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UTILITY OF A VOLUME-REGULATED DRIVE SYSTEM FOR
DIRECT MECHANICAL VENTRICULAR ACTUATION

A thesis submitted in partial fulfillment
of the requirements for the degree of
Master of Science in Engineering

By

BENJAMIN ALLYN SCHMITT
B.S., Wright State University, 2010

2013
Wright State University

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WRIGHT STATE UNIVERSITY

GRADUATE SCHOOL

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I HEREBY RECOMMEND THAT THE THESIS PREPARED
UNDER MY SUPERVISION BY Benjamin Allyn Schmitt
ENTITLED Utility of a Volume-Regulated Drive
System for Direct Mechanical Ventricular
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ABSTRACT

Schmitt, Benjamin Allyn. M.S.Egr. Department of Biomedical, Industrial, and Human Factors Engineering, Wright State University, 2012. Utility of a Volume-Regulated Drive System for Direct Mechanical Ventricular Actuation.

Direct Mechanical Ventricular Actuation (DMVA) is a non-blood contacting cardiac assist device that augments ventricular function. The purpose of this study was to determine if a volume-regulated "hand pump" drive system and a pressure-regulated "switch tank" drive system provide equivalent levels of cardiac support. Canine (n=2) and swine (n=4) were instrumented for hemodynamic monitoring and intravascular echocardiography. DMVA support was assessed during both severe heart failure and fibrillation. Pump function was evaluated using hemodynamic measures to calculate stroke work. Myocardial function was assessed using echocardiographic speckle tracking to quantify strain rate. Results were compared between groups using paired t-tests. There were no significant differences in either pump function or myocardial strain rates between the hand pump versus switch tank during support of either the failing or fibrillating heart. These results suggest functional equivalency between the two drive system mechanisms that supports development of an automated volume-regulated

system, with its corresponding benefits in reduced size, portability, and potential user-friendly control.

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I. INTRODUCTION

There is currently an unmet need in medicine to provide rapid and effective circulatory support for victims of acute cardiac failure or arrest. Pharmacological management of heart failure with inotropes can augment myocardial function. However, these drugs also exacerbate the already increased physiologic demands of heart. Judicious administration of volume and/or vasodilators can improve cardiac dynamics through alterations in preload and afterload, respectively. When these efforts fail, acute failure enters a downward cycle where the heart progressively deteriorates as failure becomes increasingly severe.

In such situations it becomes necessary to directly supplant the failing heart's inadequate pumping ability with mechanical circulatory support (MCS). Clinically available MCS devices consist of blood pumps. The use of these devices in combination with an oxygenator (i.e. cardiopulmonary bypass) allows support of the entire circulation during open heart surgery or for short-term resuscitative support. A wide variety of MCS devices have also been developed to assist the failing heart and

typically rely on the native lung function for blood oxygenation. All these devices have common drawbacks (e.g. blood contact, technically demanding installation) that limit their feasibility for resuscitative support of the acutely failing or arrested heart.

Resuscitative cardiac support therapies are predominantly limited to those defined in the Advanced Cardiac Life Support algorithms developed by the American Heart Association.³ These algorithms primarily make use of chest compressions, defibrillation, and drug interventions to provide cardiac support. Unfortunately, despite increased awareness of cardiopulmonary resuscitation techniques among the public and an emphasis on timely defibrillation, most patients who suffer cardiac arrest cannot be successfully resuscitated using these methods.³⁻¹⁰

DIRECT MECHANICAL VENTRICULAR ACTUATION

Direct Mechanical Ventricular Actuation (DMVA) is a MCS device consisting of a polymer cup that augments both systolic and diastolic ventricular function (Figure 1).¹¹ The DMVA cup is composed of a hard outer shell enclosing a flexible polymer diaphragm. The ventricles are positioned inside the cup so the epicardial surface contacts the inner membrane (Figure 2). The space between the outer shell and inner diaphragm is pneumatically isolated save for a connection with a pulsatile driving mechanism. Ventricular actuation is achieved by cyclic introduction and removal of air into this space, which act to expand and retract the flexible diaphragm, respectively. These forces are translated to the surface of the ventricle after device attachment. Attachment is achieved by a continuous low vacuum delivered via an apical port on the cup. This vacuum both prevents expulsion of the heart during systolic compression and allows the diaphragm to adhere to the heart's epicardial surface. Proper vacuum attachment is necessary for effective translation of diaphragm forces to the ventricles.

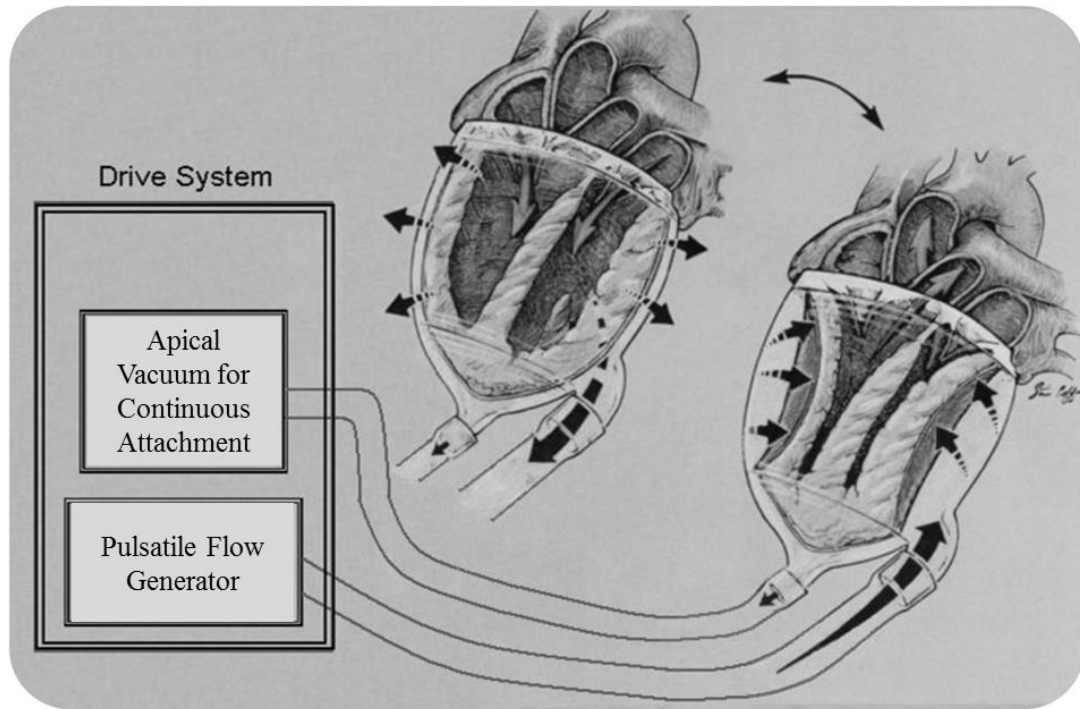


Figure 1 - Representation of the DMVA support system during diastolic and systolic support. The DMVA system consists of the DMVA cup, a pulsatile driving mechanism, and a continuous apical vacuum.

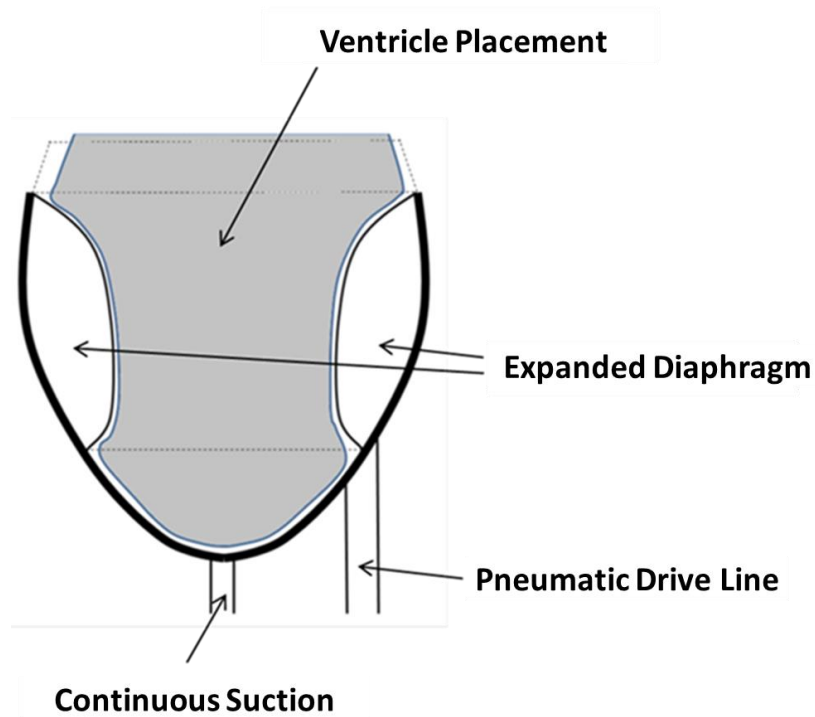


Figure 2 - Diagram showing the various features of the DMVA cup. The cup consists of a hard outer shell and a flexible inner diaphragm. The ventricles are positioned inside the cup so their epicardial surface is in contact with the inner diaphragm. The pulsatile drive system uses air to expand and retract the flexible diaphragm. A low continuous vacuum applied to heart apex facilitates a seal between the epicardium and diaphragm that allows for effective translation of diaphragm motions to the ventricles.

DMVA has a inherent advantages when compared to other MCS devices that make DMVA better suited for cardiac resuscitation.⁹ Most clinical MCS devices are best characterized as blood pumps that reroute blood around the ventricles. These devices typically require anticoagulants to prevent thromboembolic complications from interactions with MCS surfaces. In contrast DMVA only contacts the heart's surface, thereby eliminating this need.

Installation of MCS devices is relatively time-consuming and technically-challenging, sometimes requiring hours and specialized surgeons. DMVA is simple to install, requiring one to five minutes in animal^{12,13} and clinical¹⁴⁻¹⁶ studies. The ability to provide rapid resuscitative circulatory support suggests DMVA would have a favorable impact on the time-sensitive nature of cerebral resuscitation. DMVA installation is dependent on gaining adequate exposure to the heart's surface and thereby requires technically simpler surgical skills compared to other devices, which require the use of specialized techniques.

Additionally, there can be the need to install two typical MCS devices in tandem in order to provide biventricular support since many are univentricular devices. In contrast both ventricles are inserted into the DMVA cup, so support can benefit both the right and left ventricle, as is frequently necessary.

Many newer MCS devices are continuous flow pumps that use an impeller to circulate blood throughout the body.² These pumps are useful for their enhanced implantability and reduced power requirements, but sacrifice the enhanced perfusion provided by physiologic pulsatile flow. DMVA's pulsatile blood flow and use of the ventricles in pumping promote a more physiologic level of perfusion.¹⁶

DMVA should be distinguished from simple direct cardiac compression (DCC) devices, which only apply external compression forces to the surface of the heart. A key weakness of DCC is the lack of diastolic assist and the subsequent limitations on diastolic filling incurred by only compressing the heart. This produces stroke volume insufficiencies and thereby limits the efficacy of such circulatory support modalities.¹⁵ In contrast DMVA augments both systolic and diastolic function.

DMVA DRIVE SYSTEMS

Historically, positive and negative pressure tanks have been used to generate pulsatile flow for DMVA. In this type of system, known as the "switch tank", the cup is actuated by rapidly alternating between these tanks. However, this pressure-regulated approach imposes restrictions in both mobility and compactness that limit use of the device to established medical centers. Additionally, control of such devices has been imprecise and non-intuitive to unfamiliar users. Recent research in both small and large animal models has focused on volume-regulated systems using a hand-operated pneumatic piston known as the "hand pump" to actuate the DMVA cup. Both approaches are summarized in Figure 3.

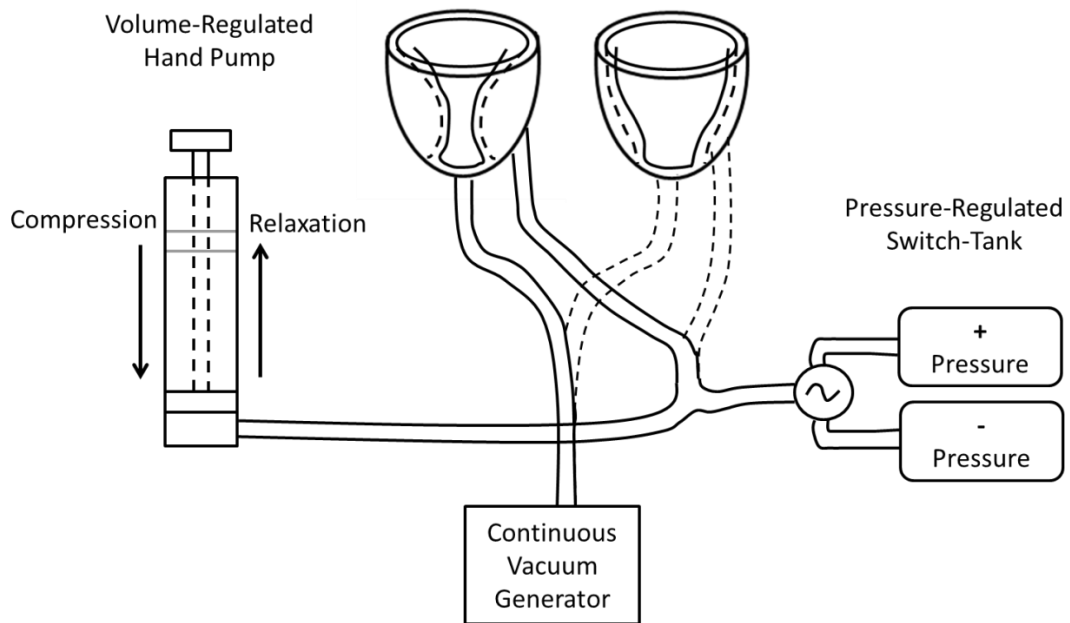
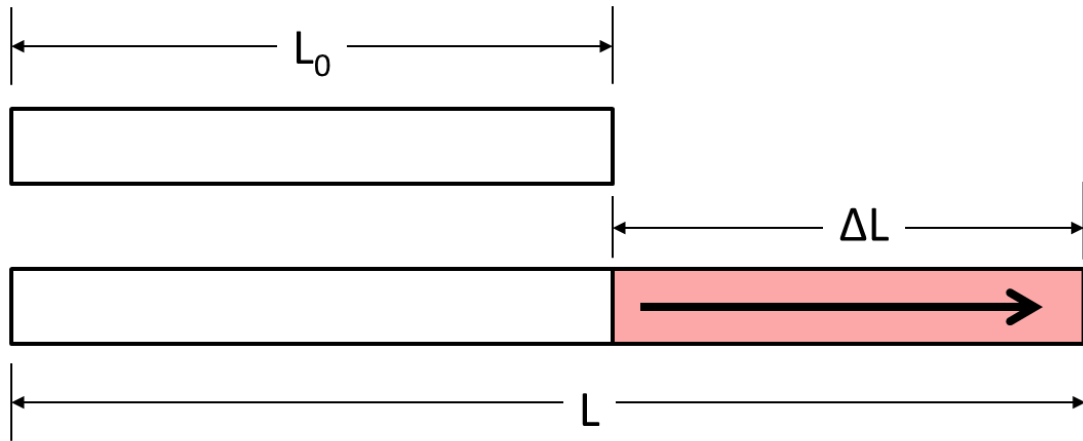


Figure 3 - (Left) Volume-Regulated (Hand Pump) and (Right) Pressure-Regulated (Switch Tank) drive systems demonstrating the means of inducing pneumatic compression and decompression for systolic and diastolic support, respectively.

ECHOCARDIOGRAPHY BACKGROUND

Echocardiography (ECHO) has been a useful tool for evaluating myocardial function, generally defined by visually tracking ventricular wall motions. Strain and strain rate in particular have emerged as quantitative estimates of myocardial function and contractility.²⁰⁻²² Strain is the deformation of an object compared to its original length while strain rate is the rate at which that relative deformation occurs (Figure 4). Strain rate in particular has shown promise as a load-independent measure of myocardial contractility.^{20,21}

To use strain and strain rate as useful parameters, however, there must be some way to track ventricular wall motions. The two primary methods of wall tracking are **tissue Doppler imaging** and **speckle tracking**.²⁰ Tissue Doppler imaging makes use of ultrasound frequency shifts when reflecting off moving objects to measure instantaneous tissue velocity gradients in small myocardial segments (which can be converted to strain rate). However Doppler is highly angle-dependent (i.e. the beam must be parallel to the tissue axis), raising questions of reproducibility.



$$\varepsilon = \frac{L - L_0}{L_0} = \frac{\Delta L}{L_0}$$

Figure 4 - Definition of Lagrangian strain (ε) as the change in length compared to the original length used in wall-tracking.

Speckle tracking uses randomly distributed acoustic markers (speckles) to uniquely characterize a section of the ultrasound image.¹⁹ Speckles are caused by reflections from microscopic boundaries in the tissue being analyzed, meaning each tissue section presents a characteristic speckle pattern. Each speckle section can be followed over a number of consecutive frames (necessitating a sufficiently high frame rate) before tissue motion brings the speckle section out of frame. Frame-to-frame changes can be tracked by using sum of absolute difference algorithms. In addition to its angle-independent nature, speckle tracking only needs a single cardiac cycle and analysis can be performed offline using captured two-dimensional images. Speckle tracking strains and strain rates have shown good correlation and agreement with sonomicrometry when measured under a variety of conditions.²⁰

Strain and strain rate can be measured along three heart axes: longitudinal, radial, and circumferential (Figure 5). Longitudinal strain measurements rely on a long-axis view of the heart while radial and circumferential strain measurements rely on a short-axis view. In this study, a

long-axis view was better obtainable due to positioning of the ultrasound transducer to avoid passing the beam through the air-filled portions of the DMVA cup. The myocardium is a complex network of overlying layers that contract, stretch, rotate, and twist in three dimensions, but longitudinal strain and strain rates (which play a large part in determining compression and relaxation of the ventricles assuming constant ventricular volumes) have been demonstrated as an accurate relative measure of myocardial function.²¹

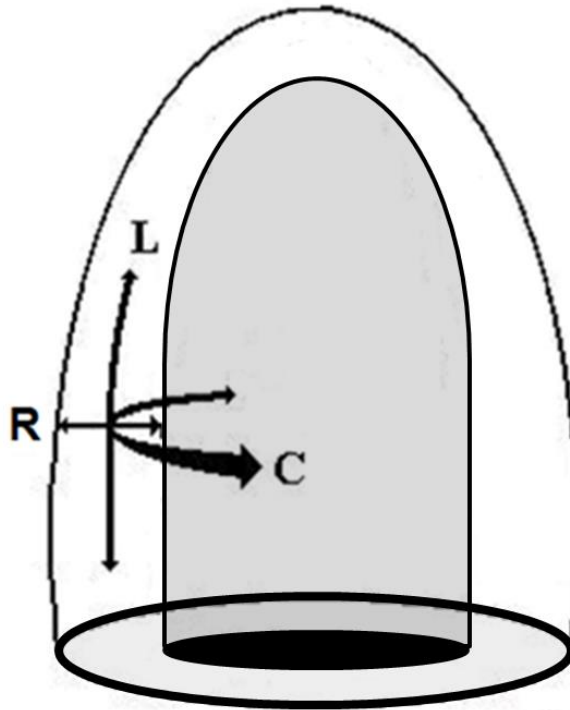


Figure 5 - Diagram showing different axes of myocardial strain (L - Longitudinal, R - Radial, C - Circumferential) on the left ventricle. The longitudinal axis was used for strain analysis during this study because of its utility in characterizing myocardial strain and attainability because the beam does not have to pass through the air-filled sealed space of the cup.

PURPOSE

The purpose of this study was to investigate whether there is functional equivalency between switch tank and hand pump driven DMVA support when applied to the severely failing or fibrillated heart.

II. METHODS

The Wright State University Lab Animal Care and Use Committee approved the experimental protocol, and all animals were treated in compliance with the *Guide for the Care and Use of Laboratory Animals*, published by the National Institutes of Health, revised 1996.

SURGICAL PROTOCOL

Large animal models, comprised of Yorkshire Swine (n = 4) and canine (n = 2) subjects, were studied. Subjects were pre-anesthetized with Telazol (6 mg/kg), Xylazine (3 mg/kg), and Atropine (0.02 mg/kg) followed by tracheal intubation and mechanical ventilation. Anesthesia was maintained with 1-2% isoflurane. Vascular access for drug infusion was achieved through bilateral femoral cutdowns. Phenylephrine was used to regulate subject arterial pressure. The subjects were instrumented for left ventricular, femoral artery, and central venous pressures. A 10-MHz Acuson AcuNav10F ultrasound catheter was positioned through the right jugular vein for intravascular imaging. Two-chamber, left heart long-axis ECHO video clips encompassing a couple heart cycles were obtained on the Acuson Sequoia C512 ECHO system. **(Note: A summary of instrumentation is in Table 1)**. A median sternotomy and pericardiotomy were performed. An ultrasound flow probe was placed on the ascending aorta to measure cardiac output. Surface electrocardiogram, hemodynamics, pulse oximetry, end-tidal carbon dioxide, and rectal temperature were monitored using a computer acquisition system.

Both the hand pump and switch tank drive systems were instrumented to measure pulsatile and continuous vacuum pneumatic pressures and pulsatile flow. The displacement of the hand pump was measured using a string potentiometer. This setup is schematically shown in Figure 6.

Table 1 – List of devices used for study measurements

	Variable	Device
Hemodynamic Measures	Left Ventricular Pressure	Spectramed P23XL Transducer
	Arterial (Femoral) Pressure	Spectramed P23XL Transducer
	Central Venous Pressure	Millar Mikro-tip Transducer (Millar Instruments, Houston, TX)
	Aortic Flow	TS420 Perivascular Module (Transonic Systems, Ithaca, NY)
	ECG, pulse oximetry, rectal temperature	LifeWindow 6000 system (Digicare, Boynton Beach, FL)
Drive Measures	Pneumatic Pressures	Honeywell Microswitch 143PC05D Pressure Transducer
	Bidirectional Flows	Hans Rudolph Model #3700 Flowmeter
	Piston Displacement	String Pot (Celesco SP1-25)
	Echocardiography	10-MHz Acuson AcuNav10F catheter (Siemens Medical Solutions, Mountain View, CA)

EXPERIMENTAL TIMELINE

After collection of post-sternotomy baseline data, a 9-volt battery was applied to the epicardial surface to induce ventricular fibrillation. Following a 5-minute fibrillation period, DMVA support was provided for 15 minutes. After this initial support period hearts were defibrillated. If defibrillation was unsuccessful, DMVA support would continue for another 15 minutes before another defibrillation attempt was made. However, if normal cardiac rhythm was restored, the current cardiac output was compared to baseline cardiac output to determine the level of failure. If severe failure was present (cardiac output \leq 60% baseline) after defibrillation, DMVA support was applied for 15 minutes. If not in severe failure the heart would remain unsupported for a 15 minute recovery period. After either completing a supported failure or recovery period, fibrillation was induced again to restart the cycle (see Figure 7). For each 15 minute period of support, the drive system was alternated between the switch tank and hand pump systems every 3 minutes. This cycle was repeated over an experimental duration of 2 hours. Appropriate physiologic and drive parameters were collected through all the experimental states: (1) baseline, (2) unsupported

fibrillation, (3) unsupported severe heart failure, switch tank support during (5) fibrillation and (6) failure, hand pump support during (7) fibrillation and (8) failure, and (9) recovery. The maximum pressure and rate settings of the (automated) switch tank system were approximated by the experimenters operating the manual hand pump system via visual timing using a computer simulated metronome and pressure feedback.

ANALYTIC MEASURES

Stroke work (SW) (Equation 1), as a measure of pump function, was estimated from the product of mean arterial pressure (MAP) and stroke volume (SV) acquired via integration of aortic flow (i.e. cardiac output (CO)/heart rate (HR) in Equation 1).

$$SW = SV \times MAP = \frac{\int_{0 \text{ sec}}^{10 \text{ sec}} CO dt}{HR} \times MAP \quad \text{Equation 1}$$

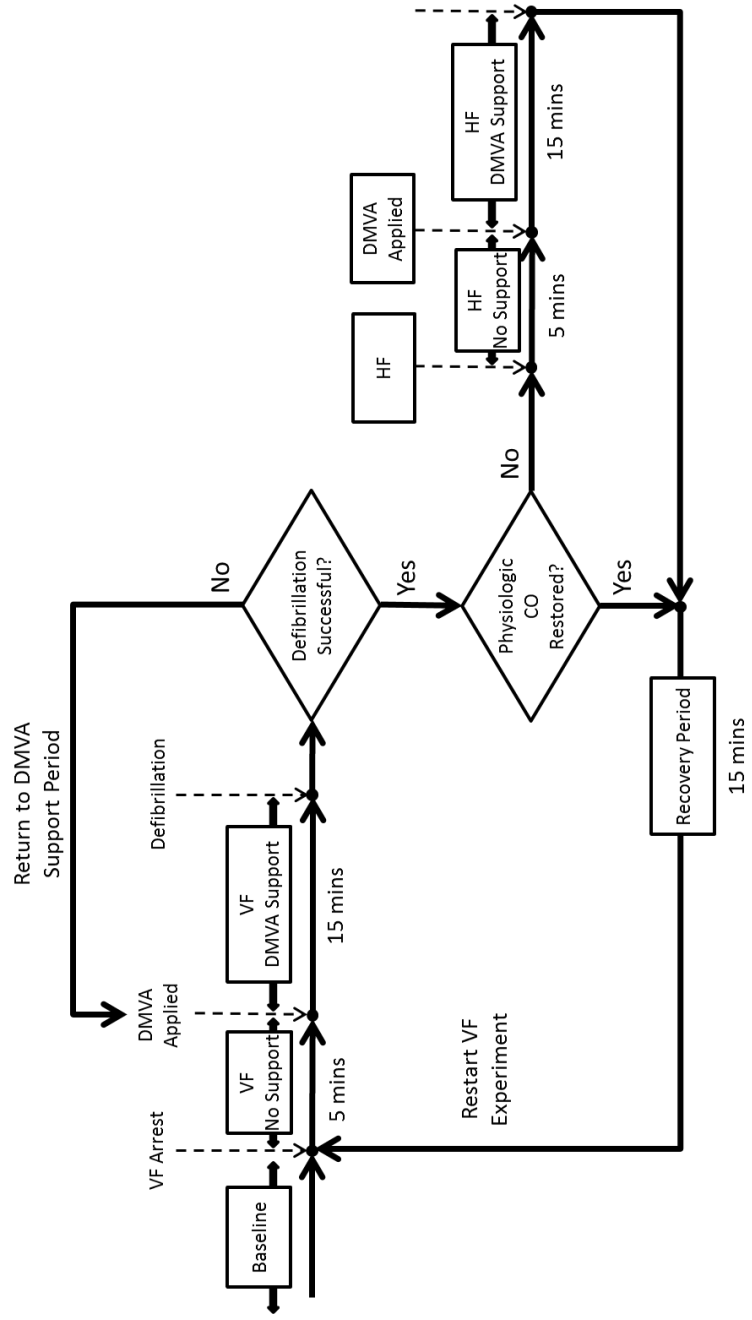


Figure 7 - Experimental timeline over a two-hour case

Digitized intravascular two-chambered long-axis ECHO video clips of the left heart were interrogated to assess myocardial function. Velocity vector imaging (VVI) software (Siemens Medical Solutions) was used to calculate longitudinal myocardial strain rates via speckle tracking. The endocardial border of a video clip was traced during end-diastole and played to ensure tracing fidelity to wall motions (Figure 8). The endocardial border was divided into six sections representing the basal, mid-wall, and apical regions of the septal and free-wall sides of the left ventricle, with each region represented by a strain rate waveform (Figure 9). Each waveform was characterized by a peak systolic and diastolic value. A systolic and diastolic average was computed for the six regions, defined in this study as global strain rate, to estimate myocardial function of the left ventricle.¹⁸ Paired t-tests were used to test for significant differences ($p < 0.05$) between drive systems.

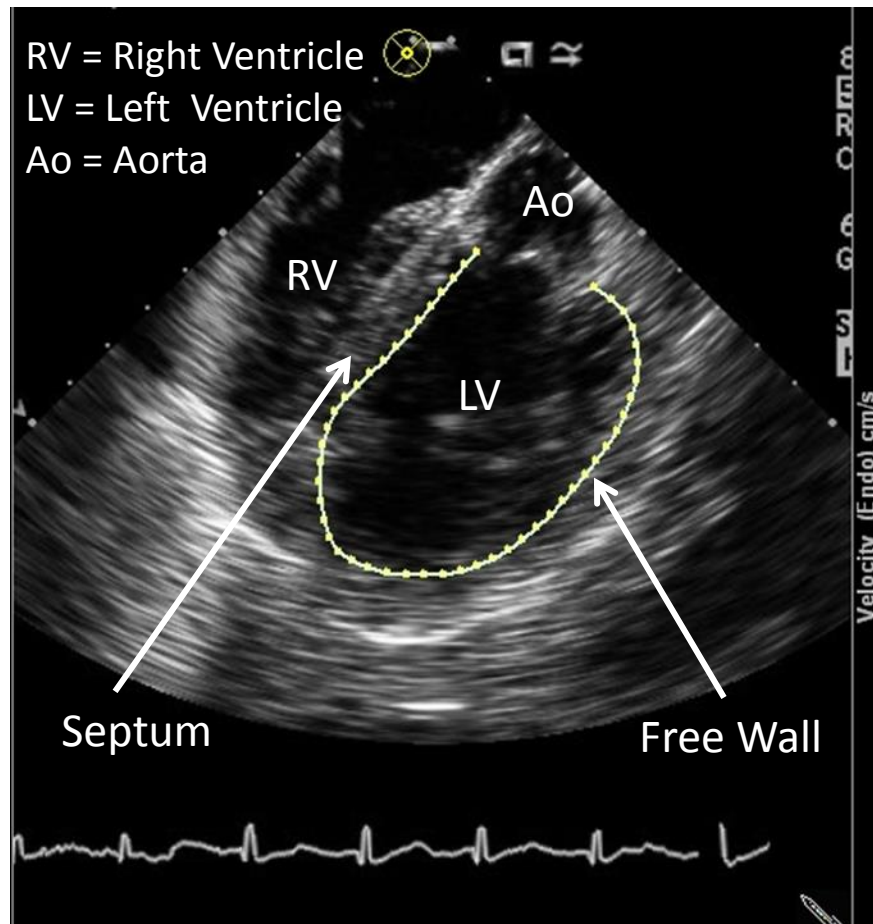


Figure 8 - This study used an intravascular echocardiography probe to capture left ventricular images. The above image is a characteristic view acquired with speckle tracking tracing along the endocardial border to compute tissue velocity, strain, and strain rate as indicators of myocardial function.

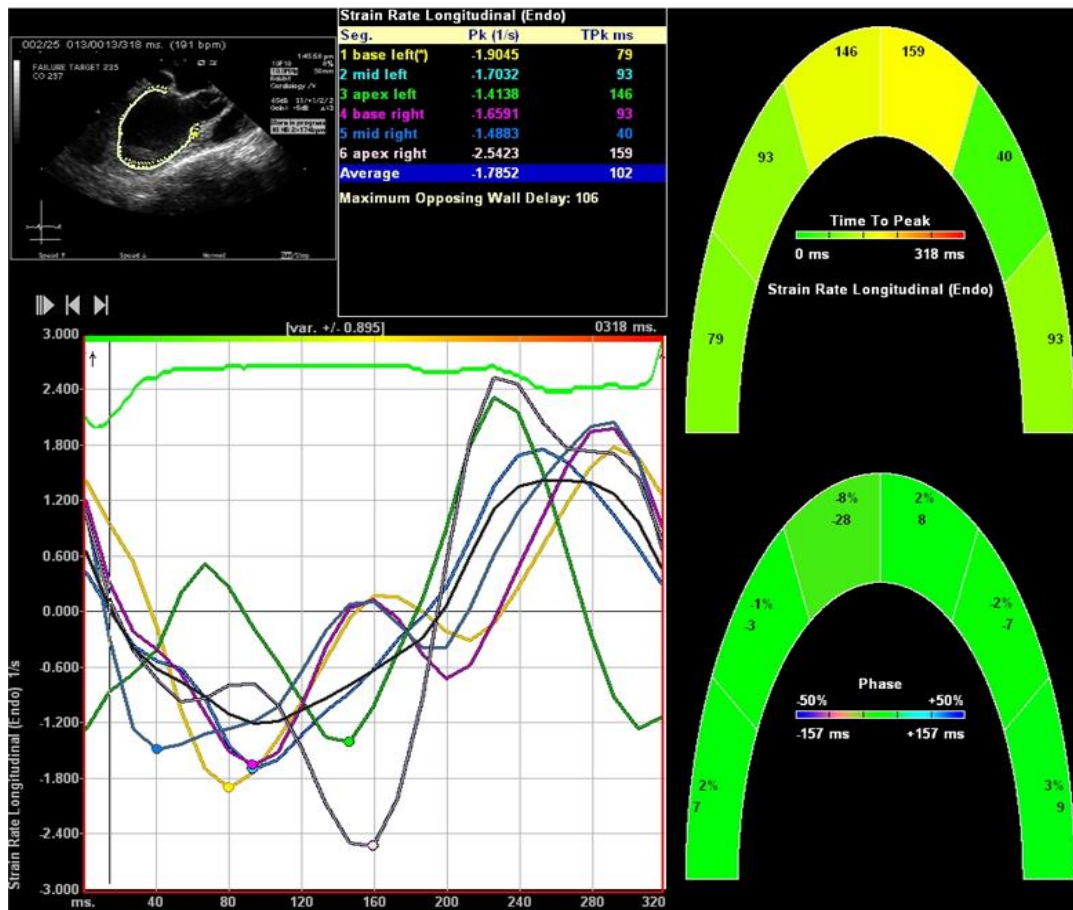
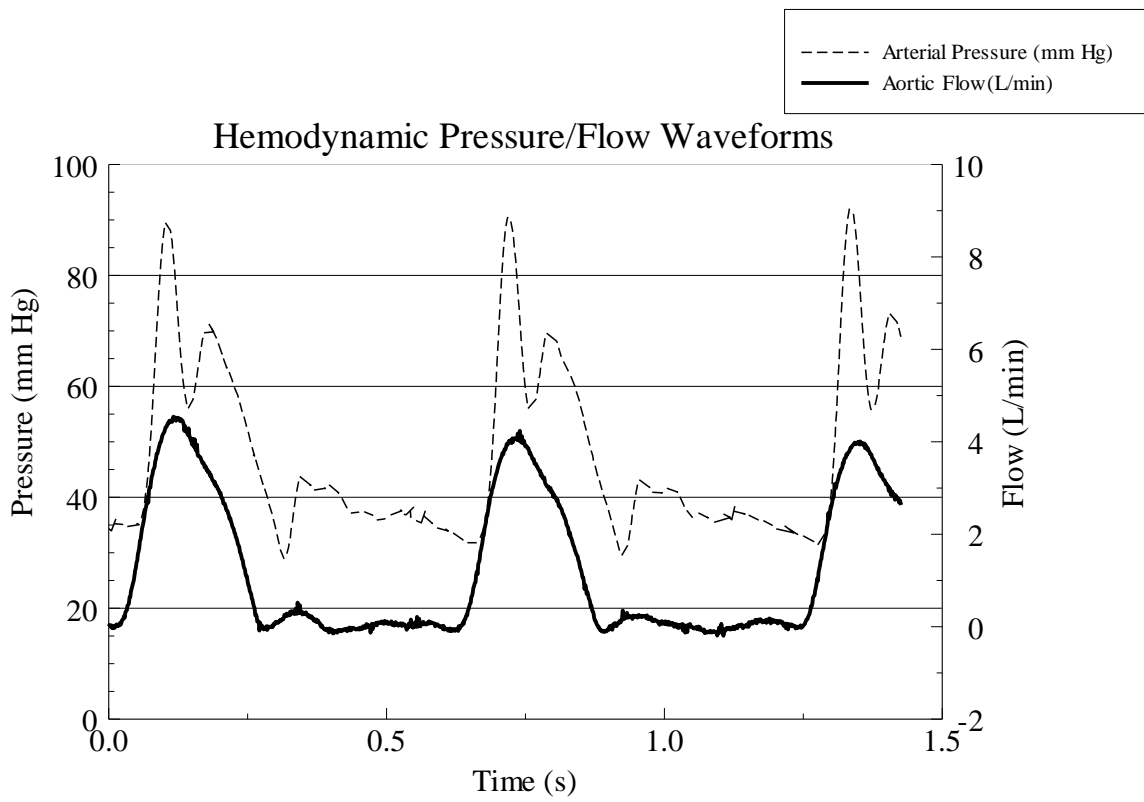


Figure 9 - Example VVI strain rate results after endocardial tracing. The heart was divided into six segments and the peak values in both systole and diastole were calculated. The averages of these six peaks (global peak strain rate) for systole and diastole were used as indicators of overall myocardial function.

III. RESULTS

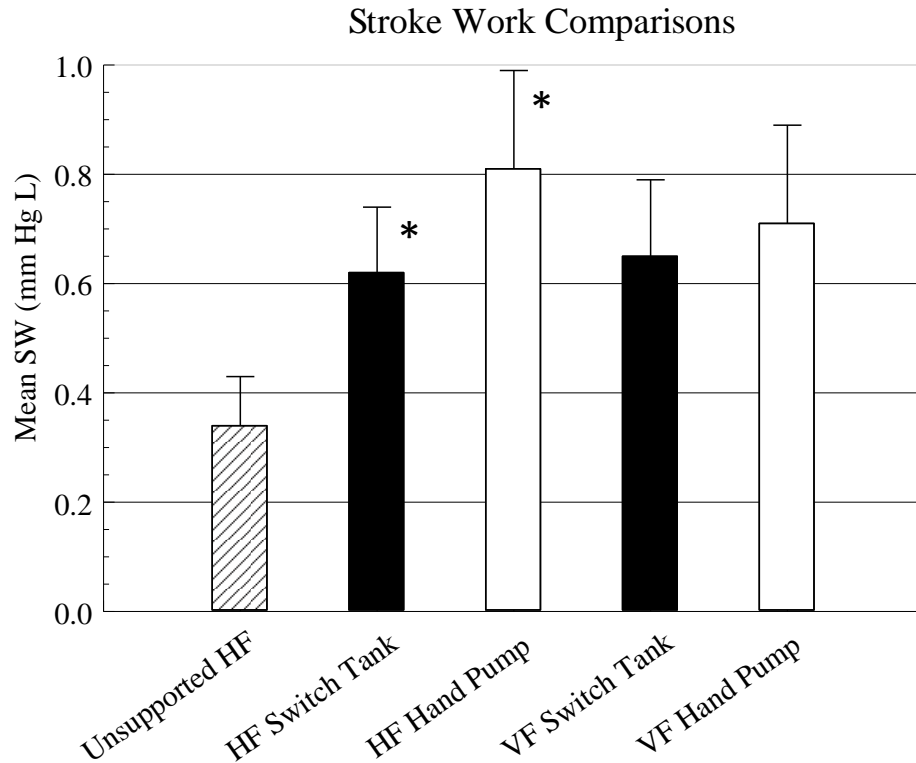
As a reminder, the main comparisons being made in this study are between the hand pump and switch tank in heart failure and the hand pump and switch tank in ventricular fibrillation. In this case, failure represents partial heart functionality while fibrillation represents negligible function (which is the reason for not including unsupported fibrillation in the results). Quantitatively, stroke work, representing overall pump function, and peak ECHO strain rates, representing myocardial function, were selected to demonstrate these comparisons.

The stroke work (computed from pressures and flows in Figure 10) data in Figure 11 shows no significant difference ($p > 0.05$) between the two drive systems in either separate failure or fibrillation comparisons while significantly higher ($p < 0.05$) values were obtained during supported failure compared to unsupported failure.²⁸



SW = Stroke Work, SV = Stroke Volume, MAP = Mean Arterial Pressure, CO = Cardiac Output, HR = Heart Rate

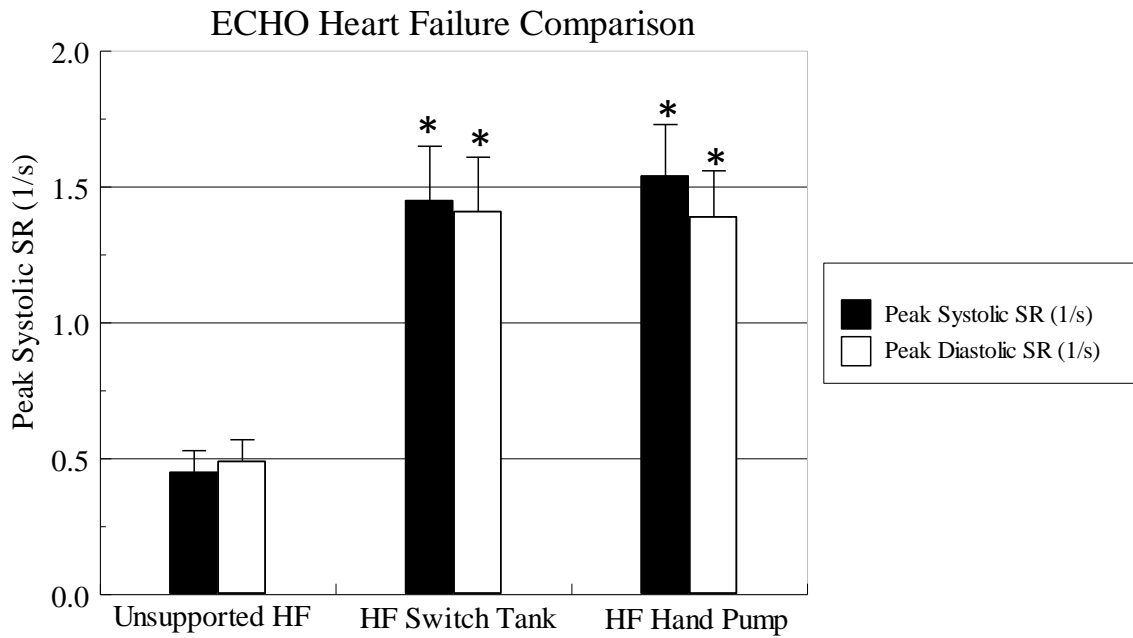
Figure 10 - Graph of representative arterial pressure (dashed line) and aortic flow (black line) waveforms. This data was used to compute the stroke work of the heart (product of mean arterial pressure and stroke volume).



*HF Support > HF Unsupported ($p < 0.05$); HF = Heart Failure, VF = Ventricular Fibrillation, SW = Stroke Work

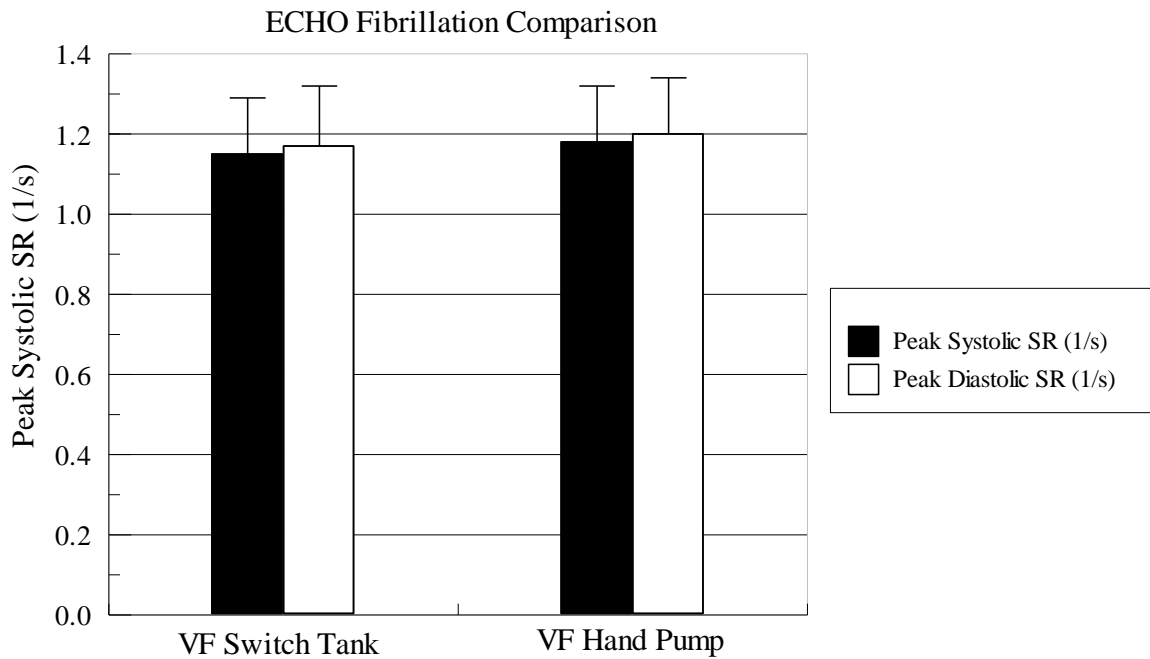
Figure 11 - Mean heart stroke work estimates for unsupported and supported heart failure and supported fibrillation. There was no significant difference between switch tank (black) and hand pump (white) support compared in either failure or fibrillation. There was a significant increase in stroke work during supported failure compared to unsupported failure (shaded).

ECHO strain rate data shows similar trends to that of stroke work. In comparing the two drive systems in both failure (Figure 12) and fibrillation (Figure 13), no significant differences ($p > 0.05$) were found between the switch tank and hand pump.¹⁷ This strain rate data was further divided into systolic and diastolic measures, also displaying non-significance when compared between drive systems. Support during failure (Figure 12) produced significant increases ($p < 0.05$) in max strain rates compared to unsupported failure.²⁸



*HF Support > HF Unsupported ($p < 0.05$); HF = Heart Failure, VF = Ventricular Fibrillation, SR = Strain Rate

Figure 12 - Peak global strain rate magnitudes for systole and diastole in the failing heart during non-support, switch tank support, and hand pump support. There was no significant difference in peak global strain rates when comparing the two drive systems during either systole or diastole. There was a significant increase in peak global strain rate during supported failure compared to unsupported failure.



HF = Heart Failure, VF = Ventricular Fibrillation, SR = Strain Rate

Figure 13 - Peak global strain rate magnitudes for systole and diastole during support of fibrillated hearts using the switch tank and hand pump drive systems. There was no significant difference in peak global strain rates when comparing the two drive systems in either systole or diastole.

DISCUSSION

ECHO interrogation has been a valuable tool that allows for a clinically-relevant assessment of device function.

Traditionally, ECHO imaging has been used to visually evaluate the heart structure and calculate estimates of key cardiac parameters such as ejection fraction, stroke volume, cardiac output and stroke work. Speckle tracking has opened up a whole new level of analysis in that tissue function can be evaluated directly.

The inclusion of both stroke work and ECHO strain rates was meant to create a bridge between traditional measures using pump function and cutting-edge measures using myocardial function. Pump function measurements are indicators of the heart's ability to circulate blood while myocardial measurements reflect cardiac muscular function, which are thought to be a more direct measure of cardiac health. Both variables (stroke work and global max strain rate) demonstrated predicted significant increases in supported failure. This demonstrates the utility of DMVA for

increasing circulatory function during heart failure (in line with previous work in small animal models).

It is important to note that the max pressure and rate settings being the same do not necessarily guarantee that the waveforms have the same shape. The different mechanisms of pneumatic support may alter the pressure dP/dt profiles in a significant manner without creating a functional difference in cardiac support.

The lack of difference between support provided by the two drive systems in either failure or fibrillation indicates a functional equivalency at approximately the same max pressure and rate settings. Given the advantages of a typical volume-regulated system (practical control features and compactness) it appears that an automated hand pump would provide the listed benefits without any significant performance degradation compared to the established switch tank system.

CONCLUSION

This study suggests that there is no significant difference between DMVA support provided by an established pressure-regulated switch tank and an experimental volume-regulated hand pump. Equivalency was established based on hemodynamic and cardiac wall motion comparison during support of severe failure and fibrillation using both drive systems. Given the lack of significant difference between the drive systems, the findings suggest that an automated drive system could be constructed that incorporates the hand pump and provides equal support to that of the switch tank.

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