Skeletal Muscle Counterpulsation

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Abstract

Skeletal muscle used for counterpulsation is one of several methods currently under investigation to provide cardiac assistance. A variety of approaches to achieve diastolic augmentation have been adopted, including skeletal muscle ventricles, hydraulic pouches or extra aortic skeletal muscle wraps. These remain experimental at present although long term results are now being published.

Key words: Skeletal muscle counterpulsation, skeletal muscle ventricles, aortomyoplasty.

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The use of skeletal muscle to support the failing circulation is an exciting area of both research and clinical interest. Skeletal muscle can be used to augment systolic function of the heart by wrapping the failing ventricles (cardiomyoplasty) or to produce counterpulsation, improving myocardial perfusion and reducing afterload. Cardiomyoplasty techniques have recently been reviewed in this journal [8] and will not be discussed further. An overview of counterpulsation techniques are presented in this communication and include the methods of assessment currently in use.

Historical Perspective

In 1959 Kantrowitz reported using the muscular portion of the left hemidiaphragm wrapped around the distal thoracic aorta [12]. The muscle was paced via the phrenic nerve to contract during diastole, and achieved a transitory rise in mean arterial pressure up to 26.5% before the muscle fatigued. This work stimulated the development of the intraaortic balloon pump [16].

During the 1970's other workers including Vachon [24], Spotnitz [23] and Von Recum [25] investigated skeletal muscle pouches, but again they encountered the problem of skeletal muscle fatigue.

The pioneering work of Buller [7] and the continuing work of Salmons and Pette's groups on muscle transformation and fatigue resistance (for reviews see [19, 22]) renewed interest in the possibility of using stimulated muscle for cardiac assistance. The development of pulse train stimulators appropriate for skeletal muscle contraction also contributed to the improved performance of the assist devices.

During the 1980's two main techniques of using skeletal muscle for counterpulsation have emerged: skeletal muscle ventricles or pouches [1, 17] and extraaortic counterpulsation involving either the ascending [9] or proximal thoracic aorta [11, 18] building upon Kantrowitz's original idea.

Techniques

Skeletal muscle counterpulsation devices have been constructed from a number of different muscles including pectoralis major, rectus abdominis, although the latissimus dorsi is the most frequently employed. The latissimus dorsi is an appropriate muscle for cardiac assistance as it is readily mobilised on an intact neurovascular pedicle, it is located close to the site of application and it leaves little residual deformity. However, whichever muscle is chosen, the problem of fatigue has to be addressed for it to be capable of long term work.

1) *Skeletal muscle ventricles:*

To construct a skeletal muscle ventricle the latissimus dorsi is mobilised leaving the thoracodorsal neurovascular bundle intact. The muscle is then wrapped around a Teflon mandrel in a multilayered spiral fashion (Figure 1). The cavity of the skeletal muscle ventricles are lined with either autogenous pleura or pericardium, in an attempt to eliminate thromboemboli.

After 4 weeks the mandrel is removed and the skeletal muscle ventricle anastomosed to the descending thoracic aorta with a polytetrafluoroethylene bifurcation graft. The

aorta is ligated between the two limbs of the graft to ensure blood flow through the neoventricle. Direct nerve stimulation is initiated in synchrony with the cardiac cycle. This technique was used experimentally for periods up to eighteen months [21].

Many of the physiological, biochemical and physical aspects of skeletal muscle ventricles have been investigated using this model. These include studies of optimal dimensions (cylindrical, conical, narrow or wide bore etc), types of lining material, the relationship of stretch to muscle composition, the effect of altered preload on muscle mechanics and muscle metabolism (eg, [5, 10]).

Other counterpulsation devices powered by skeletal muscle have been investigated including an implantable extraaortic balloon powered by transformed latissimus dorsi [14]. The dual chamber counterpulsator involves a blood pump with a Dacron graft at each end, anastomosed end to side with the thoracic aorta and running parallel to it (Figure 2a). The blood pump is powered by a hydraulic system placed beneath the latissimus dorsi which is stimulated to contract in diastole. A similar experimental model for pulmonary counterpulsation has also been investigated [15] (Figure 2b). One of the major problems with this approach currently being addressed is the slow leak of fluid from the hydraulic system. Other configurations studied include apicoaortic uni- and bi-valved conduits with a central pumping chamber [17].

2) *Extraaortic Skeletal Muscle Wraps:*

We have developed an autologous counterpulsation system, excluding foreign material / blood surface interface [18]. The left latissimus dorsi is mobilised on an intact neurovascular pedicle and two stimulating leads attached proximally to allow neuromuscular stimulation. Through a third rib resection 8 cm of the proximal descending thoracic aorta is mobilised, dividing one or two intercostal vessels as necessary. The muscle is wrapped twice around the mobilised aorta in a spiral fashion and sutured back onto itself securely. Initially a pericardial sensing lead was used but more recently with the development of an implantable stimulator a right ventricular endocardial sensing lead is used to detect the native R wave (Figure 3). Stimulation is initiated after 48 hours at our standard stimulation regime every fourth cardiac cycle. This procedure has been investigated for up to 6 months in a normal animal model

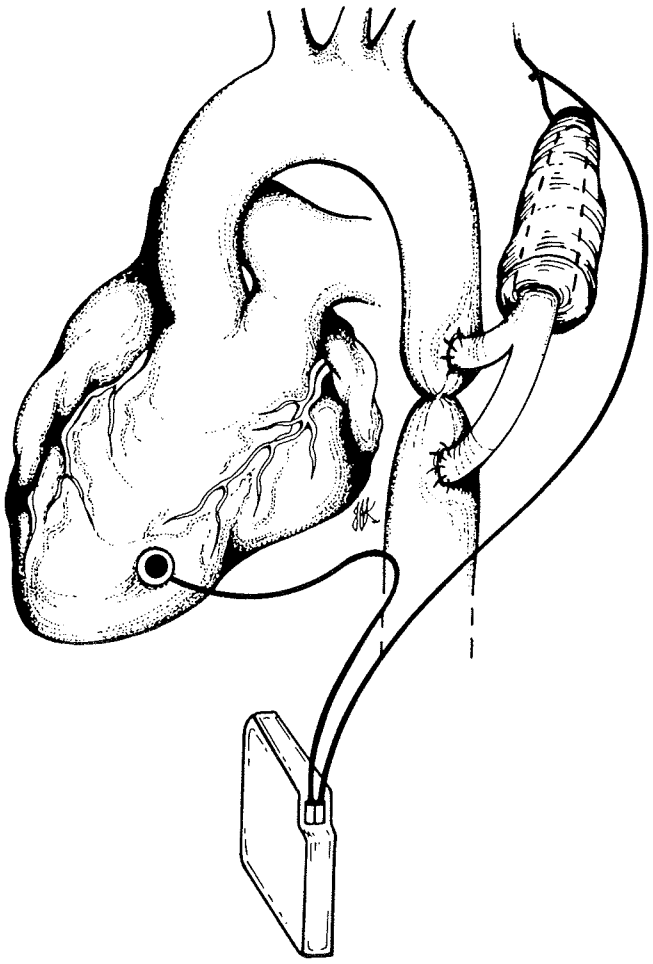


Figure 1: Skeletal muscle ventricle [21]

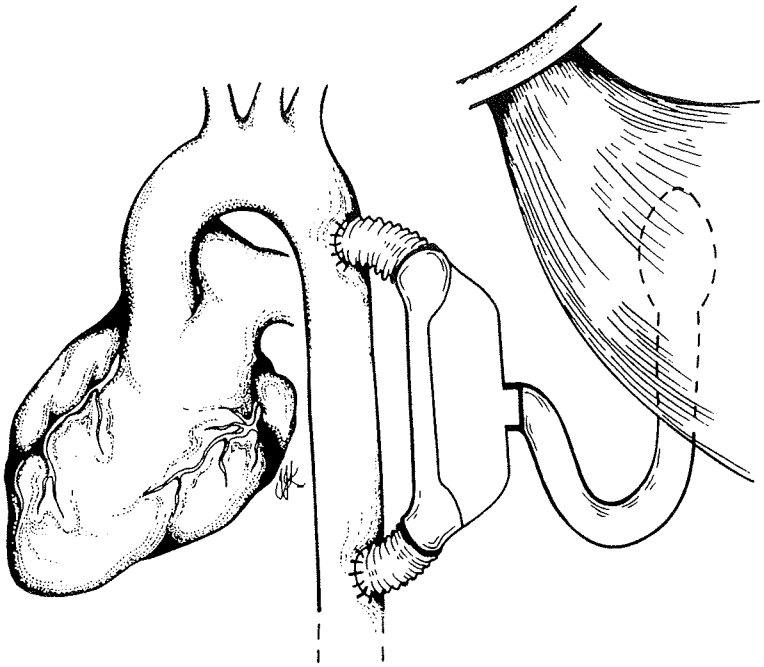


Figure 2a: Hydraulic pouch powered by skeletal muscle [14]

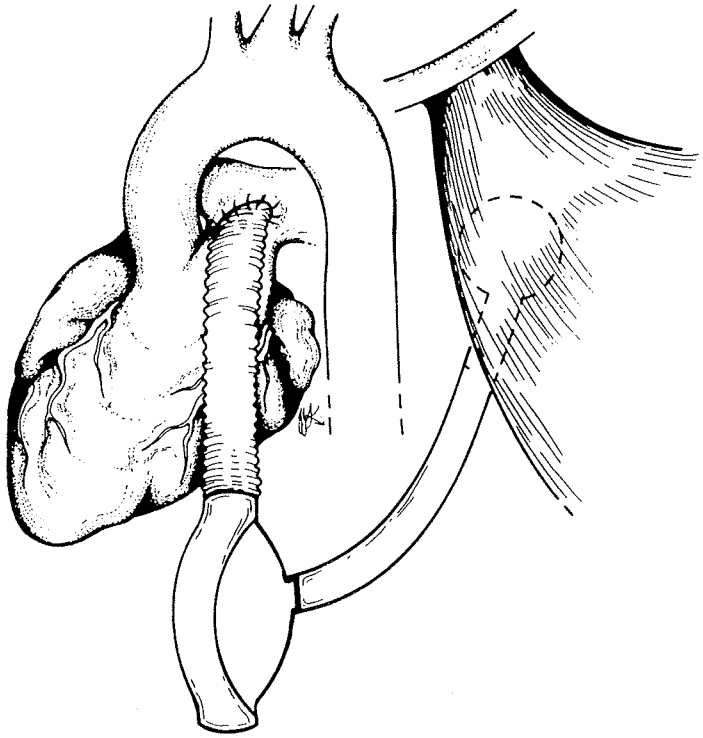


Figure 2b: Pulmonary artery counterpulsation [15]

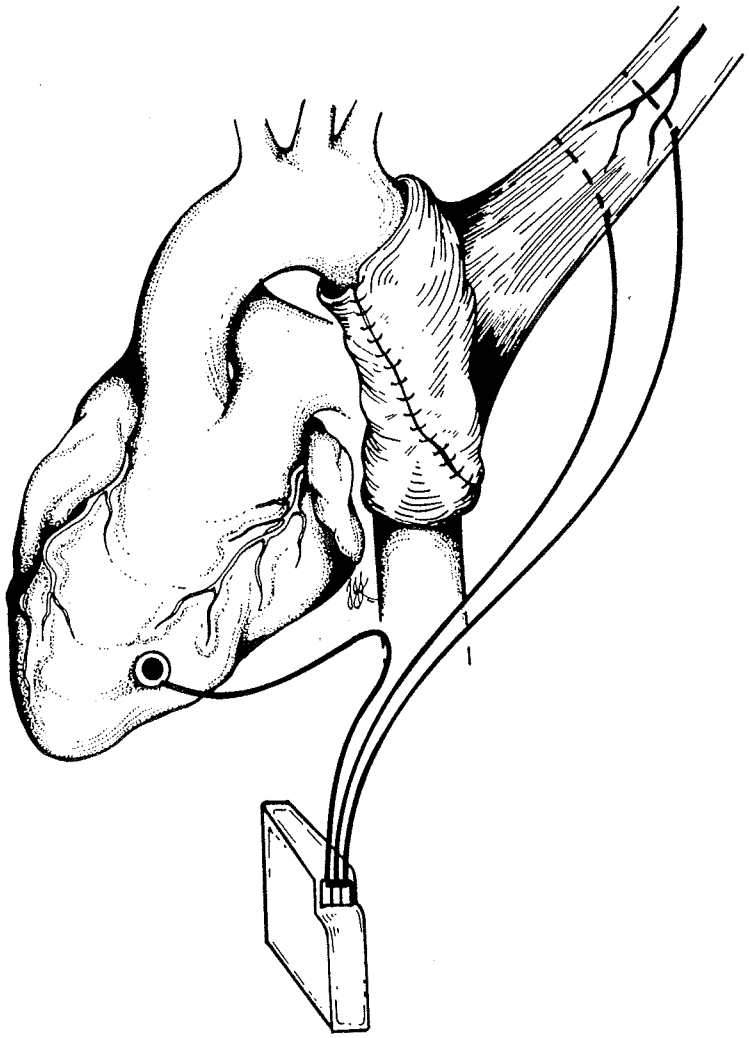


Figure 3: Extra aortic counterpulsation [18]

(sheep) [11] and its therapeutic potential is currently being investigated in dogs with end stage heart failure [26].

Recently Carpentier's group have reported their experimental experience with aortomyoplasty [9]. This involves wrapping the muscle around the ascending aorta which may be enlarged with an autologous pericardial patch (Figure 4a). The latissimus dorsi used may be split longitudinally to cover the aorta on both sides of the brachiocephalic trunk (Figure 4b). The results reported to date with this model are for acute experiments.

Stimulation Regimes and Vascular Delay

The subject of electrical stimulation for cardiac assistance is currently an extensive area of research for both cardiomyoplasty and for skeletal muscle counterpulsation, to achieve the optimum stimulation regime. Some groups opt for a graded build up of stimulation pulses over a six week time course [8]. Others adopt a stimulation protocol providing haemodynamic effect after only forty eight hours [18].

The choice of stimulation lead remains open, whether to directly stimulate the nerve using a nerve cuff electrode [21] or to achieve neuromuscular stimulation by suturing the lead through the muscle at the neurovascular pedicle [9, 18]. This latter technique may be technically easier, but may also be less efficient at delivering the burst of stimulation.

The concept of vascular delay (i.e the time between operation and the onset of stimulation) in the counterpulsation mode is of importance for the skeletal muscle ventricles for adhesions to form between the layers and the lining. It appears to be less mandatory in the extraaortic wrap application where stimulation may be initiated after forty eight hours [18]. The blood flow recovery, following mobilisation and division of the collateral is being investigated in both cardiomyoplasty and skeletal muscle counterpulsation groups. Prompt circulatory support is

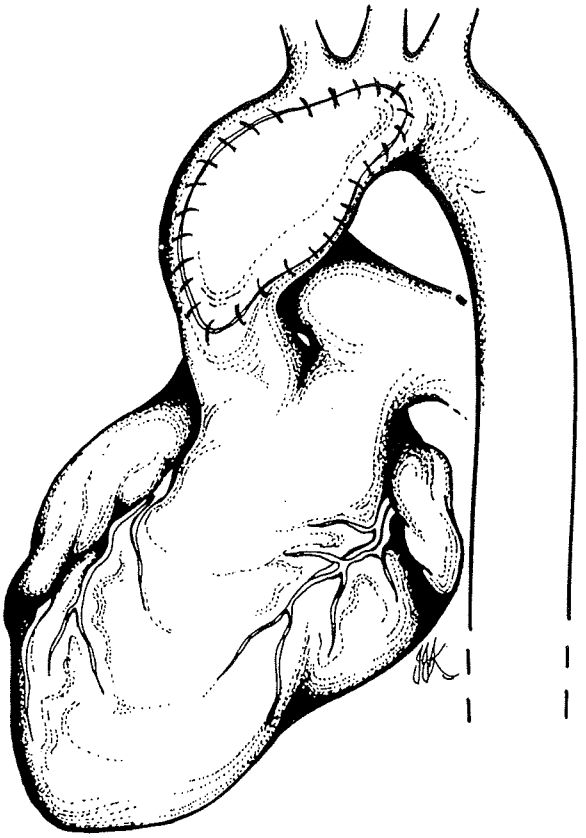


Figure 4a: Enlargement of aorta with pericardial patch [9]

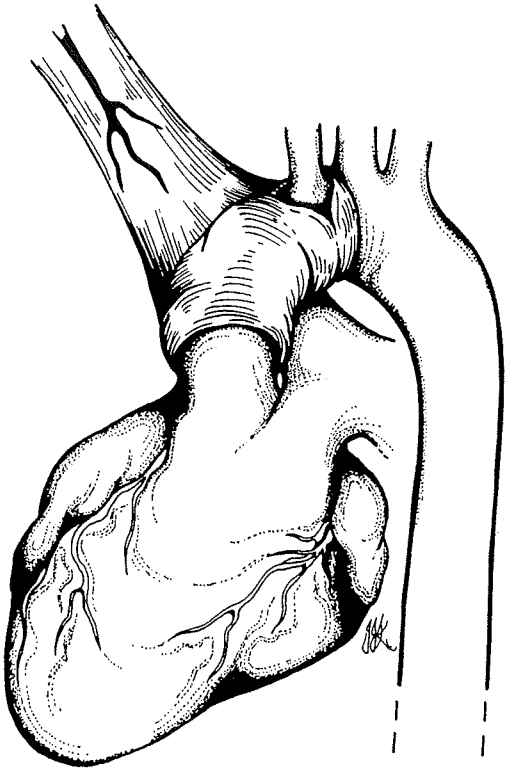


Figure 4b: Aortomyoplasty of ascending aorta [9]

desirable for the patients with severe chronic heart failure, but muscle ischaemia and damage must be avoided as this would prevent long term cardiac assistance being achieved.

Assessment of Skeletal Muscle Counterpulsation

Assessment of the performance of skeletal muscle counterpulsation devices has included a broad range of physiological and biochemical approaches, some specific to counterpulsation and others used for cardiomyoplasty as well.

1) *Endocardial viability ratios (EVR):*

Calculation of the EVR (the ratio of the diastolic time pressure index and the time tension index) [6] during assisted and non assisted cycles allows an estimate of the increase in the blood flow to the myocardium. For the dualchamber counterpulsator in short term experiments the average increase was 55% [14]. For extraaortic counterpulsation we have reported increases of between 27 and 42%, for up to 1 month of stimulation [18]. Increases in the order of 30% were noted for the aortomyoplasty acute experiments without aortic enlargement. When the aorta was enlarged the increase was 35.8% for the normal animal model and 42.2 % for those with induced cardiac failure [9], emphasising that maximum haemodynamic benefit is only likely to be observed in heart failure.

2) *Echocardiography:*

Echocardiography of the skeletal muscle counterpulsation device can be used to monitor the contractility of the mobilised muscle working as either a neoventricle or as an extraaortic counterpulsation wrap (Figure 5). Rates of contraction and relaxation may be calculated from M mode images together with the percentage occlusion of the aorta/skeletal muscle ventricle. This allows assessment of the efficiency of the system itself and also monitors the physiological characteristics of the muscle as it is transformed from a fast fatiguable muscle towards a slow fatigue resistant muscle with altered power characteristics.

3) *Mock Circulation Models:*

We have developed a mock circulation model [4] to allow assessment of the haemodynamic benefit associated with extraaortic counterpulsation in comparison to that produced by intraaortic counterpulsation. The model con-

sists of two fluid filled compliance chambers (representing the elastic component of the ascending aorta, aortic arch and the major vessels arising from it, and the second chamber representing the elastic component of the remainder of the systemic vasculature) connected together by a piece of rubber tubing representing the proximal descending thoracic aorta (Figure 6).

Table 1 illustrates the haemodynamic performance of the skeletal muscle wrap at two different lengths, when wrapped around 5 cm or 8 cm of mock aorta. In this particular experiment, the muscle has undergone two weeks of conditioning at our standard regimen (3V, 240 msec pulse width, 240 msec burst width, 35 Hz and 1:4 mode). The results confirm the fact that within the confines of the mock circulation model, the skeletal muscle wrap is capable of conferring definite haemodynamic benefit, even in the case of the 5 cm wrap. Skeletal muscle contraction was associated with near complete occlusion of the lumen.

Mock circulation models have been used by other groups to assess the potential power of skeletal muscle ventricles and investigate a variety of haemodynamic parameters (for a review see 20), including performance of the ventricles at physiological preloads and altered afterloads. The effect of stretch and burst frequency on muscle performance has also been addressed. This mock circulation approach is implantable and therefore capable of assessing skeletal muscle ventricle performance over a defined time course.

4) *Afterload Reduction:*

The mechanism of afterload reduction in the intraaortic balloon pump is well documented [2], but the potential for skeletal muscle counterpulsation devices for ventricular unloading is less clear. Lee et al [13] studied left ventricular functional mechanics in terms of stress and axis dimensions in a normal canine model where a skeletal muscle pump had been constructed using latissimus dorsi wrapped around a polyethylene bladder connected to aorta. They demonstrated a 29% reduction in mean systolic left ventricular wall stress. It should be noted though that the experiments were acute using muscle which was untrained and therefore predominantly fast twitch muscle with more rapid rates of contraction and relaxation than trained muscle. Rates of relaxation of the muscle as well as elastic recoil [3] of the occluded aorta may both contribute to the degree of afterload reduction.

5) *Biochemistry:*

This remains an integral component of any physiological assessment of skeletal muscle cardiac assistance, either for cardiomyoplasty or counterpulsation. Optimal muscle transformation to a particular fibre type composition has not yet been defined, although in the last five years there has been a change in attitude towards predominantly mixed fibre type populations and not the pure slow fibre type previously considered optimal. A broad spectrum of techniques (including molecular biology, enzymology, electrophoresis, histology, electron microscopy, magnetic resonance spectroscopy, eg [10, 11]), are currently used to ascertain the degree of transformation both in terms of protein isoforms and also for the metabolic profile. Non invasive approaches to biochemical analysis of skeletal muscle remain limited, and therefore studying correlations between mechanical function and molecular architecture in the experimental models remains crucial to our future understanding of the clinical situation.

Discussion

The precise application and indications for using skeletal muscle in humans remains highly controversial, although the exclusive use of one technique would appear restrictive. Each approach has its advantages in particular circumstances. Recently there has been an increase in the number of publications concerning research into skeletal muscle counterpulsation, particularly for extraaortic wraps.

The use of skeletal muscle for counterpulsation maximises muscle perfusion; the muscle is relaxed during the systolic phase of systemic perfusion and this may be important in diminishing fatigue. A further advantage is that the muscle is at maximum end systolic stretch prior to its contraction, which may optimise the contractility or developed tension of the muscle. The greater pressure that may be generated by multiple layers of muscle around a narrower tube, in comparison to a single or even incomplete muscle layer around the dilated heart may be an important advantage.

Skeletal muscle used for counterpulsation remains at the research stage, although long term results of the experimental approaches are now being published. These will allow a critical assessment of the role that skeletal muscle counterpulsation might have in the clinical setting. Cardiomyoplasty and skeletal muscle counterpulsation although subtly different in approach still both depend on the concept of muscle plasticity and the basic molecular architecture of the skeletal muscle used. This includes muscle specific protein isoforms, metabolic components and Ca^{2+} handling apparatus, all of which will ultimately be affected

Table 1. Investigation of the haemodynamic benefit of skeletal muscle counterpulsation. Period of conditioning: 2 weeks at standard regime.

	5 cm wrap	8 cm wrap
Volume displacement (cm^3)	14.1 (± 1.8)	18.36 (± 0.5)
Pressure augmentation (mm Hg)	14.9 (± 2.1)	17.54 (± 0.8)
Work done (J)	0.18 (± 0.07)	0.24 (± 0.07)
Power generated (W)	0.80 (± 0.1)	0.92 (± 0.04)

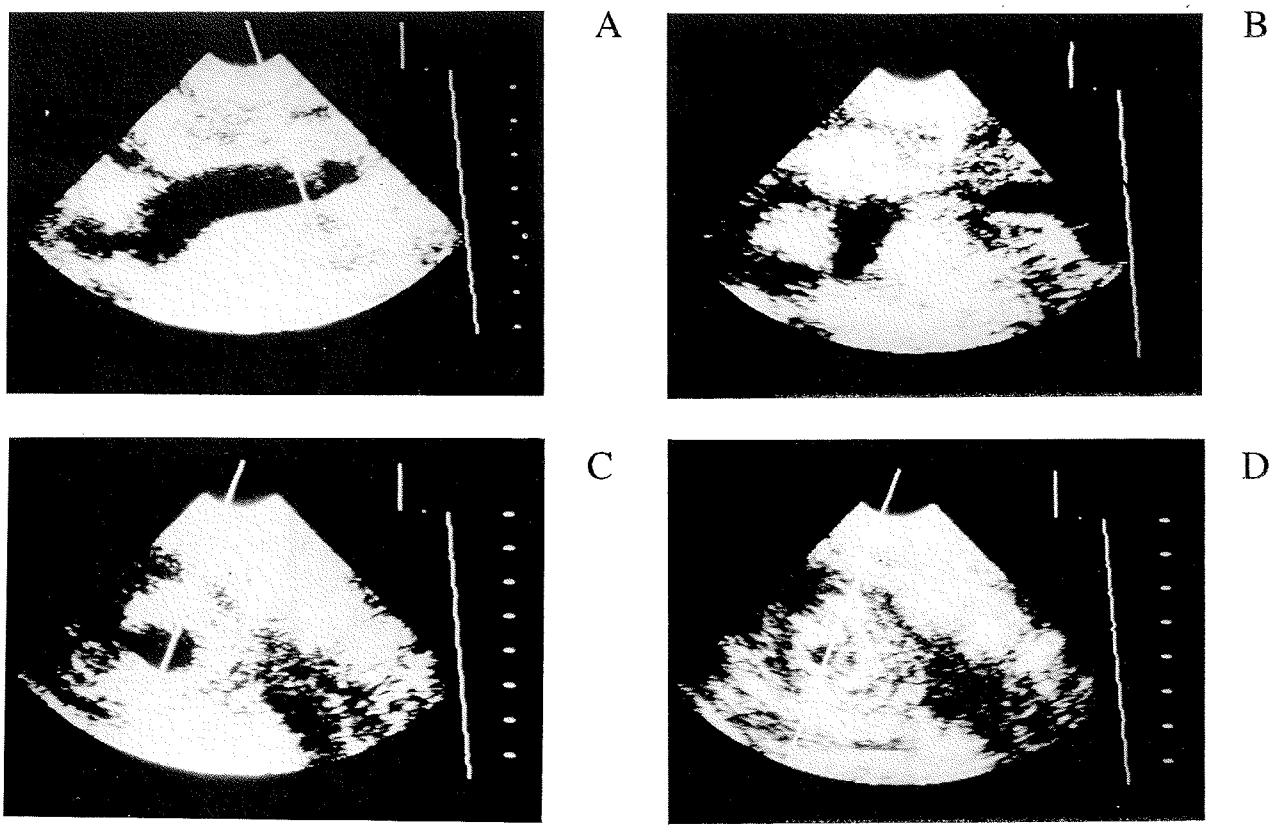
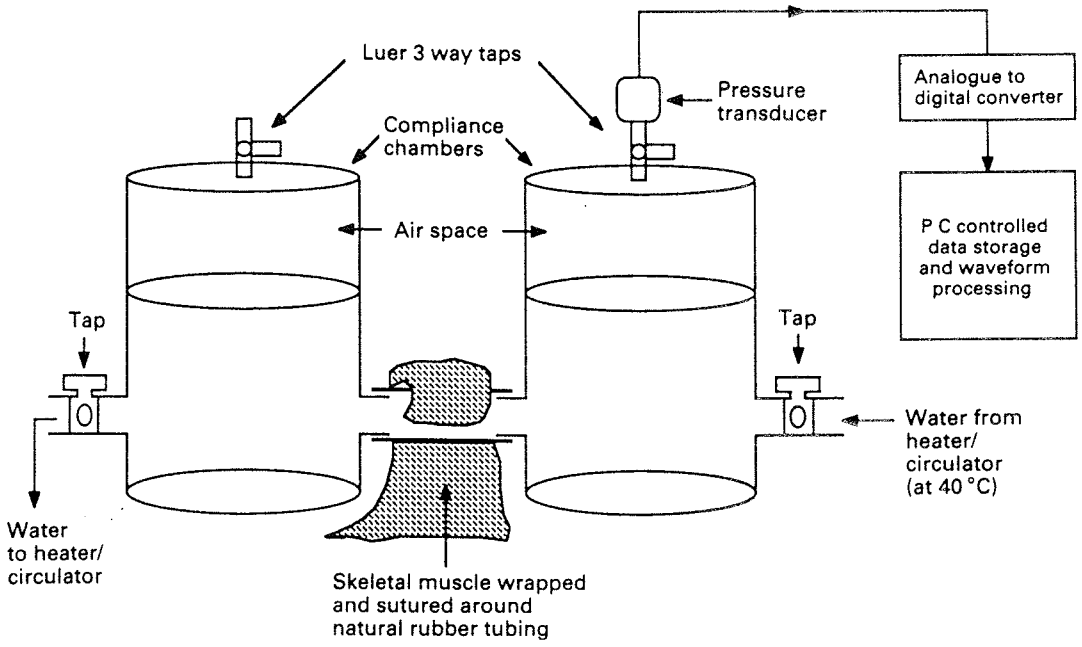


Figure 5: Longitudinal (a and b) and transverse (c and d) sections of aorta using ultrasound showing contraction of wrap and occlusion of lumen.



Apparatus for the in vivo assessment of the indices of muscle wrap performance.

Figure 6: Apparatus for the in vivo assessment of the indices of muscle wrap performance [4] (reproduced with permission).

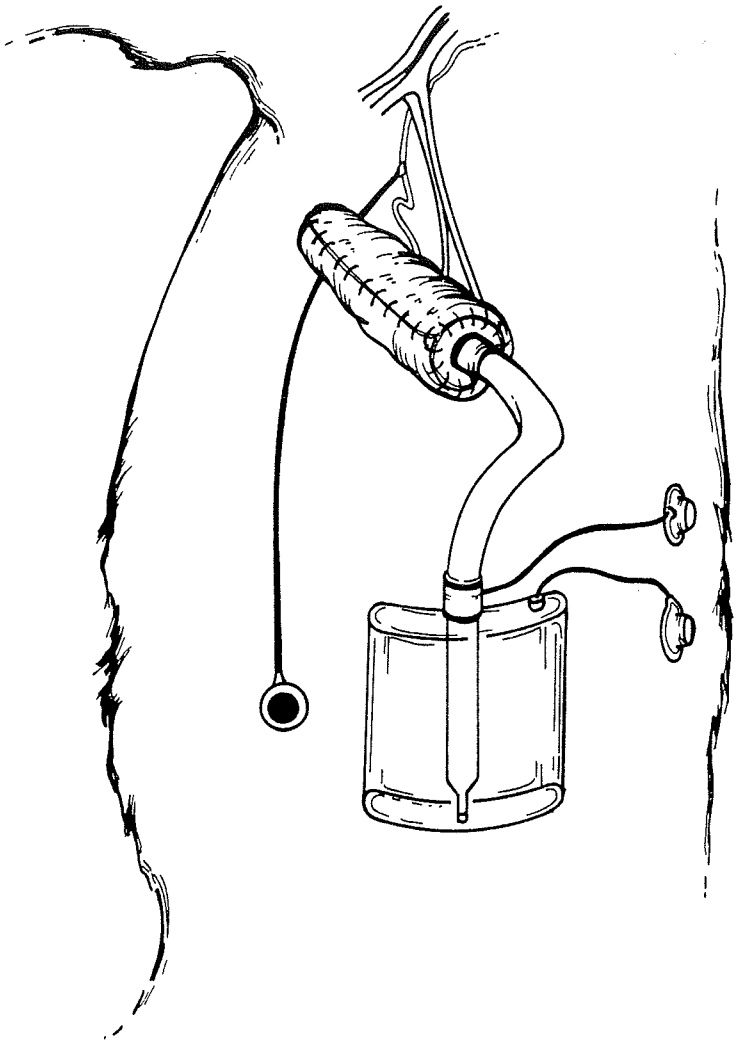


Figure 7: Implantable mock circulation apparatus [20].

by the stimulation regime adopted. Consequently research currently in progress for stimulator design (with the incorporation of feedback control loops), lead design (direct nerve or neuromuscular) and the biochemistry of muscle transformation has implications common to both approaches.

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