
2271020	74.	5.03	.28	5.9	20.1	.09
2271020	76.	3.87	.34	5.6	25.9	.14
2271020	76.	3.55	.34	4.6	23.0	.12
2271020	74.	3.89	.93	7.1	54.3	.12
2271020	74.	3.82	.31	4.6	21.9	.13
2274020	74.	1.83	.53	3.3	32.0	.07
2274020	76.	1.77	.60	3.3	35.3	.08
2274020	74.	1.87	.70	3.5	39.6	.07
2274020	74.	1.76	.66	3.4	36.0	.08
2274020	74.	1.75	.56	3.2	33.4	.08
2281030	49.	2.68	.53	2.8	41.3	.06
2281030	48.	2.77	.41	2.4	30.8	.07
2281030	48.	2.61	.51	2.6	53.1	.06
2281030	48.	2.48	.47	2.5	41.5	.07
2284030	49.	1.15	1.00	2133.1	16.4	.07
2284030	49.	1.18	1.00	1948.6	17.0	.08
2284030	51.	1.11	1.00	4763.3	14.2	.09
2284030	51.	1.09	1.00	-166.0	12.5	.09
2284030	50.	1.15	1.00	-979.1	12.8	.10
2291030	111.	1.93	.54	4.5	30.9	.06
2291030	112.	1.78	.61	4.9	39.0	.07
2291030	109.	1.69	.77	5.0	46.4	.06
2291030	112.	1.70	.64	4.9	52.3	.07
2291030	107.	1.99	.48	4.4	38.3	.07
2291030	105.	2.02	.35	4.2	46.4	.06

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2294030	103.	2.40	.34	4.2	41.3	.07
2294030	111.	1.87	.35	4.4	41.1	.08
2294030	110.	1.96	.45	4.7	30.5	.07
2294030	106.	1.66	.67	4.5	34.8	.08
2294030	108.	1.46	.62	4.2	38.3	.09
2294030	104.	1.97	.39	4.2	37.4	.08
2301040	67.	7.89	.34	19.7	13.4	.07
2301040	68.	4.82	.43	10.0	15.2	.09
2301040	65.	6.39	.35	10.9	14.2	.05
2301040	66.	5.81	.36	11.2	14.1	.06
2301040	61.	6.49	.34	9.6	13.3	.05
2304040	66.	5.58	.61	44.1	12.6	.07
2304040	64.	6.11	.38	8.5	15.1	.06
2304040	63.	6.06	.36	8.8	15.2	.05
2304040	63.	6.74	.34	10.0	15.4	.05
2304040	63.	6.93	.32	10.2	16.3	.04
2311040	81.	4.21	.46	6.8	21.8	.06
2311040	78.	4.00	.41	5.8	17.7	.06
2311040	78.	4.50	.48	7.3	19.7	.07
2311040	78.	4.63	.36	6.6	18.9	.05
2311040	88.	4.95	.35	8.1	21.1	.05
2314040	79.	6.15	.32	11.3	13.9	.06
2314040	75.	6.40	.29	9.5	13.5	.08
2314040	81.	5.87	.42	22.5	13.0	.06
2314040	80.	6.40	.36	18.8	12.4	.06
2321050	57.	3.09	.52	4.1	19.2	.03
2321050	58.	3.26	.47	4.2	15.5	.04
2321050	58.	3.31	.56	4.1	17.4	.04
2321050	57.	3.13	.66	4.3	16.3	.03
2321050	58.	3.04	.59	4.2	21.2	.04
2324050	56.	2.41	.68	3.5	21.8	.06
2324050	59.	2.14	.58	3.1	20.3	.04
2324050	56.	2.09	.51	2.9	20.2	.06
2324050	56.	2.07	.58	3.0	17.7	.05
2324050	57.	2.12	.67	3.0	24.3	.06
2331060	54.	4.07	.26	3.6	17.5	.12
2331060	48.	4.26	.30	3.2	16.7	.08
2331060	53.	4.98	.38	5.3	20.4	.13
2331060	50.	4.22	.29	3.6	16.4	.09
2331060	52.	5.06	.25	4.1	16.8	.13
2334060	54.	2.27	.76	3.0	31.2	.07
2334060	53.	2.06	.96	2.8	38.5	.08
2334060	52.	1.96	.80	2.7	26.9	.08
2334060	52.	2.06	.91	2.9	37.5	.08

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2341060	69.	1.69	.91	3.8	20.6	.07
2341060	71.	1.48	1.00	109.0	12.5	.08
2341060	69.	1.60	.92	3.6	20.9	.08
2341060	69.	1.61	1.00	29.0	18.2	.09
2341060	68.	1.53	.87	3.3	22.6	.09
2344060	68.	3.44	.49	5.4	21.6	.09
2344060	69.	3.50	.43	5.3	20.4	.10
2344060	70.	3.43	.40	5.1	20.6	.09
2344060	68.	3.44	.53	5.4	22.9	.11
2344060	67.	3.34	.43	5.2	20.4	.08
2351060	81.	3.11	.27	4.2	24.3	.09
2351060	86.	3.01	.30	4.6	23.7	.08
2351060	90.	2.80	.27	4.3	23.1	.09
2351060	87.	2.68	.30	4.6	23.0	.07
2351060	91.	2.82	.29	4.6	27.1	.10
2354060	76.	5.53	.24	7.1	20.7	.09
2354060	83.	5.00	.23	6.4	20.8	.12
2354060	80.	4.56	.23	6.0	20.0	.09
2354060	79.	4.88	.24	6.3	20.2	.10
2354060	78.	4.57	.23	5.6	19.6	.09
2361070	58.	2.63	.57	3.1	19.9	.07
2361070	63.	2.61	.58	3.7	50.2	.09
2361070	63.	2.88	.77	3.4	36.4	.07
2361070	63.	2.91	.85	3.6	39.0	.08
2361070	63.	2.62	.56	3.3	50.9	.06
2364070	57.	3.78	.23	3.2	18.8	.08
2364070	56.	3.23	.29	2.8	21.5	.09
2364070	55.	2.99	.39	2.9	24.0	.08
2364070	59.	2.76	.55	3.1	28.1	.06
2364070	63.	2.63	.41	3.3	22.2	.08
2371080	75.	2.05	.43	3.2	24.2	.08
2371080	76.	2.51	.37	3.5	22.9	.06
2371080	75.	2.54	.36	3.5	25.3	.06
2371080	76.	2.43	.30	3.5	29.2	.08
2371080	69.	2.80	.28	3.0	31.4	.08
2374080	80.	3.14	.72	5.9	32.6	.09
2374080	75.	3.15	.71	5.4	31.1	.08
2374080	75.	3.01	.50	5.1	27.3	.06
2374080	90.	2.82	.43	5.2	20.5	.05
2374080	73.	2.94	.35	4.2	20.2	.05
2381080	78.	14.13	.26	116.4	15.2	.07
2381080	77.	10.83	.32	174.8	14.8	.05
2381080	78.	15.81	.23	179.4	14.0	.12
2381080	75.	10.72	.33	248.3	14.7	.05
2381080	72.	13.58	.28	109.2	14.6	.06

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2384080	76.	3.22	.33	4.7	22.7	.05
2384080	76.	3.32	.35	5.3	25.4	.09
2384080	72.	3.28	.35	5.1	20.8	.05
2384080	70.	3.73	.29	4.5	20.2	.04
2384080	71.	3.31	.36	5.0	23.7	.05
7001109	64.	3.38	.26	3.6	18.0	.09
7001109	65.	3.50	.26	3.8	16.8	.10
7001109	67.	3.48	.25	3.7	15.8	.10
7001109	66.	3.47	.25	3.7	16.8	.10
7001109	65.	3.78	.26	3.9	16.2	.10
8011129	63.	8.47	.26	10.8	21.0	.10
8011129	66.	7.96	.25	10.0	21.2	.09
8011129	66.	7.25	.21	7.9	20.2	.08
8011129	67.	7.47	.26	9.9	22.7	.11
8011129	64.	7.86	.27	9.7	21.0	.09
8021129	65.	21.50	.18	47.7	18.5	.13
8021129	66.	14.93	.26	48.0	19.1	.11
8021129	65.	14.94	.23	25.6	18.8	.09
8021129	65.	15.36	.21	21.0	19.7	.08
8021129	68.	10.09	.22	12.9	22.8	.08
8031129	63.	3.75	.21	3.6	17.6	.11
8031129	66.	2.90	.23	3.1	19.1	.10
8031129	67.	2.62	.24	3.1	19.1	.11
8031129	66.	2.16	.30	2.9	19.3	.10
8031129	65.	2.68	.24	3.0	19.0	.11
8041129	63.	6.33	.23	6.7	19.2	.08
8041129	71.	5.84	.21	6.6	19.8	.08
8041129	75.	6.18	.24	8.1	19.8	.09
8041129	77.	5.48	.25	7.7	20.0	.09
8041129	66.	6.36	.28	8.2	20.7	.09
8051129	69.	8.68	.26	12.6	20.1	.07
8051129	67.	8.22	.27	11.3	21.0	.08
8051129	64.	8.94	.24	9.9	20.7	.06
8051129	66.	8.85	.25	10.3	21.0	.07
8051129	65.	8.82	.28	12.0	21.0	.08
8061129	68.	25.37	.15	38.7	15.7	.21
8061129	71.	25.97	.12	99.4	14.7	.23
8061129	65.	30.86	.14	39.4	15.0	.24
8061129	64.	21.09	.18	29.9	15.2	.19
8061129	65.	15.27	.22	24.6	16.1	.14
8061129	65.	18.16	.18	36.2	14.7	.13
8071129	72.	1.25	.59	2.6	39.0	.14
8071129	70.	1.32	.52	2.6	28.5	.13
8071129	70.	1.26	.65	2.6	43.6	.13
8071129	77.	1.38	.59	3.0	38.7	.13
8071129	74.	1.45	.49	2.9	29.4	.12

TABLE D-I

8081129	67.	2.42	.23	2.5	21.0	.11
8081129	69.	2.07	.28	2.7	24.9	.14
8081129	65.	1.95	.31	2.5	22.9	.08
8081129	65.	2.57	.23	2.7	21.4	.11
8081129	64.	4.20	.14	2.7	19.7	.16
8091129	70.	4.86	.16	3.8	20.8	.16
8091129	67.	4.37	.16	3.3	20.8	.15
8091129	65.	4.69	.16	3.5	19.7	.16
8091129	66.	5.54	.17	4.8	20.4	.15
8091129	68.	5.44	.17	4.3	20.3	.17
8101129	64.	10.94	.30	21.5	18.5	.05
8101129	66.	11.75	.26	22.9	18.2	.06
8101129	63.	11.24	.27	18.0	18.2	.06
8101129	61.	11.13	.24	14.9	18.6	.05
8101129	62.	12.98	.28	35.8	17.6	.08
8111129	63.	12.65	.29	33.0	17.6	.03
8111129	62.	13.01	.30	63.9	17.4	.05
8111129	65.	13.66	.28	61.8	17.1	.04
8111129	69.	10.84	.27	23.4	17.7	.06
8111129	70.	9.77	.30	20.7	18.4	.07
7001129	75.	2.60	.24	3.3	24.1	.13
7001129	75.	2.94	.23	3.6	25.4	.16
7001129	73.	2.91	.28	4.5	25.2	.16
7001129	77.	2.94	.24	3.5	23.4	.12
7001129	81.	2.84	.18	3.4	27.5	.21
7011129	74.	2.87	.21	3.2	23.0	.14
7011129	71.	2.83	.21	2.9	20.9	.12
7011129	76.	2.71	.23	3.2	22.4	.12
7011129	73.	2.55	.23	3.0	22.5	.12
7011129	72.	2.94	.22	3.1	22.1	.13
7021129	77.	4.71	.48	18.1	12.3	.08
7021129	88.	4.02	.50	18.8	12.8	.09
7021129	80.	4.23	.50	13.3	14.0	.08
7021129	78.	4.00	.38	7.7	15.7	.08
7021129	76.	4.09	.42	8.3	17.5	.12
7031129	79.	1.76	.36	3.1	24.9	.15
7031129	89.	1.54	.51	3.7	27.3	.13
7031129	78.	1.84	.37	3.1	21.6	.11
7031129	83.	1.78	.40	3.6	25.6	.12
7031129	79.	1.93	.32	3.1	21.1	.11
7041129	83.	1.98	.33	3.4	24.1	.11
7041129	85.	2.70	.27	3.7	23.7	.13
7041129	77.	2.70	.25	3.1	22.9	.15
7041129	76.	2.23	.29	3.0	19.9	.13
7041129	75.	2.04	.32	3.0	22.9	.12

TABLE D-II

MEANS AND STANDARD DEVIATIONS OF PI AND LTD FOR EACH LIMB IN THE STUDY (N = NUMBER OF WAVEFORMS ANALYSED)

N	PATIENT IDENTITY	PI	±SD	LTD	±SD
4.	1781039.	5.42	.52	.55	.05
5.	1784039.	3.30	.15	.85	.16
5.	1801049.	1.23	.08	.98	.04
5.	1804049.	1.60	.04	.98	.04
6.	1811049.	9.27	1.61	.41	.06
5.	1814049.	7.99	.89	.51	.08
5.	1821049.	7.90	.89	.41	.02
5.	1824049.	4.53	.13	.79	.27
5.	1831059.	2.28	.17	.51	.14
5.	1834059.	4.64	.47	.35	.03
5.	1841059.	3.81	.68	.33	.07
5.	1844059.	2.90	.30	.40	.06
6.	1851059.	1.35	.05	.94	.05
5.	1854059.	4.86	.50	.37	.08
4.	1861059.	2.30	.21	.46	.09
5.	1864059.	3.84	.27	.60	.18
5.	1871059.	4.85	.21	.68	.12
4.	1874059.	3.19	.25	.85	.20
5.	1881059.	8.37	2.77	.32	.03
5.	1884059.	3.92	.44	.30	.03
5.	1891059.	2.89	.22	.46	.22
5.	1894059.	4.26	.53	.27	.05
5.	1901059.	4.93	.57	.32	.02
5.	1904059.	3.32	.15	.35	.02
5.	1911059.	3.77	.21	.39	.04
5.	1914059.	4.74	.63	.45	.11
6.	1924059.	7.61	1.25	.37	.05
5.	1931059.	1.72	.08	.55	.06
5.	1934059.	1.95	.15	.51	.04
5.	1941059.	2.84	.26	.34	.04
5.	1944059.	2.82	.26	.30	.00
6.	1951069.	1.13	.08	1.00	.00
5.	1954069.	1.04	.04	1.00	.00
3.	1961069.	6.55	.79	.70	.17
5.	1964069.	4.77	.44	.36	.16
5.	1971069.	4.85	.39	.90	.04
5.	1974069.	6.97	1.02	.31	.00
5.	1981069.	1.20	.02	1.00	.00
5.	1984069.	0.89	.05	.90	.04
5.	1991069.	10.13	.62	.42	.02
4.	1994069.	6.41	.33	.80	.22
4.	2001069.	1.80	.12	.92	.10
5.	2004069.	1.89	.08	.72	.18
4.	2011069.	1.11	.07	.97	.06
5.	2014069.	1.29	.07	.98	.05

TABLE D-II

5.	2021069.	4.38	.51	.73	.07
5.	2024069.	4.26	.15	.69	.02
5.	2031079.	3.80	.33	.80	.07
5.	2034079.	3.62	.10	.81	.00
4.	2041079.	5.81	.04	.54	.02
4.	2044079.	3.85	.49	.43	.05
3.	2051079.	1.48	.05	.96	.06
5.	2054079.	6.47	.29	.35	.07
5.	2064079.	1.42	.11	.70	.21
8.	2071079.	4.83	.96	.23	.03
5.	2074079.	2.60	.36	.43	.02
6.	2081079.	1.18	.07	.99	.01
4.	2084079.	2.00	.14	.43	.02
4.	2091089.	3.07	.23	.53	.07
3.	2094089.	3.14	.12	.58	.22
6.	2101089.	1.66	.06	1.00	.01
5.	2104089.	7.15	.42	.47	.07
4.	2114089.	2.11	.09	.48	.08
5.	2121089.	5.91	.23	.64	.02
5.	2124089.	1.61	.07	1.00	.00
4.	2131089.	3.89	.39	.43	.05
4.	2134089.	3.28	.10	.64	.15
5.	2141089.	5.52	.60	.47	.08
5.	2144089.	1.94	.11	.68	.20
5.	2151089.	3.26	.27	.44	.10
5.	2154089.	3.98	.13	.36	.02
4.	2161089.	3.34	.15	.80	.13
5.	2164089.	4.32	.62	.73	.28
4.	2171089.	4.00	.23	.28	.03
5.	2174089.	6.41	.39	.59	.02
5.	2181089.	4.77	.34	.33	.06
5.	2184089.	3.75	.29	.34	.02
5.	2191099.	3.80	.24	.19	.03
5.	2194099.	6.16	.41	.32	.04
5.	2201109.	4.49	.22	.52	.07
5.	2204109.	3.58	.23	.59	.08
5.	2211109.	2.79	.30	.41	.03
4.	2214109.	2.77	.17	.44	.04
5.	2221109.	1.51	.09	.78	.14
5.	2224109.	1.50	.04	.96	.07
6.	2231109.	2.70	.28	.60	.08
5.	2234109.	3.83	.26	.50	.15
5.	2241119.	3.57	.35	.43	.04
4.	2244119.	1.57	.09	.98	.04
5.	2251010.	1.20	.05	.92	.04
4.	2254010.	4.33	.37	.40	.04
5.	2261020.	1.85	.08	.74	.18
4.	2264020.	2.53	.25	.51	.09
5.	2271020.	4.03	.57	.44	.28
5.	2274020.	1.80	.05	.61	.07
4.	2281030.	2.64	.12	.48	.05
5.	2284030.	1.14	.04	1.00	.00
6.	2291030.	1.85	.15	.57	.14
6.	2294030.	1.89	.32	.47	.14

TABLE D-II

5.	2301040.	6.28	1.12	.36	.04
5.	2304040.	6.28	.55	.40	.12
5.	2311040.	4.46	.37	.41	.06
4.	2314040.	6.21	.25	.35	.06
5.	2321050.	3.17	.11	.56	.07
5.	2324050.	2.17	.14	.60	.07
5.	2331060.	4.52	.46	.30	.05
4.	2334060.	2.09	.13	.86	.09
5.	2341060.	1.58	.08	.94	.06
5.	2344060.	3.43	.06	.46	.05
5.	2351060.	2.88	.17	.29	.02
5.	2354060.	4.91	.40	.23	.00
5.	2361070.	2.73	.15	.67	.13
5.	2364070.	3.08	.45	.37	.12
5.	2371080.	2.47	.27	.35	.06
5.	2374080.	3.01	.14	.54	.17
5.	2384080.	3.37	.20	.34	.03
5.	7001109.	3.52	.15	.26	.01
5.	8011129.	7.80	.47	.25	.02
5.	8021129.	15.36	4.06	.22	.03
5.	8031129.	2.82	.58	.24	.03
5.	8041129.	6.04	.37	.24	.03
5.	8051129.	8.70	.29	.26	.02
6.	8061129.	22.79	5.70	.17	.04
5.	8071129.	1.33	.08	.57	.06
5.	8081129.	2.64	.91	.24	.06
5.	8091129.	4.98	.50	.16	.00
5.	8101129.	11.61	.82	.27	.02
5.	8111129.	11.99	1.62	.29	.01
6.	7001129.	2.85	.14	.23	.04
5.	7011129.	2.78	.15	.22	.01
5.	7021129.	4.21	.29	.46	.05
5.	7031129.	1.77	.14	.39	.07
5.	7041129.	2.33	.35	.29	.03

TABLE D-III

VALUES OF THE COEFFICIENTS OF THE FIRST FIVE PRINCIPAL COMPONENTS FOR EACH LIMB OF THE PATIENTS (178-238) AND THE NORMAL SUBJECTS (700-811)

PATIENT IDENTITY	PC1	PC2	PC3	PC4	PC5
1781039	4.548	-.289	.519	.229	-.214
1781039	4.054	.521	.518	.953	-.225
1781039	2.232	1.206	.541	.720	.473
1781039	2.225	.987	.189	.465	.368
1781039	1.958	1.165	.424	1.151	.300
1784039	-1.015	.025	.714	1.126	-.222
1784039	-.377	-.209	.609	1.076	-.378
1784039	-1.037	.146	.459	.722	.243
1784039	-.908	.481	.845	.923	.141
1784039	-.375	-.244	.589	.816	-.032
1801049	-4.638	-.914	-.571	-.108	-.244
1801049	-3.721	-1.042	-.873	.026	-.375
1801049	-3.881	-1.438	-.262	-.307	-.268
1801049	-4.119	-1.242	-.761	-.152	-.004
1801049	-4.428	-.971	-.541	.086	-.079
1804049	-3.163	-.996	-.484	-.371	-.198
1804049	-3.095	-.662	-.204	-.220	.017
1804049	-2.765	-.829	-.262	-.419	-.155
1804049	-3.083	-.856	.132	-.193	-.081
1804049	-3.297	-.575	-.386	-.250	-.135
1804049	-3.448	-.786	-.569	-.280	-.396
1811049	6.634	-2.189	1.475	-1.294	-.651
1811049	5.069	.091	-.175	-.905	-1.082
1811049	5.978	.124	-.465	-1.540	-.358
1811049	8.209	-1.320	-.719	-2.357	-.839
1811049	8.846	.137	-1.146	-1.977	-.645
1811049	10.151	-3.648	1.110	-1.995	-.094
1814049	2.527	-1.538	1.155	-.977	.171
1814049	2.165	-1.854	1.545	-.673	-.155
1814049	2.485	-1.699	1.908	-.507	-.114
1814049	4.333	-3.577	2.922	-1.015	-.069
1814049	3.596	-1.991	1.946	-.814	.201

TABLE D-III

1821049	6.340	2.391	.528	-.108	.191
1821049	5.129	2.163	.074	-.768	.859
1821049	5.395	1.049	-.322	-.138	.356
1821049	3.275	3.160	-.200	-.389	.343
1821049	5.461	2.448	.037	-.210	.337
1824049	.684	.050	1.029	.297	.256
1824049	1.061	.236	.849	.527	-.163
1824049	.863	-.773	.321	-.348	-.226
1824049	.693	-.305	1.006	.362	-.286
1824049	.072	.636	.136	-.897	.031
1831059	-.731	-1.500	.142	.087	-.142
1831059	-.501	-1.425	.190	.194	.064
1831059	-.650	-1.045	.695	.575	.149
1831059	-.616	-1.987	.652	.074	.014
1831059	-.150	-1.216	.014	.150	.109
1841059	1.562	-1.422	-.523	-.721	-.054
1841059	1.231	-1.846	.162	-1.130	.248
1841059	1.620	-1.224	-.392	-1.098	-.083
1841059	3.217	-1.209	-.692	-1.305	.506
1841059	1.471	-1.792	.715	-.203	-.178
1844059	.474	-1.058	.443	-.186	-.007
1844059	1.463	-1.534	-.085	-.895	-.015
1844059	.040	-.831	.176	-.220	.024
1844059	-.077	-.336	-.050	-.842	-.086
1844059	.089	-.602	-.275	-.726	.207
1851059	-3.094	-.379	-.145	-.147	-.330
1851059	-3.406	-.203	-.339	-.323	-.133
1851059	-3.589	-.252	-.215	-.119	-.300
1851059	-3.382	-.226	-.100	-.133	-.239
1851059	-3.650	-.261	-.279	-.283	-.180
1851059	-3.386	-.232	-.061	-.144	-.187
1854059	4.203	-.165	-.577	.221	.695
1854059	2.768	1.283	-1.133	-.041	.242
1854059	3.247	-.215	-.996	-.409	.052
1854059	4.393	-.410	-.336	.125	.673
1861059	-1.150	-1.804	.393	.432	.007
1861059	-1.014	-1.413	.404	.121	.027
1861059	-.835	-1.868	.805	.549	-.468
1861059	-.989	-1.096	.273	.246	-.015
1861059	-.423	-1.684	.643	.381	-.143
1864059	.996	-.638	.546	-.093	.481
1864059	1.431	-.731	.406	-.080	.143
1864059	.827	.281	-.067	-.414	.396
1864059	1.576	-1.076	1.410	.349	-.205
1864059	1.310	-.822	.935	.479	.011

TABLE D-III

1871059	-.874	1.951	1.618	-.503	.730
1871059	-.047	1.732	1.435	.240	.950
1871059	.152	1.356	2.084	-.026	.783
1871059	.383	1.610	1.787	.160	.675
1871059	.034	3.285	1.194	-.746	.386
1874059	-.458	.760	.554	.533	.302
1874059	-1.780	.366	.671	.329	.251
1874059	-1.092	.421	.968	.501	.221
1874059	-.788	.272	.711	.746	.347
1874059	-1.342	.268	1.135	.227	.354
1881059	9.303	1.584	-2.864	.143	-.602
1881059	5.967	-1.449	-1.637	-.147	.137
1881059	5.889	-.791	-1.297	.508	-.256
1881059	1.102	.888	-.798	.097	.086
1881059	3.683	-.405	-1.093	.966	-.416
1884059	.602	-.616	-.247	.886	-.128
1884059	-.334	.977	-.416	.284	.576
1884059	-1.280	.294	-.094	.529	.281
1884059	-.510	.599	-.431	.704	.082
1884059	-1.448	1.149	-.315	.598	.716
1891059	.178	-.526	.067	.419	-.106
1891059	.539	-1.451	.248	.434	-.405
1891059	-.676	.315	-.062	-.062	.493
1891059	-.217	-1.228	-.521	-.610	-.177
1891059	-.237	-.585	.431	.521	-.200
1894059	1.083	1.635	-.997	.781	-.083
1894059	-.471	.839	-.314	.410	-.112
1894059	1.332	.761	-1.237	1.082	-.621
1894059	.589	.264	-.841	.864	-.536
1894059	.029	1.494	-.386	.704	.089
1901059	1.877	1.630	-.332	.482	.405
1901059	1.626	.586	-.721	.208	-.406
1901059	1.476	.756	-.557	.757	.061
1901059	2.075	2.585	-.826	.424	.111
1901059	.725	1.287	-.679	.313	-.024
1904059	.608	.186	-.250	.557	-.499
1904059	.071	.392	-.271	.217	-.291
1904059	-.367	.769	-.418	.040	.057
1904059	.039	.892	-.792	.187	-.259
1904059	.464	.505	-.660	.024	-.341
1911059	.913	-1.385	.886	-.034	.132
1911059	.983	-1.020	.278	-.534	.669
1911059	1.158	-1.305	.544	-.294	.425
1911059	1.223	-1.115	.291	-.272	.770
1911059	.789	-1.379	.637	-.125	.570

TABLE D-III

1914059	4.255	-.510	.462	-.018	.441
1914059	1.361	1.190	-.974	-.532	.373
1914059	2.061	.147	.174	.093	.152
1914059	1.280	.606	-.705	-.795	.315
1914059	2.630	.195	-.092	-.399	.310
1924059	5.596	-1.658	-.028	-3.075	.520
1924059	7.059	-1.849	.188	-2.781	.960
1924059	4.006	-2.611	.590	-.845	.369
1924059	5.744	-2.711	.912	-2.693	.472
1924059	4.053	-2.662	.756	-2.378	.635
1931059	-5.786	-.156	-.274	-.475	-.639
1931059	-5.070	.065	-.312	-.634	-.372
1931059	-5.437	.065	-.455	-.491	-.469
1931059	-5.727	-.357	-.317	-.578	-.662
1931059	-5.436	-.100	-.279	-.546	-.495
1934059	-5.958	-.269	-.069	-.551	-.337
1934059	-5.950	-.481	-.213	-.616	-.488
1934059	-5.854	-.520	-.433	-.690	-.395
1934059	-5.581	-.338	-.183	-.632	-.486
1934059	-5.573	-.081	-.134	-.445	-.459
1941059	-1.410	.805	-1.286	-.687	-.065
1941059	-1.438	.666	-1.734	-.972	-.351
1941059	-2.417	.942	-1.291	-.719	-.247
1941059	-.968	-.360	-.183	-.592	.315
1941059	-1.716	.451	-1.088	-.742	.050
1944059	-1.616	2.091	-1.252	.091	-.429
1944059	-3.090	2.333	-.782	.112	-.267
1944059	-2.972	1.860	-.953	.172	-.484
1944059	-2.246	1.899	-.964	.065	-.243
1944059	-2.330	1.565	-.870	-.047	-.065
1951069	-3.409	-.564	-.435	-.127	-.047
1951069	-3.281	-.830	-.122	.100	.042
1951069	-3.426	-.573	-.388	-.023	-.017
1951069	-3.607	-.650	-.292	-.035	.030
1951069	-3.336	-.647	-.248	-.050	.050
1951069	-3.679	-.461	-.407	-.055	-.159
1954069	-3.182	-.924	-.347	-.094	.085
1954069	-2.950	-1.088	-.133	.111	-.025
1954069	-3.419	-.880	-.310	-.062	.081
1954069	-3.902	-.761	-.602	-.014	-.194
1954069	-3.608	-.896	-.468	-.045	-.051
1961069	4.522	-2.451	3.963	.034	-.607
1961069	4.964	-4.914	6.410	2.281	.754
1961069	4.860	-2.833	4.486	-.202	.367
1961069	4.191	-2.814	3.845	-.195	.262
1961069	3.816	-2.823	3.213	-.613	.962

TABLE D-III

1964069	1.629	-2.351	2.029	-.618	.634
1964069	1.681	-3.761	2.851	.015	-.151
1964069	1.976	-3.625	3.074	.666	-.080
1964069	2.450	-2.548	2.545	-.012	.152
1964069	1.138	-2.403	1.520	-.327	.684
1971069	.735	.126	1.629	1.062	-.505
1971069	2.048	-1.028	1.943	1.701	-2.003
1971069	1.738	-.826	1.778	1.605	-1.780
1971069	.664	.332	1.686	.867	-.371
1971069	1.743	-.655	1.877	1.500	-1.142
1974069	-2.238	7.552	-.588	-2.278	-1.091
1974069	-1.524	7.005	-.525	-2.507	-.861
1974069	-2.139	7.486	-.170	-2.845	-1.368
1974069	-3.545	5.727	-.273	-2.194	-1.026
1974069	-2.654	5.789	-.393	-2.560	-.887
1981069	-3.948	-1.048	-.311	.120	-.085
1981069	-4.012	-1.063	-.274	.179	-.131
1981069	-3.856	-.999	-.362	.058	-.083
1981069	-3.577	-.918	-.132	.158	-.174
1981069	-3.813	-1.094	-.260	.126	-.101
1984069	-4.887	-1.455	-.690	.172	.013
1984069	-4.816	-1.556	-.582	.154	-.058
1984069	-4.788	-1.570	-.472	.257	.000
1984069	-4.752	-1.458	-.461	.168	-.030
1984069	-4.615	-1.435	-.621	.148	-.039
1991069	6.570	-2.424	-.376	.209	-1.073
1991069	5.484	2.123	-.611	.907	-1.197
1991069	5.965	-.001	-.896	.846	-1.242
1991069	6.490	.989	.310	1.845	-1.249
1991069	3.658	2.480	-.128	1.400	-1.039
1994069	2.221	-1.850	.639	.994	-.447
1994069	2.177	-1.674	1.089	1.146	-.425
1994069	1.593	-.725	.506	.736	-.166
1994069	2.100	-.477	.449	.398	-.089
1994069	1.796	-2.242	1.440	.955	-1.133
2001069	-3.185	-.455	-.135	-.205	.033
2001069	-3.336	-.613	-.171	-.008	-.039
2001069	-3.321	-.286	-.050	-.076	-.050
2001069	-3.192	-.675	-.116	-.068	-.122
2001069	-3.715	-.455	-.182	-.038	-.098
2004069	-3.253	-.011	-.206	-.276	.061
2004069	-3.272	-.334	.025	-.124	-.082
2004069	-2.809	-.222	.065	-.087	-.048
2004069	-2.585	-.369	-.142	.008	-.039
2004069	-3.604	.143	-.304	-.280	.010

TABLE D-III

2011069	-3.456	-.783	-.373	.072	-.070
2011069	-4.236	-.599	-.448	-.179	-.141
2011069	-4.112	-.721	-.569	.054	-.131
2011069	-3.730	-.659	-.456	.057	-.181
2011069	-3.783	-.463	-.265	.048	-.030
2014069	-3.144	-.089	-.474	-.162	-.128
2014069	-3.282	-.618	-.496	-.156	-.123
2014069	-3.146	-.333	-.359	-.177	.010
2014069	-3.322	-.365	-.295	-.195	.044
2014069	-3.360	-.391	-.517	-.085	-.097
2021069	2.433	1.247	.902	.433	.198
2021069	2.525	.185	1.303	.700	-.483
2021069	1.340	.469	1.396	.776	-.402
2021069	1.238	.493	.976	.572	-.161
2021069	1.134	.381	.973	.688	-.158
2024069	.589	1.846	1.204	-.240	-.079
2024069	-.117	2.123	1.063	-.057	-.324
2024069	.098	1.507	.547	-.214	-.180
2024069	.602	2.015	1.038	.042	-.379
2024069	.158	1.884	1.011	-.075	-.347
2031079	-1.539	.246	.995	.044	-1.004
2031079	-.998	-.240	1.073	.130	-1.167
2031079	-2.020	.075	.557	-.187	-.636
2031079	-1.340	.089	1.420	-.309	-.900
2031079	-1.674	.053	1.339	-.068	-1.010
2034079	-2.651	.438	.592	-.054	-.599
2034079	-2.838	.604	.796	-.366	-.432
2034079	-2.539	.818	.442	-.049	-.793
2034079	-2.348	.964	.551	-.046	-.650
2034079	-2.730	.498	.701	-.362	-.365
2041079	3.752	1.064	.116	.321	-1.283
2041079	4.120	.571	.863	.374	-1.775
2041079	4.993	.425	.382	.314	-1.665
2041079	4.256	.245	.989	.713	-1.463
2041079	3.832	-.008	1.317	1.018	-1.398
2044079	.912	-1.808	1.089	.249	-.228
2044079	1.561	-1.224	.496	-.082	.425
2044079	.640	-1.623	.805	.211	-.138
2044079	1.347	-1.231	.653	.118	.002
2051079	-3.999	-.285	-.510	-.140	-.132
2051079	-3.688	-.498	-.254	-.193	-.087
2051079	-3.762	-.398	-.490	-.227	-.103
2051079	-3.233	-.596	-.158	-.094	-.086

TABLE D-III

2054079	3.220	1.590	-1.173	1.048	.328
2054079	3.768	1.015	-1.434	.819	.504
2054079	4.962	1.234	-.707	1.565	-.083
2054079	3.108	2.613	-.303	1.119	.206
2054079	4.228	1.933	.082	1.526	-.010
2071079	-2.446	.384	-1.359	.330	.332
2071079	1.404	1.284	-.976	.854	1.168
2071079	.622	1.562	-1.569	1.074	.777
2071079	.540	.113	-.906	1.186	.236
2071079	1.586	.956	-.893	.980	1.080
2071079	1.016	.926	-1.016	1.121	1.154
2071079	2.134	.654	-.703	1.577	.874
2071079	1.497	1.334	-1.022	1.493	1.218
2074079	-1.909	.606	-.715	-.210	-.245
2074079	-2.579	.866	-.660	-.393	-.541
2074079	-2.544	.587	-.346	.052	-.329
2074079	-2.066	-.154	-.425	-.359	-.379
2074079	-2.102	.683	-.771	-.085	-.410
2081079	-3.998	-1.086	-.178	.105	-.115
2081079	-4.372	-.966	-.363	-.039	.030
2081079	-4.401	-.893	-.250	-.088	-.062
2081079	-4.189	-1.084	-.297	.072	-.063
2081079	-4.218	-1.118	-.242	.054	-.100
2081079	-4.374	-.902	-.448	-.125	-.002
2084079	-2.961	.363	-.094	-.042	-.071
2084079	-3.255	.464	.006	-.194	.112
2084079	-3.082	.420	-.030	-.187	-.124
2084079	-3.215	.655	-.174	-.301	-.106
2084079	-2.939	.649	.140	-.112	.017
2091089	-1.192	.088	.491	-.274	.503
2091089	-1.053	.401	.120	-.400	.330
2091089	-.133	-.299	.604	.043	.383
2091089	-.395	-.775	.493	.107	-.123
2091089	-.612	-.208	.296	.024	.081
2094089	-.888	.276	.440	-.189	-.012
2094089	-.610	.150	.505	.380	-.284
2094089	-.152	-.281	.768	.600	-.106
2094089	-1.082	.558	-.031	-.122	.330
2094089	-.996	.854	.241	-.064	.278
2101089	-3.230	-.696	.004	.104	-.285
2101089	-3.710	-.628	.029	.149	-.142
2101089	-3.791	-.576	.057	.004	-.043
2101089	-2.877	-.823	.143	.210	-.636
2101089	-3.401	-.655	.401	-.021	-.176
2101089	-3.611	-.511	.084	.183	-.145

TABLE D-III

2104089	2.591	3.371	.209	-.442	.292
2104089	2.513	1.179	-.251	.436	.185
2104089	2.706	1.302	.052	.639	.478
2104089	2.048	2.072	.272	.554	.374
2104089	2.852	.225	.365	.345	-.458
2114089	-.482	.128	-.127	-.118	-.353
2114089	-.412	.089	-.021	-.121	-.255
2114089	-.532	.333	-.757	-.367	-.258
2121089	-.157	2.200	1.722	-.357	.701
2121089	.298	2.101	1.415	-.364	.462
2121089	.160	2.119	1.488	-.168	.174
2121089	1.883	1.329	.981	.241	-.371
2121089	1.326	1.749	1.575	.380	-.337
2124089	-3.732	-.742	-.116	-.027	-.213
2124089	-4.237	-.753	-.176	-.179	-.162
2124089	-4.211	-.633	-.017	-.341	-.018
2124089	-3.499	-.494	.137	.061	-.200
2124089	-3.730	-.814	-.008	.050	-.138
2131089	.320	-.501	.452	.206	.928
2131089	.454	-1.052	.899	.567	.735
2131089	-.269	-.128	.035	.032	1.181
2131089	.192	-1.318	1.004	.698	.014
2131089	-.375	-1.297	1.045	.788	.218
2134089	-.436	-.271	.738	.299	.317
2134089	-.421	-.203	.708	.108	.249
2134089	-.399	.313	.155	-.354	.563
2134089	-.206	-.400	.877	.451	-.106
2134089	-.382	-.431	.986	.533	.050
2141089	1.641	.941	.215	1.026	-.108
2141089	.538	1.120	.499	.494	-.004
2141089	1.123	1.281	.795	1.060	.050
2141089	1.238	.087	.248	.227	-.213
2141089	.687	2.417	.763	.216	.145
2144089	-3.603	-.066	-.345	-.388	-.212
2144089	-4.239	.150	-.190	-.414	-.162
2144089	-3.707	-.259	-.334	-.269	-.148
2144089	-3.458	-.253	.034	.010	-.099
2144089	-3.414	-.063	.037	-.176	-.010
2151089	.368	-1.875	.887	.360	-.035
2151089	.147	-1.335	.739	.093	.054
2151089	-.215	-.452	-.322	-.716	.427
2151089	.261	-1.185	.316	-.919	.713
2151089	.021	-1.238	.674	.310	.199

TABLE D-III

2154089	.548	-.829	.180	-.437	.653
2154089	1.205	-1.745	.613	-.531	.161
2154089	1.125	-1.648	.737	-.287	.337
2154089	1.290	-2.096	.990	-.032	.343
2154089	.952	-1.874	.643	.087	.097
2161089	-.135	-.141	.375	.403	.046
2161089	.214	-.229	.483	.756	-.356
2161089	.119	-.928	.870	.808	-.611
2161089	.092	-1.187	1.054	.897	-1.169
2161089	.120	-.666	.673	.737	-.425
2164089	.560	.067	.821	.013	-.213
2164089	-.092	.091	-.002	.037	.449
2164089	2.510	-.168	-.202	-.502	.333
2164089	1.099	-1.135	1.525	.598	-.741
2164089	.523	-.345	1.538	.532	.019
2171089	-2.840	2.571	1.464	-.350	.045
2171089	-2.676	2.545	1.728	-.443	.139
2171089	-1.504	2.550	.648	.700	.319
2171089	-1.990	2.649	1.648	-.331	-.017
2174089	2.526	2.747	1.792	-.176	.400
2174089	1.605	3.387	1.843	-.857	-.021
2174089	1.585	3.354	1.821	-1.209	.055
2174089	3.578	3.075	.819	-.482	-.059
2174089	1.826	3.187	1.250	-.455	.047
2181089	1.274	1.440	-1.289	-.031	.146
2181089	1.515	.778	-.806	.054	.379
2181089	1.541	.212	.063	-.011	.451
2181089	1.267	.528	-.148	.122	.575
2181089	.857	.522	-.245	.142	.376
2184089	1.093	.582	-.340	-.052	.187
2184089	.058	.929	-.496	-.019	-.125
2184089	-.092	1.182	-.418	-.052	-.030
2184089	.121	.876	-.252	-.192	.185
2184089	-.269	1.040	-.619	-.273	.313
2191099	-.040	-1.290	-.944	-.596	.330
2191099	.221	-3.398	1.236	-.269	.134
2191099	.760	-3.552	.762	-.635	.353
2191099	.927	-2.738	.314	-.745	.469
2191099	.956	-2.460	-.071	-.785	.168
2194099	5.893	.117	-1.080	-.099	.230
2194099	3.425	2.308	-1.462	.543	.169
2194099	4.106	1.683	-.835	.555	.432
2194099	2.710	2.948	-1.547	.416	.098
2194099	3.359	2.402	-1.114	.475	.444

TABLE D-III

2201109	1.438	2.753	.147	-.442	.375
2201109	.983	2.459	.500	-.237	.584
2201109	.350	2.479	.760	-.664	.879
2201109	.692	2.707	.588	-.672	.880
2201109	1.573	1.762	.643	-.252	.564
2204109	.118	.141	.823	.028	.713
2204109	.573	-.068	.738	-.026	.731
2204109	.082	-.244	.467	-.492	.825
2204109	-.282	.002	.573	-.168	.938
2204109	-.459	.081	.677	-.056	.774
2211109	-1.432	.393	-.555	-.319	-.011
2211109	-1.703	.727	-.339	-.146	.267
2211109	-1.181	.721	-.460	-.266	.540
2211109	-1.363	.633	-.314	-.233	.185
2211109	-1.295	.575	-.232	-.202	.017
2214109	-.526	.067	.219	.145	.163
2214109	-1.118	.495	-.046	-.297	.548
2214109	-1.333	.649	-.644	-.542	.251
2214109	-1.657	.551	-.574	-.534	.308
2221109	-3.975	-.778	-.187	.019	-.132
2221109	-4.331	-.993	-.191	.028	-.004
2221109	-3.887	-.765	-.069	.064	-.241
2221109	-4.277	-.705	.046	-.161	-.054
2221109	-3.853	-.688	.025	.049	-.178
2224109	-3.943	-.747	-.549	-.098	-.183
2224109	-3.763	-.915	-.301	.028	-.135
2224109	-4.077	-.801	-.348	-.078	-.094
2224109	-3.993	-.967	-.420	.060	-.215
2224109	-3.706	-.941	-.427	-.028	-.149
2231109	-.543	-.230	.424	.324	.064
2231109	-.665	-.134	.420	.228	.061
2231109	-1.401	.542	.068	.009	.006
2231109	-1.364	.433	.015	-.262	.216
2231109	-.794	-.167	.479	.246	-.069
2231109	-.618	-.161	.276	.315	.005
2234109	.344	1.201	.152	.018	.504
2234109	.237	1.138	-.108	.023	.368
2234109	.733	-.107	.252	.202	-.004
2234109	.226	.639	-.177	-.287	.022
2234109	.923	-.253	.881	.526	.336
2241119	-1.295	.253	-.427	-.816	.336
2241119	-.611	.731	-.147	-.204	.201
2241119	-.077	.451	.081	-.361	.583
2241119	-.599	.030	-.026	-.143	.330
2241119	-.033	-.195	.408	.011	.244

TABLE D-III

2244119	-4.215	-.491	-.599	-.168	-.203
2244119	-4.038	-.708	-.560	-.069	-.161
2244119	-3.982	-.384	-.469	-.107	-.050
2244119	-4.028	-.520	-.655	-.151	-.100
2251010	-4.469	-1.016	-.674	-.055	-.106
2251010	-4.097	-1.271	-.472	-.038	-.048
2251010	-4.696	-1.179	-.776	.041	-.110
2251010	-4.529	-1.183	-.620	.169	.068
2251010	-4.405	-1.089	-.466	.032	-.052
2254010	-.680	3.138	.659	-.484	.557
2254010	.628	3.723	.160	.269	.124
2254010	.049	2.578	-.093	.081	.250
2254010	-.751	2.947	.231	-.362	.634
2261020	-2.438	.036	.192	-.102	-.164
2261020	-2.628	-.015	-.163	-.054	-.138
2261020	-2.361	-.133	-.315	-.094	-.197
2261020	-2.281	.138	-.205	.042	-.355
2261020	-1.689	.120	-.064	.241	-.633
2264020	-.557	-1.285	.571	.125	-.311
2264020	-1.106	-1.227	.346	-.017	-.027
2264020	-.854	-.471	.406	.132	.164
2264020	-1.051	-1.048	-.295	.150	-.068
2264020	-.874	-1.146	.177	.474	-.205
2271020	1.636	.576	-.710	.618	.634
2271020	1.247	-1.312	.090	.553	-.301
2271020	.276	-.375	-.035	.815	.291
2271020	1.083	-.935	.314	1.364	-.591
2271020	.338	-.180	-.088	.918	.361
2274020	-2.032	-.907	-.020	.024	.246
2274020	-2.165	-1.079	-.119	.206	.102
2274020	-2.121	-.921	.229	.409	.051
2274020	-2.084	-.833	.098	.284	.079
2274020	-2.100	-.752	.039	.245	.131
2274020	-2.145	-.913	-.017	.073	.274
2281030	-1.689	-.619	.446	.366	-.087
2281030	-1.839	-.823	.362	.277	-.271
2281030	-1.643	-.745	.144	.149	-.004
2281030	-1.801	-.998	.577	.470	-.203
2281030	-1.727	-.843	.336	.313	-.173
2284030	-4.012	-1.269	-.267	.089	-.010
2284030	-4.086	-1.223	-.168	.267	-.048
2284030	-4.188	-1.319	-.325	.090	-.069
2284030	-4.189	-1.455	-.374	.241	.036
2284030	-4.234	-1.389	-.555	.212	.044

TABLE D-III

2301040	3.158	5.652	.215	.383	-.509
2301040	.624	3.422	1.090	.238	-.386
2301040	.863	4.920	.734	.171	-.061
2301040	.831	4.731	.965	.201	-.087
2301040	-.585	4.937	1.529	-.930	-.136
2304040	1.867	2.468	1.424	.164	-.074
2304040	.161	3.675	.611	-.992	.340
2304040	.401	3.647	.653	-.391	.424
2304040	1.130	3.748	.343	.108	.566
2304040	2.192	3.315	-.348	.401	.241
2311040	.181	.406	.091	-.315	.715
2311040	-1.195	1.612	-.253	-1.049	.901
2311040	-.231	1.135	.013	-.608	1.003
2311040	.138	1.462	-.835	-.661	.388
2311040	2.072	.426	-.538	-1.086	.649
2314040	.575	5.442	.834	-.073	.142
2314040	-.956	6.091	.572	.013	-.127
2314040	2.176	4.374	1.298	.104	-.046
2314040	1.265	5.834	1.362	-.595	.111
2321050	-2.676	.471	-.301	-.486	.167
2321050	-3.375	.958	-.068	-.342	-.500
2321050	-3.214	.539	-.259	-.605	-.488
2321050	-3.740	.355	-.304	-.839	-.412
2321050	-2.455	.298	-.086	-.360	.039
2324050	-3.152	.106	.065	-.195	-.070
2324050	-3.268	.019	-.241	-.316	-.020
2324050	-3.118	-.001	-.179	-.003	-.082
2324050	-3.855	-.030	-.174	-.281	.070
2324050	-3.155	-.190	-.077	-.073	-.094
2331060	-.675	1.501	.307	.458	.151
2331060	-1.646	1.270	.061	-.327	-.063
2331060	.971	1.378	.548	.443	.119
2331060	-1.423	1.800	.402	-.278	-.229
2331060	.329	2.514	.610	.221	-.037
2334060	-2.870	-.213	.126	-.218	-.051
2334060	-3.080	-.244	.197	-.193	-.109
2334060	-3.512	-.235	.025	-.383	-.054
2334060	-2.961	-.300	.097	.048	-.164
2341060	-3.850	-.160	-.158	-.169	-.279
2341060	-3.699	-.328	-.038	-.174	-.128
2341060	-3.948	-.279	-.259	-.058	-.216
2341060	-3.857	-.162	.019	-.146	-.242
2341060	-3.757	-.198	-.129	-.143	-.201

TABLE D-III

2344060	-.511	.902	.383	-.169	.399
2344060	-.388	1.012	.341	-.093	.515
2344060	-.226	.886	.061	-.147	.428
2344060	-.440	.842	.507	.171	.198
2344060	-.501	.953	.173	-.126	.144
2351060	-.085	-1.427	-.481	-.157	.586
2351060	.071	-1.122	-.560	-.327	.611
2351060	-.215	-1.323	-.708	-.152	.192
2351060	-.158	-.890	-.633	-.313	.249
2351060	-.176	-1.982	.021	-.175	.351
2354060	2.633	-1.098	-1.549	-.169	.258
2354060	2.481	-1.358	-1.451	.364	.934
2354060	1.911	-.311	-1.399	.430	.341
2354060	2.211	-.489	-1.467	.408	.254
2354060	1.571	.028	-1.451	.381	.558
2361070	-3.257	.313	.028	-.982	.374
2361070	-2.246	-.612	1.414	.485	-.089
2361070	-2.508	-.369	.602	-.849	.773
2361070	-2.318	-.073	.802	-.459	.569
2361070	-1.947	-.807	1.113	.311	.316
2364070	-.553	.675	-.683	-.000	.592
2364070	-1.418	-.423	-.360	.266	.778
2364070	-1.743	-.330	-.105	.077	.633
2364070	-2.275	-.256	.115	-.250	.747
2364070	-1.665	.165	-.050	-.113	.523
2371080	-2.061	-.581	-.419	.102	.436
2371080	-1.600	-.295	-.571	-.412	.285
2371080	-1.388	-.580	-.293	-.640	.541
2371080	-.958	-1.555	.232	-.211	.568
2371080	-1.130	-1.814	.128	.047	.475
2374080	-.406	.060	.742	.562	.335
2374080	-.771	.134	.579	.507	.490
2374080	-.468	-.189	.416	-.316	.467
2374080	-.965	.611	-.469	-.631	.145
2374080	-1.005	.580	-.659	-.330	-.051
2381080	13.587	-.852	.333	.672	2.660
2381080	10.712	-.116	1.158	.135	.316
2381080	17.874	3.273	.849	-2.217	.342
2381080	10.807	-.379	1.476	-.307	.789
2381080	12.790	1.342	.198	-.654	.308
2384080	-.053	-.247	-.426	-.583	.082
2384080	.489	-.984	.071	-.123	-.418
2384080	-.149	.519	-.531	-.449	.074
2384080	-.211	.697	-1.214	-.826	-.170
2384080	-.026	-.289	-.191	-.594	-.100

TABLE D-III

7001109	-.769	1.290	-.370	.294	.074
7001109	-.995	1.912	.035	.250	-.022
7001109	-1.558	2.229	.136	-.064	.111
7001109	-1.066	1.902	-.219	.428	-.014
7001109	-1.125	2.405	.049	.225	-.044
8011129	4.579	-2.256	-1.382	-.029	-.441
8011129	4.335	-2.216	-1.232	-.114	-.322
8011129	3.525	-1.133	-2.130	.251	-.362
8011129	3.869	-3.092	-.686	-.798	-.537
8011129	3.942	-1.754	-1.252	.151	.060
8021129	12.141	-4.965	.086	-2.032	-2.191
8021129	8.529	-5.360	1.002	-1.385	-1.834
8021129	8.970	-2.222	-1.206	-1.177	-1.408
8021129	9.646	-2.569	-1.543	-2.520	-1.376
8021129	5.882	-5.278	.025	-2.410	-1.051
8031129	-.291	1.504	-.567	.765	.558
8031129	-.903	.246	-.813	.540	.138
8031129	-1.123	.242	-.595	.646	.157
8031129	-1.867	.187	-.512	.233	.276
8031129	-1.220	.211	-.649	.634	.085
8041129	2.155	.332	-1.432	.766	.250
8041129	2.412	-.440	-1.991	.360	.039
8041129	3.339	-.528	-1.854	.491	.093
8041129	2.793	-.323	-1.367	.570	-.142
8041129	2.947	-.871	-.776	.608	.066
8051129	5.563	-1.879	-2.173	-.394	.498
8051129	4.866	-2.093	-1.356	-.327	-.222
8051129	4.503	-1.761	-2.199	-.897	-.160
8051129	4.607	-1.932	-1.499	-.475	-.203
8051129	5.047	-2.414	-1.279	-.089	-.146
8061129	11.877	3.673	-1.481	.488	-.864
8061129	12.667	3.970	-1.018	1.110	-1.554
8061129	9.671	4.604	-1.393	.895	-.811
8061129	7.976	4.439	-1.461	1.163	-.694
8061129	6.157	2.124	-1.088	1.355	-.579
8061129	8.854	4.197	-1.025	1.273	.567
8071129	-2.474	-1.435	-.531	.428	.144
8071129	-2.615	-1.031	-.643	.308	.209
8071129	-2.454	-1.426	-.561	.406	.046
8071129	-2.343	-1.364	-.446	.290	-.172
8071129	-2.332	-1.126	-.492	.282	.215
8081129	-1.313	-.807	-1.158	.270	-.012
8081129	-1.249	-1.517	-.519	.389	-.065
8081129	-1.929	-.908	-.910	-.094	.044
8081129	-1.008	-.934	-.984	.263	.288
8081129	.766	-.674	-2.380	1.204	-.004

TABLE D-III

8091129	2.320	-1.690	-2.088	.628	.447
8091129	1.282	-1.630	-1.708	.767	-.079
8091129	1.903	-.466	-1.724	1.136	.484
8091129	3.326	-1.107	-2.078	.849	-.112
8091129	2.997	-1.530	-1.693	1.405	.386
8101129	6.881	-1.813	-1.785	-.244	.040
8101129	7.649	-1.998	-2.249	-.013	-.360
8101129	6.697	-.388	-1.873	.667	-.300
8101129	6.094	-.469	-2.139	.417	.228
8101129	8.234	-2.781	-1.376	.501	-.718
8111129	8.860	-2.413	-1.866	-.254	.519
8111129	8.575	-4.465	-.908	-.640	.710
8111129	10.094	-4.202	-1.366	-.096	.559
8111129	8.254	-1.429	-3.130	-.048	-.047
8111129	7.529	-1.767	-2.397	.269	-.041
7001129	-.345	-1.509	-.540	.100	-.113
7001129	.302	-1.841	-.208	.324	-.165
7001129	-.133	-1.413	-.678	.130	.222
7001129	-.177	-1.297	-.734	.045	.172
7001129	-.160	-1.629	-.504	.094	.227
7001129	-.084	-2.898	-.023	.707	-.346
7011129	-.130	-1.527	-.843	.078	-.119
7011129	-.559	-.709	-1.126	.507	-.061
7011129	-.515	-1.074	-.901	.188	.145
7011129	-.594	-1.297	-.895	.058	.131
7011129	-.255	-1.103	-.821	.295	-.091
7021129	.093	4.014	1.775	-.560	-.790
7021129	.460	3.635	1.614	.052	-.761
7021129	.247	3.412	1.463	-.147	-.382
7021129	-.060	2.996	.579	-.016	-.509
7021129	1.086	2.248	.469	.613	-.369
7031129	-1.600	-.894	-.526	.446	-.067
7031129	-1.850	-.723	-.526	.213	-.013
7031129	-2.001	-.324	-.632	.358	.090
7031129	-1.453	-.711	-.454	.178	.050
7031129	-1.702	-.344	-.812	.334	.051
7041129	-1.405	-.938	-.780	.075	.106
7041129	-.316	-1.250	-.850	.238	.027
7041129	-.645	-.974	-.636	.706	.218
7041129	-1.636	-.060	-.689	.617	.258
7041129	-1.503	-.653	-.589	.273	.289

TABLE D-IV

MEANS AND STANDARD DEVIATIONS OF FIRST 3 PRINCIPAL COMPONENTS

PC1	±SD	N	PATIENT IDENTITY	PC2	±SD	PC3	±SD
3.00	1.08	5.	1781039.	.72	.56	.44	.13
-.74	.30	5.	1784039.	.04	.26	.64	.13
-4.16	.34	5.	1801049.	-1.12	.19	-.60	.21
-3.14	.21	6.	1804049.	-.78	.14	-.30	.23
7.48	1.75	6.	1811049.	-1.13	1.42	.01	.96
3.02	.81	5.	1814049.	-2.13	.74	1.89	.59
5.12	1.01	5.	1821049.	2.24	.68	.02	.29
.67	.33	5.	1824049.	-.03	.48	.67	.37
-.53	.20	5.	1831059.	-1.43	.32	.34	.28
1.82	.71	5.	1841059.	-1.50	.27	-.15	.52
.40	.56	5.	1844059.	-.87	.41	.04	.25
-3.42	.18	6.	1851059.	-.26	.06	-.19	.10
3.65	.67	4.	1854059.	.12	.68	-.76	.32
-.88	.25	5.	1861059.	-1.57	.29	.50	.19
1.23	.28	5.	1864059.	-.60	.46	.65	.50
-.07	.43	5.	1871059.	1.99	.68	1.62	.30
-1.09	.45	5.	1874059.	.42	.18	.81	.21
5.19	2.72	5.	1881059.	-.03	1.11	-1.54	.72
-.59	.74	5.	1884059.	.48	.62	-.30	.12
-.08	.41	5.	1891059.	-.69	.62	.03	.32
.51	.66	5.	1894059.	1.00	.50	-.75	.35
1.56	.46	5.	1901059.	1.37	.71	-.62	.17
.16	.34	5.	1904059.	.55	.25	-.48	.21
1.01	.16	5.	1911059.	-1.24	.15	.53	.23
2.32	1.09	5.	1914059.	.33	.56	-.23	.54
5.29	1.15	5.	1924059.	-2.30	.45	.48	.35
-5.49	.26	5.	1931059.	-.10	.16	-.33	.07
-5.78	.17	5.	1934059.	-.34	.16	-.21	.12
-1.59	.48	5.	1941059.	.50	.46	-1.12	.51
-2.45	.54	5.	1944059.	1.95	.26	-.96	.16
-3.46	.14	6.	1951069.	-.62	.11	-.32	.11
-3.41	.33	5.	1954069.	-.91	.10	-.37	.16
4.47	.43	5.	1961069.	-3.17	.89	4.38	1.09
1.77	.43	5.	1964069.	-2.94	.62	2.40	.56
1.39	.57	5.	1971069.	-.41	.54	1.78	.12
-2.42	.67	5.	1974069.	6.71	.80	-.39	.15
-3.84	.15	5.	1981069.	-1.02	.06	-.27	.08
-4.77	.09	5.	1984069.	-1.49	.06	-.57	.09
5.63	1.06	5.	1991069.	.63	1.76	-.34	.41
1.98	.24	5.	1994069.	-1.39	.68	.82	.38
-3.35	.19	5.	2001069.	-.50	.14	-.13	.05
-3.10	.36	5.	2004069.	-.16	.20	-.11	.14
-3.86	.28	5.	2011069.	-.65	.11	-.42	.10
-3.25	.09	5.	2014069.	-.36	.17	-.43	.09
1.73	.61	5.	2021069.	.55	.36	1.11	.20
.27	.28	5.	2024069.	1.88	.21	.97	.22

TABLE D-IV

-1.51	.34	5.	2031079.	.04	.16	1.08	.30
-2.62	.17	5.	2034079.	.66	.20	.62	.12
4.19	.44	5.	2041079.	.46	.36	.73	.43
1.11	.36	4.	2044079.	-1.47	.25	.76	.22
-3.67	.28	4.	2051079.	-.44	.12	-.35	.15
3.86	.68	5.	2054079.	1.68	.56	-.71	.55
.79	1.32	8.	2071079.	.90	.46	-1.06	.26
-2.24	.27	5.	2074079.	.52	.35	-.58	.17
-4.26	.14	6.	2081079.	-1.01	.09	-.30	.09
-3.09	.13	5.	2084079.	.51	.12	-.03	.10
-.68	.40	5.	2091089.	-.16	.39	.40	.17
-.75	.34	5.	2094089.	.31	.38	.38	.27
-3.44	.31	6.	2101089.	-.65	.10	.12	.13
2.54	.27	5.	2104089.	1.63	1.05	.13	.22
-.48	.05	3.	2114089.	.18	.11	-.30	.32
.70	.77	5.	2121089.	1.90	.33	1.44	.25
-3.88	.29	5.	2124089.	-.69	.11	-.04	.11
.06	.33	5.	2131089.	-.86	.47	.69	.39
-.37	.08	5.	2134089.	-.20	.27	.69	.29
1.05	.40	5.	2141089.	1.17	.75	.50	.25
-3.68	.30	5.	2144089.	-.10	.15	-.16	.17
.12	.20	5.	2151089.	-1.22	.45	.46	.43
1.02	.26	5.	2154089.	-1.64	.43	.63	.26
.08	.12	5.	2161089.	-.63	.40	.69	.25
.92	.88	5.	2164089.	-.30	.45	.74	.73
-2.25	.54	4.	2171089.	2.58	.04	1.37	.43
2.22	.76	5.	2174089.	3.15	.23	1.50	.41
1.29	.25	5.	2181089.	.70	.41	-.48	.49
.18	.47	5.	2184089.	.92	.20	-.43	.13
.56	.40	5.	2191099.	-2.69	.81	.26	.74
3.90	1.09	5.	2194099.	1.89	.97	-1.21	.26
1.01	.46	5.	2201109.	2.43	.36	.53	.21
.01	.36	5.	2204109.	-.02	.13	.66	.12
-1.39	.17	5.	2211109.	.61	.12	-.38	.11
-1.16	.41	4.	2214109.	.44	.22	-.26	.36
-4.06	.20	5.	2221109.	-.79	.11	-.08	.10
-3.90	.14	5.	2224109.	-.87	.09	-.41	.08
-.90	.35	6.	2231109.	.05	.31	.28	.18
.49	.28	5.	2234109.	.52	.61	.20	.38
-.52	.46	5.	2241119.	.25	.32	-.02	.27
-4.07	.09	4.	2244119.	-.53	.12	-.57	.07
-4.44	.20	5.	2251010.	-1.15	.09	-.60	.12
-.19	.57	4.	2254010.	3.10	.41	.24	.27
-2.28	.32	5.	2261020.	.03	.10	-.11	.17
-.89	.19	5.	2264020.	-1.04	.29	.24	.30
.92	.53	5.	2271020.	-.45	.65	-.09	.34
-2.11	.04	6.	2274020.	-.90	.10	.03	.11
-1.74	.07	5.	2281030.	-.81	.12	.37	.14
-4.14	.08	5.	2284030.	-1.33	.08	-.34	.13
.98	1.21	5.	2301040.	4.73	.73	.91	.43
1.15	.79	5.	2304040.	3.37	.48	.54	.57
.19	1.06	5.	2311040.	1.01	.51	-.30	.35
.76	1.14	4.	2314040.	5.44	.65	1.02	.33
-3.09	.47	5.	2321050.	.52	.23	-.20	.10

TABLE D-IV

-3.31	.28	5.	2324050.	-.02	.10	-.12	.11
-.49	1.00	5.	2331060.	1.69	.45	.39	.19
-3.11	.25	4.	2334060.	-.25	.03	.11	.06
-3.82	.09	5.	2341060.	-.23	.07	-.11	.10
-.41	.10	5.	2344060.	.92	.06	.29	.16
-.11	.10	5.	2351060.	-1.35	.37	-.47	.26
2.16	.38	5.	2354060.	-.65	.51	-1.46	.05
-2.46	.44	5.	2361070.	-.31	.40	.79	.47
-1.53	.56	5.	2364070.	-.03	.41	-.22	.28
-1.43	.39	5.	2371080.	-.96	.60	-.18	.31
-.72	.25	5.	2374080.	.24	.31	.12	.57
13.15	2.61	5.	2381080.	.65	1.50	.80	.48
.01	.25	5.	2384080.	-.06	.61	-.46	.43
-1.10	.26	5.	7001109.	1.95	.38	-.07	.19
4.05	.37	5.	8011129.	-2.09	.64	-1.34	.46
9.03	2.01	5.	8021129.	-4.08	1.39	-.33	.93
-1.08	.51	5.	8031129.	.48	.51	-.63	.10
2.73	.41	5.	8041129.	-.37	.39	-1.48	.43
4.92	.38	5.	8051129.	-2.02	.23	-1.70	.40
9.53	2.22	6.	8061129.	3.83	.82	-1.24	.20
-2.44	.10	5.	8071129.	-1.28	.17	-.53	.07
-.95	.91	5.	8081129.	-.97	.29	-1.19	.63
2.37	.74	5.	8091129.	-1.28	.46	-1.86	.18
7.11	.75	5.	8101129.	-1.49	.93	-1.88	.31
8.66	.84	5.	8111129.	-2.86	1.25	-1.93	.78
-.10	.20	6.	7001129.	-1.76	.53	-.45	.25
-.41	.18	5.	7011129.	-1.14	.27	-.92	.11
.36	.40	5.	7021129.	3.26	.60	1.18	.55
-1.72	.19	5.	7031129.	-.60	.23	-.59	.12
-1.10	.52	5.	7041129.	-.77	.40	-.71	.09

CUMULATIVE INFORMATION CONTENT OF THE 32 PRINCIPAL COMPONENTS

1	69.76	9	99.47	17	99.94	25	99.99
2	87.56	10	99.62	18	99.95	26	100.00
3	93.09	11	99.72	19	99.96	27	100.00
4	95.70	12	99.80	20	99.97	28	100.00
5	97.12	13	99.85	21	99.98	29	100.00
6	98.31	14	99.88	22	99.98	30	100.00
7	98.91	15	99.91	23	99.99	31	100.00
8	99.24	16	99.93	24	99.99	32	100.00

TABLE D-V

This table contains the summarised data of all the patient assessments, including the Doppler methods. Grading of the femoral pulse, pressure study and arteriograms is as described in Chapter 5. The key to the abbreviated symbols is as follows:

PAT	Patient identity code
FP	Clinical grade of femoral pulse (1 - 4)
RG	Resting pressure gradient between test and control (in mm Hg)
HG	Hyperaemic pressure gradient (in mm Hg)
P	Pressure grade (1 - 4); 9 = not done or inadequate
AF	Arteriography of the aorto-femoral segment (1 - 4); 9 = not done or inadequate
SFA	Arteriography of the femoro-popliteal segment (1/0); 9 = not done or inadequate
CLIN	Standard clinical assessment (see Chapter 9)
PI	Pulsatility index
LTD	Laplace transform damping
PC1	Coefficient of the first principal component
PC2	Coefficient of the second principal component

PAT	FP	RG	HG	P	AF	SFA	CLIN	PI	LTD	PC1	PC2
1781	1	-8	10	1	9	1	3	5.42	.55	3.00	0.72
1784	1	4	10	1	9	0	2	3.30	.85	-0.74	0.04
1801	4			9	4	0	1	1.23	.98	-4.16	-1.12
1804	1	30	60	4	3	0	1	1.60	.98	-3.14	-0.78
1811	1	4	8	1	1	1	3	9.27	.41	7.48	-1.13
1814	1	1	2	1	1	0	2	7.99	.51	3.02	-2.13
1821	1	6	18	2	1	1	3	7.90	.41	5.12	2.24
1824	1	0	4	1	1	0	2	4.53	.79	0.67	-0.03
1831	2			9	1	0	2	2.28	.51	-0.53	-1.43
1834	3			9	1	1	4	4.64	.35		
1841	1	18	30	4	1	0	2	3.81	.33	1.82	-1.50
1844	2	-10	4	1	1	0	2	2.90	.40	0.40	-0.87
1851	3			9	3	0	1	1.35	.94	-3.42	-0.26
1854	1	0	23	3	1	1	4	4.86	.37	3.65	0.12
1861	1	-6	18	2	9	0	2	2.30	.46	-0.88	-1.57
1864	1	0	29	4	9	1	4	3.84	.60	1.23	-0.60
1871	1	2	20	3	1	1	3	4.85	.68	-0.07	1.99
1874	1	-2	8	1	2	0	2	3.19	.85	-1.09	0.42
1881	1	-4	2	1	9	1	3	8.37	.32	5.19	-0.03
1884	1	1	6	1	9	1	3	3.92	.30	-0.59	0.48
1891	1	-2	11	1	9	0	2	2.89	.46	-0.08	-0.69
1894	1	8	14	1	9	1	3	4.26	.27	0.51	1.00
1901	1	-1	4	1	1	1	3	4.93	.32	1.56	1.37
1904	2	4	22	3	2	0	4	3.32	.35	0.16	0.55
1911	1			9	1	0	2	3.77	.39	1.01	-1.24

TABLE D-V

PAT	FP	RG	HG	P	AF	SFA	CLIN	PI	LTD	PC1	PC2
1914	1			9	1	1	3	4.74	.45	2.32	0.33
1921	4			9	4	9	1				
1924	1			9	2	0	3	7.61	.37	5.29	-2.30
1931	3	30	50	4	9	1	1	1.72	.55	-5.49	-0.10
1934	4	30	50	4	9	1	1	1.95	.51	-5.78	-0.34
1941	1	6	-10	1	1	0	2	2.84	.34	-1.59	0.50
1944	1	22	26	4	2	1	4	2.82	.30	-2.40	1.95
1951	4	60	100	4	9	1	1	1.13	1.00	-3.60	-0.62
1954	4	60	100	4	9	1	1	1.04	1.00	-3.41	-0.91
1961	2			9	1	0	2	6.55	.70	4.47	-3.17
1964	2	-8	-8	1	1	0	2	4.77	.36	1.77	-2.94
1971	1	4	10	1	1	0	2	4.85	.90	1.39	-0.41
1974	1	-2	10	1	1	1	3	6.97	.31	-2.42	6.71
1981	4			9	4	0	1	1.20	1.00	-3.84	-1.02
1984	4			9	3	0	1	0.89	.90	-4.77	-1.49
1991	1	-1	21	3	1	1	3	10.13	.42	5.63	0.63
1994	1	2	6	1	1	0	2	6.41	.80	1.98	-1.39
2001	3	40	80	4	2	1	1	1.80	.92	-3.35	-0.50
2004	3	20	60	4	2	1	1	1.89	.72	-3.10	-0.16
2011	4	120		4	4	1	1	1.11	.97	-3.86	-0.65
2014	4			9	3	1	1	1.29	.98	-3.25	-0.36
2021	1			9	1	1	3	4.38	.73	1.73	0.55
2024	2			9	1	0	4	4.26	.69	0.27	1.88
2031	3	38	70	4	9	0	1	3.80	.80	-1.51	0.04
2034	2	10	40	4	9	0	4	3.62	.81	-2.62	0.66

TABLE D-V

TABLE D-V

PAT	FP	RG	HG	P	AF	SFA	CLIN	PI	LTD	PC1	PC2
2041	1	4	20	3	9	1	3	5.81	.54	4.19	0.46
2044	1	-4	12	1	2	0	2	3.85	.43	1.11	-1.47
2051	4	120	140	4	9	9	1	1.48	.96	-3.67	-0.44
2054	1	4	19	2	9	1	3	6.47	.35	3.86	1.68
2061	4			9	4	9	1				
2064	1	60	90	4	3	0	1	1.42	.70		
2071	1	-31	-24	1	1	1	3	4.83	.23	0.79	0.90
2074	4	36	71	4	4	1	1	2.60	.43	-2.24	0.52
2081	4	26	56	4	3	1	1	1.18	.99	-4.26	-1.01
2084	3	30	60	4	2	1	1	2.00	.43	-3.09	0.51
2091	2	0	19	2	1	0	4	3.07	.53	-0.68	-0.16
2094	2			9	1	0	4	3.14	.58	-0.75	0.31
2101	1	8	4	1	1	0	3	1.65	1.00	-3.44	-0.65
2104	1	-9	10	1	1	1	3	7.15	.47	2.54	1.63
2111	4			9	9	9	1				
2114	1			9	9	0	2	2.11	.48	-0.48	0.18
2121	1	0	37	4	3	1	4	5.91	.64	0.70	1.90
2124	2	78	120	4	3	0	1	1.61	1.00	-3.88	-0.69
2131	1	0	10	1	1	0	2	3.89	.43	0.06	-0.86
2134	1	2	16	2	1	0	2	3.28	.64	-0.37	-0.20
2141	1	9	21	3	2	1	3	5.52	.47	1.05	1.17
2144	3	20	54	4	3	1	1	1.94	.68	-3.68	-0.10
2151	1	-4	16	2	2	0	2	3.26	.44	0.12	-1.22
2154	1	6	12	1	2	0	2	3.98	.36	1.02	-1.64
2161	1	0	4	1	2	0	2	3.34	.80	0.08	-0.63

TABLE D-V

PAT	FP	RG	HG	P	AF	SFA	CLIN	PI	LTD	PC1	PC2
2164	1	1	6	1	1	0	2	4.32	.73	0.92	-0.30
2171	1	-4	26	4	3	1	4	4.00	.28	-2.25	2.58
2174	3	1	21	3	3	0	1	6.41	.59	2.22	3.15
2181	1			9	9	1	5	4.77	.33	1.29	0.70
2184	1			9	9	1	5	3.75	.34	0.18	0.92
2191	1	-8	6	1	2	0	2	3.80	.19	0.56	-2.69
2194	2	0	28	4	2	1	4	6.16	.32	3.90	1.89
2201	2	2	7	1	9	1	3	4.49	.52	1.01	2.43
2204	3			9	9	0	4	3.58	.59	0.01	-0.02
2211	2	9	33	4	1	0	4	2.79	.41	-1.39	0.61
2214	1	-8	1	1	1	0	1	2.77	.44	-1.16	0.44
2221	2	104	124	4	3	1	1	1.51	.78	-4.06	-0.79
2224	3	126	148	4	4	1	1	1.50	.96	-3.90	-0.87
2231	2	-10	9	1	1	0	2	2.70	.60	-0.90	0.05
2234	2	10	19	2	1	1	3	3.83	.50	0.49	0.52
2241	2	-2	20	3	2	0	4	3.57	.43	-0.52	0.25
2244	4			9	4	0	1	1.57	.98	-4.07	-0.53
2251	4			9	4	1	1	1.20	.92	-4.44	-1.15
2254	2	6	14	2	2	1	4	4.33	.40	-0.19	3.10
2261	3			9	4	1	1	1.85	.74	-2.28	0.03
2264	1	10	37	3	2	0	4	2.53	.51	-0.89	-1.04
2271	1			9	2	0	4	4.03	.44	0.92	-0.45
2274	2	-6	3	1	2	0	4	1.80	.61	-2.11	-0.90
2281	2	6	34	4	1	1	4	2.64	.48	-1.74	-0.81
2284	3	50	110	4	3	1	1	1.14	1.00	-4.14	-1.33

PAT	FP	RG	HG	P	AF	SFA	CLIN	PI	LTD	PC1	PC2
2291	3			9	2	0	1	1.85	.57		
2294	1			9	2	0	2	1.89	.47		
2301	2	12	46	4	2	1	1	6.28	.36	0.98	4.73
2304	2	2	19	2	2	1	1	6.28	.40	1.15	3.37
2311	2	-6	2	1	9	0	2	4.46	.41	0.19	1.01
2314	2	4	27	4	9	1	4	6.21	.35	0.76	5.44
2321	3			9	4	0	1	3.17	.56	-3.09	0.52
2324	3			9	4	1	1	2.17	.60	-3.31	-0.02
2331	1	-16	15	3	2	1	3	4.52	.30	-0.49	1.69
2334	2	16	45	4	3	1	1	2.09	.86	-3.11	-0.25
2341	3	54	97	4	4	1	1	1.58	.94	-3.82	-0.23
2344	2	-58	-38	2	2	1	4	3.43	.46	-0.41	0.92
2351	1			9	9	0	2	2.88	.29	-0.11	-1.35
2354	1			9	9	1	5	4.91	.23	2.16	-0.65
2361	1	1	13	1	2	0	2	2.73	.67	-2.46	-0.31
2364	1	0	27	4	2	1	3	3.08	.37	-1.53	-0.03
2371	1	-6	17	2	9	0	4	2.47	.35	-1.43	-0.96
2374	1	3	24	3	2	1	4	3.01	.54	-0.72	0.24
2381	1	0	19	2	2	1	3				
2384	2	-1	12	1	2	0	2	3.37	.34	0.01	-0.06
7001	1			9	9	1	5	3.52	.26	-1.10	1.95
8011	1			9	9	1	5	7.80	.25	4.05	-2.09
8051	1			9	9	1	5	8.70	.26	4.92	-2.02

TABLE D-V

TABLE D-VI

This table is a summary of the direct pressure studies performed on the majority of the patients. Most patients underwent a standard test as described in Chapter 8. In a few cases it was not possible to needle the femoral artery on both sides and an arm cuff was used as control; this is indicated in the comments column below, together with the reason which was usually iliac disease on the control side. In a further small number of cases operative pressure studies were used, and these are noted as 'theatre' below. Some patients were frail and elderly and only underwent a limited assessment without pressure studies. Pressure gradients for each limb are listed in Table D-V.

LIMB	TYPE OF TEST	COMMENTS
1781	Standard	
1784	"	
1801	---	Not attempted: amputation
1804	Theatre	
1811	Standard	
1814	"	
1821	"	
1824	"	
1831	---	Attempted: could not needle vessel
1834	---	" " " " "
1841	Standard	
1844	"	
1851	---	Attempted: could not needle vessel
1854	Theatre	
1861	Standard	
1864	"	
1871	"	
1874	"	
1881	"	
1884	"	
1891	"	
1894	"	
1901	"	
1904	"	
1911	---	Not attempted: patient ill
1914	---	" " " "

TABLE D-VI

LIMB	TYPE OF TEST	COMMENTS
1921	---	Not attempted: patient ill
1924	---	" " " "
1931	Standard	Brachial control: bilat. iliac disease
1934	"	" " " " "
1941	"	
1944	"	
1951	"	Brachial control: bilat. iliac disease
1954	"	
1961	---	Not attempted: patient ill
1964	Theatre	
1971	Standard	
1974	"	
1981	---	Not attempted: absent femoral pulse
1984	---	" " " " "
1991	Standard	
1994	"	
2001	"	Brachial control: bilat. iliac disease
2004	"	" " " " "
2011	Theatre	
2014	---	Not attempted: patient anxiety
2021	---	Not attempted: patient ill
2024	---	" " " "
2031	Standard	
2034	"	Brachial control: iliac disease
2041	"	
2044	"	
2051	Theatre	
2054	"	
2061	---	Not attempted: amputation
2064	Standard	Brachial control: iliac disease
2071	"	
2074	"	
2081	"	
2084	"	Brachial control: iliac disease
2091	"	Brachial control
2094	---	Attempted: could not needle vessel
2101	Standard	
2104	"	
2111	---	Not attempted: patient ill
2114	---	" " " "
2121	Standard	Brachial control: iliac disease
2124	Theatre	
2131	Standard	
2134	"	
2141	Theatre	
2144	Standard	
2151	"	
2154	"	
2161	"	
2164	"	

TABLE D-VI

LIMB	TYPE OF TEST	COMMENTS
2171	Standard	
2174	"	
2181	---	Not attempted: Raynaud's syndrome
2184	---	" " " "
2191	Standard	
2194	"	
2201	Theatre	
2204	---	Attempted in theatre: inadequate study
2211	Standard	
2214	"	
2221	Theatre	
2224	"	
2231	Standard	
2234	"	
2241	"	Brachial control: iliac disease
2244	---	Not attempted: absent femoral pulse
2251	---	" " " " "
2254	Theatre	
2261	---	Not attempted: absent femoral pulse
2264	Standard	Brachial control: iliac disease
2271	---	Inadequate recording
2274	Standard	
2281	Theatre	
2284	"	
2291	---	Not attempted: patient ill
2294	---	" " " "
2301	Standard	
2304	"	
2311	"	
2314	"	
2321	---	Not attempted: absent femoral pulse
2324	---	" " " " "
2331	Standard	
2334	"	
2341	"	
2344	"	
2351	---	Not attempted: child
2354	---	" " "
2361	Standard	
2364	"	
2371	"	
2374	"	
2381	"	
2384	"	
7001	---	Not attempted: healthy volunteer
8011	---	" " " "
8051	---	" " " "

TABLE D-VII

This table contains details of those limbs classified in clinical Group 4 (those in whom there was uncertainty about the adequacy of the aortoiliac segment after femoral pulse palpation, arteriography and direct pressure studies). In addition to the reasons for this initial classification, data is also available from clinical follow-up of these patients. Some of these results are discussed at the end of Chapter 9. The key to the table is as follows:

PAT Patient identity code

FP Clinical grade of femoral pulse (1 - 4)

P Pressure grade (1 - 4); 9 = not done

AF Arteriography of the aorto-femoral segment (1 - 4); 9 = not done or inadequate

PAT	FP	P	AF	REASON IN GROUP 4	FOLLOW-UP DATA
1934	3	9	1	Disagreement; no pressure test	Had a fem-pop which failed; subsequent iliac reconstruction and amputation
1854	1	3	1	Irregularity on XR and moderate pressure gradient	Endarterectomy revealed >50% stenosis
1864	1	4	9	Marked pressure gradient despite good femoral pulse: X-rays lost	Patient died from mesenteric vascular occlusion
1904	2	3	2	All assessments equivocal	Had SFA occlusion: did well on conservative treatment
1944	1	4	2	Slight narrowing on X-ray; large gradient	Lost to follow up

TABLE D-VII

2024	2	9	1	Pulse felt to be weak by several observers	Elderly and frail; died shortly after
2034	2	4	9	Pulse thought to be weak; X-rays out of date, but showed AF segment probably adequate	Conservative treatment; pulse still fairly good 3 years later
2091	2	2	1	19mm Hg hyperaemic gradient and weakish pulse	Had femoro-popliteal bypass; good result 2 years later so inflow was probably adequate
2094	2	9	1	Pulse definitely weak by several observers; pressure test not satisfactory	No operation; good pulse 2 years later
2121	1	4	3	Marked disagreement between assessments	Had significant disease on opposite side; bifurcation graft
2171	1	4	3	Marked disagreement between assessments	Eventually had femoro-popliteal bypass; gpod result 2 years later
2194	2	4	2	Disagreement between assessments	Treated conservatively; no worsening of symptoms
2204	3	9	9	Narrow vessels; X-rays lost	Had bifurcation graft with little improvement; better after addition of fem-pop bypass
2211	2	4	1	Disagreement between assessments	Treated conservatively; femoral pulse remained the same for 2 years
2241	2	3	2	All assessments equivocal	Treated conservatively; femoral pulse remained the same for 2 years

TABLE D-VII

2254	2	2	2	All assessments equivocal	Had bifurcation graft with little improvement; better after addition of fem-pop bypass
2264	1	3	2	Disagreement between assessments	Had bifurcation graft because of contra-lateral disease
2271	1	9	2	Borderline arterio-gram	Eventually had femo-ro-popliteal bypass with good result, so inflow probably good
2274	2	1	2	Equivocal pulse and X-ray	Had ilio-popliteal graft with good result
2281	2	4	1	Disagreement between assessments	Had bifurcation graft because of contra-lateral disease; still has claudication
2314	2	4	9	Disagreement	Did not have arter-iogram; treated con-servatively
2344	2	2	2	All assessments equivocal	Had bifurcation graft because of contra-lateral disease; did well
2371	1	2	9	Inadequate X-ray	Ilio-profunda done; not improved, so had fem-tib; failed; amputation
2374	1	3	2	Disagreement between assessments	Treated conservat-ively; femoral pulse good 2 years later

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UNIVERSITY OF LEICESTER

CANDIDATURE FOR HIGHER DEGREE

NOTES FOR GUIDANCE OF EXAMINERS

These notes appear on the examiners' report form and are here reproduced for the benefit of internal examiners.

1. Examiners are requested to submit (as an agreed report, if possible):

   (a) a reasoned assessment of the candidate's performance and

   (b) a recommendation of conferment or non-conferment of the degree, or re-examination of the candidate.

   If an agreed report cannot be submitted, each examiner should report separately. The candidate's work will then be referred to the adjudication of a second external examiner.

   (As a gloss on this section, examiners are requested to include in their report a brief description of the main problems under study, so that their reasoned assessment of the candidate's performance might be understood by all members of the Faculty Board or relevant Board of Studies).

2. (a) Where a candidate offers a thesis an oral examination is required.

   (b) Where the candidate offers both written papers and a dissertation the examiners should report on each part of the examination separately, though basing their recommendation on the candidate's performance as a whole, including the oral examination. The examiners may at their discretion fail or refer without an oral examination a candidate whose written performance they consider inadequate.

3. The written papers, dissertation or thesis should comply with the requirements (including those relating to length, presentation, relevance, and style) laid down in the notes issued for the guidance of candidates. Examiners should state that these requirements have been met, or indicate any departure from them. Examiners should note that no change should be made in the title of a dissertation or thesis once it has been submitted for examination.

4. Where the examiners recommend the award of a Ph.D degree, they must certify that the thesis contains work worthy of publication.

5. A candidate for the Master's degree, including the degree of M.Phil in the Faculty of the Social Sciences and Faculty of Arts may be recommended for a mark of distinction but only for a performance of outstanding merit.

6. Examiners may recommend the conferment of a degree subject to minor amendments to a dissertation or thesis, provided two copies, amended as required, are lodged with the University not later than one month after the date of examination.

7. If referred for re-examination, a candidate proceeding to a Master's degree by written papers only will be required to resit the whole examination, but it is open to examiners to recommend that a candidate proceeding to the degree by a combination of dissertation or thesis and written papers should be referred either in both parts of the examination or in one part only. The oral examination on a re-submitted dissertation or thesis for a Master's or a Doctor's degree may be omitted at the examiners' discretion.

8. Examiners may, if they wish, specify a minimum period which should elapse before any re-examination (in no case less than three months), and a maximum period within which a student must submit (in no case more than one year of full-time or two years of part-time study).

9. Examiners for the degree of Doctor of Philosophy in the Faculties of Arts, Science and of Law may recommend that a candidate shall pass either for the degree of Doctor of Philosophy or the degree of Master of Philosophy, or shall fail, or shall be referred either for re-submission for the degree of Ph.D or Master of Philosophy.

Examiners for the degree of Doctor of Philosophy in the Faculties of Social Sciences and Medicine may recommend that a candidate shall pass, shall fail or shall be referred for re-submission for either the degree of Doctor of Philosophy or the degree of Master of Philosophy.

Examiners for the degree of Doctor of Philosophy in the School of Education may recommend that a candidate shall pass either for the degree of Doctor of Philosophy or the degree of Master of Education, or shall fail, or shall be referred either for re-submission for the degree of Master of Education or Doctor of Philosophy.

THE ASSESSMENT OF AORTOILIAC NARROWING by David Symon Macpherson

A thesis submitted for the degree of Doctor of Mecicine to the University of Leicester, December 1983

SUMMARY

The deficiencies of arteriography in the assessment of arterial narrowing proximal to the inguinal ligament are well recognised. This thesis has set out to examine the usefulness of continuous wave Doppler ultrasound as a method of providing more reliable diagnostic information in this segment.

After a review of the literature, the methods used in the study are described. Two series of animal experiments are then presented. In the first, three methods of analysis are applied to Doppler waveforms recorded from below stenoses of known dimensions implanted in the canine iliac artery. Pressure and flow measurements are used to calculate peripheral and stenosis resistance. The conclusion from this study is that neither pulsatility index (PI) nor Laplace transform damping factor (LTD) is consistently sensitive to stenoses of less than 88% area reduction and that this is in part due to the effect on these parameters of peripheral resistance. A third method, principal component analysis (PCA) appeared to give slightly better results.

In the second series of canine experiments, the extent of turbulence produced by stenoses of varying degree is investigated. There is a clear relationship between increased tightness of stenosis and increased turbulence propagation.

In the final part of the thesis the same methods of Doppler waveform analysis are investigated in a clinical study. The main reference material for comparison with the Doppler methods is direct arterial pressure measurement rather than arteriography. Although there are clear trends seen with all the indices examined, there is marked overlap between their values for different clinical groups, especially for PI and LTD. In particular,

the effect of superficial femoral artery disease on common femoral Doppler waveforms is identified as a major factor which limits the usefulness of the methods. Again PCA appears to perform best, although the use of two dimensional information seems necessary to get the most out of the technique. In practice, it seems unlikely that the use of these methods of Doppler waveform analysis will be helpful in those specific cases where there is genuine doubt about the state of the proximal vessels.

In conclusion, none of these methods is sufficiently accurate to be recommended for widespread adoption without more research. The present work would suggest that the information about lesser degrees of proximal narrowing is simply not contained in the outline of the Doppler waveform. Direct pressure studies provide the best current method of assessing aortoiliac narrowing.