

Linear Muscle Power for Cardiac Support: a Progress Report

Dennis R. Trumble and James A. Magovern

Cardiothoracic Surgery Research, Allegheny-Singer Research Institute, Department of Surgery, Allegheny General Hospital, Pittsburgh, Pennsylvania

Abstract

The use of electrically-stimulated skeletal muscle as an endogenous power source is an attractive approach to long-term cardiac assistance. The principle advantage of this technique over current methods is that it obviates the need for extracorporeal power sources and provides a reliable, low-cost, self-sustaining source of energy without immune compromise or loss of patient autonomy. This article briefly examines the various approaches to harnessing muscle power, details the rationale for the use of muscle in a linear configuration, and reviews our progress to date regarding development of a ventricular assist device powered by in situ skeletal muscle.

Key words: skeletal muscle, cardiac assist, electrical stimulation, conditioning, linear contraction, prosthesis, latissimus dorsi.

Basic Appl. Myol. 9 (4): 175-186, 1999

Cardiovascular disease is the leading killer in the United States, claiming more than 954,000 lives annually. Despite intense efforts to prevent and treat these disorders, the incidence and prevalence of congestive heart failure (CHF) continues to rise and is now estimated to afflict up to three million people in this country alone [8, 12]. Current pharmacological therapies result in symptomatic improvement in many patients but do not appreciably alter the natural progression of this disease. Heart transplantation is a very effective treatment but is limited by a small donor pool and by the serious side-effects of immunosuppressive drugs. Consequently, there is an urgent need to develop new interventions to treat CHF.

A safe and effective permanent ventricular assist device (VAD) would be a powerful tool for physicians, but the complexities of transcutaneous power delivery and problems associated with percutaneous drive lines have severely limited this approach. Most mechanical prostheses currently employ electric or pneumatic power delivered via tubes, wires, or electromagnetic transformers. These schemes work well in acute settings, but are inappropriate for chronic use due to problems with infection, concerns over long-term reliability, expense, and quality-of-life issues. Clearly, an alternative means of energy production and transmission is needed to avoid the problems inherent to extracorporeal power schemes.

The use of stimulated skeletal muscle as a natural, internal energy source offers an attractive alternative to drive systems currently in use. Muscle-powered systems have the potential to greatly simplify motor prostheses by eliminating electro-mechanical components and obviating the need to transmit power across the skin. This strategy is especially appealing when one considers the quality-of-life benefits to be gained from a self-contained implant free from extracorporeal components and daily maintenance. Moreover, the relative simplicity of such systems would serve to improve mechanical reliability and drastically lower the cost of long-term cardiac support - increasing its viability from a societal perspective [45].

In this article, we briefly summarize the rationale supporting the use of in situ muscle as an endogenous power source and detail our efforts to develop a practical means to harness this energy to aid the failing heart.

Early use of skeletal muscle for cardiac assistance

The earliest application of skeletal muscle for cardiac assist purposes dates back to 1935 when Beck and Tichy first employed static muscle grafts to revascularize the myocardium [2]. These early studies promptly led to the use of both pedicled and free muscle grafts for ventricular repair. The contractile nature of these muscle flaps was first utilized in 1958 when Kantrowitz stimulated pedicled diaphragm muscle to assist cardiac function in dogs [18]. Since then, many investigators have shown that untrained skeletal muscle can provide cir-

Linear muscle power for cardiac support

culatory support for brief periods [19, 30, 43], but early attempts to provide long-term cardiac assistance invariably failed due to the onset of muscle fatigue.

Conditioning skeletal muscle for fatigue resistance

Despite early advances, the problem of muscle fatigue hindered further progress toward muscle-powered cardiac support until 1969 when Salmons and Vrbova demonstrated that changes in impulse activity can influence the physiologic properties of skeletal muscle [36]. This prompted researchers to explore the possibility of “conditioning” skeletal muscle via chronic electrical stimulation. The objective was to transform muscle to a fatigue-resistant state so that it would function much like the myocardium. Cardiac and skeletal muscle both contain contractile proteins which transform chemical energy into mechanical work, but skeletal muscles comprise several types of muscle cells, each with a unique set of physiologic and metabolic characteristics. These contractile fibers may be either glycolytic (fatigue-susceptible) or oxidative (fatigue-resistant). Slow-twitch muscle is generally oxidative, while more powerful fast-twitch muscle can be either glycolytic or oxidative. In order to utilize skeletal muscle for long-term circulatory assist, a conditioning scheme is needed to uniformly convert these fibers to an oxidative metabolic state.

The feasibility of conditioning skeletal muscle via chronic electrical stimulation was first demonstrated by Salmons and Soter in 1976 [35]. Early studies revealed that stimuli delivered at a constant rate of 2-10 pulses/sec were effective in producing oxidative muscle fibers with excellent endurance characteristics [6, 23, 35]. However, practical application of this stimulation pattern was limited since constant, low-frequency pulses cannot fuse twitch responses to produce prolonged, forceful contractions. Several groups addressed this concern by studying the effects of repeated “burst” stimuli on muscle phenotype expression. These studies confirmed that long-term stimulation via discrete pulse trains (30-50 Hz) can be used to elicit useful, rhythmic contractions from fatigue-resistant muscle fibers [3, 10, 41]. Work to determine how best to preserve the strength and speed of electrically conditioned skeletal muscle is ongoing [4, 7, 13].

Limitations of muscle wrap and oblique compression techniques

Refinements in muscle training and burst stimulation methods have spurred development of numerous techniques designed to utilize the transposition of conditioned contractile tissue for circulatory support. The most popular methods employed to date include: wrapping the heart for direct mechanical assistance (cardiomyoplasty); wrapping the aorta for counterpulsation (aortomyoplasty); shaping the muscle into a neoventricle to pump blood (skeletal muscle ventricle); and posi-

tioning a compressive device beneath the muscle. Low power production however, has proven to be a major limitation common to all these assist schemes [34].

The primary cause of this poor performance is most likely the mechanical inefficiencies that result when muscle is wrapped to compress the heart or some fluid-filled conduit [45, 48]. Skeletal muscles comprise individual myofibers arranged in parallel to produce shortening in a single direction. Muscles wrapped in this manner therefore tend to pull and twist the enveloped vessel rather than provide the compression forces needed to pump blood. Likewise, devices placed beneath the muscle utilize only a small portion of the available contractile energy because their motion is nearly perpendicular to the muscle's primary force vector.

Another important factor which limits the effectiveness of these heterotopic methods is the functional loss induced via muscle mobilization. Wrap-around techniques require isolation of the muscle from its surrounding structures, sacrificing collateral blood supply and depriving the muscle of its optimal orientation and preload. Surgical isolation of skeletal muscle has been shown to produce an abrupt 37% decrease in contractile power due to trauma and physical separation from surrounding synergistic musculature [42]. In the long term, reduced blood flow caused by the separation of collateral blood vessels further compromises function and often leads to chronic ischemia and muscular atrophy [52].

In light of these limitations, it is apparent that current wrap-around methods for muscle-powered cardiac assistance are sub-optimal and that alternative schemes for harnessing the contractile energy of skeletal muscle should be explored.

Advantages of using in situ muscle in a linear configuration

Given the linear, tensile nature of muscular function, the most effective way to collect contractile energy is to place a compressive device at one end of an otherwise undisturbed skeletal muscle. This approach, first proposed by Guizzi and Ugolini in 1979 [14], allows the muscle to operate at maximum efficiency by preserving biomechanical mechanisms perfected through evolutionary adaptation. This scheme also serves to preserve the primary and collateral blood vessels needed to fuel the muscle and remove metabolic waste products. This is especially important in that conditioned muscles depend on oxidative metabolic processes to prevent fatigue during extended periods of activity. This hypothesis has recently been tested by Badhwar et al. [1], who studied the function of latissimus dorsi (LD) muscle in three orientations: sub-dorsi (compressive); circular (wrap); and linear-pull. In this study, linear actuation produced a 3-fold improvement in work output over

Linear muscle power for cardiac support

wrap-type, and yielded a 5-fold increase over the compressive arrangement.

Another experiment, completed by Geddes and associates at Purdue University [11], used isolated canine muscles (contracting linearly) to compress a valved pouch in a hydraulic model of the circulation (10-40 contractions/min). Dramatic increases in muscle blood flow was observed during periods of work, and fatigue was not a factor despite the fact that unconditioned muscles were used. All three muscle groups studied (LD, gastrocnemius, and triceps), pumped over 1.5 L/min against a pressure load of 100 mmHg with an energy conversion efficiency approaching that of cardiac muscle (roughly 10%). Based on these results, Geddes concluded that an energy conversion scheme should be sought in which linear shortening of skeletal muscle could be used to assist the circulation.

Studies that have employed skeletal muscle in a non-isometric, linear configuration have generally isolated the muscle from its collateral circulation, leaving only the origin with its neurovascular supply intact. This practice has clearly compromised the integrity of these muscles and diminished their performance. One notable exception may be found in a 1990 report by Salmons and Jarvis [33] on the force-velocity relationships of normal and trained rabbit tibialis anterior muscles. These tests, performed on fully-vascularized muscles, led the authors to conclude that "sustained work at a rate of 4 W/kg is not an unrealistic proposition for a suitably conditioned muscle." Another group examined the power output of in situ canine gastrocnemius-plantaris muscle contracting linearly against a "pneumatic muscle lever" [42]. Initial power levels of 19.0 mW/gram were reported for untrained muscle in these acute experiments. Moreover, our own studies of linear in situ muscle power using normal and conditioned canine LD have yielded power levels of 5.76 and 2.06 mW/gram respectively [46, 48]. These data support the hypothesis that certain skeletal muscles can produce mechanical power at levels sufficient for cardiac assistance and thereby validate the development of implants designed to harness this energy.

Linear muscle-powered pumps - work by others

Previous attempts to harvest in situ skeletal muscle for cardiac assist have employed a variety of mechanisms. The concept of powering a pump with linearly-contracting muscle appeared in the literature as early as 1964, when Kusserow and Clapp employed a quadriceps femoris muscle to drive a spring-loaded diaphragm pump [20]. Since that time, a number of investigators have addressed this topic, yet no attempts to develop a working device were published until 1992 when Sasaki reported use of a flexible rod, sheath, crank, and cam system to transmit muscle power to a pusher-plate pump [37]. This scheme was tested in dogs using an untrained

LD muscle and a mock circulatory system. At 60 beats per minute, this device maintained 0.8-2.0 L/min for 200 minutes against an afterload of 75 mmHg. Output power was 2.5 mW/gram of muscle, and system efficiency approached 50%. Later that same year, Farrar and Hill described a spring-loaded piston-type actuator designed to harness in situ LD power to actuate a hydraulic blood pump [5]. Because no attempt was made to minimize energy losses or address durability issues, the efficiency of their initial prototype was less than 25%. A refined version of this device however, has reportedly transmitted over 1 J per contraction from goat LD after two weeks implantation - enough energy to provide significant circulatory support given an effective means to transmit this hydraulic power to the bloodstream [32]. Other systems include a "linear-push actuator" [44] comprising bellows supported by two interlocking cylinders, as well as a cable-driven scheme which includes a roller screw-nut assembly and translation unit designed for actuation of pusher-plate pumps [38].

These studies have added much to the conceptual development of in situ muscle-powered devices and have served to demonstrate the viability of this approach from a theoretical perspective. Little emphasis however, has been placed on developing mechanisms that require little maintenance and preserve function over the long term. As a result, efforts to date have failed to produce a tenable means by which contractile energy may be collected and transmitted in vivo to perform work within the body.

In Situ Muscle Power for Cardiac Assist: Progress at Allegheny

Work in the area of muscle-powered circulatory support began at Allegheny in the mid 1980's with the advent of dynamic cardiomyoplasty as a novel means to treat patients suffering from congestive heart failure [24]. However, equivocal results from nearly a decade of clinical and experimental trials [9, 21, 22, 25-29] led us to seek a more effective means of harnessing muscle power to aid the failing heart. The following pages detail our efforts to date, from basic studies of muscle energetics to device design and testing.

Measuring Contractile Energy Available for Cardiac Assist

A novel apparatus for muscle power measurement

In order to measure in situ muscle performance under realistic cardiac assist conditions, a custom hydrodynamic skeletal muscle ergometer was designed and constructed [47]. This device quantifies the amount of external work extracted from stimulated muscle by efficiently transferring contractile energy to a mock circulatory loop. The ergometer is attached to the muscle via

Linear muscle power for cardiac support

a thin cable which traverses a stationary pulley and is fixed to one end of a lever. Attached to the opposite end is a piston mounted on a rolling diaphragm. Beneath the piston lies a fluid-filled chamber with a valve stationed at each end to provide uni-directional flow. As the muscle shortens along its natural line of contraction, it pulls up on the lever and forces the piston down an equal distance. Pressures are monitored within the pump chamber and in the systemic and venous compliance chambers of the mock loop. Fluid flow is measured using a sensor positioned at the outlet port of the pump chamber. Bench tests show no discernible energy losses within this system, due primarily to the frictionless nature of the rolling diaphragm that supports the piston head. As a result, this system allows the energy of muscular contractions to be measured directly in the form of hydraulic pressures and flows.

Ergometric studies of untrained (normal) skeletal muscle

Three male mongrel dogs were used to study the contractile energetics of six untrained LD muscles using the hydraulic ergometry system described above [48]. The LD was chosen because of its large size, surgical accessibility, and proximity to the thoracic cavity. A left flank incision was made to expose the LD muscle while preserving its vasculature. Sutures were placed 10 cm apart along the oblique segment to mark normal resting length. A bipolar pacing lead was placed over the thoracodorsal nerve for subsequent activation via an Itre pulse-train stimulator. The LD was then freed from its humeral insertion and connected to the ergometer so that complete filling of the piston pump stretched the muscle to its original resting length. The resistance and compliances of the mock circulation were adjusted to allow the LD to complete one pump cycle with each contraction. Contractions were activated once each second via burst stimuli comprising 11 pulses delivered at 43 Hz. Upon completion of the left-side study, the incision was closed and the same experiment repeated on the contralateral LD.

Under these conditions, the six canine LD delivered an average of 1.14 watts of continuous power, which translates to 5.76 mW per gram of muscle tissue. On average, peak power levels reached 10.75 watts, while power during shortening exceeded 5.5 watts. This level of work production far exceeds that reported in studies of isolated skeletal muscle and can be attributed in large part to improved perfusion that results when the LD is left in situ and not mobilized from the chest wall. Moreover, the fact that these muscles were roughly one third the size of human LD suggests that even higher work outputs can be expected clinically (although the deleterious effects of heart failure on muscle function must be taken into account).

Ergometric studies of trained skeletal muscle

The experiment described above was repeated using electrically conditioned muscle in order to assess physiologic changes induced by training and to quantify the capacity of these muscle to perform cardiac-like work [46]. Six male mongrel dogs were used to study the morphology and function of stimulated and normal muscles. One LD from each dog (three left, three right) was conditioned using an Itre pulse-train stimulator programmed to deliver burst stimuli (7 pulses/burst; 210 msec pulse width; 40 msec delay between pulses) at an initial rate of six per minute. Pulse amplitude was maintained at the lowest level needed to induce forceful contractions. The stimulation rate was gradually increased to 60 contractions/min over the course of eight weeks to complete the training process. Full muscle recruitment was later confirmed via histology.

Upon completion of the training period, LD muscles were prepared for in situ testing using the same methodology used in prior ergometry studies (see above). Force data were collected as a function of stimulation frequency over a range of fixed muscle lengths. Burst stimuli lasting 250 msec were delivered once each second in all force experiments. Following these tests, the LD tendon was attached to the hydraulic ergometer which was positioned so that maximum pump filling stretched the muscle to its original in vivo length. Contractions were induced at a rate of 60/min with burst stimuli averaging 12 pulses delivered at 46 Hz. Hydraulic pressures and flows were continuously monitored for four hours to measure contractile and fatigue properties. Upon completion of the left-side study, the same experiment was performed on the contralateral LD. Tissue samples were subsequently collected from both LD muscles to determine myosin heavy chain (MyHC) fiber type distribution and metabolic/glycolytic enzyme activities.

The training process reduced muscle mass and cross-sectional area by 16 and 17% respectively. Immunohistochemical analysis of myofibrillar ATPase activity revealed the existence of three fiber types (1, 2A, and mixed). On average, chronic burst stimulation produced a 142% increase in the number of type 1 fibers, while the abundance of type 2A fibers dropped 82% relative to control. Biochemical assays of malate dehydrogenase did not demonstrate a significant difference between control and stimulated muscle. However, a significant increase in citrate synthase activity (indicative of O_2 metabolic capacity) was observed with training (28.4 ± 4.9 to 38.3 ± 7.4 $\mu\text{mol/g/min}$, $p < 0.01$). Glycolytic capacity was significantly reduced in trained LD as evidenced by a substantial decrease in lactate dehydrogenase levels from 433.6 ± 134 to 164.4 ± 45 $\mu\text{mol/g/min}$ ($p < 0.01$). Force generation was reduced 54% and contractile duration increased 13%. Fatigue resistance was

markedly enhanced and chronic stroke work increased from 0.19 to 0.72 mJ/g. The highest steady-state power output (2.06 mW/g) was obtained from one muscle fully converted to a slow (type 1) phenotype. These data suggest that single LD trained via conventional techniques can provide sufficient energy to provide substantial cardiac assistance.

Development of a Prototype Muscle Energy Converter (MEC)

Physical and functional characteristics

Based on results obtained from in situ muscle testing (described above), two prototype muscle energy converters (MECs) were built and tested in vitro (Figure 1). The purpose of these devices is to efficiently convert the power of in situ muscle contractions into a form which can be used to drive a wide variety of motor prostheses - cardiac assist devices in particular. The objective is to eliminate the need for external power supplies which contribute significantly to infection and device failure.

Work to date has yielded prototype devices that resemble simple hydraulic piston pumps [49, 50]. These prostheses are designed to be implanted along the axillary line, beneath the humeral insertion of the LD. The cylindrical housing is fixed to the ribcage with its outlet port stationed distally and its long axis placed parallel to the line of contraction. The muscle is attached to the top of the piston via its humeral tendon so that linear shortening pulls the piston into the cylinder. As the muscle shortens, hydraulic energy is transmitted from the MEC under conditions of high pressure and low flow. Short stroke lengths (1-2 cm) are employed to increase device durability, reduce trauma to surrounding tissues, and minimize the kinetic components of muscle-power transmission.

The central piston shaft rides within the cylindrical housing on a single low-friction bushing which provides radial stability and guides the piston shaft through the center of the pumping chamber. Two edge-welded metal bellows are used to seal the pump: the inner bellows provides a seal to sequester the energy transmission fluid while the outer bellows protects the bearing surfaces from biological debris. These bellows also provide a return force which extends the MEC during muscle relaxation to refill the pump and preload the muscle. Internal air vents are stationed around the bearing site to prevent damping caused by pressure swings within the bellows seals (each bellows acting as volume compensation for the other). MEC compression length is ultimately limited by either a passive magnetic bearing (MEC1) or the total collapse of the outer bellows (MEC2). Piston arm extension during periods of muscle relaxation is limited in both devices by the complete collapse of the inner bellows seal.

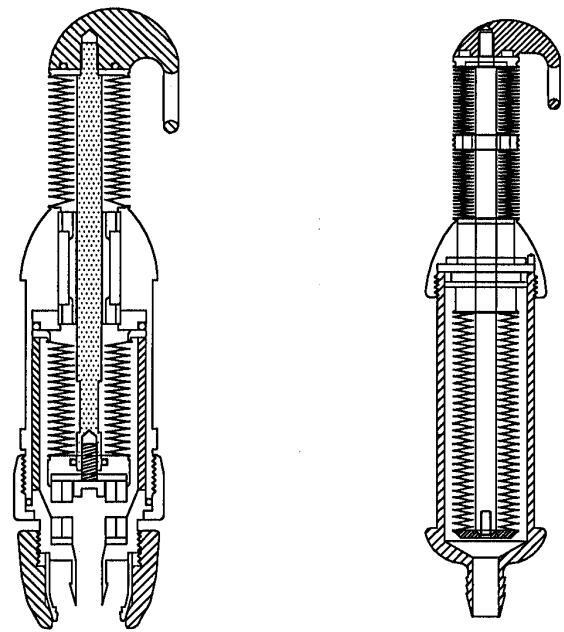


Figure 1. Two muscle energy converter prototype designs (MEC1, left; MEC2, right) drawn to scale. MEC1 features a magnetic thrust bearing (bottom) and thin titanium bellows for low-energy applications. MEC2 employs thicker stainless steel bellows capable of transmitting nearly 1 joule/stroke to meet higher energy demands. Devices are shown with tendon loop attachment schemes wherein the LD tendon is threaded through the piston head and sutured to itself - tendon clamp mechanisms (Fig. 2) are also being evaluated. Ribcage attachment hardware is not shown.

MEC function can be tailored to various applications via simple changes in bellows design. For the first prototype (MEC1), thin titanium bellows were chosen to create low preload forces and a stroke work capacity of 150 mJ. MEC1 stroke work capacity is ultimately limited by the deformation of the bellows diaphragms at high pressures ($> 20 \text{ N/cm}^2$), but offers the advantage that modest actuation forces (20-30 N) can be used to impart partial cardiac assist. The second-generation device (MEC2) features thicker stainless steel bellows designed to increase maximum pressure capacity by 750% and hence, significantly improve energy transmission to 0.93 J per 1.5 cm stroke. While more contractile work must be used to compress these stiffer bellows, this energy is recovered during LD relaxation as active pump filling and muscle preload work.

Muscle mechanics and MEC2 design

The MEC2 was designed to operate at contractile force and velocity levels which correspond to peak power generation in fully-conditioned human LD mus-

Linear muscle power for cardiac support

cle. Anatomical measurements taken from cardiomyoplasty patients at this institution ($n = 11$, 3 female) and cadaver studies performed elsewhere ($n = 10$, 5 female) suggest average LD lengths of 35-40 cm and mean cross-sectional areas of 19-20 cm² [31, 49]. Since maximum force generation in normal skeletal muscle is known to be 34 N/cm² [15] and shortening velocities typically peak at five times total muscle length per second [39], $F_{\max}$ and $V_{\max}$ for these LD can be calculated at 646 N and 175 cm/s respectively. Fully conditioned muscles however, typically demonstrate a 50% loss in force generating capacity and show a 5-fold reduction in shortening velocity [33, 46]. Moreover, maximum contractile power production is known to occur near 0.3 $F_{\max}$ and 0.3 $V_{\max}$ [16, 17]. It is therefore reasonable to postulate that power from trained LD will be greatest when the muscle is allowed to generate about 95 N force while shortening at a rate near 10 cm/s. Given a contraction time of 0.25 seconds (corresponding to typical cardiac systolic durations) and a sinusoidal shortening trajectory centered around 10 cm/s (mean = 6.37 cm/s), LD shortening would total 16 mm - near the maximum stroke length of the MEC2. Taking the combined spring rate (24 N/cm) and effective pressure area (0.6 cm²) of the bellows into account, the forces required to actuate the MEC2 against peak rated pressures (1034 kPa) range from 62 to 100 N. Hence, MEC2 actuation requirements are consistent with conditioned LD muscle operating near the peak of its power-velocity curve.

Biocompatibility issues

Tissue reaction to chronic MEC implantation will likely mimic pathobiological responses which are known to occur with other metallic implants (e.g., cardiac pacemakers). In most instances, wound healing and tissue repair begins shortly after device placement and comprises three distinct phases: inflammation, cell proliferation and tissue remodelling [40]. The inflammatory response occurs first and serves to limit bleeding and attract circulating macrophages and other leukocytes in order to remove damaged tissue, bacteria, and necrotic cells. The proliferative phase includes migration of fibroblasts, endothelial cells, and epithelial cells to the wound site and is often accompanied by angiogenesis, re-epithelialization, and alterations to the extracellular matrix. The remodelling phase completes the healing process and involves the formation of a fibrous capsule via deposition of collagen fibers.

A corrugated PTFE sheath will be placed over the outer bellows to prevent tissue infiltration during the early phases of wound healing. As with pacemaker implants, the entire device will, in a matter of weeks, become encapsulated by a layer of fibrous tissue that will act as a permanent barrier against biological infiltration. This supposition has recently been tested by Reichen-

bach et al. through short-term (6-week) implantation of a similar device in goats [32]. They report that "upon explant, a fibrous layer was encapsulating the implanted [energy] converter; however, the layer was not adherent to device surface[s] and did not appear to hinder device function." In addition, serous fluids secreted within this fibrous capsule should provide added protection against piston binding by acting as a natural lubricant.

Device dimensions

The original MEC device (MEC1) readily lends itself to implantation beneath the latissimus dorsi muscle due to its compact size and short stroke length. The titanium housing, including the outlet port, is 8.3 cm long with a maximum outside diameter of 3.0 cm. The inner and outer diameters of both bellows measure 0.59 cm and 1.57 cm respectively, yielding an effective pressure area of 0.92 cm². Stroke length is limited to 1.3 cm, corresponding to a peak stroke volume of about 1.2 mL. The maximum length of the MEC, including the outlet port and fully-extended piston, is 12.9 cm. The entire device weighs 142 grams and occupies a volume of 50 cm³.

The second-generation device (MEC2), designed for high-power applications, is even smaller. The stainless steel housing, including the outlet port, is 7.7 cm long with a maximum outside diameter of 2.3 cm. The inner and outer diameters of both bellows measure 0.48 cm and 1.27 cm respectively, yielding an effective pressure area of 0.60 cm². Stroke length is limited to 1.6 cm, corresponding to a peak stroke volume of about 0.96 mL. The maximum length of the MEC, including the outlet port and fully-extended piston, is 12.9 cm. The entire device weighs 91 grams and occupies a volume of 26 cm³.

Results from in vitro testing

A fully-functional MEC1 prototype was tested in vitro to determine energy conversion efficiency and characterize device function under various load conditions [49]. The experimental setup described below was designed to simulate the high-pressure pumping and low-pressure filling conditions anticipated in vivo.

Muscular compression was simulated on the bench using a rotary motor attached to a reciprocating metal rod. This rod, in turn, was fixed to the MEC1 muscle interface via a Teflon felt strip to simulate the pull of the LD muscle on the piston head. Device actuation rate and stroke length were set at 60 cycles/min and 1.05 cm respectively. Fluid expelled from the MEC1 (silicone oil) was channelled through a needle valve to regulate afterload pressure. Fluid pumped past this valve entered a graduated cylinder (for stroke volume measurement) and returned to the MEC1 via a reservoir connected to the outlet port through a check valve. A load cell was mounted between the drive rod and MEC1 to measure forces applied to the muscle interface. Piston motion

Linear muscle power for cardiac support

was monitored with an linear potentiometer attached to the MEC piston head. Pressures were measured with a transducer positioned proximal to the needle valve.

For mean stroke pressures between 8 and 20 N/cm², 20-33% of input (i.e., muscle) energy was converted to preload work while the remaining 67-80% appeared as hydraulic power. Transmission losses in this operating range were too small to be detected. Mean pressures above 25 N/cm² caused significant decreases in device efficiency and MEC1 stroke volumes. These losses were due to bellows deformation caused by increased pressure gradients across the thin bellows diaphragms. Hence, for this particular prototype, mean output pressures must be kept below 20 N/cm² to optimize energy transfer efficiency and preserve inner bellows durability.

These data confirm the efficacy of this device by demonstrating very high mechanical efficiencies (> 98%) and energy transmission losses that are vanishingly small. While the energy transfer capacity of this first prototype is limited (roughly 170 mJ/stroke), it is important to note that stiffer bellows can be readily substituted to achieve energy levels compatible with full circulatory support.

Implant testing of tissue attachment sites

In order to assess device fit and test preliminary tissue attachment schemes, a dummy MEC2 device was implanted in a 40 Kg mongrel dog. Tissue anchoring hardware was machined from titanium and included a toothed tendon clamp attached to the MEC piston head (Figure 2) and a perforated titanium plate attached to the main housing for rib cage fixation (Figure 3). Piston motion was restricted in order to induce isometric loading conditions and hence maximize stresses applied to the attachment sites.

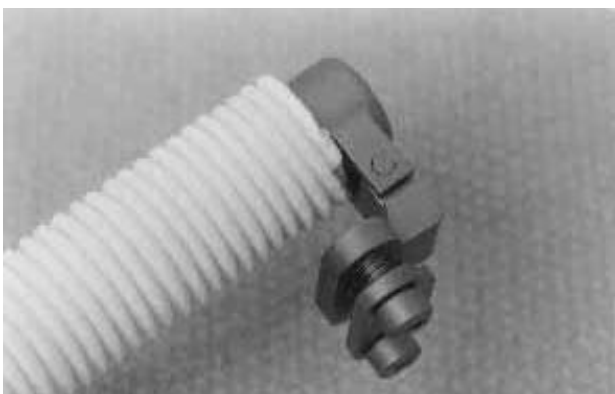


Figure 2. Tendon clamp mechanism designed to secure the LD humeral insertion to the MEC2 piston head. Four raised “teeth” on one plate are matched with depressions machined on the opposite surface to improve tissue adhesion. The tendon may either be placed directly between the plates or reinforced with surgical fabric (e.g., Teflon felt) prior to clamping.

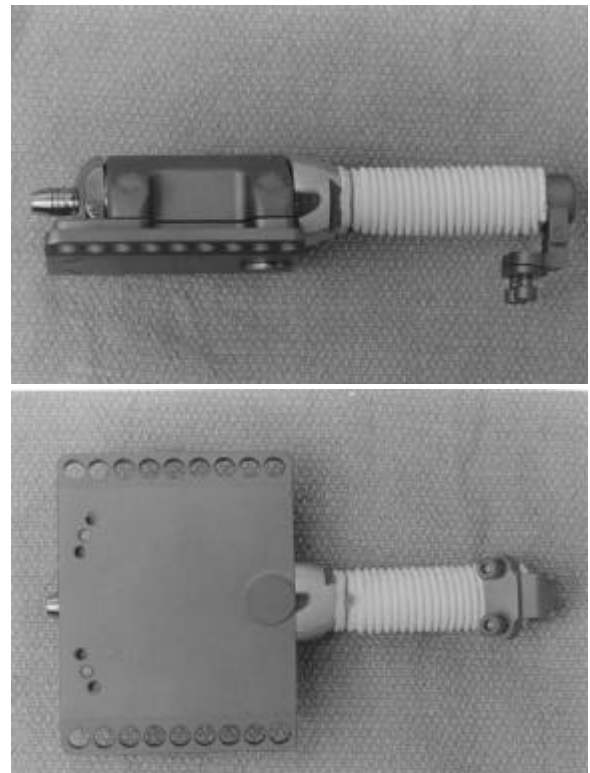


Figure 3. Tissue interface scheme for muscle and rib-cage attachment. The humeral insertion of the LD muscle is transected and inserted into a toothed clamp to form a stable connection. A titanium plate is used in conjunction with four bone screws to anchor the entire device to the ribs (flat surface facing out). A swivel mechanism allows MEC position to be adjusted relative to the main anchor plate (to fine-tune muscle alignment). Attachments designed and manufactured in cooperation with Encore Orthopedics, Inc. (Austin, TX).

Under general anesthesia, a right flank incision was made to expose the LD muscle while carefully preserving its vasculature. With the forelimb relaxed, markers were placed 15 cm apart near the middle of the muscle (along its line of contraction) to establish in situ resting length. A bipolar pacing lead was placed around the thoracodorsal nerve for subsequent activation via an Itrtel pulse-train stimulator. The LD was then freed from its humeral insertion to expose the implant site. Sections of the first three ribs were resected and the MEC placed plate-side up with its long axis parallel to the line of LD contraction. The anchor plate was secured to ribs 2 and 3 using four bone screws (two on each side). A short section of rib 1 was removed to prevent contact with the MEC piston. The LD tendon was then inserted into the piston head clamp and the plates screwed together. LD resting length was maintained following device attach-

Linear muscle power for cardiac support

ment (14.8 mm marker separation) and anatomic fit was good.

All tendon and rib cage fixation points tolerated repeated LD contractions generating > 100 N force. Long-term evaluation of fixation stability was hampered however when the thoracodorsal nerve was inadvertently damaged, but the study was continued for 35 days to assess chronic tissue reaction. Wound healing was complete by day 25 and the dog remained ambulatory throughout the implant period. Upon explant, the device was found to be firmly fixed to the ribs due, in large part, to tissue ingrowth (despite the loosening of three bone screws). The entire device was encapsulated with a layer of fibrous tissue and the LD attachment site was secure.

Based on these findings, the ribs were determined to be too thin to reliably hold bone screws and that alternate methods should be explored. Plans to improve rib cage attachment include replacing screws with clamping bolts and/or substituting thick tantalum wire mesh for the main anchor plate (to maximize tissue ingrowth and adhesion). Device placement may also be adjusted so that the main housing lies in the plane of the ribcage (rather than just below). This is expected to obviate the need to resect any portion of the first rib.

Implantable Afterload Chamber Design and Testing

In order to assess MEC performance in vivo, an implantable afterload chamber (IAC) has been designed and fabricated [50]. The IAC comprises a thin metal cylinder machined to accept insertion of a fluid-filled balloon which communicates directly with the outlet port of the MEC via non-compliant pressure tubing (Figure 4). The IAC housing connects to a vascular access port which allows percutaneous measurement and adjustment of air pressure between the housing and latex balloon. A second subcutaneous access port is used to adjust balloon filling volumes and measure fluid pressures generated by MEC activation.

Fluid is pumped from the MEC only after LD contraction generates fluid pressures sufficient to overcome IAC resting pressure (P_1). Once fluid pressure exceeds

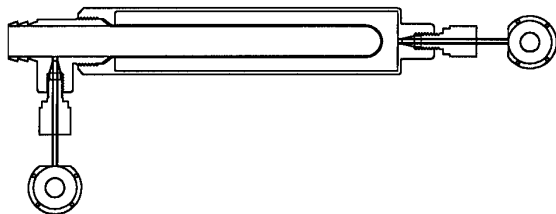


Figure 4. Implantable afterload chamber (IAC) used to monitor chronic MEC performance in conscious animals. Latex balloon insert is shown inside the main housing. Vascular access ports are connected via high-pressure PEEK tubing and sealed with medical grade UV-curable adhesive.

P_1 , bladder volume will increase in proportion to MEC fluid displacement. This will cause the volume of air within the IAC housing to decrease by an equal amount and thus increase housing pressure in accordance with Boyle's law ($V_1P_1 = V_2P_2$ at constant temperature). MEC stroke volume is calculated based on the change in IAC air pressure, which is directly proportional to the amount of fluid pumped into the bladder. Since P_1 and P_2 are measured directly, and V_1 (initial air volume) is known at the time of IAC fabrication, the change in volume can be readily calculated as: $V_1 - V_2 = V_1 (1 - (P_1/P_2))$. This technique eliminates the need for an implantable flow sensor and allow the MEC/IAC system to function long-term with minimal risk of infection.

Results from MEC2/IAC bench testing

A fully-functional MEC2/IAC system was evaluated on the bench to measure the accuracy of this monitoring system. IAC pressures were measured under numerous contraction profiles and loading conditions and used to calculate MEC2 performance parameters. The accuracy of this method was established by comparing calculations of MEC performance parameters (based on IAC pressures measurements alone) to direct measurement of MEC actuation forces and piston displacements.

LD actuation was simulated on the bench using an instrumented pull-bar which was operated manually. This bar was attached directly to the MEC2 muscle interface via a thin cable to simulate the pull of the muscle on the piston head. Actuation rate and stroke length were varied to cover a wide range of fluid ejection profiles. Fluid from the MEC2 was pumped through a 30 cm length of high-pressure PVC tubing (4.8 mm ID) into the inlet port of the IAC. A miniature load cell was mounted between the drive rod and MEC2 to measure forces applied to the muscle interface. Piston motion was monitored with a linear potentiometer attached to the MEC piston head. IAC pressures were measured through a subcutaneous access port via a miniature pressure sensor mounted on a Huber-point needle.

Air pressure within the IAC housing was seen to change in proportion to MEC2 piston displacement over a wide range of actuation speeds and stroke lengths. Piston displacement was calculated for stroke lengths ranging from 0.5 to 17.9 mm and was found to be in substantial agreement with measured values (less than 5% difference between calculated and measured values). Likewise, estimates of MEC2 actuation forces were found to closely approximate those forces measured directly at the LD tendon attachment site (calculated values exceeded measured force by an average of 5.4 ± 3.3 N). These data confirm that MEC actuation force and stroke length can be accurately calculated based solely on IAC pressure measurements, and thus validate this method of monitoring chronic MEC function in vivo.

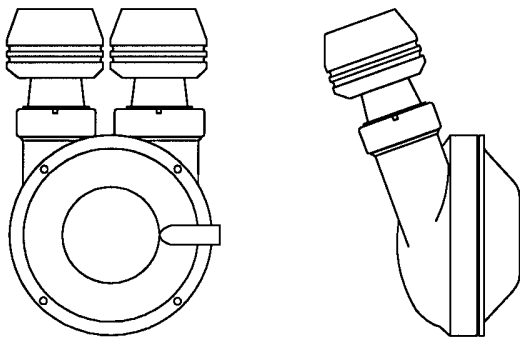
Hydraulic Ventricular Assist Device (HVAD) Design and Testing

Perhaps the most obvious way to harness MEC power for cardiac assist is to modify an existing blood pump for low-volume hydraulic actuation. The advantage of this approach is that it employs previously established blood pump technology and alters only the mechanism by which the blood sac is compressed. As a first step toward reducing this concept to practice, we have devised a means to power a commercial ventricular assist device (VAD) via low-volume hydraulics and have measured blood pump performance in a mock circulatory loop under simulated muscle actuation conditions [51].

Blood pump design modifications

In order to retrofit a pneumatic blood pump for MEC actuation, the pneumatic drive chamber must be replaced with a hydraulic actuation scheme. This may be

Sarns / 3M pneumatic VAD



Sarns / 3M VAD modified for hydraulic actuation

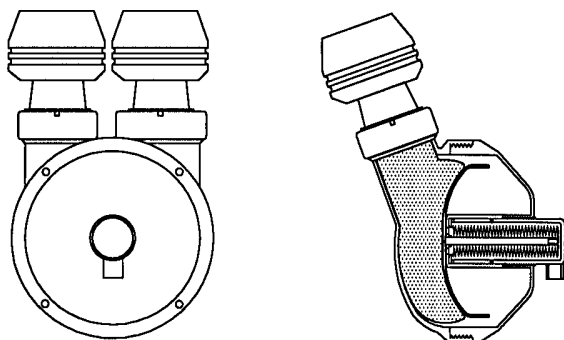


Figure 5. Pneumatic VAD modified for hydraulic actuation (compliance chamber not shown). HVAD actuation is accomplished by shuttling fluid directly from the MEC to the bellows/pusher-plate mechanism (bottom right). Blood sac compression occurs simultaneously with muscle shortening and can be adjusted to pump in synchrony with the heart or timed for counterpulsation.

accomplished by expanding the space between the blood sac and casing in order to insert a bellows/pusher-plate mechanism designed to compress the blood sac (Figure 5). As fluid from the MEC enters the actuation cylinder, it collapses the metal bellows and forces the pusher-plate against the polyurethane bladder, expelling blood through a valved cannula. Piston alignment is maintained via a central bushing and the axi-symmetric pressures applied by the blood sac. A low-pressure air line connects a compliance chamber to the pump housing to provide for volume compensation as the blood sac empties and fills.

Results from in vitro testing

A prototype HVAD was designed and fabricated in order to measure the efficiency of piston-style pump actuation and to validate pusher-plate design. Device assembly was accomplished by removing the drive mechanism from a pneumatic blood pump (Sarns/3M) and substituting a piston/bushing mechanism. A hollow, contoured pusher-plate was employed to maximize ejection fraction, minimize device size and weight, and support the lateral convolution formed during blood sac compression. The pusher-plate shaft was supported by a central bushing machined into a backing plate secured to the main pump housing. The pusher-plate shaft was connected to the central shaft of the MEC via a direct mechanical linkage to simulate LD actuation. Both bellows were removed from the MEC and the outer bellows replaced by a coil spring to mimic the return forces produced by the high-pressure bellows of the hydraulic MEC2/HVAD system. As with prior MEC bench tests, muscular actuation was simulated using a rotary motor attached to a reciprocating rod guided by a Teflon bushing. MEC stroke length was fixed at 12 mm during tests designed to measure energy transfer efficiencies and the effects of afterload pressure on muscle force and stroke work requirements. A thin-beam load cell was mounted between the drive rod and MEC to measure forces applied to the muscle interface while piston motion was monitored with an inductive displacement transducer attached to the MEC piston head. Standardized inlet and outlet cannulae were used to connect the HVAD to a Penn State mock circulatory system. Preload pressure was set near 60 mmHg (to mimic counterpulsation conditions) while afterload resistance was adjusted to produce mean pressures of 70-110 mmHg.

Blood pump actuation was realized without difficulty and no damage to the blood sac was detected as a result of repeated piston compression. HVAD stroke volume was found to be a linear function of piston displacement (3 mL/mm) and reached an maximum value of 45 mL. Flow rates were found to be a linear function of MEC stroke length and actuation frequency (as expected). Energy losses due to friction and inertial effects amounted to roughly 5% of the total stroke work produced by the

Linear muscle power for cardiac support

muscle - thus, 95% of LD input energy was either transferred to the blood-analog fluid or stored in the return spring as potential energy. Mean input forces of 46 to 56 N acting over a 12 mm stroke (2.1 L/min) were sufficient to generate mean afterload pressures of 70 to 110 mmHg within the mock circulation. Peak force generation ranged from 72 to 86 N and work input was calculated to be 552 to 672 mJ/stroke. Energy transfer efficiencies increased slightly with higher afterloads and ranged from 69% at 70 mmHg to 74% at 110 mmHg.

These results suggest that a muscle-powered VAD can, in principal, provide significant cardiac support with LD actuation forces under 90 N and stroke work levels under 700 mJ. Previous studies have shown that fully-conditioned human LD muscle (comprising 100% type 1 fibers) can be expected to generate forces of 164 N and sustain work levels approaching 1000 mJ/stroke [46, 49]. Thus, these data indicate that this method for delivering muscle power to the bloodstream is both mechanically tenable and consistent with the functional capabilities of trained LD muscle.

Summary

The use of in situ skeletal muscle as an endogenous power source affords a unique opportunity to bring a completely implantable, tether-free cardiac assist system to fruition. Muscle-powered devices offer an attractive alternative to current long-term support schemes by eliminating the need to transmit energy across the skin, thereby reducing hardware requirements significantly. Through this mechanism, external battery packs, power conditioning hardware, transmission coils, and internal power cells could all be replaced by natural biomechanical processes, serving to greatly enhance patient quality-of-life by improving reliability and eliminating all external components. Moreover, muscle-based blood pumps would be much less expensive to implement and maintain, resulting in wider availability and reduced costs for health-care providers.

This report summarizes our efforts to develop a functional prosthesis for transforming contractile energy into hydraulic power for chronic circulatory support. Results from in vitro testing of prototype devices are encouraging, but potential problems associated with long-term implantation have yet to be fully addressed. Should the MEC prove to be a reliable means for transmission of contractile energy, this device could be paired with a hydraulic VAD to form a permanent muscle-powered ventricular assist device free of external hardware. Such a system could potentially represent an inexpensive alternative to heart transplantation and enable patients with heart failure to maintain a higher quality of life.

Address correspondence to:

Dennis R. Trumble, Cardiothoracic Surgery Research, Allegheny-Singer Research Institute, 9th floor - South

Tower, 320 East North Avenue, Pittsburgh, PA 15212, phone (412) 359 3660, fax (412) 359 3878, Email trumble@pgh.auhs.edu.

References

- [1] Badhwar V, Badhwar RK, Oh J-H, Chiu RCJ: Power generation from four skeletal muscle configurations: design implications for a muscle powered cardiac assist device. *ASAIO Abstracts* 1997; 43 (2): 48.
- [2] Beck CS, Tichy VL: Surgical development of a new blood supply to the heart. *Am Heart J* 1935; 10: 849-873.
- [3] Dewar M, Chiu R: Cardiomyoplasty and the pulse-train stimulator, in Chiu RCJ (ed): *Biomechanical Cardiac Assist, Cardiomyoplasty and muscle-powered devices*. Futura Publishing Company, Inc., 1986, pp 43-58.
- [4] Duan C, Trumble DR, Scalise D, Magovern JA: Intermittent stimulation enhances function of conditioned muscle. *Am J Physiol* 276 (Regulatory Integrative Comp Physiol 45) 1999; R1534-R1540.
- [5] Farrar D, Hill J: A new skeletal linear-pull energy converter as a power source for prosthetic circulatory support devices. *J Heart and Lung Trans* 1992; 11: 341-50.
- [6] Frey M, Thoma H, Gruber H, Stohr H, Huber L, Havel M, Steiner E: The chronically stimulated muscle as an energy source for artificial organs. *Eur Surgical Research* 1984; 16: 232-237.
- [7] Fritzsche D, Krakor R, Asmussen G, Widera R, Caffier P, Berkei J, Cesla M: Anabolic steroids (metenolone) improves muscle performance and hemodynamic characteristics in cardiomyoplasty. *Ann Thor Surg* 1995; 59: 961-970.
- [8] Funk M: Epidemiology of heart failure. *Critical Care Nursing Clinics of North America* 1993; 5: 569-573.
- [9] Furnary AP, Magovern JA, Christlieb IY, Trumble DR, Magovern GJ: Component analysis of bilateral anterior cardiomyoplasty. *Ann Thor Surg* 1993; 55: 72-77.
- [10] Furnary A, Trumble D, Vu T, Magovern G, Kao R: Perineural leads and burst stimulation optimize contraction of skeletal muscle. *ASAIO Transactions* 1991; 37: 164-166.
- [11] Geddes L, Badylak S, Tacker W, Janas W: Output power and metabolic input power of skeletal muscle contracting linearly to compress a pouch in a mock circulatory system. *J Thoracic and Cardio-vasc Surg* 1992; 104: 1435-1442.

Linear muscle power for cardiac support

- [12] Gillum RF: Epidemiology of heart failure in the United States. *Am Heart Journal* 1993; 126: 1042-1047.
- [13] Guldner NW, Eichstaedt HC, Klapproth P, Tilmans MHI, Thuaudet S, Umbrain V, Ruck K, Wyffels E, Bruyland M, Sigmund M, Messmer BJ, Bardos P: Dynamic training of skeletal muscle ventricles. A method to increase muscular power for cardiac assistance. *Circulation* 1994; 89: 1032-1040.
- [14] Guizzi GL, Ugolini F: Proposal for a total orthotopic muscle-powered artificial heart system for live application. *XII Int Conf on Med and Biol Eng*, Jerusalem, Israel, Aug 19-24, 1979.
- [15] Guyton AC: Contraction of skeletal muscle, in: *Textbook of Medical Physiology* (6th edition). Philadelphia, Pennsylvania, WB Saunders Company, 1981, pp 122-137.
- [16] Johnson AT, BF Hurley: Factors affecting mechanical work in humans, in: *The Biomedical Engineering Handbook*. Boca Raton, Florida, CRC Press, 1995, pp 400-410.
- [17] Josephson RK: Contraction dynamics and power output of skeletal muscle. *Ann Rev Physiol* 1993; 55: 527-546.
- [18] Kantrowitz A, McKinnon W: The experimental use of the diaphragm as an auxiliary myocardium. *Surg Forum* 1959; 9: 266.
- [19] Kochamba G, Desrosiers C, Dewar M, Chiu RC: The muscle-powered dual-chamber counterpulsator: rheologically superior implantable cardiac assist device. *Ann Thorac Surg* 1988; 45: 620-625.
- [20] Kusserow B, Clapp J: A small ventricle-type pump for prolonged perfusions: construction and initial studies, including attempts to power a pump biologically with skeletal muscle. *Trans ASAIO* 1964; 10: 74-78.
- [21] Lazzara RR, Park SE, Cmolik BL, Trumble DR, Magovern JA: Static left cardiomyoplasty: Effect on left ventricular function. *J Heart Lung Trans* 1993; 12: 1024-1028.
- [22] Lazzara RR, Trumble DR, Magovern JA, Magovern GJ: Clinical and experimental effects of the unstimulated (static) right latissimus dorsi cardiomyoplasty on left ventricular function. *Basic Appl. Myology* 1993; 3 (4): 281-288.
- [23] Macoviak JA, Stephenson LW, Armenti F, Kelly AM, Alavi A, Mackler T, Cox J, Palatianos G, Edmunds LH: Electrical conditioning of *in situ* skeletal muscle for replacement of myocardium. *J Surg Res* 1982; 32: 429-439.
- [24] Magovern GJ, Heckler FR, Park SB, Christlieb IY, Magovern GJ Jr, Kao RL, Benckart DH, Tullis G, Rozar E, Liebler GA, Burkholder JA, Maher TD: Paced latissimus dorsi used for dynamic cardiomyoplasty of left ventricular aneurysms. *Ann Thor Surg* 1987; 44: 379-388.
- [25] Magovern GJ, Park SB, Kao RL, Christlieb IY, Magovern GJ Jr: Dynamic cardiomyoplasty in patients. *J Heart Transplant* 1990; 9: 258-263.
- [26] Magovern GJ, Simpson KA: Clinical cardiomyoplasty: Review of the ten-year United States experience. *Ann Thor Surg* 1996; 61: 413-419.
- [27] Magovern JA, Hunter TJ, Cardone JC, Christlieb IY: Long-term results of right latissimus dorsi cardiomyoplasty. *J Card Surg* 1996; 11: 264-270.
- [28] Magovern JA, Magovern GJ Sr: Cardiomyoplasty, in LR Kaiser (ed): *Mastery of Cardiothoracic Surgery*. Philadelphia, Pennsylvania, Lippincott-Raven Publishers, 1998, pp 574-582.
- [29] Magovern JA, Park SE, Cmolik BL, Trumble DR, Christlieb IY, Magovern GJ: Early effects of right latissimus dorsi cardiomyoplasty on left ventricular function. *Circulation* 1993; 88 [part 2]: 298-303.
- [30] Park SE, Cmolik BL, Lazzara RR, Trumble DR, Magovern JA: Right latissimus dorsi cardiomyoplasty augments left ventricular systolic performance. *Ann Thorac Surg* 1993; 56: 1290-1295.
- [31] Perier P, Acar C, Chachques JC: Anatomy of the latissimus dorsi muscle: description, in: *Cardiomyoplasty*. Mount Kisco, New York, Futura Publishing Company, Inc., 1991, pp 63-68.
- [32] Reichenbach SH, Farrar DJ, Diao E, Hill DJ: *In vivo* studies of an implantable energy convertor for skeletal muscle powered cardiac assist. *ASAIO J*, 1997; 43: M668-M672.
- [33] Salmons S, Jarvis JC: The working capacity of skeletal muscle transformed for use in a cardiac assist role, in: *Transformed Muscle for Cardiac Assist and Repair*. Mount Kisco, New York, Futura Publishing Company, Inc., 1990, pp 89-104.
- [34] Salmons S, Jarvis JC: Cardiac assistance from skeletal muscle: a critical appraisal of the various approaches. *Br Heart J* 1992; 68: 333-338.
- [35] Salmons S, Sroter F: Significance of impulse activity in the transformation of skeletal muscle type. *Nature* 1976; 263: 30-34.
- [36] Salmons S, Vrbova G: The influence of activity on some contractile characteristics of mammalian fast and slow muscles. *J Physiol* 1969; 201: 535-549.
- [37] Sasaki E, Hirose H, Murakawa S, Mori Y, Yamada T, Itoh H, Ishikawa M, Senga S, Sakai S, Katagiri Y, Hashimoto M, Fuwa S, Azuma K: A skeletal muscle actuator for an artificial heart. *ASAIO J* 1992; 38: 507-511.

Linear muscle power for cardiac support

- [38] Sasaki Y, Chikazawa G, Nogawa M, Nishida H, Koyanagi H, Takatani S: Ex vivo evaluation of a roller screw linear muscle actuator for an implantable ventricular assist device using trained and untrained latissimus dorsi muscle. *Artificial Organs* 1999; 23 (3): 262-267.
- [39] Schneck DJ: Mechanics and energetics of muscular contraction. In: *Mechanics of Muscle* (2nd ed). New York, New York University Press, 1992, pp 165-196.
- [40] Silver F, Doillon C: Wound healing: in vivo response to biomaterial implantation, in: *Biocompatibility. Interactions of Biological and Implantable Materials*. New York, VCH, 1989, pp 97-128.
- [41] Sreter FA, Pinter K, Jolesz F, Mabuchi K: Fast to slow transformation of fast muscles in response to long-term phasic stimulation. *Exp Neurology* 1982; 75: 95-102.
- [42] Stainsby WN, Andrew GM: Maximal blood flow and power output of dog muscle in situ. *Med Sci Sports Exercise* 1988; 20: S109-S112.
- [43] Stevens L, Brown J: Can noncardiac muscle provide useful cardiac assistance? Preliminary studies of the properties of skeletal muscle. *Am Surgeon* 1986; 52: 423-427.
- [44] Takahashi M, Misaki T, Watanabe G, Ohtake H, Tsunozuka Y, Wada M, Sakakibara N, Matsunaga Y, Kawasuji M, Watanabe Y: Efficacy of a skeletal muscle-powered dynamic patch: Part 1. Left ventricular assistance. *Ann Thor Surg* 1995; 59: 305-312.
- [45] Trumble DR: Cardiomyoplasty fundamentals and muscle-powered blood pump, in Webster J (ed): *Encyclopedia of Electrical and Electronics Engineering*. New York, John Wiley and Sons, Inc., 1999, pp 662-665.
- [46] Trumble DR, LaFramboise WA, Duan C, Magovern JA: Functional properties of conditioned skeletal muscle: implications for muscle-powered cardiac assist. *Am J Physiol* 273 (Cell Physiol 42) 1997; C588-C597.
- [47] Trumble DR, Kao RL, Magovern GJ: Quantification of skeletal muscle work capacity for circulatory assistance, in *Cardiovascular Science and Technology: Basic and Applied: II*. Louisville, Kentucky, Oxymoron Press, 1990, pp 388-390.
- [48] Trumble DR, Magovern JA: Ergometric studies of untrained skeletal muscle demonstrate the feasibility of muscle-powered cardiac assistance. *J Appl Physiol* 1994; 77 (4): 2036-41.
- [49] Trumble DR, Magovern JA: A permanent prosthesis for converting in situ muscle contractions into hydraulic power for cardiac assist. *J Appl Physiol* 1997; 82 (5): 1704-1711.
- [50] Trumble DR, Magovern JA: A muscle-powered energy delivery system and means for chronic in vivo testing. *J Appl Physiol* 1999; 86 (6): 2106-2114.
- [51] Trumble DR, Magovern JA: Muscle-powered blood pump: Design and initial test results, *ASAIO J* 1999; 45: 178-182.
- [52] van Doorn CA, Bhabra MS, Hopkinson DN, Barman D, Cranley JJ, Hooper TL: Latissimus dorsi muscle blood flow during synchronized contraction: implications for cardiomyoplasty. *Ann Thor Surg* 1996; 61: 603-609.