A VIEW OF THE CARDIOVASCULAR DEVICE INDUSTRY

A Record of Study

by

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ABSTRACT

This record of study details the experience and the knowledge applied by an engineering doctoral candidate during two internships with two separate organizations in the cardiovascular device industry. The first internship was with an early startup company with a large focus in early research and design. The second was in a more mature organization with a focus in process control and increasing efficiencies.

The startup company provided the appropriate dynamic for applying engineering design methods such as generating customer requirements, generating product functional requirements, building a quality function deployment, and proposing a basic high level design approach. With the mature company the focus was on investigating procedural inefficiencies through root cause analysis and mitigating the inefficiencies through integrated software solutions.

The detailed accounts of these experiences provide a broad overview of the many challenges facing the cardiovascular device industry and the organizations involved. These accounts also illustrate the importance and value of engineering design principles and systems based engineering management in the industry.

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INTRODUCTION TO THE INDUSTRY

The cardiovascular device industry is, not unlike many other industries, in a slower than normal growth state as compared to figures over the past decade. With the regulatory burden continuing to increase and increasing pressures to reduce costs, the industry faces a significant number of challenges in the immediate future. Capital is now more difficult to come by than it has been in the past, therefore the number of successful startup companies has been limited. Pricing pressures continue to increase forcing companies to search for creative ways to market their products. In the face of all these pressures however, the demand for improved cardiovascular devices is unchanged.

According to a 2011 report from the American Heart Association (AHA), Cardiovascular Disease (CVD) accounted for 406,351 deaths in the United States in 2007; that figure equates to roughly 1 of every 6 deaths for the year. The report also estimated a cost of $286 Billion related to CVD and stroke in the United States. While new medical devices such as Ventricular Assist Devices (VADs) and Cardiac Rhythm Management (CRM) units have improved patient outcomes over the recent past, these devices are certainly not without their problems. There remains an unmet need for novel solutions for the treatment of heart failure.

ABOUT CORINNOVA

CorInnova Inc. is an early stage medical device company with a focus in device-based therapies for congestive heart failure. Founded in 2004 by Dr. John Criscione, Biomedical Engineering professor at Texas A&M University, CorInnova is developing a cardiac assist device and is currently in the early stages of product development. The company utilizes fully patented cardiac assist technology and is seeking further patents for other intellectual property. Mr. William Altman serves as Chief Executive Officer and is charged with developing the company's business strategy, building a team, and raising venture capital funds while Dr. Criscione serves as Chief Technology Officer overseeing product development and preclinical testing while maintaining involvement in all other aspects of the business. With just a handful of engineers working for the company, CorInnova seeks to introduce an innovative product to a highly complex and increasingly competitive cardiovascular assist device market.

With an early startup company, there is usually a great deal work to be done and not nearly enough people to accomplish it. From a strategic standpoint, the company was and continues to develop a portfolio of intellectual property centered around unique interventions for congestive heart failure. In an industry which has seen significant reductions in investment dollars, this puts CorInnova in a challenging position. The drastic differences between the company's unique therapeutic approach and those which have become more common practice both set the company apart from competitors and present a high level of risk due to regulatory uncertainties and inevitably large costs for human trials. Nevertheless, the therapy has produced promising results from animal

studies, and a number of advantages over current treatments put the company in a competitive position. The heart assist device which the therapy centers around can however use some improvement before. These improvements would serve both to expand the company's limited portfolio as well as present more attractive treatment technologies.

Market Overview

As the condition of patients with congestive heart failure worsens, the number of treatment options becomes more limited. In recent years, ventricular assist devices have gained traction, largely improving over first generation devices which featured a large number of moving parts which led to a high rate of mechanical failure. In addition to VADs, there are also multiple total artificial heart (TAH) devices available in the clinical environment with the CardioWest device from Syncardia having FDA approval as a bridge to transplant therapy. As discussed, these therapies are not without their limitations and improvements can certainly be made. A common feature between VADs and TAHs is that both devices are in direct contact with the patient's blood. VADs supplement the heart's ability to pump blood by pumping blood in parallel through inflow and outflow cannulas in peristaltic and continuous flow. TAH's require complete removal of the patient's failing heart and are directly linked to the patients' vena cava, pulmonary vein and artery, and the aorta. For both of these major treatment interventions, patients are administered potent anticoagulation drugs which reduce the risk of the patient forming blood clots in response to contact with the implant. These anti-clotting therapies can however lead to problems with forming clots at other

locations where they are needed. In the case of VADs that utilize continuous flow pumps

there is even evidence linking the treatment to the formation of clotting disorders

(Nicolini & Gherli 2009)

VADs and TAHs are viable alternatives for patients at end stage heart failure, but

other less drastic alternatives are gaining in popularity. Cardiac rhythm therapy (CRT)

has quickly emerged as a very effective treatment for patients suffering heart failure. By

pacing the atrium and ventricles in a synchronized rhythm, cardiac output can be

drastically improved and has even led to cardiac remodeling in some many cases such as

shown by Solomon et al. in Circulation (Solomon et al. 2010). The impact of CRT on

overall function however seems to lower as the patient reaches more advanced disease

states. These patients often have to turn toward other alternatives. Notwithstanding this

limitation, CRM therapy is quickly becoming a first line of treatment in the long struggle

against congestive heart failure. (Nicolini & Gherli 2009)

With most of the treatments and interventions discussed designed primarily to

help slow the progression or compensate for the effects of congestive heart failure, it is

important to consider the growing evidence of the heart's ability to remodel itself and

improve cardiac output in response to cardiac support treatment. As evident in the

previously mentioned Solomen et al. study for CRT, other therapies have seen similar

results. While the exact mechanism responsible for reverse remodeling is not well

understood, the key device attribute common to the phenomena is temporarily reducing

the load on cardiac muscle then following this support period with a gradual increase in

load until the support device can be removed completely thereby putting the complete load on the natural cardiac tissue. CorInnova's support therapy is largely based on the reverse remodeling phenomena. In contracts to VADs however, the CorInnova device features some key differences in design. The most prominent difference stems from the fact that the CorInnova device is not in contact with the patient's blood stream. Instead the device supports the heart from the outside of the heart. Before reviewing the design further, I thought it worthwhile to consider the problem in a more systematic form as commonly done in product development cycles.

Customer Needs

The first step in product development is generating a list of key customer requirements. Therefore using information collected from market research and clinical research we can clarify the important customer needs in both a clinical sense as well as a patient impact sense. We will first consider the clinical need. Cardiac output is a key measure of cardiac function and can be calculated as:

C.O. = S.V. x H.R.

where S.V. stands for stroke volume and H.R. stands for heart rate. The common CO observed in healthy patients is typically 5-6 liters/minute but in congestive heart failure these numbers can reach figures as low as 3 liters/minute in patients with congestive heart failure. The requirement to increase cardiac output for CHF patients is critical to improving patient conditions and quality of life. One challenge this requirement presents is that increasing cardiac output would put a large strain on heart muscle tissue,

myocardium. These cells are responsible for their individual contraction and as when aggregated the contraction of the 4 heart chambers the Right Atrium, Right Ventricle, Left Atrium, and Left Ventricle. With the limitation of cardiac output directly linked to the limited ability of myocardium to undertake increased pump loads, the device must increase cardiac output while also decreasing workload on myocardium. In close relation to these two requirements is the atrium and ventricle chamber contraction synchrony must also be enhanced, thereby improving the movement of blood between the chambers, hemodynamics. With atrial and ventricular contractions out of sync, the workload undertaken by myocardium would increase dramatically and leave cardiac output unchanged or even reduced.

While increasing cardiac output is a reasonably obvious need, it is worthwhile to consider the broader reason for this requirement. A brief statement describing the function of the heart can help in this respect. The heart is the body's blood pump which delivers blood to throughout the body which in turn delivers oxygen to the tissue while removing carbon dioxide through capillaries. The heart's right chambers also deliver blood to the lung capillaries in which carbon dioxide is removed from blood and oxygen is taken up by hemoglobin cells in the blood. In order to drive the delivery of blood to throughout the body, sufficient systemic blood pressure is required to improve tissue perfusion to firstly vital organs such as the brain and kidneys, and secondly to the rest of the body. Proper perfusion throughout the body would improve tissue oxygenation throughout allowing the patient to perform such seemingly trivial tasks as walking up and down the hall or sitting up in bed without placing a large strain on the body. Finally,

the patients' safety should always be considered top priority and the level of risk

associated with the treatment device must justify its utilization. Therefore the risk of life

threatening blood clotting must be limited on one hand but the risk of excessive bleeding

must be limited on the other.

From a patient perspective, there are a few things to consider in addition to the

clinical needs required to improve their medical condition. The invasiveness of the

implant and procedure must be limited for one. The less invasive the surgery, the better

chances the patient has of surviving the operation itself and the more attractive the

device becomes to the patient receiving the implant and the physician implanting it.

Recognizing the large portion of these patients in need of a bridge to transplant therapy,

two things are considered. Most obviously, there must be an explants procedure which

must also be limited in invasiveness as much as possible. But a more subtle requirement

is that the therapy must not risk the patient eligibility for a heart transplant. This further

emphasizes the need to balance clotting and bleeding risks since any adverse event of

that nature could compromise the patient's eligibility status. Patients and their families

seek options that not only improve their state of health but also improve their overall

quality of life, allowing them to resume a more normal lifestyle. So in addition to the

clinical benefits, the system should also allow for patient mobility within the hospital

and even outside the barriers of the hospital or a home care environment. Finally, there is

a wide range in age and size within the patient population and therefore the system must

be scalable to some extent to address limited implant real estate and the like.

From a more system approach and with consideration of the principal of reverse remodeling, the treatment system must allow for adjustable support. This would allow physicians the ability to fine tune support systems to maximally improve their patient's condition and after appropriate periods improved condition, follow up with a reduction in support. Even after the system is initially tuned to the patients needs, the level of support required can change either progressively or rapidly, therefore the system must have some intrinsic ability to automatically detect altered patient physical state and adjust its output appropriately. Finally, the proposed system must limit its power requirement to a level sustainable within a typical hospital room setting and, in light of the patient mobility need, sustainable for a reasonably sized battery.

Therefore in light of the needs discussed, we conclude with the customer requirements list as shown in Table 1.

Table 1. Customer Needs List.

Category	Description of Need
Clinical	Improve cardiac output (S.V. x H.R.)
Clinical	Decrease work load on myocardium.
Clinical	Improve synchrony of chamber contraction and thereby hemodynamics
Clinical	Improve systemic pressure & thereby tissue perfusion throughout body
Clinical	Keep Patient's heart transplant eligibility uncompromised.
Clinical	Keep patient free from risk as much as possible.
Clinical/Patient	Limit invasiveness of implant & explant procedures.
Patient	Allow for patient mobility.
Patient	Allow patient to resume a more normal lifestyle
Patient/System	Scalability of system size
System	Allow adjustment and variability of support output

Table 1. Continued.

Category	Description of Need
System	Respond to patient needs and changes in need
System	Limit the external power requirement to support device function

Function Set

With our list of customer requirements generated, we now move to a functional

approach through which we convert the customer requirements to a set of possible

functions to utilize in order to address these customer requirements. A further analysis of

the links between these functions and the customer needs is necessary but we must first

identify a comprehensive set of functions which the design could utilize. The functions

and system characteristics as listed in Table 2 are considered:

Table 2. Function/Characteristics of Design.

To Address Fundamental System Requirements	To Address Patient Requirements	To Address System Requirements
Pressure differential	Size of implanted device	Convert energy to pressure differential
Synchrony with cardiac rhythm and hemodynamics	Size of external subsystem	Transfer pressure differential to patient heart
Detection of atrial and ventricular contraction	Size of delivery mechanism	Alert patient of malfunction or damage
Post-ventricular blood pressure	Internal and external battery sizes	
Measurement of systemic oxygenation demand	Size of whole system	
	Steps required during operation	
	Scalability of system	

With this list of functions, I could move forward with a deeper analysis of the relationships between the customer needs and the device functions listed. To accomplish this task, I utilized traditional quality function deployment (QFD) technique as commonly applied in product development processes.

Quality Function Deployment

Before going over the QFD for this device, I felt it worthwhile to review the purpose and value of performing a QFD. A quality function deployment is a design tool used to both identify and quantify the relationships between system functions and the more generalized customer requirements. The calculations made in QFDs allow for the quantification of how different design functions align with or do not align with customer requirements. Additionally with as multiple design functions are linked to single customer requirements, a QFD can identify whether the design functions are in conflict, are in line with each other, or have no impact on each other. This clear identification and the quantification of key design elements allow for balancing the system design. Additionally some QFDs even consider competitive technologies and thereby help identify opportunities for novel approaches and solutions. Therefore the value of QFD can bring to the design process is considerable and well worth the effort especially for complex design undertakings such as cardiac support devices.

I started my QFD process with the competitive analysis using traditional ventricular assist devices, total artificial hearts, and cardiac rhythm management

therapies as the competitors. Figure 1 summarizes this analysis with respect to the

defined user requirements.

Row Number	Demanded Quality (a.k.a. "Customer Requirements" or "Whats")	Weight / Importance	Relative Weight	Competitive Analysis (0=Worst, 5=Best)				
				CorInnova Product	Traditional VAD	Artificial Heart	Cardiac Rhythem Management	
1	Improve cardiac output (S.V. x H.R.)	10	10.53	4	5	3	2	
2	Decrease work load on myocardium.	10	10.53	4	4		2	
3	Improve synchrony of chamber contraction	10	10.53	2	2		5	
4	Improve systemic pressure & tissue perfusion	10	10.53	4	4	3	2	
5	Limit risk of clotting	8	8.42	4	2	2	4	
6	Limit risk of excessive bleeding	8	8.42	4	2	2	4	
7	Allow for patient mobility	5	5.26	4	1	1	3	
8	Allow patient to resume a more normal lifestyle	5	5.26	4	1	1	3	
9	Scalability of system size	6	6.32	4	4	1	4	
10	Allow adjustment and variability of support output	8	8.42	4	4	2	4	
11	Respond to patient needs and changes in need	8	8.42	4	3	3	4	
12	Limit the power requirements	7	7.37	3	2	2	5	

Figure 1. QFD – Competitive Analysis

The QFD allows for prioritizing customer requirements as well and for this

competitive analysis segment, allows for identifying opportunities in the competitive

landscape. Without going into a great deal of detail, we can see that while competitive

therapies can address cardiac output and load reduction requirements, the risk to the

patient for clotting or bleeding complications tends to increase. The advantage of

significantly limiting the risk of clotting and bleeding through the fact that CorInnova's

device does not come into contact with the patient's blood stream rather it delivers

support while remaining external to the heart. Another disadvantage of the competitive

solutions is that current technologies keep patients significantly limited in their ability to

be mobile and live normal lives. Most VADs require percutaneous lines which keep patients tethered to external control systems. The same holds true for artificial heart solutions. For this design problem the patients considered would face later stages of heart failure and therefore CRT does not score well in most of the requirements listed with the exception of improving synchrony. Therefore the opportunities in the competitive landscape present themselves around limited complication risk therapies which allow significant patient mobility. I continued with the functional relationships with the customer requirements. This is a bit more involved so I will not describe every detail but rather focus on more general observations.

A number of observations can be made in this section of the QFD. The relationship between our customer requirements and the functions listed as shown in Figure 2, allows us to generate a relative requirement weight for each of the functions or design aspects considered. We see that the conversion of energy to a pressure differential is the design aspect with the highest weight while transferring the pressure differential to the heart is a close second. Synchronizing the heart, increasing post-ventricular pressure, and the pressure differential itself were not unsurprisingly high in weight the steps required during operation and the internal battery size were of small weight by comparison.

Figure 2. QFD – Functional Relationships with Customer Requirements.

Column Number	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18
Max Relationship Value in Column	9	9	9	9	9	9	3	9	9	3	9	9	9	1	9	9	9	9
Requirement Weight	375.8	447.4	314.7	398.9	274.7	118.9	114.7	226.3	234.7	36.84	217.9	47.37	16.84	73.68	97.89	525.3	451.6	47.37
Relative Weight	9.35	11.13	7.83	9.92	6.83	2.96	2.85	5.63	5.84	0.92	5.42	1.18	0.42	1.83	2.43	13.06	11.23	1.18
Difficulty (0=Easy to Accomplish, 10=Extremely)	6	10	8	8	8	1	7	7	10	8	9	7	9	6	3	10	10	7
Minimize (▼), Maximize (▲), or Target (x)	x	▲	▲	x	▲	▼	x	▼	▼	▼	▼	▼	▼	▼	▲	▲	▲	x

Quality Characteristics (a.k.a. "Functional Requirements" or "Hows"):
1. Pressure Differential
2. Synchrony with cardiac rhythm and hemodynamics
3. Detection of atrial and ventricular contraction
4. Post-ventricular blood pressure
5. Measurement of systemic demand
6. Surface area in contact with blood
7. Surface area in contact with heart
8. Size of implanted device
9. Size of external system
10. Internal battery size
11. External battery size
12. Complexity of maintenance
13. Steps required during operation
14. Size of Delivery mechanism
15. Scalability of system
16. Convert energy to pressure differential
17. Transfer differential to patient heart
18. Alert patient of malfunction or damage

Row Number	Max Relationship Value in Row	Relative Weight	Demanded Quality (a.k.a. "Customer Requirements" or "Whats")	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18
1	9	10.53	Improve cardiac output (S.V. x H.R.)	9	9	3	9			3	9								9	9	
2	9	10.53	Decrease work load on myocardium.	9	9	3	3			3	3								9	9	
3	9	10.53	Improve synchrony of chamber contraction		9	9	3	1											1	1	
4	9	10.53	Improve systemic pressure & tissue perfusion	9	9	3	9	9											3	3	
5	9	8.42	Limit risk of clotting	3	3	1	3		9	1	1					1	1			1	
6	9	8.42	Limit risk of excessive bleeding	3	1	1	9									1	1				
7	9	5.26	Allow for patient mobility	1	1		3	1			1	9	1	9				1	9	3	
8	9	5.26	Allow patient to resume a more normal lifestyle	1	1		3	1			1	9	1	9	9			1	9	9	9
9	9	6.32	Scalability of system size	1			1		3	3	9	9	3	9			9	9	9	9	
10	9	8.42	Allow adjustment and variability of support output	1	1	3		9	1	1	1	1									
11	9	8.42	Respond to patient needs and changes in need	1	1	9		9	1	1	1	1						1	9	3	
12	9	7.37	Limit the power requirements	1	1	1	1	1	1	1	1	9	1	9				3	9	9	

The final portion of the quality function deployment is commonly referred to as the roof and it characterizes the correlations between the design functions and characteristics. Figure 3 illustrates the contents of the so called roof for our design problem in table form.

Row Number	Quality Characteristics (a.k.a. "Functional Requirements" or "Hows")	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18
1	Pressure Differential																		
2	Synchrony with cardiac rhythm and hemodynamics	•																	
3	Detection of atrial and venctricular contraction		•																
4	Post-ventricular blood pressure	•	•																
5	Measurement of systemic demand			•	•														
6	Surface area in contact with blood																		
7	Surface area in contact with heart	•		•	•		•												
8	Size of implanted device	•		•		•		•											
9	Size of external system	•		•		•			•										
10	Internal battery size			•		•			•										
11	External battery size			•		•				•									
12	Complexity of maintenance					•													
13	Steps required during operation												•						
14	Size of Delivery mechanism								•			•							
15	Scalability of system	-							•	-	-	-	-		-				
16	Convert energy to pressure differential	•			•			•	•	•			•		-	-			
17	Transfer differential to patient heart	•	•	•	•			•	•	•			•			-	•		
18	Alert patient of malfunction or damage			•					-	-			-	-		-	•	•	

Figure 3. QFD – Cross-Functional Interactions.

Here we can see that the transfer of differential pressure to the patient heart has a large amount of correlations, making this design aspect crucial for the success of the overall product design. Detecting atrial and ventricular contractions, the size of the

implanted device, and the conversion of energy to the pressure differential also have a number of correlations with other design aspects.

After applying the QFD method to CorInnova's design challenge, a number of key design functions were identified one of which I would investigate in greater detail. The fundamental customer requirement key for both setting the therapy apart and improving market interest and general reception of such a different and unique therapy was the requirement to allow for patient mobility and a lifestyle closer to normal.

Sub-System Design

The CorInnova device would need to offer a fully implantable system with external power support or battery packs as needed. In light of the inefficiencies of transcutaneous energy transfer systems, the system would limit its utilization of TETS technology for direct pressure driving purposes as is common in other fully implantable approaches. For initial acute animal studies, the proposed system would have 2 subsystems, one to be implanted and partially in direct contact with the epicardium or the outer tissue of the heart, and the other to be external to the patient but linked to the internal system through a proprietary transcutaneous driver system. While the driver system design addresses the function of driving a pressure differential, there is one key function missing. That is the function of measuring and detecting the natural rhythm of the heart is left ill-defined. As shown in our QFD, the detection of the natural heart rhythm is essential for providing dynamic support which is also in synchrony with the patient intrinsic pacing mechanisms. Therefore to ensure the system works with the

patient's heart and not against it, there needs to be a system for measuring the natural rhythm and communicating this rhythm with the main pressure driver – the external subsystem. With a strict elimination of any percutaneous wiring or tubing, the signal would have to be communicated wirelessly. Surface ECGs were briefly considered but the significant level of interference from electro-myogram potentials (EMG) would lead to possible misrepresentations, leading to over-stimulation or inactivation when required.

The proposed system would therefore take advantage of stronger signals measured at the epicardium. These signals would be free of EMG interference and not as vulnerable to surface electrode placement and movement related errors as is a concern in moving patients. The system would also communicate an appropriate trigger signal to the external pressure driver in a manner sufficient as to allow the driver to activate and transfer the pressure to pressure cuff placed around the heart, thus supporting heart pump function in a synchronous fashion. In simple terms, the system would have to detect and send a signal for the beginning of the heart beat in time for the pressure driver to receive the signal and apply the pressure back inside the patient when the ventricle begins to contract or just thereafter.
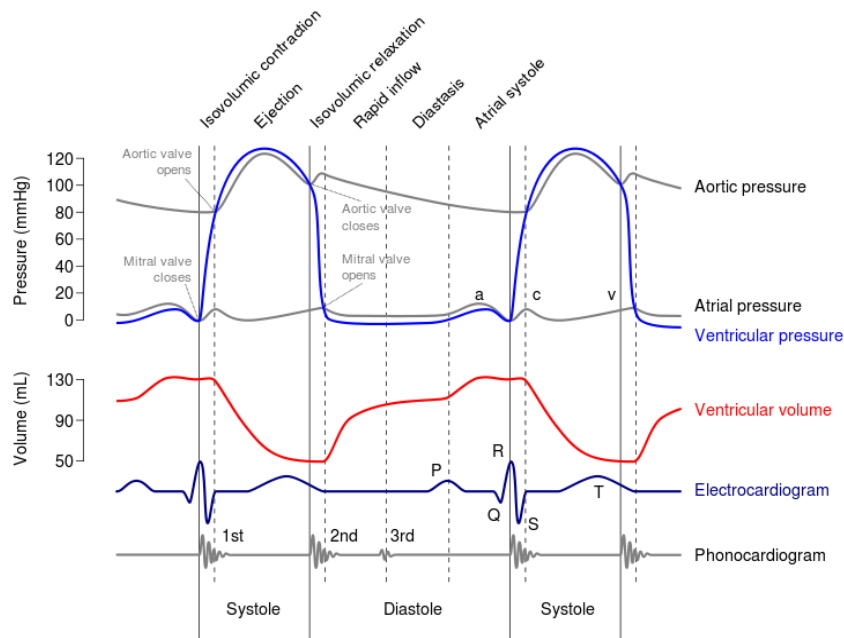
Figure 4. Wiggers Diagram
*Reprinted from "Wiggers Diagram.png" by Daniel Chang, MD, DestinyQX, and xavax, 2012. *Wikipedia*, Copyright 2012 by Creative Commons

To get a better understanding for the timing requirement, let us review the electromechanical aspects of the heart. One very useful tool first which I was first introduced to in a Cardiac Mechanics course is the Wiggers diagram such as shown in Figure 4. The ECG is a very useful measure of the electrical activity in the heart, but with the heart being an electromechanical system the ECG also holds a great deal of mechanical information. A normal cardiac cycle begins with atrial contraction which starts with an electrical action potential at the sinoatrial node located at the top of the right atrium. As the signal propagates in the atrium along the myocardium, the atrial chamber contracts, first increasing pressure within the atrium and then forcing the valve

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open between the atrium and ventricle, delivering blood into the ventricle. As this is happening the electrical signal makes its way to the atrioventricular node which slows the signal allowing the atrium to eject blood into the ventricles. Then the signal continues to propagate into first the bundle branches along the septum or the inner ventricular wall, then spreading through the Perkinje fibers to the outer walls of the ventricles. While the electrical signal starts near the right atrium it is carried to the left atrium through Bachmann's bundle and to the left ventricle through the left bundle branches. Although slightly delayed in relation to the right atrium and right ventricle, the left atrium and left ventricle follow the same contraction pattern.

The Wiggers diagram illustrates the interrelationship between ECG propagation and atrial and ventricular contractions by plotting the pressure inside the left ventricle, the left atrium, and the aorta. Chamber volumes are also plotted along with a plot of the audible sound of valves closing in some cases such as in the one shown in figure. Looking at a typical 60 beat per minute ECG signal, the start of atrial contraction as denoted by the start of the P-wave and the start of ventricular contraction as signaled by the beginning of the R peak in the QRS segment complex are only separated by roughly 120-200 ms. This small window is the maximum time which our system can take to detect the p-wave, transmit the trigger signal, receive the trigger signal at the pressure driver, and apply the pressure differential at the epicedium through the pressure cuff.

Functional Breakdown

The function of the ECG trigger mechanism as proposed can be broken into three high level functions. The subsystem must detect the action potential at the SA node, transmit the trigger signal, and receive the signal at the external driver control subsystem. Detecting the action potential can be accomplished in a fairly straightforward way using a sensor or electrical lead, and an analog circuit to detect the voltage differential between the lead placed near the SA node and some other reference point such as another lead at the apex of the pressure cuff. The analog measurement can be taken by differential amplifiers, however, because of the small scale differences in potential, specialized operational amplifiers are often utilized in ECG applications. Typically, ECG signal amplitudes are in the single mV range with a typical DC offset two to three magnitudes higher. Luckily, there are a number of operational amplifiers with characteristics tuned specifically for such signal detection.

The second function of transferring a trigger signal wirelessly presents three challenges. First the analog signal coming from the AFE needs to be digitized. After the digital signal is encoded in the chosen format, the signal must then be passed to a wireless communication circuit which then sends the wireless signal. The signal is then received, decoded, and relayed to the pressure activation control circuit. With advancements in radiofrequency technologies, there are RF transceiver chips now available which can encode, transmit, and receive RF signals. The added challenge in our case is the fact that the transmitting chip will actually be implanted into the patient. The RF signal must then be able to penetrate the patient's tissue and do so in a manner

that does not put the patient at risk from overheating but also does not risk the integrity of the signal.

As mentioned above, the analog signal must be digitized. This digital conversion is commonly accomplished by microcontrollers with embedded analog to digital converters. The microcontroller must be programmed to interpret the analog signal appropriately, thereby producing the preferred digital signal to be relayed to the communication circuit or chip.

Finally, with all functions accounted for through the AFE, the microcontroller, and the transceiver chips, the components must be interconnected into one system. The function of integrating these components can be accomplished through the use of smart boards which provide a hardware platform on which to interconnect the functional components. Smart boards also manage power consumption which in our case would come from an internal battery source.

Limitations

The proposed design approach is feasible and, through the utilization of standard communication protocols and commercially available components, can be relatively in-expense to create. However, the application of the proposed system being of life-threatening nature, would almost certainly require a continuous RF signal to be transmitted. This requirement would be a tremendous limitation to the life of the implanted system. Therefore a recharging system would be essential for long-term applications. While a limited life system would be sufficient for acute animal studies, a

recharging mechanism or a different approach altogether would be necessary for a human implant application. Recharging circuits direct our attention back to TETS technologies which we were trying to avoid. However, when we compare the use of TETS in our design approach versus that of many other fully implantable approaches, there is a significant difference in our use. With our approach, the pressure driving circuit remains outside of the patient, therefore the TETS system would only be required to recharge the ECG trigger communication circuit rather than supporting the pressure driving circuit as well. This system would consume much less power than a complete support system. So although we cannot fully abandon TETS technology, the way in which we apply it places this inefficient technology in a much lower risk area. Thus our application decouples it from the primary device objective of applying pressure to the heart.

Though plans were in place to move forward with a prototype, the battery life limitation and the complexity of the system along with the consideration of our limited experience in this type of application, CorInnova was led to consider different solutions which are still under investigation. Unfortunately, my experience at CorInnova was cut short of my originally planned duration when an opportunity to work with a more established and experienced company presented itself. Given the uncertainties surrounding the future of such a young company, I made the decision to work for Biotronik, a leading company in the cardiac rhythm management market.

ABOUT BIOTRONIK

Biotronik is one of the leading manufacturers of electronically active implants for the cardiovascular field. Considered among the top competitors, Biotronik continues to gain market shares in Europe as well as in the United States. One notable difference at Biotronik is that the company is privately owned as opposed to the publically traded companies at the top of the list such as Medtronic, St. Jude Medical, and Boston Scientific. While capital may be limited at times for the low key company, its private ownership allows flexibility unmatched by any publically traded organization. Led by the visionary leadership of Dr. Max Schaldach, son of co-founder Max Schaldach, the company has continued to deliver high quality devices for over 30 years, pioneering key innovations such as fractal coating which was considered a breakthrough in lead performance.

Although small with just over 5000 employees worldwide, Biotronik is represented in over 100 countries. With a vertically integrated approach to product development, Biotronik has subsidiaries manufacturing device components such as leads, batteries, and headers as well as the complex electronic modules which device output. The modules development takes place in two key manufacturing and development centers. One is located in Berlin, Germany and is directly linked to the worldwide headquarters while the other is located in Lake Oswego, Oregon and forms the subsidiary company of Micro Systems Engineering, Inc (MSEI). All device components are shipped to Berlin, where final product assembly takes place, however a large portion of the development takes place right here in the United States.

Although, Biotronik and its subsidiaries have a great deal of flexibility regarding vision and leadership, the same regulations for both for both the financial and clinical aspects apply as they do for the larger corporations. For MSEI in particular, in the financial realm accountants and financial controllers ensure the company follows generally accepted accounting principles (GAP) and reports their annual income on which they pay taxes to the internal revenue service (IRS). In the clinical and device design functions, MSEI must also comply with regulatory requirements such as requirements from the FDA or the European Commission to get products out to market. With electronically active implantable medical devices of the CRM nature having such direct impact on the life-sustaining function of the heart, CRM devices are considered Class III medical devices by the FDA and Class A medical devices by the EU. These classes of medical devices face the utmost scrutiny and the bar continues to be raised in an effort to ensure the quality of the devices making it to market and being implanted in patients.

For engineering design, the key regulatory requirement is to establish a quality system in compliance with 21CFR820 for FDA compliance and ISO 13485 for EU compliance. The primary impact on design is the requirement to set and continually follow appropriate design controls from initial market needs definition all the way through to the first product sale in the clinical field.

For many medical device companies the responsibility of ensuring product design efforts follow the appropriate processes falls to the design team for each of their

respective areas of concentration and to program managers who ensure the aggregate design effort for the product as a whole is in compliance with the established policies. Quality however is just one aspect of program management. Additionally program managers (PMs) are responsible for driving the design effort, projecting costs along the way, solving technical problems that arise and finally controlling design project outcomes and costs. With an incredible portion of product costs stemming from the design effort costs which are spent long before the first product sale, it is vital that projects come within budget and, of equal importance, within schedule. The final responsibility of PM is to ensure that the final product design meets customer needs as defined by the customer requirement scope. With the length and complexity of meeting scope requirements directly linked to the duration and cost of the design effort required, PMs have to balance the set of requirements with the schedule and available resources to ensure all stakeholders are satisfied and confident in the product feature set. PMs are those responsible for ensuring the design effort meets the established customer requirements, the established control policies and the estimates cost and schedule targets.

For single projects, these functions are exactly those of a project manager. When these responsibilities extend across multiple projects often sharing resources (equipment, dollars, and staff) it is considered program management according to the Program Management Book of Knowledge printed by the Program Management Institute.

With MSEI involved in a number of such complex product design efforts, the program management office is vital to the success of the organization both within MSEI

and extending to the Biotronik family of companies altogether. With program management so closely related to company spending in R&D company, as most R&D company spending revolves around the product development efforts. It is only natural that the PM team also be responsible for established the overall budget for the foreseeable future. Hence, MSEI formed the Budget & Program Management team which consisted of four highly experienced and knowledgeable engineers directed by the department's director, Andreas Gute.

Problem Statement

I was lucky enough the join the Budget and Program management team as an intern and was given information regarding a number of possible internship projects from which to pursue. One particularly caught my interest partly because it seemed to compliment my knowledge and experience very well. In addition to the aligned interests, this project was given high priority with direct visibility for senior management. With such high visibility and such high impact on the organization it was given first priority. To better understand the nature of the problem let us review the basic problem definition. In simple terms the integration between program management and financial management software systems was poor. This forced a number of inconsistencies between financial reports and program management reports, which forced many complex reports to be manually created using information from a number of sources. Not surprisingly, there were often mistakes in data entry due in large part to the heavy use of manual data input. These mistakes forced accounting and financial controlling staff to spend a large amount of their time to make sense of input from all these sources

and tracking down any inconsistencies. While the problem persists in many areas, the most crucial problem was observed in its impact on the program cost forecast and the financial forecast for the entire MSEI company.

In light of this fact, it quickly became apparent why the project was given such high priority. As a subsidiary of an international organization, not unlike most subsidiaries, MSEI must come up with a forecast of future costs which then determine their annual budget after senior management review and approval. As miscue in these figures could lead to mistakes in budget setting, therefore any and all measures, including many hours of tracking down inconsistencies, were taken to ensure the accuracy of the numbers requested.

Root Cause Analysis

My first step was to find the root cause of possible errors and I was lucky enough to find an example of freshly observed errors having been pointed out the week before my internship started. The problem observed was simply that financial report figures and PM system report figures were not matching up. I was to figure out why there were not matching up and resolve the problem within a few weeks to ensure proper budget entry reporting for the coming budget request cycle. For financial and accounting questions, I had my finance team, for program management questions I had my department, and for technical questions, I had support staff from our program management software system as well as for our financial software system. I would start by comparing the two reports

which were labeled as inconsistent and checking whether there were true errors or the problem stemmed from miscommunication or data.

A closer look at the nature of these reports revealed a few key reporting practices which could account for part of the misunderstanding. The financial report which I'll refer to as Report A consisted of a list of active projects for which actual costs and/or forecasted costs exist which are expected to be spent before year end. With the numbers not clearly separated for spend versus future estimate, it could not be distinguished how much had already been spent with Report A alone. The program management report which I'll refer to as Report B was a comprehensive report of all program management budget entries for all projects under the entire program management software system. Therefore Report B had much more detail than Report A, but the totals reported in Report B for all projects was expected to match the totals reported for Report A. This was not the case however.

The information that was entered into Report A was the responsibility of our accounting and financial controlling staff. As with any other major financial reports, this data was carefully collected and quite often took several days, if not weeks, of work to compile. I spent a large amount of time with our accounting staff to better understand their input and the work it took to get this data. As expected there was no flaw in the final results of their data collection, though the nature of their process to gather the numbers was inconsistent and quite often highly inefficient. Actual costs were collected directly from the financial system and could be identified to each of the projects for

which they were incurred. Forecasted costs on the other hand were collected from the MSEI program management staff in the form of a number of spreadsheets. This process seemed fairly simple and was only complicated in cases where program managers made last minute changes to their forecast. The addition of the program management system however quickly complicates matters.

The program management system utilized at MSEI is the system used throughout the Biotronik product development and manufacturing entities. It is a robust system which supports a large number of users spread throughout the world, and it is used not only for project timelines and cost planning, but also for employee time reporting throughout Biotronik. While the system features a large number of capabilities in its own right, the system must also be interconnected with the financial system for functions such as purchasing material against a project or charging employee labor costs to the project. With respect to the forecast report, Report B, it is based on a report template which pulls cost information from the entire system database which includes all active projects in the system. The data is collected directly from the program planning tools which is where PM staff update project schedules and expense projections. To identify company specific expenses such as those for MSEI, an organization code is included in the report. Finally, the report makes one very important assumption. That is the report assumes PM staff update the planning on a monthly basis including the reconciliation of actual costs in the planning tool. This assumption very quickly raised a red flag in my review and it quickly became apparent that the assumption was in most cases incorrect.

Therefore with the assumed actual expenses in Report B not equaling the actual expenses incurred through the financial system included in Report A, the two reports would simply never agree with each other. With the reconciliation of actual costs in the planner placing such a considerable burden PM staff for reasons beyond the scope of my project, the cause was communicated to senior management and the limitation was accepted. Therefore actual costs and forecasted costs would be separated in Report A and it would be understood that only the forecast numbers from Report A and Report B would be consistent.

While this revelation accounted for some of the smaller scale differences between report numbers there was still a large number discrepancy between the two reports, with Report A totals being considerably higher than Report B totals. Our finance team soon revealed the exclusion of administrative or overhead expenses in the program management system. With the PM system viewed as a purely project related system, it was assumed that overhead expenses would be omitted from the system. To make up for the large discrepancy, it was quickly decided that overhead expenses be included in the PM system for the sake of consistency across financial and program management system forecast figures.

With the root causes of the observed inconsistencies identified and a clear plan in place for the immediate forecast cycle, my short term objective was successfully completed, though my work was just getting started.

Automation of Data Transfer

The next undertaking would be to automate the transfer of forecast data from the PM software system to the financial software system. I again gathered insight from each of the parties at my disposal and mapped the flow of information between systems. I was quickly reminded of the large amount of manual data entry throughout the process which reiterated the importance of automating the data transfer between the systems. Figure 5 below illustrates the flow of information required to put together a comprehensive budget for MSEI. This particular view shows a clear separation between the software systems utilized including the financial and program management systems but also a number of MS excel spreadsheets.
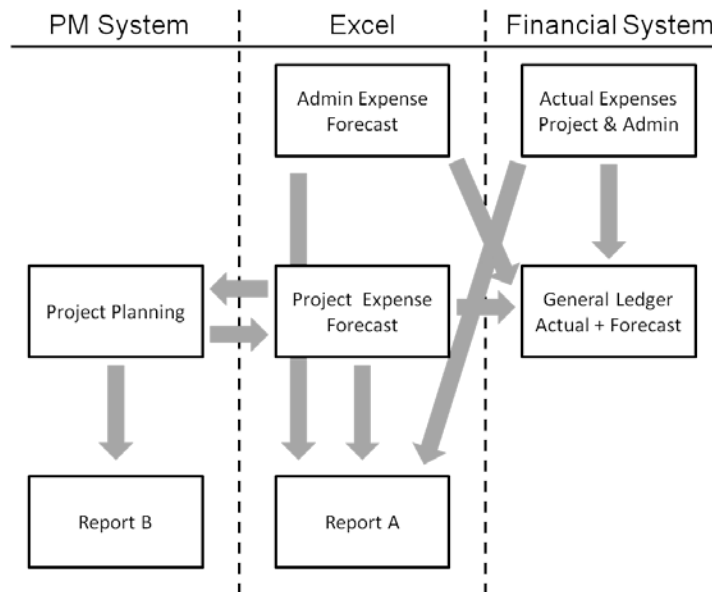

Figure 5. Data Flow Diagram.

Starting with the excel spreadsheets containing project related expenses, these provide data to be entered into the program management system as well as the data to be entered in the financial system and Report A. In the PM system the data was entered in the planning tools for the affected projects while in the financial system, the data was entered in the affected cost accounts. Once this data is entered in the program management system, the project expense forecast would then show up in Report B. For the administrative related expense forecast, the data comes from the financial system since the forecast is largely based on incurred expenses during previous periods. Prior to the decision of including administrative expense forecasts in the program management system, the data related to these administrative costs was only entered directly into Report A. Lastly, actual expenses as shown in the financial system would be entered into Report A, but would not in the planner tool within the PM system. The proposed changes to the data flow would include administrative related forecasts in the PM system and as a measure toward eliminating error all forecast data included in the Report A would originate from the PM System. This would assure that the forecast figures shown in Report A would match the forecast figures in the PM system and as shown in Report B. For the actual costs, it was understood and accepted for the time being that they would not be reconciled in the PM system and therefore would not match the numbers from Report A. To further illustrate this point and to provide additional information, the actual costs and the forecasted costs would be separated in Report A. After these changes were implemented, the data flow would change to that shown in figure 6. With

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an agreed upon plan in place, the technical work could begin toward forming a working

automation solution.
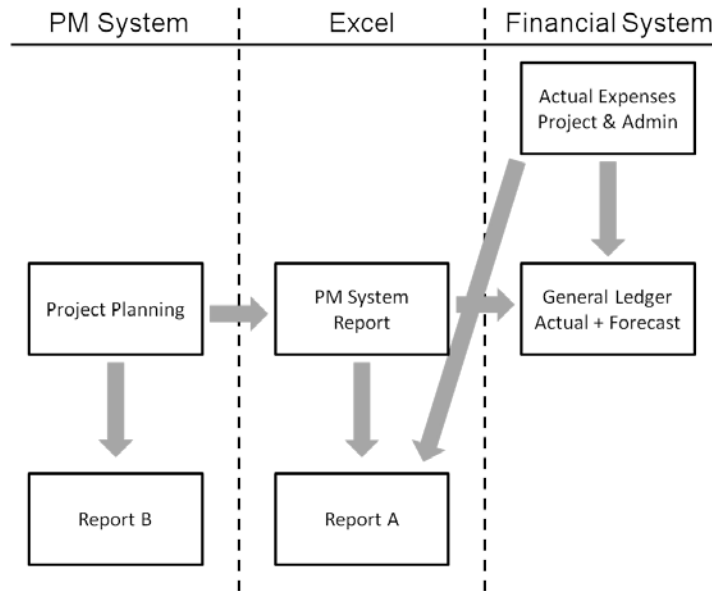
Figure 6. Improved Data Flow Diagram.

For the automation of data transfer, a number of solutions were considered as

shown in the Table 3 below. The solutions considered can be described as follows:

1. Using an intermediate MS Access database and a few report variants to pass
   data between the systems

2. Using MS Excel VB scripting coupled with PM system reports to generate
   files that can be imported into the financial system

3. Using a 3rd party system integration tool to pass data between the two
   systems automatically

4.   Using system integration tools built in to the existing systems to set up direct communication between the two.

Table 3. Decision Matrix

Requirement/Attribute	wt.	MS Access Database	MS Excel VBA	System Integration tool	Direct system communication
Read data from source	3	3	3	4	5
Interpret data	5	5	5	5	5
Calculate data	5	5	5	5	5
Deliver data to destination	3	3	3	4	4
Ease of Use	3	2	4	4	5
Resources required	5	3	5	1	1
Maintenance	5	1	4	1	1
Complexity	4	2	5	1	2
Total Score		102	**145**	100	110

Largely due to its small level of resource requirements, maintenance, and complexity level as compared to the other solutions, the solution based on Excel Visual Basic Script was chosen for its simplicity and low maintenance nature. Programming the systems to communicate directly was a close second but its heavy resource requirements and the likely maintenance costs made it less attractive.

With the approach decided upon, my next step in creating a solution was to break up the programming requirements into the major coding functions required to deliver the

required output. This high level breakdown shown in Figure 7 would serve as an outline for code development.
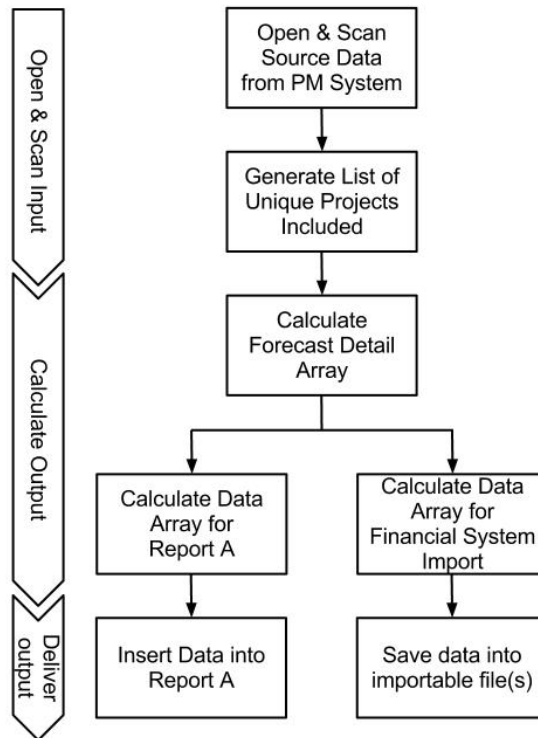
Figure 7. High Level Breakdown of Script Functions.

As used to compare the functional advantages for each of the solutions considered, the function of the script can be broken into the three sections of opening and scanning the input, calculating the output, and then delivering the output in a usable form. For the first section, the script was to open and scan the source data then generate a list of unique projects included in the source data since the number of lines per project varied. After the initial scan of the data, our calculations could then take place first calculating a Forecast Detail array then out of this calculation continuing with a calculation of a data array for the Report A input and an array of financial system data to

be imported into it. Finally to deliver the data to each of their destinations, the data for Report A could be inserted directly while the data to be imported into the financial system would be saved in a format that could be imported into the financial system.

Execution and Code Development

In addition to the task of generating the code, there were a few supporting tasks that needed to take place that would have significant influences on the code. First a report with all of the relevant information for both Report A and the financial system input would need to be created in the PM system. This required coordination with the PM system technical support group to create an appropriate report template and coordination with the financial system support group to help define data needs. Based on the template utilized for Report B, the group was able to include month by month data spanning across the 24 months following the date of report generation which would cover the financial system's requirement of month by month data for the following 18 months at the end of each fiscal quarter. Another more administrative and process oriented was related to the way expense forecasts were entered into the PM system. With a description field in the PM system at our disposal, the script could take advantage of custom text to identify each department's expenses without adding to the program manager's project administration burden. Finally, the output file which was to be imported into the financial system would have to be formatted into an acceptable layout that could be properly interpreted by the financial system import toolset.

With the supporting tasks in place and under way, the process of writing the code to perform the functional requirements could also begin. However, the risk of changes to the supporting tasks and reports was mitigated by first addressing the functions with more definite input and output expectations. With the efficient handling of arrays in Excel VBS, virtually all subroutines and functions utilized arrays allowing the script an added advantage of minimized memory consumption even during large file runs.

As the development of the code regarding the functional block for the financial system data came up a few questions surfaced. One was related to the financial system cost accounts as compared to the PM system cost types while the other was a bit more complex. The cost types in the two systems were not set up identically and as a result there were several accounts in the financial system which did not have clear equivalents in the PM system. This required some negotiating with our accountants as well as our PM staff to ensure there was a clear mapping of cost types between the PM system and the financial system. Thereby ensuring that financial system input would have a clear destination for all entries put into the PM system. After agreements were reached, I quickly wrote down the terms in a formal document and made it available for all PM and finance staff reference.

After weeks of coding, a demonstration was schedule with the finance group and a few key enhancements were immediately requested. First, it became well apparent that there had to be a method for selecting the data document. The code had to be verified in different generations of software, at least one older and one newer generation. After a

few more weeks of coding, the next solution was ready for demonstration and with the

coming budget cycle quickly approaching, it was ready just in time.

Delivery

The final version of the script, now embedded in the template file for Report A

allowed the user to first select their data file, generated out of the PM system, from their

file directory and an appropriate start date for the budget period being calculated. After a

number of heavy array calculations and sub-functions, the forecast data would be

inserted in the appropriate location in Report A and the user would be then be prompted

to enter a filename for the output files to later be imported into the financial system.

With great reception from our financial department and agreement from all PM staff

regarding adjustments in their forecast entries, the final solution ensured consistency

between forecast figures in the PM system, the financial system, and the data in Report

A. Also just as importantly, the amount of time spent putting together this information

went from several days to weeks of work to a few seconds it took the code to run. With a

solution delivered and all supporting documentation including user instructions for script

as well as PM system data entry, my internship project was complete.

CONCLUSION

This concludes the summary of my internship experiences with first CorInnova and then Micro Systems Engineering, Inc. a subsidiary of Biotronik. I feel very blessed to have had these experiences and am eternally grateful to those who have influenced me along the way. I feel confident that my contributions to these organizations were valuable and this would not be possible without the education and skills I gained at the Dwight Look College of Engineering and Mays Business school of Texas A&M University. In an industry full of engineering challenges and operational obstacles, I feel well prepared to be a valuable asset in the industry. The knowledge and experiences gained throughout my education and internships are and will always be invaluable.

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