Method for measuring long-term function of muscle-powered implants via radiotelemetry

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Received 18 September 2000; accepted in final form 27 November 2000

Trumble, Dennis R., and James A. Magovern. Method for measuring long-term function of muscle-powered implants via radiotelemetry. J Appl Physiol 90: 1977–1985, 2001.—Long-term remote monitoring of muscle-powered implants has been made possible with development of an adjustable workload that can be remotely monitored to assess device function. This technique obviates the need for percutaneous access lines and allows test animals to remain untethered, eliminating deleterious effects caused by infection, sedation, or animal stress. Hardware components include a latex bladder fixed within a hermetically sealed canister, multichannel implantable telemetry unit, and subcutaneous access port (for pressure charge adjustment). To validate this method, in vitro tests were performed by using a third-generation muscle energy converter designed to function as an implantable hydraulic pump. Two channels of telemetered pressure data were collected and used to calculate six indexes of device function. Calculated parameters were then compared with measured values to determine accuracy. Correlation between measured and calculated parameters was high in all instances, with most estimates yielding errors of <3%. These results demonstrate the utility of this approach and support its use as a means to monitor muscle-powered devices during long-term animal trials.

motor prostheses; latissimus dorsi; muscle energy converter; blood pump

THE POTENTIAL HEALTH BENEFITS to be gained by harnessing skeletal muscle power for circulatory support are substantial. Successfully tapping this autologous energy source would breach an important barrier that has prevented current blood pump technology from becoming a viable, cost-effective means to treat congestive heart failure, which is a devastating disease that continues to increase in prevalence in our society despite the aggressive application of advanced pharmacological therapies (5). The availability of a practical muscle energy transmission scheme would breathe new life into the field of mechanical cardiac support, providing a means to develop self-contained systems fueled by the same metabolic processes that drive the heart itself. Hybrid implants of this sort would provide a much-needed alternative to cardiac transplantation without the limitations of donor availability, the complications of coronary artery vasculopathy, and the expense of immunosuppressive drugs.

Progress toward developing a practical prosthesis to harvest muscle power has been slowed, however, because of complexities of device design and difficulties associated with monitoring long-term device function in vivo. System durability and energy transfer efficiency have proven to be key design considerations from a mechanical perspective, and important refinements in device architecture have been realized in recent years. Still, fundamental questions regarding device biocompatibility (14) and steady-state work capacity (12) have remained largely unanswered for lack of a simple, reliable means to assess system performance under chronic implant conditions.

Long-term monitoring of motor implants has now been made possible with development of a subcutaneous muscle-actuated accumulator and radiotelemetry (SMART) system designed to provide both regulated pressure loads and a means to measure device and muscle function via remote sensing. Through this mechanism, device loading can be easily adjusted and performance data collected at any time without the need for sedation or general anesthesia, which may influence contractile function. Moreover, this system obviates the need for percutaneous access lines and allows test animals to remain untethered, thereby eliminating deleterious effects caused by infection and animal stress. As a result, long-term studies of in vivo device performance, steady-state muscle function, and
tissue response to device implantation can now be performed by using this novel test system.

This report outlines the fundamental principles of SMART system operation and describes individual hardware components, data transmission techniques, and results from preliminary in vitro testing. Recent improvements in muscle energy converter (MEC) design and functional parameters are also described.

MEC DESIGN AND OPERATION

The most salient aspects of MEC design and function have not changed appreciably since they were first described in 1997 (13). In brief, this device assumes the form of a cylindrical pump, 12–14 cm in length, with a reciprocating piston stationed at one end. The MEC is positioned beneath the humeral insertion of the latissimus dorsi (LD) muscle so that the tendon can be attached to the piston head and the muscle used to actuate the pump. LD contractions are governed by an implanted stimulator that sends short bursts of electrical impulses to the thoracodorsal nerve. Contractile energy is transferred to the transmission medium (water or silicone oil) via an internal metal bellows that serves as a low-friction piston seal. The entire mechanism is mounted to the chest wall by using a perforated titanium backing plate to provide a stable anchor point for pump operation.

Extensive in vitro testing of earlier prototype devices has yielded an improved third-generation muscle pump (MEC3) capable of delivering contractile energy at rates exceeding 340 mJ per actuation cycle (Fig. 1). Device modifications were implemented to improve power transfer capacity beyond that of the original MEC prototype (135 mJ/stroke) while reducing the relatively high muscle force requirements imposed by the second-generation device (owing to high bellows spring rates). Current MEC3 configuration and component parts are illustrated in Fig. 2. Details regarding device form and function are summarized below.

The MEC3 features a low-pressure stainless steel bellows seal with an effective pressure area of 3.16 cm², a nominal spring rate of 4.4 N/cm, and a volumetric compliance of $9.67 \times 10^{-8}$ cm³/kPa. The bellows is heat treated to cycle in compression for maximum durability, and, as a result, resting fluid pressures of ~40 kPa are needed to both extend the piston and preload the muscle. Bellows integrity is further safeguarded by limiting piston stroke lengths to ~16 mm. The outer bellows seal used in previous designs has been replaced with a length of reinforced expanded polytetrafluoroethylene graft (18 mm) that prevents body fluids from contacting the bearing surface. Elimination of the outer bellows minimizes overall device length and reduces MEC3 spring rate by an additional 50% beyond the low value already afforded by the
lighter inner bellows. Moreover, MEC3 spring rates now assist LD shortening rather than working against the muscle as in prior designs.

The central shaft of the MEC3 is supported by two sleeve bearings lined with FrelonGOLD, a low-friction, Teflon-based compound manufactured by Pacific Bearing (Rockford, IL). Two bearings placed end to end are required to prevent piston binding due to the cantilevered load generated by the muscle. Internal volume compensation is achieved via circular vents machined into the hollow central shaft. The lower portion of the shaft is stepped to a slightly larger diameter to provide a stop mechanism that limits the bellows compressed length, thereby protecting the welded surfaces from wear due to impact stresses.

**TECHNIQUE FOR REMOTE MONITORING OF MEC FUNCTION**

As detailed in a previous report (14), MEC loading conditions can be regulated in vivo using a subcutaneous muscle-actuated accumulator (SMA). This device, adapted from an implantable mock circulation system developed by Acker et al. (1, 2), comprises a latex bladder fixed within a hermetically sealed titanium canister (Fig. 3). The bladder insert receives fluid pumped from the MEC via a noncompliant conduit; pressure loads are altered by simply injecting or removing air through a vascular access port connected to the canister. Both fluid and gas compartments are equipped with luer lock fittings for pressure measurement purposes.

By using this loading scheme, it becomes possible to calculate every key MEC performance parameter on the basis of accumulator pressure readings alone, including actuation force, stroke length, contraction time, piston velocity, stroke volume, and energy output. This information is computed by combining pressure readings with known system constants such as bellows properties (e.g., effective area, spring rate, and compliance) and resting canister air volume, a parameter used to determine fluid volume displacement via Boyle’s law. Despite the relative simplicity of this approach, however, there remains the need to insert a small-gauge needle though both skin and access port septum to measure accumulator pressures. Percutaneous access thus limits data collection to relatively brief time periods during which the animal must be either restrained or sedated. Thus it is important that a means be developed to monitor these waveforms non-invasively, without having to disturb the animal under study.

To this end, a fully implantable radiotelemetry system (Data Sciences International, St. Paul, MN) has been developed specifically for use with the SMA. The housing of this device resembles a cardiac pacemaker and comprises a silicone elastomere capsule that contains a battery, two pressure sensors, and an electronics module (Fig. 4). A pair of fluid-filled catheters, each capped with luer lock fittings, transmit device pressures to solid-state transducers modified to accommodate the supraphysiological pressures generated during MEC actuation. A proprietary silicone-oil-like fluid is used as the transmission medium within the catheter to improve frequency response and effect minimal diffusion losses for a long working life (>2 yr). For this application, standard amplifier gains are reduced to increase peak measurement capacity roughly fivefold to 1,550 mmHg. Atmospheric pressure is monitored continuously via an ambient pressure reference (model APR-1, Data Sciences International) and added to tele-

![Fig. 3. Subcutaneous muscle-actuated accumulator shown with luer lock fittings for fluid (left) and gas (right) chamber access. A thin metal rod is used to prevent longitudinal collapse of the latex bladder, allowing preload and afterload pressures to be set independently. Inset: the bladder fully inflated (top) and completely evacuated (bottom) in both longitudinal and axial views. Total device length = 14 cm; external housing diameter = 2 cm.](http://jap.physiology.org/Downloadedfrom10.220.33.5onApril18,2017)
metered gauge pressure readings to yield absolute pressure data needed for stroke volume calculations. Biopotential leads sheathed in silicone are used to monitor muscle activity and provide temporal data relating LD activation and energy transfer times. The electronics module converts these analog readings to frequency-modulated digital signals and transmits them as a series of pulses to a nearby receiver hard-wired to a computerized data-acquisition system. Data from each channel are transmitted at a rate of 400 Hz. Transmitter power may be cycled on and off via a magnetically activated switch to extend battery life in studies in which only intermittent monitoring is needed. Estimated battery life under conditions of continuous use is 4 mo.

The integration of this remote sensing scheme with SMA technology has yielded a totally implantable, self-contained system for chronic testing of muscle-powered devices (Fig. 5). The principal advantage of this approach is that it allows device function to be readily (and continuously) monitored in conscious, untethered animals, thereby avoiding the potential impact of sedation, anesthesia, or stress on muscle performance. Moreover, the SMART system eliminates the risk of percutaneous access line infection and thus can potentially be used to test long-term implant function for periods of months or even years. In fact, this technique requires only that the test animal be handled during those brief periods when air is injected or withdrawn from the accumulator to adjust loading conditions (note: a second subcutaneous access port can be added should preload adjustments be required). At all other times, device performance may be monitored without the need for any direct contact with the animal under study.

DEVICE TESTING: MATERIALS AND METHODS

The MEC-SMART complex was tested in vitro to assess both muscle pump function and the accuracy of telemetric monitoring before live animal implantation. Muscle contractions were simulated via a programmable linear actuator (SmartActuator, UltraMotion) attached to a reciprocating rod guided by a Teflon bushing. The actuator arm was attached to the MEC3 via a light metal chain terminated by a 2 cm length of braided artificial tendon (8) to simulate in vivo fixation conditions and allow the piston to extend under its own power (the chain becoming slack during rapid extension of the actuator arm to mimic low tension during LD relaxation). The hydraulic output generated by these “contractions” was pumped into the SMART system to 1) test the accuracy of device performance calculations based on telemetry pressure readings and 2) provide a controlled pressure load for MEC3 bench testing. A miniature load cell (model ELH-TC401, Entran Devices) was mounted between the drive rod and MEC3 to measure forces applied to the muscle interface. Piston motion was monitored with a low-friction linear potentiometer (model LP804-01, Omega Engineering) attached to the piston head. An in-line flow probe (model 8N, Transonic) was inserted into the pressure tubing and used to quantify fluid volume displacement. Force, displacement, and flow wave-
forms were digitized at a rate of 500 samples/s and saved to a Compaq Armada E700 laptop computer using another data-acquisition package (DI-720-P DAS with WinDaq/Pro+, Dataq Instruments).

To simulate in vivo measurement conditions, gas and fluid pressures were measured by using an implantable telemetry unit (model TL11M3-D70-PCP) and saved to a Dataquest A.R.T. data-acquisition system (Data Sciences International). Waveforms were collected simultaneously on both data-acquisition systems with the actuator cycled off-on-off and system clocks synchronized to produce event and time markers common to both data sets. These data were then postprocessed by using XANALYZE, a comprehensive cardiovascular waveform analysis program developed at the National Institutes of Health (11).

Calculations of device stroke volume, stroke work, stroke length, contraction time, actuation speed, and muscle force based on telemetered pressure measurements alone were compared with values obtained via direct measurement over a wide range of resting gas (afterload) pressures (50, 100, 150, and 200 kPa) and peak “contraction” speeds (10–100 mm/s; increments of 10), with the duration of actuation set at 250 ms and actuator stroke length limited to 16 mm. Resting fluid pressure (preload) was fixed at 38.7 kPa to rapidly extend the piston between actuation cycles, plus provide an additional 5-N force at full extension (to overcome anticipated LD resting tension and pressure from surrounding tissues). Once the system was primed with fluid, a complete battery of 40 tests was performed over a period of several days. Static pressure tests were also performed over longer periods (up to 2 wk) to detect leakage of fluid or gas from the system. These data were then used to 1) quantify the accuracy of this telemetric monitoring technique, 2) calculate MEC3 energy transfer capacity at various afterload pressure settings, and 3) determine whether system leakage rates are compatible with extended in vivo use.

Data analysis and statistical methods. All summary data are expressed as means ± SD. Linear regression analyses were performed by using the Marquardt-Levenberg algorithm for iterative, least squares estimation of curve-fit parameters.

RESULTS

Typical force, displacement, and flow waveforms measured during device testing are shown in Fig. 6 along with corresponding gas and fluid pressure readings recorded via radiotelemetry. No fluid leakage was

![Fig. 6. Simultaneous recordings of actuation force, piston displacement, fluid flow, and accumulator pressures acquired during MEC3-SMART system bench testing. Telemetered pressure readings (bottom) were used to calculate 6 key muscle pump performance parameters. These calculations were then compared with measured values to test the accuracy of this monitoring technique.](http://jap.physiology.org/)
detected during the course of system testing, and gas pressures were found to be stable under both static and dynamic operating conditions. As anticipated, fluid pressure tracings were seen to change in proportion to actuation force over a broad range of shortening speeds and stroke lengths. Similarly, gas pressure waveforms were found to closely follow changes in volumetric flow for stroke lengths ranging from 2.7 to 15.0 mm. These observations are consistent with the fundamental premise that accumulator pressure readings alone contain sufficient information to calculate key pump performance parameters.

The accuracy of MEC performance parameters computed from SMART pressure readings is shown graphically in Fig. 7, in which calculated values are plotted against those obtained via direct measurement. SMART system measurement errors are further delineated in Fig. 8 by using a method described by Bland and Altman (3) in which differences between estimated and measured values are plotted against their true value. Estimates of peak actuation forces ranged from 12.5 to 73.6 N and were in substantial agreement with measured values, differing by an average of $10.9 \pm 6.5\%$. Contraction times, defined as the period from initial force development to peak piston displacement, were calculated at 0.247 to 0.310 s on the basis of the time course of fluid pressure fluctuations. Absolute differences between calculated and measured times averaged 0.005 $\pm$ 0.008 s. Relative differences averaged 2.2%.

Device performance parameters calculated from accumulator gas pressure readings (illustrated in panels C–F of Figs. 7 and 8) were found to be even more precise. Discrepancies between calculated and mea-
sured stroke volumes averaged $-0.02 \pm 0.05$ ml, a difference of $<1\%$ over a range of 0.42–3.93 ml. Stroke length estimates, based on stroke volume calculations and bellows effective area and compliance, differed from measured values by $-0.01 \pm 0.66$ mm, with the average reading exceeding the true distance by 2.8%. Similarly, mean stroke velocity, derived from these stroke length measurements plus estimated contraction time, deviated only slightly from actual values, differing by $-0.85 \pm 3.19$ mm/s over a span of 8.4–60.1 mm/s. Perhaps the most important performance parameter, stroke work output, was calculated as the product of stroke volume and pressure generation. Calculated values ranged from 6.0 to 332.9 mJ, with the average reading being 0.5% less than that determined by direct measurement. Absolute differences averaged $1.7 \pm 5.6$ mJ.

The amount of mechanical energy transmitted by the MEC3 was strongly influenced by both stroke length and afterload conditions (Fig. 9). Stroke work outputs of 324–344 mJ were realized against pressure loads of 150–200 kPa at full piston compression. Peak energy transfer was achieved with actuation forces of 65–80 N peak (45–55 N mean) applied over a period of 0.25 s. Under these conditions, total input energy needed to actuate the device was measured at 521–796 mJ per pump cycle. This “contractile work” was converted into hydraulic power with an efficiency of 87 ± 3%. Of this, just over one-half (53 ± 3%) was transmitted to the accumulator, with the remainder being stored as po-

Fig. 8. Graphs showing difference between calculated (Calc) and measured (Meas) values plotted against their mean for 6 key muscle pump performance parameters. Horizontal lines define mean difference and 95% confidence intervals. Avg, average. A: peak actuation force (F). B: contraction duration (CT). C: stroke volume (SV). D: stroke length (SL). E: mean piston velocity during actuation (PV). F: stroke work output (SW).
potential energy within the metal bellows seal. Hydraulic conversion efficiencies were found to be independent of stroke length and afterload pressures.

DISCUSSION

The principal aim of this study was to evaluate the prospect of using radiotelemetry as a noninvasive means to monitor functional parameters of muscle-powered implants in conscious, untethered animals. This test scheme was developed to allow on-demand assessment of muscle and device performance over extended implant periods (3–24 mo) without the need for percutaneous access lines or the administration of tranquilizing drugs. Its ultimate purpose is to simulate, to the degree possible, the clinical conditions under which these devices will operate to better predict implant performance before human trials.

To this end, the SMART system was designed and its function assessed in vitro. Two channels of telemetered pressure data (gas and fluid) were collected and used to calculate six indexes of device function. Calculated parameters were then compared with measured values to determine their accuracy. Estimates of peak force based on fluid pressure readings were found to consistently underestimate actual values by ~11%. This small, invariable error is thought to be due to low-level shear loads supported by the piston bearing and thus not detectable by pressure measurement. This discrepancy can be offset, however, by simply adding a 5-N correction constant to the force equation, effectively reducing mean calculation errors to 0.02 ± 3.2 N. All other calculated parameters fell within 3% of measured values, with stroke volume and work output estimates proving most accurate (mean errors <1%). These data confirm that important MEC performance parameters can be accurately derived from telemetered pressure readings alone, without the need to physically manipulate the system under study.

This remote monitoring scheme could potentially be used to facilitate a variety of studies involving the transduction of muscle power into hydraulic energy, whether for circulatory support purposes or other applications (e.g., actuation of artificial limbs). In addition to aiding development of other in situ muscle energy transformers (10), the SMART system may similarly prove beneficial to myoplasty researchers studying the long-term effects of loading conditions on skeletal muscle ventricle performance (6, 7, 15). Moreover, this telemetric loading system could also be employed to examine functional changes brought about by various electrical training protocols, including those enhanced via drug infusion (4, 7, 9), myoblast transfer, or gene therapy. The ability to study muscle mechanics in conscious, unstressed animals could thereby significantly improve our understanding of skeletal muscle plasticity and help determine the feasibility of motor prostheses powered by electrically stimulated skeletal muscle.

The next phase of MEC development, made possible by validation of the telemetric monitoring technique detailed here, will involve use of the SMART system to assess device function in vivo. Implant studies of extended duration will be required to examine a number of biological factors that may impact long-term MEC operation, including muscle function, tendon and chest wall attachment stability, and chronic tissue reactions. By providing a quick and simple means to access device functional status, postimplant problems will be more rapidly identified and the time course of performance degradation documented before explantation. Thus causes of system failure will be quickly and accurately diagnosed, leading to more effective design modifications and more efficient animal use.

In the absence of mechanical difficulties, the SMART system will be used to chart MEC and muscle function for up to 2 yr, documenting the feasibility of operating an internal reciprocating pump powered by muscle contractions over an indefinite period of time. Information regarding optimum patterns of muscle activation and peak sustainable power production will also be obtained by periodically altering loading conditions and muscle stimulation regimens. This novel monitoring technique may thus yield important information regarding tissue encapsulation of long-term kinetic implants, the steady-state work capacity of electrically trained skeletal muscle, and the degree to which in situ skeletal muscle can be used to support the failing heart.

Conclusion. In summary, this report details development of a third-generation MEC and implantable test system designed to provide a practical means to regulate pressure loads and monitor MEC function via...
remote sensing. Bench studies confirm that key device parameters can be calculated with high precision by using pressure readings received via radiotelemetry from an implantable transmitter. This innovative approach to chronic implant testing will allow muscle-powered motor prostheses to be closely monitored for extended periods in conscious, untethered animals, yielding performance data unadulterated by tranquilizing drugs or adrenergic reactions. Implementation of this experimental technique represents an essential step toward determining the feasibility of harnessing muscle power for cardiac-assist purposes.

This work was supported by National Heart, Lung, and Blood Institute Grant 1 R01 HL-59896-01A1.

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