

Characteristics of Disruptive Innovation Within the Medical Device Industry

By

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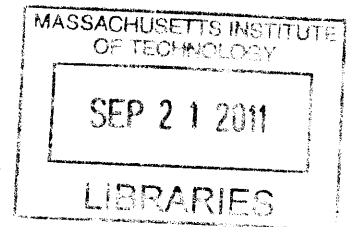
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Master of Science in Health Sciences and Technology

Abstract

Innovation within the medical device industry had led to tremendous advances in the provision of care for patients worldwide. Continued progress in the treatment of disease will require effective processes for managing and analyzing innovation within this industry. Popular models of innovation exist for many industries outside of the medical realm; however, an extensive literature search uncovered a limited body of work related to innovation within the medical device industry. Specifically, literature that examines the application of the principles of disruptive innovation to the medical device industry is limited in scope and in quantity. It is theorized that the medical device industry may have unique characteristics for disruptive innovation due to the unique economic and regulatory structures that exist within this industry.

This thesis applies the principles of disruptive innovation that were popularized by Clayton Christenson's seminal work, *"The Innovator's Dilemma"*, to the medical device industry. These characteristics are subsequently delineated and evaluated through examination of the prosthetic cardiac valve industry. This industry serves as an effective case study due to the long history of innovation and the emergence of new disruptive technology within this specialty. The categorization of a "disruptive" innovation was made when a given technology altered the value proposition for treating a disease, relative to incumbent technology.

This case study was evaluated along metrics of performance characteristics, the perception of leading customers, the ability to prospectively analyze markets, and the profitability of disruptive innovation for the incumbent firm. Conclusions were reached based on an examination of relevant literature and primary research conducted with thought leaders in this area. This research supports the conclusion that the cardiac valve industry has experienced unique characteristics in the development and commercialization of disruptive innovations. Specifically, incentives appear to exist within this industry that support development and commercialization of disruptive innovations by industry incumbents. Furthermore, the importance of understanding what value proposition is being disrupted is paramount in effectively understanding the incentives of manufacturers to innovate. When a technology is developed that is disruptive to a procedure, then the manufacturer tends to behave similar to a "new-entrant" within the Christenson framework. This appears to also be true when the innovation is disruptive to that manufacturer's legacy products. Additional research is warranted in extrapolating this finding to the broader medical device industry.

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This thesis is dedicated to:

My mother for always telling me, *"You can do anything you put your mind to"*,
My father for teaching me that *"Anything worth doing is worth doing right"*,
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Introduction:

The intersection of technological progress and medical care has provided tremendous advances in the health outcomes of worldwide populations.¹ Implantable pacemakers, defibrillators, left ventricular assist devices, cochlear implants, robotic surgery, prosthetic heart valves, and cardiac stents are just a limited number of innovations that have drastically shifted the paradigm of care for patients worldwide. Some have described these types of innovations as “disruptive” or “discontinuous” in nature – implying that the innovations present a radical new value proposition for physicians and patients.^{2,3} Given the tremendous historic, and potential future, impact of medical device innovation on the provision of medical care it is important to fully understand the characteristics of innovation within this industry.

The characteristics of discontinuous or disruptive innovation have been previously delineated by academic researchers including James Utterback and Clayton Christenson.^{4,5} In the case of Dr. Utterback’s work, the proposed model of innovation rests upon a foundation of analysis with a primary focus on historic industrialized products. The work segments innovations into assembled and non-assembled products, with subsequent categorization of the innovation lifecycle into fluid, transitional, and specific phases. In the case of Dr. Christenson’s model, innovations are characterized as “sustaining” or “disruptive” in nature with specific characteristics ascribed to each category. The foundation for formulating Christenson’s model was evaluation of innovation within the disk-drive industry with subsequent verification of the model through analysis of the steel, mechanical excavator, thin film, and retailing industries among others.

While both models represent significant and valuable concepts for evaluating the process of innovation, it is unclear if these models apply specifically to the medical device industry. In particular the market for high-tech interventional medical devices has distinct economic and regulatory characteristics, which may uniquely impact the characteristics of innovation within this industry. First, the US medical device industry is subject to significant regulation from the Food and Drug Administration (FDA), which both limits entry into the market and restricts marketing of a product to clearly defined uses that are substantiated by clinical evidence. Second, while the ultimate end user of an implantable or surgical device is a patient, the physician, in most instances, is the intermediary agent who chooses the specific product to use in providing care to that patient. However, the physician does not directly incur the economic cost of his/her decision, which therefore creates a moral hazard in which the cost of an innovative device is less likely to influence product choice than pure performance of that device. Furthermore it is unlikely that medical technology could over-perform what the market demands when performance is measured in terms of clinical outcomes. The characteristics of over-performance are a core tenant of Christenson’s model of innovation, which theorizes that consumers will shift to a lower cost option when the traditional technology out performs that consumer’s needs. However in the medical device industry, even if a technology were significantly more expensive, the physician may choose to use this expensive product due to an improved patient outcome. This dynamic is a significant deviation from traditionally studied industries where product adoption is based upon a customer’s perception of value, which includes the economic costs of their product choice.

Thesis Intent

The intent of this thesis is to explore the characteristics of radical innovations within the interventional medical device industry. The traditionally accepted characteristics of disruptive innovation will be enumerated; hypotheses will be generated according to these characteristics; a case study of innovation within the medical device industry will be examined and conclusions will be drawn regarding the validity of traditional models of innovation when applied to medical devices.

Thesis Relevance

The conclusions of this work will inform strategic decision at many levels within the medical device industry including entrepreneurs, incumbent firms, investors, and technology transfer offices.

Incumbent medical device firms are often faced with emerging technologies and must evaluate the extent to which these emerging technologies threaten their existing businesses. In addition, incumbent firms must allocate resources toward either internal innovation or the acquisition of innovation developed by independent medical device entrepreneurs. The latter model of innovation has become more prevalent in recent years and it is worth examining whether this model of acquiring innovative products is theoretically optimal in the context of disruptive technology. Furthermore, when firms pursue internal technological development that is disruptive to their existing product lines there must be a deliberate organizational structure to allow sufficient resources to be directed towards the disruptive technology. Understanding the dynamic of internal disruption and the characteristics of what is being disrupted is of central importance to successfully commercializing a disruptive product.

Additionally, this research may help inform the decisions of technology transfer offices. The primary objective of technology transfer offices at academic medical facilities is often to ensure that the intellectual property be developed and reach clinical use. These licensing offices are often faced with multiple licensing options including licensing to an entrepreneurial company, which has no track record for success, or licensing to a larger organization, which may have incentives to prevent commercialization of the product if it could cannibalize their existing product sales. While these offices often have legal covenants that try to incentivize development of technology following licensure, it would be preferential to license technology to organizations with characteristics consistent with successful development of innovative medical technology. One example of this dynamic would be the licensing of smart infusion pump technology. The initial licensee of this technology lacked an incentive to commercialize the device because it represented a less profitable business opportunity than their traditional technology. Eventually the academic licensing office was able to force commercialization of the technology, but only after protracted negotiations.⁶ It is unclear whether the current model of disruptive innovation, which espouses development of radical technology by new-entrant firms, would be applicable to the medical device industry.

Review of Existing Literature

Christenson Model of Innovation

The Christenson model of innovation was popularized with his 1997 book *The Innovator's Dilemma* and since that time has become the most well know, popular, model of innovation. Within Christenson's model, innovation is characterized as either sustaining or disruptive. Sustaining innovation is generally defined as innovation that improves a given product along traditional performance standards. By contrast, disruptive innovation changes the metric of performance upon which the product competes. As such, sustaining innovation competes within the historic value proposition while disruptive innovation competes within a new value paradigm.

With this framework Christenson demonstrates, using the rapidly changing disk drive industry, that incumbent firms tend to effectively manage sustaining innovation, while being incapable of managing the development of disruptive innovations from within existing organizational structures. This implies that disruptive innovations must come from either new entrant firms, primarily through the form of entrepreneurs, or through independent organizations within an incumbent firm.

In addition Christenson describes the following characteristics of disruptive innovations:⁷

- Disruptive technology is "*simpler, cheaper, and lower performing*"
- Incumbent firms' "*most profitable customers generally can't use and don't want*" disruptive technology
- Disruptive technology is "*first commercialized in emerging or insignificant markets*"
- Disruptive technology promises "*lower margins, not higher profits*"

The overriding premise of Christenson's model is that disruptive innovations initially do not represent attractive areas of investment for incumbent firms given the small markets, low margins, and lack of interest from leading customers. However, once commercialized within these small markets, disruptive innovations tend to have a technological trajectory that improves performance at a rate higher than both the rate at which sustaining innovations take place for incumbent technologies and the rate at which market performance demands increase. Furthermore, Christenson has demonstrated that the rate of sustaining innovation for incumbent technologies causes those products to exceed the market demands for performance. This "over-performance" provides an opportunity for lower performing technologies with ancillary benefits and lower costs to enter the market and undercut the incumbent product. Initially the disruptive product will enter the market at a very low performing level, according to traditional performance metrics. However, with time the disruptive technology will improve to the point at which it will satisfy market demand, despite being inferior to incumbent technology. Pairing this market adequacy with the lower costs of the disruptive technology creates an incentive for leading customers, who initially could not use the disruptive innovation, to switch to the lower cost, higher value, disruptive product. However, the premise of this model requires low performing innovations to

reach the market and for experimentation to take place with these products to more clearly define the market, while technological capabilities improve.

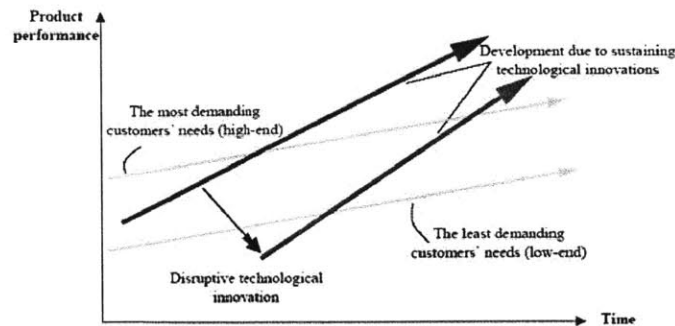


Figure 1: Representation of the impact and interaction of sustaining and disruptive innovation.⁸

One current example of disruptive technology would be the rising popularity of smartphones and tablet computing. The early models of smartphones were lower cost, and lower performing, than laptop computers. Leading customers, for example students who often rely on laptops for note-taking during class, could not use smartphones as a replacement for laptop technology due to the limited performance of smartphones. However, with time the smartphone technology has improved to the point where it can power low cost tablet computing. While tablets are still inferior to their more powerful laptop competitors, they are adequate for the demands of the student market. This dynamic is leading to disruption within the computing market as customers who used to rely upon laptops are now able to switch to lower cost, higher value, disruptive technology such as tablet computing. In addition, the tablet market is beginning to threaten even higher end business customers as multiple companies have transitioned their sales forces from laptop computers to tablet computers.⁹

The Christenson model of innovation, and the example just listed, are both taken from the high tech electronics industry. While Christen has validated this model through examination of additional industries including steel manufacturing, excavation, automotive, and retailing the economic and regulatory dynamics of the medical device industry present distinct issues that may cause innovation in this area to deviate from the model outlined by Christenson.

Healthcare Innovation Literature Review

A review of literature related to innovation within the medical device industry was undertaken. Numerous articles were reviewed that focus on the nature of innovation within healthcare, broadly defined.^{10,11,12} Literature was also uncovered dealing with the sources of medical device innovation, and in particular literature was focused on the industry's traditional dominance by physician generated innovations, also described more broadly as user generated innovations. The process of integrating innovations into surgical practice has also been previously researched in detail. However, the availability of literature focused on the characteristics of innovation within the interventional medical device industry is of limited quantity.

Christenson touched on the topic of healthcare innovation in *"The Innovator's Dilemma"* by briefly discussing the issues that Eli Lilly Inc. faced when developing an ultra-pure form of insulin. In addition, Christenson's most recent book, *"The Innovator's Prescription"*, is focused on healthcare innovation. This book examines the ways in which the principles of disruptive innovation could be applied to the system of healthcare delivery. While much of the book is focused on systemic issues facing healthcare, there are several insights related to the medical device industry. Christenson even identifies Johnson & Johnson and GE Health Care as masters of the process of commercializing disruptive innovation. This is in contrast to his analysis of high-tech industries where it was exceedingly rare to see disruptive innovation emerge from an incumbent firm. However, even within this analysis there is not a detailed examination of whether surgical devices adhere to the same characteristics of innovation enumerated in Christenson's earlier model.

The most cited example of disruptive innovation within the surgical device industry is the example of angioplasty. From afar, this example seems to fit within the framework of a disruptive innovation. It has radically changed the way in which patients with coronary artery disease are treated, and angioplasty competed with coronary bypass surgery using an entirely new value proposition. However, when you consider the perspective of the medical device manufacturer, and the incentives for commercialization of this technology, it is unclear that Christenson's framework is entirely applicable.

First, it is unclear that angioplasty and stenting disrupted another medical device. While the procedure of angioplasty disrupted the procedure of coronary bypass it is less clear that the device itself, a catheter delivered balloon, disrupted a specific device for coronary bypass. In bypass surgery the majority of surgical tools are basic clamps and scalpels that are made productive through the skill and experience of a surgeon. Therefore it may be that the angioplasty devices disrupted the need for advanced cardiothoracic surgical skill, but that is a different dynamic than the previous examinations of disruptive innovation where a device or product disrupts another device or product.

Secondly, the market for angioplasty products was well defined, in the sense that epidemiologic studies existed that allowed manufacturers to determine the prevalence and incidence of coronary artery disease. In addition the indicated uses for angioplasty technology were fixed according to regulatory guidelines. While physicians often broadened the market for this technology through off-label implantation, data existed that allowed the manufacturer to assess whether the market for the indicated use was sufficient to warrant investment. This is different from the circumstances of disk drive development discussed by Christenson, wherein the products were used by consumers in ways that were largely unimaginable to the manufacturer and therefore the markets were exceedingly difficult to prospectively analyze.

Finally, with regard to angioplasty and stenting, the procedure represented a major opportunity for profitable growth within the medical device industry, and has subsequently attracted significant investment and competition. Contrary to other examples of disruptive innovation where firms are not attracted to innovation because of small markets and low profitability, angioplasty and stenting was a

major source of profitable growth for medical device manufacturers. This conclusion could be different if examining the healthcare system as a whole. One could argue that the costs of an angioplasty procedure are less than coronary bypass, and therefore represent a lower margin business for the hospital. However, when focused on the perspective of the medical device manufacturer, the disruptive opportunity deviates from established characteristics of innovation.

The concept that medical devices may deviate from established models of innovation is further supported by the work of Neo, et al. in their examination of the automatic external defibrillator (AED) market.¹³ In this paper the authors argue that entrance of AED technology into the mainstream market followed a unique technological trajectory that deviates from established models of innovation. Specifically the AED, by virtue of its status as a Class III FDA regulated device requiring pre-market approval (PMA) prior to market introduction, cannot be labeled as an inferior technology. The authors expand on this topic by establishing the concept of market “adequacy”. In contrast to traditional models of innovation, where inferior products enter the market and then through positive technological trajectory succeed in capturing larger portions of the market, in the AED market the technological trajectory was inverted from a high-end hospital model defibrillator down to an “adequate” general use AED.

Despite the work of various authors in examining innovation within the healthcare industry, the characteristics of medical device innovation have yet to be delineated. Specifically innovation within the area of surgical or interventional devices may have unique properties due to the previously described economic and regulatory structure.

Hypotheses:

This thesis seeks to evaluate whether interventional medical devices adhere to the previously defined characteristics of disruptive innovation. The following four hypotheses will be evaluated:

1. **H₀:** Disruptive innovation in the interventional medical device industry will always have inferior traditional performance and higher ancillary performance than incumbent technology.
2. **H₀:** Disruptive innovation in the interventional medical device industry will always be rejected by leading customers.
3. **H₀:** Disruptive innovation in the interventional medical device industry is always first commercialized in a small or insignificant market.
4. **H₀:** Disruptive innovation always represents a lower margin business opportunity relative to traditional products.

Method of Evaluation:

Evaluation of the hypotheses enumerated above will take place through detailed examination of the prosthetic cardiac valve industry. This industry represents a useful case study for numerous reasons.

First, the medical device industry has an extended development cycle resulting from the complex design process, the need for enabling clinical science, and the requirements for extensive clinical testing prior to market release. The cardiac valve industry has one of the longest innovation timelines among interventional medical devices. The first human prosthetic valve was implanted in 1952.¹⁴ Since that time various designs, materials, and anatomic locations have been used for implantation. This provides a rich history from which to draw evidence regarding the characteristics of radical innovation.

Second, the prosthetic valve industry is representative of the unique characteristics that are theorized to impact the characteristics of disruptive innovation in the medical device industry. Specifically, the surgeon chooses which valve to implant in a patient, and does not directly bear the economic impact of his/her decision. In addition, the development and market introduction of cardiac valve technology is highly regulated by the FDA, which limits the entry of inferior technologies as well as the indicated use for each product.

Finally, emerging technologies for cardiac valve replacement have the potential to significantly disrupt the current paradigm for treating patients with valvular heart disease. Specifically, technologies have been developed to deliver valves through a catheter, which drastically changes the value proposition for both patients and providers. These emerging procedures may open care to a previously untreated population, while also shifting the provision of care from a high-cost surgical setting into a lower cost interventional setting. The impending changes associated with such disruptive technology, in addition to the quantity of scientific literature being produced around this technology, make the field of cardiac valve technology ideal for examining the characteristics of innovation and drawing broad conclusions about innovation in the medical device industry.

In analyzing the cardiac valve industry, focus will be placed on radical innovation, as opposed to sustaining innovation. A detailed history of prosthetic valves will follow. Two discontinuous innovations from within this history will form the basis of further analysis according to the hypotheses established above. These discontinuous innovations include the transition between mechanical and tissue valves and the emerging transition between surgically implanted valves and transcatheter aortic valve implantation (TAVI). In addition, the analysis will focus on innovations in aortic valve replacement. While many of these innovations have also been developed for mitral valve repair, including minimally invasive options, the techniques and technologies used in mitral valve repair are generally not applicable for aortic valve repair, primarily as a result of natural anatomic and physiologic differences, and therefore are beyond the scope of this analysis.

Valvular Disease Overview:

The heart contains four major valves, as illustrated in Figure 2 below. These are the right sided tricuspid and pulmonary valves, and the left sided mitral and aortic valves. While much could be written about the pathologies associated with each valve, the focus of this analysis will remain on pathologies and associated therapies for aortic valvular disease.

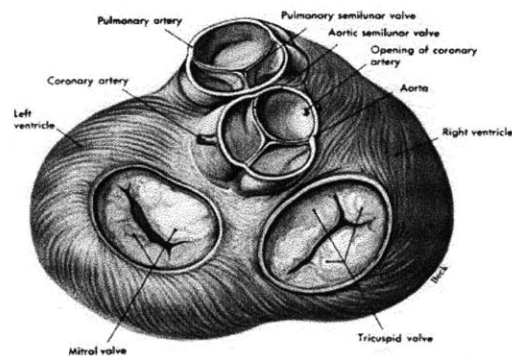


Figure 2: Anatomy of the cardiac valves, viewed from above.¹⁵

The aortic valve is positioned between the left ventricle and the aorta and serves to regulate systemic blood flow. When the left ventricle contracts pressure develops within the chamber. When this pressure exceeds the afterload pressure of the aorta and systemic vasculature, the aortic valve will open and blood will be ejected into systemic circulation. As the left ventricle finishes contracting, and begins to relax, pressure will begin to fall in the ventricle and the aortic valve will close to prevent regurgitant flow from the systemic vasculature back into the ventricle. Mechanical dysfunction of the aortic valve can be rooted in multiple etiologies, but the resulting mechanical dysfunction can generally be segmented into valvular insufficiency or stenosis.

Aortic insufficiency is often caused by dilatation of the aortic root. Rheumatic fever used to be a major precipitating factor in aortic insufficiency; however, as the use of antibiotics has become more prevalent the complication of aortic insufficiency has decreased dramatically.¹⁶ In the developing world, where antibiotic use is limited, rheumatic fever remains a prominent factor in the development of aortic

insufficiency. Common etiologies of acute aortic insufficiency are infective endocarditis or aortic dissection, while etiologies of chronic aortic insufficiency include presence of a bicuspid aortic valve, trauma, myxomatous degeneration, or idiopathic degeneration of the valve leaflets.¹⁷ Aortic insufficiency affects 5 out of 10,000 people and has the highest prevalence among men between the ages of 30 and 60.¹⁸ The regurgitant flow of aortic insufficiency leads to volume overloading of the left ventricle, which results in dilation and eccentric hypertrophy. Aortic insufficiency can present with shortness of breath, dyspnea, fatigue, and palpitations. Left untreated a patient with aortic insufficiency is likely to develop heart failure, left ventricular impairment, and have a higher risk of arrhythmias. For patients with mild or moderate aortic insufficiency who receive treatment, the 10 year survival is 80-95%. However for patients with severe aortic insufficiency and heart failure the prognosis is significantly worse.¹⁹ Treatment includes pharmacologic and surgical options. Pharmacologic options are generally reserved for mild aortic insufficiency and include vasodilators, nitrates, and diuretics. Surgical replacement of the aortic valve is the only curative treatment for aortic stenosis and can be indicated in either symptomatic or asymptomatic patients. For acute onset aortic insufficiency surgical intervention is indicated in any patient without surgical contraindications. For chronic severe aortic insufficiency surgical intervention is indicated for all symptomatic patients, and asymptomatic patients with ejection fractions below 50% or severe LV dilation.²⁰ Current surgical intervention involves replacement of the valve with a tissue or mechanical prosthesis; however, percutaneous methods of aortic valve replacement are also under development. The current developmental focus for percutaneous valve replacement technology is for the treatment of aortic stenosis.

Aortic stenosis is most commonly a result of progressive age-related calcification of the valve leaflets. The prevalence of aortic stenosis has been shown to increase with age and ranges between 2% and 7% of patients older than 65 and is the most common valvular lesion.²¹ However, in patients less than 70 years old the most common cause of aortic stenosis is a congenital bicuspid valve, which occurs in roughly 1% of all live births.²² In aortic stenosis the valve leaflets thicken and impede the flow of blood during systole. The impeded flow results in higher pressures on the left ventricle during systole and can lead to concentric hypertrophy and heart failure. The thickening of valve leaflets during aortic stenosis may also prevent proper closure of the valve during diastole, which causes aortic regurgitation. A recent study of patients undergoing aortic valve repair surgery noted that 84% of patients had aortic stenosis and that 47% of patients had aortic insufficiency; implying that a significant percentage of patients undergoing surgery had both stenosis and insufficiency, but showing that stenosis is the primary driver for aortic valve replacement surgery.²³ Surgery for aortic stenosis is generally limited to symptomatic patients, who left untreated face a mean survival of 2-3 years.²⁴ Current surgical methods involve performing a sternotomy and placing a patient on cardiopulmonary bypass support while replacing the native valve with a prosthetic valve. However, less invasive surgical methods are under development in addition to emerging valve technology that can be placed through a catheter using minimally invasive techniques that do not require a sternotomy or cardiopulmonary support.

History of Prosthetic Valve Development:

The first implantation of a prosthetic heart valve into a human patient was performed by Dr. Charles Hufnagel in 1952, one year prior to the first successful clinical use of the heart and lung machine.²⁵ The

valve was a “caged-ball” design that was patented in 1958 and modeled after the concept of a wine bottle stopper.²⁶ Dr. Hufnagel implanted the valve in the descending aorta, presumably to assist with the prevention of regurgitant flow. This initial proof of concept unleashed a torrent of innovation and in 1960 the first mitral valve replacement, and the first aortic valve replacement, was performed by Dr. Albert Starr and Dr. Dwight Harken, respectively. Since these seminal clinical accomplishments it is estimated that more than 70 different mechanical valve designs have been implanted in patients, and multiple tissue valves have also been used clinically. Valve technology continues to undergo innovation to this day, with significant developmental efforts being focused on percutaneous transcatheter technologies.

Mechanical valves have undergone the most significant clinical experimentation in both structural design and materials. The primary categorization of design iterations includes the “Caged Ball”, “Non-Tilting Disc”, “Tilting Disc”, and “Bileaflet” valves.²⁷ The caged ball valve design formed the basis of early clinical experience in valve replacement. The Starr-Edwards design became dominant within the industry. These valves underwent significant evolution in the materials of construction, but the core caged ball design remained relatively unchanged over decades. Until recently the same caged ball design developed by Starr and Edwards continued to be marketed in certain geographies due to its adequate performance and low cost of production. It is estimated that over 250,000 patients have received a prosthetic valve based on the caged ball design.



Figure 3: Caged ball mechanical valve design.²⁸

Another major design development was the creation of pyrolytic carbon and the application of this material to biomedical implants. Pyrolytic carbon was originally developed for the encapsulation of nuclear fuel rods, but was also useful as a biomaterial due to its strong clinical thromboresistant properties. Innovators subsequently worked to construct valve components from pyrolytic carbon and applied this technology to each of the major mechanical valve design categories.

In the mid-1960 a new design emerged, which used a flat-disc as the valve poppet in place of a spherical ball. This design faced significant structural complications and was subject to multiple design iterations. Ultimately the design was used in only approximately 20,000 patients and was discontinued in the mid-1980s.²⁹



Figure 4: The Kay-Shiley flat-disc valve design.

The late 1960s also saw emergence of the tilting disc valve design. Rather than relying on a cage and poppet, this design utilized a tilting disc, which was expected to improve hemodynamic performance by reducing the obstruction to flow during systole. Popular models of the tilting disc design include the Bjork-Shiley, Lillehei-Kaster, Omniscience, and Hall-Kaster Medtronic-Hall valves. These valves were implanted in more than 850,000 patients and are still marketed in certain forms today.³⁰ The convexo-concave tilting disc valve manufactured by Bjork-Shiley was the subject of scrutiny related to early reports of structural failure that were later tied to a minor change in manufacturing processes for early products.

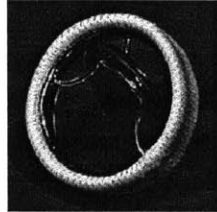


Figure 5: Bjork-Shiley tilting disc valve design.³¹

The bileaflet valve, which is constructed of two hinged leaflets, has become the dominant mechanical valve design. The original design was proposed and clinically implemented by Dr. Gott and Dr. Daggett in 1963. However, after implantation of this bileaflet valve in roughly 500 patients the clinicians discovered that the design could create stagnant flow and risk thromboembolism. Therefore the product was removed from the market in 1966. It was not until 1977 that this design was again tried in a meaningful way by St. Jude Medical. However, in this design the valve was constructed in such a way that stagnant flow was greatly reduced. Furthermore, the entire valve was constructed of pyrolytic carbon to reduce embolic risk. The bileaflet design has been implanted in approximately 1.8 million patients, with 1.3 million patients having received their valve from St. Jude Medical. Surprisingly the valve design has remained relatively unchanged since its introduction.³²

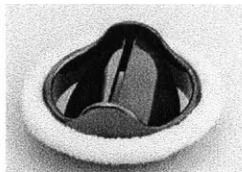


Figure 6: St. Jude bileaflet valve design.³³

While mechanical valves competed on multiple factors including hemodynamic performance, structural integrity, and thromboembolic risk no design was able to reduce the thromboembolic risk to a point where patients were not required to be chronically anticoagulated. To address the thrombogenic concerns, in addition to attempting to improve hemodynamic performance, development of tissue based valve solutions were pursued.³⁴ Development began in the 1960 with the use of homograft valves, and progressed through the early 1970s with experimentation on the ideal methods for chemically fixating heterograft tissue.^{35,36} It should be noted that the FDA gained regulatory authority over medical devices in 1976 and therefore this development took place in an environment devoid of

federal regulation. Dr. Alain Carpentier proposed washing the heterograft tissue in glutaraldehyde and fixing it to a mechanical structure to maintain its geometry. This approach ultimately proved to be viable and has remained the dominant tissue design. Iterations have been made to improve the chemically fixation process and the source of tissue has been expanded from porcine to bovine pericardium. Despite these sustaining innovations the foundation of tissue valve technology rests upon the core design of Dr. Carpentier. For this contribution to clinical medicine Dr. Carpentier was awarded the 2007 Lasker Award for Clinical Medical Research. Dr. Albert Starr also received the Lasker Award in 2007 for his contributions to the development of mechanical valve technology.³⁷

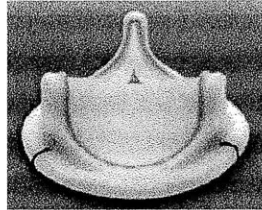


Figure 7: Edwards-Carpentier bovine pericardium valve.³⁸

A major focus of current innovation in valve technology is the development of percutaneous techniques for replacing or repairing diseased valves. While the initial concept was demonstrated to be feasible in animal trials as early as 1992, the first human clinical use of percutaneous valve technology was not seen until 2002.³⁹ Development in this area has progressed at a rapid pace and transcatheter valve replacement is being pursued by at least six companies.⁴⁰ The closest valve to FDA approval is the "Sapien" valve, which is manufactured by Edwards Lifesciences. This valve has received European regulatory approval and is currently in clinical use within that geography. Significant data is being accumulated for the performance of this technology and it has been speculated that this technology could receive FDA clearance by the end of 2011.

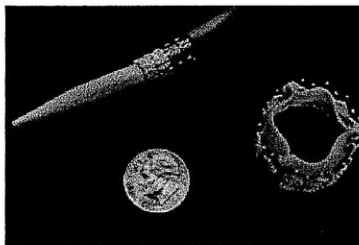


Figure 8: Edwards Lifesciences "Sapien" transcatheter aortic valve.⁴¹

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Hypothesis 1:

Disruptive innovation in the interventional medical device industry will always have inferior traditional performance and higher ancillary performance than incumbent technology.

Shifting Performance Metrics and Innovation:

A core tenant of traditional theories of disruptive innovation involves technologies that enter the market with inferior performance and lower costs than incumbent technologies. Once these technologies have entered the market they are used in unexpected ways and eventually, through subsequent sustaining innovation, are able to satisfy the market demands of traditional customers.⁴²

However, the current medical device regulatory structure does not appear to allow this type of innovation development process. Devices are restricted in their marketed use, and must exhibit certain performance characteristics before regulators allow that product to enter the market.⁴³

It is therefore hypothesized that radical medical device innovation will demonstrate unique performance characteristics and will not enter the market with inferior performance. Evaluation of this hypothesis will be performed through delineation of performance metrics for cardiac valves, evaluation of the regulatory constraints placed upon cardiac valve developers, and evaluation of the performance trade-offs that existed, or continue to exist, between mechanical and tissue valves, and surgically implanted and transcatheter valves.

Prosthetic Heart Valve Performance Metrics:

The evaluation of performance for medical technology is often a complex process that may vary based upon the perspective used to evaluate the technology. Variation between disease states of individual patients, or the training and preferences of surgeons can impact the perceived performance of a given technology. Furthermore, the clinical endpoints used for evaluation can vary based on a physician's clinical objectives. For instance performance metrics could focus entirely upon mortality benefits, which would miss any quality-of-life benefits that may accrue through the use of new technology. In considering the appropriate performance characteristics of prosthetic valves, the scientific literature was examined for key performance metrics. Surprisingly, a visionary list of performance criteria was developed in the 1950s by pioneering surgeon Dr. Dwight Harken⁴⁴, which is still relevant today and widely cited as the basis for ideal valve performance. The ten "Commandments" set forth by Harken are as follows:

1. It must not propagate emboli.
2. It must be chemically inert and not damage blood elements.
3. It must offer no resistance to physiological flows.
4. It must close promptly (less than 0.05 seconds).
5. It must remain closed during the appropriate phase of the cardiac cycle.
6. It must have lasting physical and geometric features.
7. It must be inserted in a physiological site (generally the normal anatomical site).
8. It must be capable of permanent fixation.
9. It must not annoy the patient.
10. It must be technically practical to insert.

Various iterations of these ideals formed the basis for over 50 years of prosthetic valve development. While sustaining innovations tended to provide improved performance across one of these performance characteristics, radical innovations shift the competitive performance metric away from the competitive characteristics of incumbent technology and towards a new value proposition. The subsequent analysis of performance will use these ten metrics as the basis of determining and evaluating traditional versus ancillary performance.

Regulatory Role in Cardiac Valve Approval:

The FDA regulates medical devices according to a three tier classification system (I, II, and III), which corresponds to both the risk presented to the patient by the device and subsequently, the regulatory requirements that apply to the given device. In the case of prosthetic heart valves the FDA has classified these devices as class III, which is defined as *“those that support or sustain human life, are of substantial importance in preventing impairment of human health, or which present a potential, unreasonable risk of illness or injury”*.⁴⁵

The FDA has two regulatory processes for medical devices, although this structure is currently under revision by the FDA and may soon result in significant changes to these regulatory requirements.⁴⁶ The FDA gained regulatory authority over medical devices in 1976. These regulations stipulated that products substantially equivalent to those marketed prior to 1976, referred to as predicate devices, could be approved through the guidelines of section 510(K). Once a product has been determined to be substantially equivalent by the FDA, that product may form the basis for a subsequent product’s 510(k) approval. Under this structure certain products may gain approval by claiming a postamendment device as the predicate for comparison of equivalence. The 510(K) approval process presents a relatively low barrier to entry, but by definition is generally not an applicable regulatory process for disruptive medical devices given that approval is based upon similarity to predicate technology.

The second, more stringent, regulatory process is referred to as premarket approval (PMA). Class III devices are required to undergo PMA certification, which involves both nonclinical laboratory studies and clinical investigations involving human subjects. Also, all new products are by default classified as class III, unless they pursue the FDA’s *de novo* reclassification process. However, in practice most

devices do not fall under Class III guidelines. In 1987 the FDA issued a final rule (52 FR 18162) requiring PMA approval for all predicate replacement heart valves. Therefore all future cardiac valve prostheses are also subject to the more rigorous PMA regulatory structure. The objective of PMA regulation, as set forth by the FDA, is *“to assure that the device is safe and effective for its intended use(s)”*.⁴⁷ With regard to cardiac valve technology the FDA determines clinical efficacy through the comparison of trial data to objective performance criteria (OPC), which is established through aggregation of peer-reviewed analyses of existing similar technologies.⁴⁸ In an earlier version of the FDA guidance document, these OPC were established as follows:

Complications (% per year)	Mech. valves	Biol. valves
Embolism	3.0	2.5
Valve Thrombosis	0.8	0.2
Bleeding	3.5	1.4
Paravalvular Leak	1.2	1.2
Endocarditis	1.2	1.2

Figure 9: Objective performance criteria set forth by the FDA in their 1994 Heart Valve Guidance document.⁴⁹

Accordingly these guidelines establish clinical thresholds that must be satisfied before a device can enter the market. This supports the hypothesis that medical devices cannot enter the market with significantly inferior traditional performance. Even if a device were to have drastically improved rates of one of the metrics listed above, it would still be required to not significantly exceed the other established event thresholds. Furthermore, this threshold criterion is often used by the data advisory boards that evaluate performance during clinical trials. Any deviation above established thresholds can be cause for halting the clinical trial, which would prevent submission of a PMA application to the FDA and subsequent commercialization of the technology.⁵⁰

Given the regulatory structure discussed above it is expected that traditional performance of innovative cardiac valves will not be inferior to incumbent technology, but ancillary performance of innovative technology will be improved relative to traditional technology.

Performance of Tissue Valves Compared to Mechanical Valves:

The first prosthetic cardiac valves implanted in human subjects were mechanical and utilized a “caged ball” design. While not ideal, this design dramatically extended the lives of implanted patients and incited waves of sustaining innovations. The optimal mechanical valve design evolved over the successive decades from a caged ball, to a tilting disk, to the bileaflet valve, which today is the most popular mechanical valve design.⁵¹ In addition to evolution of the structural design for mechanical valves, changes in material composition drastically improved the thrombogenic properties of these valves. Specifically the development and application of pyrolytic carbon to heart valves represented a dramatic reduction in the thrombogenicity of mechanical cardiac valves. Despite major improvements in this arena, development of a thrombus free mechanical valve has not been achieved; the result being that patients receiving mechanical valves require indefinite anticoagulation therapy. The traditional basis of competition among mechanical valves was along hemodynamic parameters and structural integrity.

In 1969 a surgeon by the name of Alain Carpentier developed what became the dominant method for preserving and fixing heterograft tissue valves.⁵² These valves, first made of porcine tissue and later from bovine pericardium, represented a dramatic shift from traditional mechanical valves. The process of curing these valves removed the associated embolic risks inherent with mechanical valves. However, it was eventually discovered that over time tissue valves are susceptible to calcification and leaflet degradation.⁵³ Comparing tissue to mechanical valves using standard performance metrics would indicate inferior structural integrity, but higher performance in terms of thrombogenicity, as illustrated in Figure 10 below. Given this shift in value proposition the introduction of tissue valves can be considered a disruptive or discontinuous innovation.

Valve type	Model(s)	Hemodynamics	Freedom from thrombosis/thromboembolism	Durability
Mechanical				
Caged ball	Starr-Edwards	+\$	+	+++
Single tilting disk	Bjork-Shiley	++	++	+++ [†]
	Hall-Medtronic Omnicarbon			
Bileaflet tilting disk	St. Jude Medical	+++	+++	+++ [‡]
	Carbomedics Edwards-Duromedics			
Tissue				
Heterograft/xenograft bioprostheses	Carpentier-Edwards (porcine and bovine pericardial)	++	+++	++
	Hancock (porcine) Ionescu-Shiley (bovine pericardial)			
	Mitroflow (bovine pericardial)			
Homograft/allograft	Cryopreserved human aortic/pulmonic valve	++++	++++	++

*Presently or previously.

[†]Except Bjork-Shiley 60°/70° convexo-concave valve (see text).

[‡]Except Previous model of Edwards-Duromedics valve (see text).

[§] Performance criteria: + = least favorable to + + + + = most favorable.

Source: Data adapted from Vongpatanasin et al.¹⁸⁹

Figure 10: Types and characteristics of commonly used substitute heart valves (from *Cardiac Surgery in the Adult - 3rd Ed.*)⁵⁴

At first pass, the lower traditional performance and higher ancillary performance of tissue versus mechanical valves appears to fit the classic model of disruptive innovation. However, the analysis is not fully valid as tissue valves were first introduced in the late 1960s and early 1970s, prior to the FDA receiving full regulatory power over medical devices. Despite this inconsistency, the characteristics

associated with tissue valves are worth further evaluation as they remain a central innovation in this industry.

While it is apparent that tissue valves have lower hemodynamic and structural performance than mechanical valves, it is important to evaluate the technological trajectory of tissue valves. Given the constraints of tissue calcification and structural degradation, tissue valves were initially utilized in limited circumstances, and primarily in older patients in whom valve durability was less likely to be a major concern. However, with time, sustaining innovation within the tissue valve materials has enabled this device to significantly improve its structural performance, by reducing the tissue's susceptibility to calcification and degradation. Specifically there are three innovations that have increased the structural performance of tissue valves. These improvements are the development of glutaraldehyde fixation methods, the transition from porcine to bovine pericardium valves, and the elucidation of the factors that lead to accelerated calcification. As illustrated in Figure 11, the shift from porcine to pericardial tissue provided for significantly improved outcomes, especially within defined patient populations.

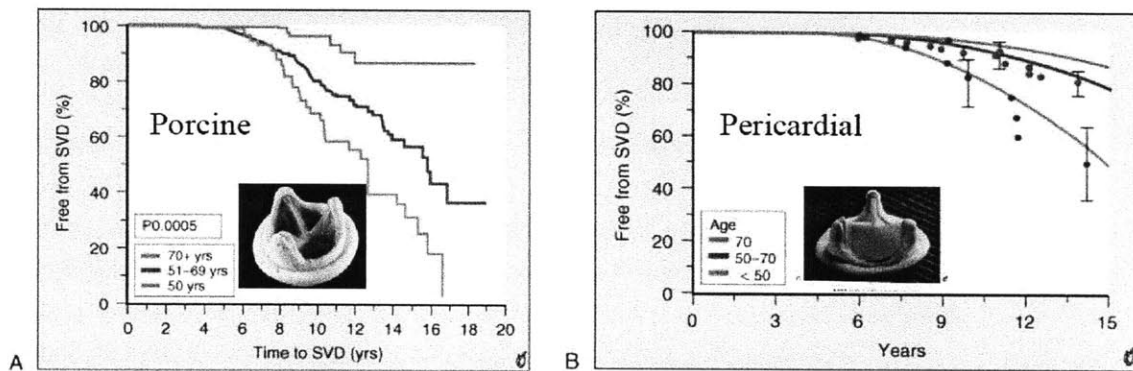


Figure 11: Comparison of structural valve dysfunction at varying ages and with varying tissue.⁵⁵

Additionally, simulation analysis has demonstrated that the use of bioprosthetic valves may have benefits in patients younger than are currently indicated to receive this type of valve.⁵⁶ This simulation is based upon the known rates of failure within varying and specific patient populations. The analysis demonstrates that even with lower structural performance, the benefits of lower thromboembolic events will make tissue valves a preferred choice for certain patients. Furthermore, it clearly demonstrates the impact of sustaining innovations, with regard to structural integrity, on the ability of tissue valves to meet a greater segment of market demand. It was estimated in 2010 that a tissue valve now has freedom from structural deterioration of 80% at 20 years, as compared to early formalin-fixed tissue valves with failure rates of 35% at just 11 months.^{57,58}

The aggregate impact of these changes can be seen in Figure 12. This graphic illustrates the effect of sustaining innovation on the market acceptance of tissue valves. As bovine pericardium became more widely accepted, and the various factors impacting structural integrity were understood, the acceptance of tissue valves began to increase dramatically. Interestingly the implantation rate of mechanical valves also increased over this time period, which indicates a symbiotic competitive dynamic. This dynamic is explored in greater depth within the chapter addressing the market size for disruptive innovation.

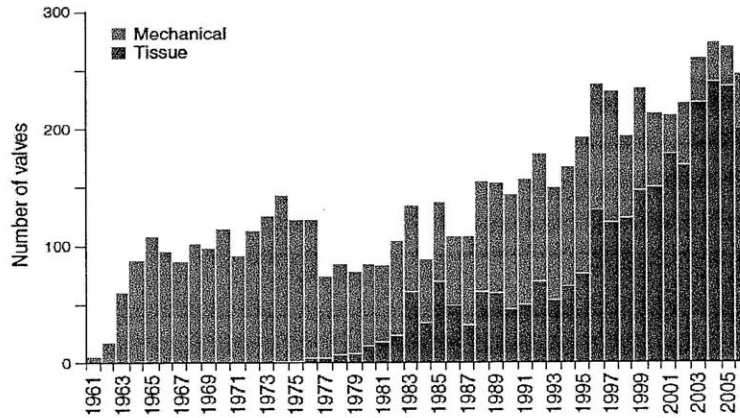


Figure 12: Number of tissue and mechanical valves implanted in the aortic position at Providence St. Vincent Hospital.⁵⁹

Performance of Transcatheter Aortic Valve Implantation (TAVI) compared to Surgical Implantation:

The development of TAVI has taken place in some form over the past 20 years.⁶⁰ However, within the past 10 years the development of this technology has leapt forward.^{61,62} The technology closest to US market release is the “Sapien” valve, which is manufactured by Edwards Lifesciences. This technology has recently gained market clearance in Europe and has been evaluated in a number of clinical trials, which have contributed to a substantial amount of newly available data regarding the performance characteristics of this technology compared to traditionally implanted valves.

In comparing TAVI with surgically implanted valves the characteristics enumerated by Dr. Harken are worthy of consideration. According to those guidelines, TAVI represents an inherent improvement with regard to Dr. Harken’s last two commandments:

- It must not annoy the patient
- It must be technically practical to insert.

A transcatheter valve that can be effectively delivered through the femoral artery, would represent a vast improvement, in terms of ease of insertion, as compared to the need to perform a sternotomy and place a patient on cardiopulmonary bypass. In addition, the patient would likely prefer the transcatheter option, assuming it provides similar clinical efficacy, as it reduces cosmetic concerns in addition to reducing the psychological stress of open chest surgery. When Dr. Harken initially wrote the commandment that, “It must not annoy the patient” he was likely referring to the noise made by early valves during each cardiac cycle. However, the characteristic is interpreted here as an increase in patient convenience.

While it is clear that TAVI competes along a new value plane, it is less clear how the traditional performance metrics compare between TAVI and surgical valve implantation. These performance characteristics are worthy of examination as the level of traditional performance represents an important characteristics of disruptive innovation.

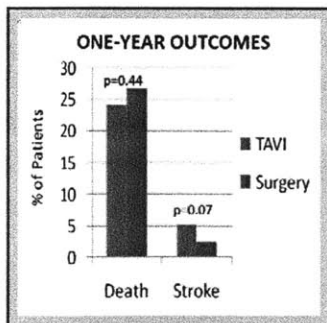


Figure 13: PARTNER Trial, Cohort A results comparing TAVI and Surgery.⁶³

A multicenter randomized clinical trial, referred to as the “PARTNER” trial, recently concluded and presented data regarding the performance of TAVI.⁶⁴ The trial contained two patient cohorts. Cohort A

contained high risk surgical patients; cohort B contained patients who were not candidates for traditional surgery. Each cohort was randomized to either TAVI or standard therapy, being surgery or medical management with possible valvuloplasty. The results of cohort A were recently presented at the American College of Cardiology 2011 Scientific Sessions. Cohort A is most relevant for this examination as it compared the performance of TAVI with surgical performance in high risk patients.

This trial reported data at 30 days, and at 1 year, with a primary endpoint of mortality and a secondary endpoint of major stroke. The trial demonstrated non-inferiority of TAVI to surgery in these high-risk patients with aortic stenosis, as illustrated in Figure 13 above. While the rate of stroke is nominally higher in the TAVI group, it did not reach the level of statistical significance prospectively specified by the researchers for determination of non-inferiority. Furthermore the increased rate of stroke was apparent on longer-term evaluation and therefore appears to be a latent effect as opposed to an operative difference. The authors of this trial stated, *“The primary hypothesis was that transcatheter replacement is not inferior to surgical replacement”* and subsequently concluded that, *“In this study, we affirmed the primary noninferiority hypothesis”*.⁶⁵

Conclusions:

The appropriate metrics of performance were delineated. Subsequently the trade-offs between these performance metrics were evaluated with respect to the mechanical valves versus tissue valves and surgical implantation versus TAVI.

In the transition between mechanical and tissue valves clear differences in performance are evident. Specifically, the structural and hemodynamic performance of tissue valves is inferior to that of mechanical valves.⁶⁶ However, it can also be noted that there is a positive technological trajectory with tissue valves that with time may allow tissue valves to disrupt mechanical valves due to their improved thromboembolic ancillary performance. The emergence of tissue valves appears to hold true to the model of disruptive innovation with regard to performance. The technology initially had inferior traditional performance and with time and continued sustaining innovation may replace the incumbent. Furthermore the structural performance of mechanical valves may over-perform what the market demands in many patients in that mechanical valves have durability predictions that vastly exceed many patients' expected longevity. Despite this adherence to the characteristics of disruptive innovation, this analysis is not entirely valid. Due to the limited regulatory oversight during the emergence of tissue valves, they may not represent a valid example of medical device innovation in the modern regulatory setting.

The examination of TAVI versus surgical implantation illustrates an improvement in ancillary performance metrics, specifically ease of implantation, without sacrificing traditional performance as measured through mortality or thromboembolic risk. Therefore, TAVI represents an example of disruptive innovation in the medical device industry that does not appear to strictly adhere to Christenson's model of innovation, in that it will not enter the market with inferior traditional performance. While certain performance characteristics cannot be immediately ascertained, such as structural durability of TAVI, when measured on the primary outcome of mortality, this innovation does not appear to have inferior traditional performance when compared to surgical valve implantation. Therefore the hypothesis that *"Disruptive innovation in the interventional medical device industry will always have inferior traditional performance and higher ancillary performance than incumbent technology"* can be rejected on the basis that traditional performance is not necessarily inferior. Additional clinical data regarding the long term performance of TAVI could lead to a change in this conclusion.

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Hypothesis 2:

Disruptive innovation in the interventional medical device industry will always be rejected by leading customers.

The Role of Leading Customers in Disruptive Innovation:

Another core tenant of Christenson's model of disruptive innovation is that leading firms' most valuable customers initially do not want, or cannot use, disruptive innovations.⁶⁷ Therefore, firms with rigorous processes in place to evaluate markets through evaluation of the needs of their most profitable customers will often discount the potential impact of disruptive innovation, and subsequently make the seemingly rational decision to forgo investment in disruptive technology. It is only after a new-entrant, or competing firm, has entered the market for this disruptive technology, and begun to improve that technology's performance using sustaining innovation, that incumbent firms will begin to recognize the competitive threat and devote resources to this emerging technology.

This characteristic of disruptive innovation implies that incumbent organizations must make a conscious effort to perform research of customer needs beyond their most profitable customers. Furthermore, it indicates that by rigorously performing market research on the most profitable customers, firms may not be aware of, or may unrealistically discount the potential success of, disruptive innovations. In addition, the analysis of emerging disruptive technologies may conclude that its technological performance is insufficient to create a competitive threat as the technology would only service the low end of the market. However, this analysis is often incorrect as it fails to account for the rate of sustaining innovation along traditional performance metrics, as well as the ancillary performance provided by a disruptive technology.

The question of the role of leading customers in the development of disruptive technology is particularly relevant in the context of the medical device industry. Multiple studies have demonstrated a consistently influential role for physician contributions in the development of radical innovation.^{68,69} Given this documented role of leading customers as innovators in the medical device industry the validity of Christenson's model is worth examining in more detail.

In evaluating whether the characteristic of leading customers reject disruptive technology, it is hypothesized that, "*Disruptive innovation in the interventional medical device industry will always be rejected by leading customers*". This hypothesis will be evaluated through analysis of the initial customer perceptions of tissue valves, as well as current perceptions of TAVI among cardiothoracic surgeons.

Customer Perceptions of Tissue Valves:

An extensive literature review was undertaken to characterize the reaction of leading cardiothoracic surgeons to the introduction of bioprosthetic tissue valves. Given the focus of this analysis on incentives to develop and commercialize products, the use of allograft or autologous tissue transplantation was not included. The use of the term “tissue valve” refers primarily to heterograft tissue mounted on a stent to maintain valve geometry, and chemically cured and preserved prior to implantation. The literature review of this topic focused on the transcribed minutes from leading conferences where the development of valve technology was discussed, and published commentary in peer reviewed journals. In addition, the rate of implantation for mechanical versus tissue valves was reviewed to determine the rate of adoption for this technology by leading customers.

The analysis of tissue valve perceptions is also interesting because the dominant design for this technology was developed through collaboration between Dr. Albert Starr and Dr. Alain Carpentier.^{70,71} Both individuals were leading cardiovascular surgeons and Dr. Starr was also instrumental in development of the mechanical ball-valve prosthesis.⁷² This initial knowledge of the historical development of tissue valve technology would seem to contradict the tenant that leading customers reject disruptive innovation. Furthermore, the customers certainly “could” use this technology as it fit within the same surgical procedure that was used for implantation of mechanical valves.

However, review of literature published during the initial introduction of this technology illustrates significant skepticism among other leading cardiothoracic surgeons. As described above, tissue valve technology shifted the metric of performance from structural integrity to thromboembolic risk. The ancillary thromboembolic performance was greater than that of mechanical valves, but the traditional structural performance was initially quite low.⁷³ As a result many leading physicians were skeptical about the viability of this technology and its ability to represent a practical alternative to traditional mechanical valves. In 1969 the first international workshop on tissue valves was held and the leading cardiothoracic surgeons were asked their perceptions of tissue valve technology. With regard to heterograft valves, surgeons said the following:⁷⁴

“Aortic heterografts proved to be the least satisfactory of all...”

– Dr. Dwight C McGoon

“I suspect there will be a tendency not to start using...heterografts, among those of us who have not already employed these techniques.”

– Dr. Hugh H. Bentall

Even with additional clinical data supporting the Carpentier method of fixating valves in glutaraldehyde, Dr. Robert Wallace, a leading cardiothoracic surgeon from the Mayo Clinic, wrote in 1975 that:⁷⁵

“...experience should continue to be accumulated with [glutaraldehyde-treated tissue valves]. It seems likely, however, that continued improvements in mechanical prostheses will ultimately lead to the most acceptable valve replacement.”

It would appear from the sentiment of these statements that leading customers maintained an academic interest in the development of tissue valve technology, but that most were not highly optimistic that tissue valves would be capable of performance levels that would allow meaningful competition with mechanical valves.

This assessment is further validated through the rates of implantation of tissue versus mechanical valves by leading customers. As illustrated in Figure 14, the implantation rates of tissue valves consistently lagged that of mechanical valves until the mid-1990’s. As previously discussed this inflection point was a result of advances in clinical science that enabled tissue valves to dramatically improve their structural integrity. However, the literature referenced above illustrates skepticism among leading customers during the initial development of tissue valve technology, and the implant data below supports the view that leading customers initially did not want to use tissue valves in place of mechanical valves for the majority of their patients.

Another interesting interaction noted in the graph below is the rising use of both mechanical and tissue valves over the same time period. This demonstrates a unique mode of symbiotic competition where the rise of new technology spurs increased adoption of incumbent technology. Possible explanations for this behavior include the ability of tissue valves to treat a unique patient population, combined with more clinical awareness of surgical treatment options for both mechanical and tissue valve candidates. Other considerations may include the training and preferences of established surgeons who may not have felt comfortable transitioning to tissue valve implantation for their patients and therefore continued to use mechanical valves while more recently trained surgeons began using tissue valves.

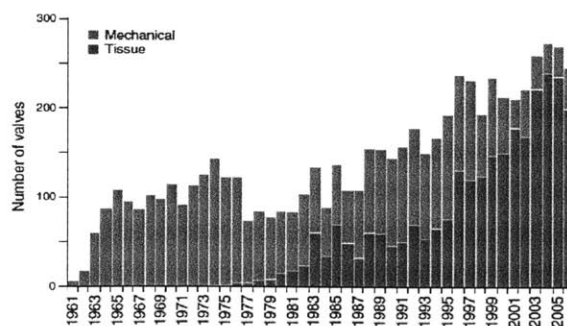


Figure 14: Number of tissue and mechanical valves implanted in the aortic position at Providence St. Vincent Hospital.⁷⁶

The hypothesis that disruptive innovation is initially rejected by leading customers does not appear to rigidly hold under this circumstance. While certain leading customers were skeptical of the chances for success with tissue valves, they also seemed to acknowledge that additional development on tissue valve technology offered the prospect of reasonable clinical value and therefore *did not completely reject* the premise of tissue valves.

Customer Perceptions of Transcatheter Valves:

In contrast to tissue valves, development of TAVI was primarily led by interventional cardiologists who, prior to development of this technology, were not customers for prosthetic valve manufacturers. The first human trial of this disruptive technology was performed by interventional cardiologist Dr. Alain Cribier in 2002.⁷⁷ The technology and procedure for TAVI is dramatically different from traditional surgery, such that leading customers for surgically implanted prosthetic valves will generally not be capable of using transcatheter technology. While certain “hybrid” forms of transcatheter technology exist that are amenable to surgical use, specifically transapical implantation, the main developmental focus is on products that will be used by interventional cardiologists to replace the aortic valve without requiring the specific skills of a cardiothoracic surgeon. The transcatheter technology clearly meets the characteristic that leading customers, in this case cardiothoracic surgeons, will be unable to use this technology. However, it is also instructive to evaluate whether cardiothoracic surgeons, or even leading interventional cardiologists, acknowledge that transcatheter valve replacement could represent a viable alternative to surgical replacement.

In evaluation of the sentiment of cardiothoracic surgeons with regard to TAVI, most appear to believe that the technology represents an advance from the viewpoint that it will allow therapy to be provided to high-risk, or non-surgical, patients but that TAVI will not soon replace the core surgical procedure for aortic valve replacement (AVR). For instance Dr. Michael Mack, an esteemed cardiothoracic surgeon at Baylor Healthcare System writes:⁷⁸

“Just as the rumors of the demise of surgical bypass were premature, conventional AVR will continue to be the predominant technique for the treatment of aortic stenosis during at least the next decade.”

Also of interest is an editorial published by Dr. R. David Fish in *Circulation*. The editorial espouses the author’s “enthusiasm” for percutaneous valves, but also contrasts the impact of TAVI with that of the first mechanical valve implantation. In this comparison Dr. Fish warns that:⁷⁹

“This stunning success [of the first mechanical valve implantation] will not soon be matched by current percutaneous aortic valve procedures. We have a long way to go.”

Despite these pronouncements, the authors also acknowledge that over 20,000 transcatheter aortic valve procedures have been performed since Cribier’s first case in 2002, and that roughly 20% of aortic valve procedures in Germany today are performed using transcatheter techniques.⁸⁰ While these stakeholders now see a potential role for transcatheter devices, the knowledge that these devices were invented, and the development pursued, by interventional cardiologists supports the hypothesis that technology disruptive to the skill sets of leading customers tends not to be developed, or openly accepted, by those leading customers.

Further discussions with a practicing cardiothoracic surgeon indicated that TAVI technology is approached with some “*skepticism and trepidation*” by surgeons who feel they will be unable to learn

these new techniques. These clinicians also seem to recognize that TAVI technology represents a real and significant threat to their surgical practices. Often patients with valvular disease are evaluated by cardiologists and subsequently referred to cardiothoracic surgeons when appropriate. Concern exists within the cardiothoracic community that more interventional cardiologists are likely to recommend TAVI, which that physician could perform, as opposed to referring a patient for surgical intervention, which would be performed by a cardiothoracic surgeon. This sentiment supports the notion that leading customers are resistant to technologies that they are unable to utilize and are disruptive to their primary skillset.⁸¹

Conclusions:

The analysis of leading customers' perceptions regarding the introduction, and development, of tissue valves and TAVI appear to provide conflicting conclusions. In the case of tissue valves, the innovation originated from a leading customer of traditional mechanical valves. Other leading cardiothoracic surgeons were skeptical of the chances for success, but also recognized the value in developing this technology further. This perception from leading customers does not support the hypothesis that disruptive innovations will be rejected.

In the case of TAVI, the innovation took place away from the traditional customer. Additionally most of the development work has been driven by interventional cardiologists, with the involvement of surgeons mostly during randomized controlled trials.⁸² Furthermore, while cardiothoracic surgeons recognize the future potential of TAVI, they also appear to discount the speed at which the technology will impact their traditional patients. The lack of involvement from leading cardiothoracic surgeons in the early development of TAVI technology, combined with the general inability for surgeons to use the TAVI technology, appears to support the premise that leading customers are not the source of this disruptive innovation. Furthermore, the expression of "*skepticism and trepidation*" among leading customers, who would be unable to use TAVI technology, supports the hypothesis that leading customers reject disruptive innovations that are disruptive to their business or skillsets.

Additionally, one may ask whether tissue valve technology is appropriately classified as a disruptive innovation. Arguments could be made that tissue valves represent a sustaining innovation due to their development by leading customers. However, this presents a self-sustaining semantic argument wherein technologies are defined by the characteristic of the model as opposed to the characteristics of the technology. Tissue valves presented a radically new value proposition. They also initially were not adopted by most leading customers, despite interest in the technology. The hesitance of leading customers to adopt tissue valve technology was a function of traditional performance that was below clinically acceptable standards for most patients. However, over an extended 20 year course of innovation, tissue valves have begun to unseat mechanical valves in younger and younger patient populations.⁸³ It appears therefore that the timeline for evaluating the technological trajectory of disruptive medical technology is extensive in this instance, but that tissue valves do indeed represent a disruptive innovation.

Given the reaction of cardiothoracic surgeons to tissue valve technology, the hypothesis that "*Disruptive innovation in the interventional medical device industry will always be rejected by leading customers*" cannot be conclusively rejected.

⁶⁷ Christensen CM. *The Innovator's Dilemma: When New Technologies Cause Great Firms to Fail*. Boston, Mass.: Harvard Business School Press, 1997.

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- ⁷⁶ Starr A. Lasker clinical medical research award. The artificial heart valve. *Nat Med.* 2007; 13(10):1160-1164.
- ⁷⁷ Cribier A, Eltchaninoff H, Bash A, et al. Percutaneous transcatheter implantation of an aortic valve prosthesis for calcific aortic stenosis: First human case description. *Circulation.* 2002; 106(24):3006.
- ⁷⁸ Mack MJ. Does transcatheter aortic valve implantation mean the end of surgical aortic valve replacement? *Texas Heart Institute Journal.* 2010; 37(6):658.
- ⁷⁹ Fish RD. Percutaneous heart valve replacement: Enthusiasm tempered. *Circulation.* 2004; 110(14):1876.
- ⁸⁰ Fish RD. Percutaneous heart valve replacement: Enthusiasm tempered. *Circulation.* 2004; 110(14):1876.
- ⁸¹ Davidson, M. Personal Communication. June 2011
- ⁸² Leon M, Smith C, Mack M, et al. Transcatheter aortic-valve implantation for aortic stenosis in patients who cannot undergo surgery. *N Engl J Med.* 2010; 363(17):1597-1607.
- ⁸³ Frost and Sullivan. Feb. 2009. Cardiovascular Business Digest - U.S. Heart Valve Market. Available from: <http://www.frost.com>

Hypothesis 3:

Disruptive innovation in the interventional medical device industry is always first commercialized in a small or insignificant market.

Indicated Use and Epidemiologic Analyses in Medical Device Innovation:

Another central tenant to Christenson's model of disruptive innovation is that the initial market for disruptive technologies is limited and therefore unattractive to incumbent organizations. In addition to markets being small, they are also initially ill-defined and require customers to experiment with technology before uncovering the ideal application, which subsequently leads to increases in market size. Christenson goes on to say:⁸⁴

"When [disruptive technologies] initially emerge, neither manufacturers nor customers know how or why the products will be used, and hence do not know what specific features of the product will and will not ultimately be valued."

The implication of this tenant is that successful commercialization of disruptive technology requires experimentation by customers and that market research prior to commercialization would likely be ineffective as customers are unaware of the optimal use for disruptive technologies prior to the opportunity to experiment with applications for the technology.

The application of this premise to the medical device industry is challenging on a number of levels. First, the concept of experimentation with the use of medical devices is difficult from the perspective of both regulatory guidelines and general utility of the product to multiple pathologies. FDA regulations require medical devices be approved for specific indicated uses and that manufacturers subsequently label the device with these approved indications. According to the FDA's General Program Memorandum #G91-1:⁸⁵

"The general statement of the 'Indications for Use' identifies the target population in a significant portion of which sufficient valid scientific evidence has demonstrated that the device as will provide clinically significant results and at the same time does not present an unreasonable risk of illness or injury associated with the use of the device."

Manufacturers are further constrained in marketing their products within these FDA approved indications. This dynamic is in significant contrast to the introduction of novel consumer electronics wherein the product can be marketed and used in any number of ways. In the medical device industry the indicated and expected use for the product is well known prior to market introduction. Additionally the experimentation with usage of medical devices outside defined indications cannot be supported by manufacturers due to the statutory regulations above.

Furthermore, given the well-defined indications for use, epidemiologic market research can be undertaken to define the potential size of a market prior to a product's clinical introduction. Indeed, prior to introduction most products are required to have undergone a thorough process evaluating their

efficacy within the target market. This represents a significant deviation from the scenarios described by Christenson, wherein the markets for disruptive innovations cannot be analyzed because the markets do not yet exist. With interventional medical devices the target market can be quite easily approximated. Using epidemiologic studies, combined with the indications for device use, an affected patient population can be identified. Furthermore, the incidence of disease can also be approximated, which provides an estimation of changes in market size with time. This market sizing is not possible in the types of disruptive technologies and products traditionally examined. For instance with disruptive consumer electronics it is difficult to understand the rate of adoption, or even the ultimate use, for that product.

The unique characteristics discussed above warrant exploration of the hypothesis that, "*Disruptive innovation in the interventional medical device industry is always first commercialized in a small or insignificant market.*" To evaluate this hypothesis the initial indicated market size will be estimated for tissue valves and for transcatheter valves. An analysis of this market size will be performed and compared to the existing market for prosthetic valves, at the time of the given technology's introduction. This comparison will inform conclusions regarding the initial size of markets in which disruptive medical technologies are introduced.

Market Size and Indications for Tissue Valves:

Within a short time of the introduction of tissue valves it was apparent that this technology had limitations that would prevent its widespread use in all patients needing aortic valve replacement. Specifically it was suggested that, “...the most appropriate use of tissue valves might be in those patients whose life expectancy is less than the proved durability of the valve”.⁸⁶ Indeed the use of tissue valves has been most prevalent in older adults with shorter life expectancy. This segment of the population also represented an ideal market for tissue valves as these patients often have contraindications for anticoagulation, and the biological process of valve calcification is also reduced in this population.⁸⁷ However, as the structural integrity of valves has improved, as discussed in the earlier chapter, the market size has correspondingly increased.

As illustrated in Figure 15 from Brown et al, the percentage of patients receiving bioprosthetic valves has steadily increased since the mid-1990s and the percentage of patients receiving mechanical valves has decreased steadily over the same period.⁸⁸ The increased market size for bioprosthetic valves was driven by sustaining innovations in the structural integrity of tissue valves, which has led to clinical recommendations that bioprosthetic valves be utilized in larger segments of the population. Specifically clinical recommendations have continued to emerge that recommend the use of tissue valves in younger patient populations.^{89, 90}

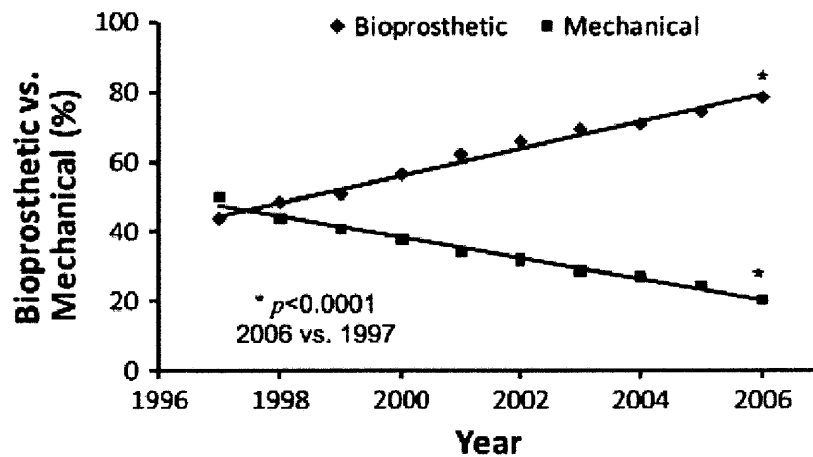


Figure 15: Percentage use of bioprosthetic valves relative to mechanical valves from 1997 through 2006.⁹¹

Evaluating this shift in market size over time it is recognized that initially the technology was in fact commercialized in a rather insignificant market, specifically elderly patients with limited life expectancy and contraindications for anticoagulation. However, with time and investment in sustaining innovation the market size grew and tissue valves are steadily replacing the use of mechanical valves for more patients. This dynamic adheres closely to that espoused by Christensen when he claims that disruptive innovations are commercialized in small markets.

However, the implication of Christensen's claim is that these small markets are difficult to analyze, because they often do not exist prior to introduction of the disruptive technology, and are not attractive areas of investment for incumbent firms. Despite being first commercialized in a small market the implication that incumbents are not incentivized to invest appears not to hold in this circumstance. Specifically, tissue valves received significant investment over the past thirty years by industry incumbents including Edwards Lifescience, Medtronic, and St. Jude Medical. Each of these companies also manufactured mechanical valves, but saw value in investing in the potentially disruptive technology of tissue valves despite the initially small market size.

The dynamics and incentives of medical device innovation may vary from traditionally studied industries due to the relatively well known potential market and value drivers that exist within the surgical setting. In this instance epidemiologic studies could inform the decision to invest in tissue valve development, as it is readily apparent that a large market exists for the technology, should sustaining innovations provide comparable structural integrity. Furthermore the drivers of value for valve technology were clearly delineated by Harken as early as the 1950s. Therefore, incumbent organizations knew that with investment and continued innovation bioprosthetic valve technology could provide ancillary performance that was important to their customers and improved patient outcomes. These specific value drivers are often more obscure within a consumer driven setting and may vary more significantly between different customers.

Based on the initially small market size for tissue valve technology, the hypothesis that, "*disruptive innovation in the interventional medical device industry is always first commercialized in a small or insignificant market*" cannot be rejected. However, unique incentives for investing in the development of disruptive innovations do appear to exist within this market.

Market Size and Indications for Transcatheter Valves:

In 2008 a position paper was published in *European Heart Journal* outlining the current expert guidelines for clinical use of transcatheter valve implantation.⁹² These guidelines recommend restriction of TAVI to “*high-risk patients or those with contraindications for surgery*”. However, the statement goes on to say that “[*indications for use*] may be extended to lower risk patients if the initial promise holds to be true after careful evaluation”. The sentiment of this European statement is echoed in a similarly timed 2008 AHA Scientific Statement, which concluded, “...*percutaneous AVR ...should be limited in use to patients considered to be high risk or to inoperable surgical candidates. In this context, even after FDA approvals, percutaneous devices should be used in only a small number of centers...until they are thoroughly tested in the clinical arena*”.⁹³

On initial examination it would appear that transcatheter valves are indeed restricted to a small or insignificant market, in that their use is initially being limited to non-surgical or high-risk patients. However, further analysis of epidemiologic studies of the target demographic indicates that this is in fact not a small or insignificant market. It is estimated that 30% of patients with severe symptomatic aortic stenosis are not surgical candidates due to associated comorbidities.⁹⁴ Furthermore, age-related aortic stenosis is the most common cause of isolated aortic valve disease in the adult population and in 2006 it was estimated that over 60,000 aortic valve replacement procedures were performed in the United States.^{95,96} Assuming that the patients undergoing aortic valve replacement represent approximately 70% of the total eligible population, then there are over 25,000 patients per year in the United States that are not surgical candidates, and represent the initial market for TAVI. Furthermore, in the 8 years following Cribier’s first clinical use of TAVI in 2002, over 20,000 patients have been treated using this method and it is estimated that nearly 20% of all aortic valve replacement in Germany is performed using TAVI, which clearly indicates a large and significant market for this technology.⁹⁷

The significance of this patient pool represents a deviation from the traditional model of disruptive innovation on multiple levels. First, the technology has a clearly defined market prior to introduction. It is prospectively known that the value inherent in this device will be its ability to provide clinical therapy to patients who are not surgical candidates. It is also widely speculated that with time indications for the use of transcatheter technology will expand into lower risk patients, therein creating a disruptive effect.⁹⁸ Secondly, the market for this disruptive technology can be readily quantified, using assumptions about device reimbursement and the known prospective patient population, and represents a significant share of the overall market.

For both of these reasons the hypothesis that “*disruptive innovation in the interventional medical device industry is always first commercialized in a small or insignificant market*” can be rejected.

Conclusions:

Market dynamics were evaluated for the introduction and continued development of tissue valve technology and for transcatheter valve technology. A determination was made that tissue valve technology was initially developed in a small or insignificant market, but that transcatheter technology is being developed in a larger market that creates a significant incentive for incumbent investment in this disruptive innovation.

The finding that transcatheter technology is being developed in a significant market allows rejection of the hypothesis that, *“disruptive innovation in the interventional medical device industry is always first commercialized in a small or insignificant market”*. Furthermore, the initial market dynamics for tissue valves suggest that unique characteristics of innovation also existed within this market. Specifically the continued investment in disruptive technology by multiple industry incumbents suggests that a market incentive existed to spur this investment in spite of an initially small market for the product.

It may again be considered whether tissue valves represent a sustaining innovation and not a disruptive innovation. However, this argument again becomes self-fulfilling if the technology is retrospectively classified based on its adherence to Christenson’s characteristics. Given the increasing market share for bioprosthetic valves, and the new value proposition that they offer, this technology continues to meet the criteria for consideration as a disruptive innovation.

The unique characteristics leading to incumbent innovation in disruptive technology may be driven by an improved ability to prospectively analyze the market for disruptive technology. Specifically the ability to quantify a patient population using epidemiologic data allows for estimation of future market potential, as opposed to initial market size. This may lead to increased willingness of incumbent organizations to invest in technology that may not have an initial market, but which could be applied to a disease state with a large future market. This opportunity to perform informed analysis of a market that does not yet exist is limited when evaluating a discretionary purchase, such as consumer electronics or the retail marketplace.

Furthermore, the drivers of value are more readily discernible within the interventional medical device industry. Dr. Harken’s prescient delineation of performance criteria allows informed investment in technology that shifts competition from traditional performance metrics to an ancillary performance metric. Both tissue and transcatheter technologies shift competition in this manner. Incumbent organizations are able to confidently pursue disruptive innovations because they can validate the ancillary value proposition at an early stage of development, and subsequently have confidence that investments in sustaining innovation that provide comparable traditional performance will be worthwhile.

Given the analysis above, it can be concluded that disruptive innovation in the medical device industry may emerge in a small, or large, market; but the characteristics of innovation that incentivize

investment by incumbent firms is different in this industry than those traditionally examined by academic researchers.

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⁹⁰ Puvimanasinghe J, Takkenberg J, Edwards M, et al. Comparison of outcomes after aortic valve replacement with a mechanical valve or a bioprosthesis using microsimulation. *Heart*. 2004; 90(10):1172.

⁹¹ Brown JM, O'Brien SM, Wu C, Sikora JAH, Griffith BP, Gammie JS. Isolated aortic valve replacement in North America comprising 108,687 patients in 10 years: Changes in risks, valve types, and outcomes in the society of thoracic surgeons national database. *J Thorac Cardiovasc Surg*. 2009; 137(1):82-90.

⁹² Vahanian A, Alfieri O, Al-Attar N, et al. Transcatheter valve implantation for patients with aortic stenosis: A position statement from the European association of cardio-thoracic surgery (EACTS) and the European society of cardiology (ESC), in collaboration with the European association of percutaneous cardiovascular interventions (EAPCI). *Eur Heart J*. 2008; 29(11):1463.

⁹³ King III SB, Smith Jr SC, Hirshfeld Jr JW, Jacobs AK, Morrison DA, Williams DO. 2007 focused update of the ACC/AHA/SCAI 2005 guideline update for percutaneous coronary intervention: A report of the American college of Cardiology/American heart association task force on practice guidelines: 2007 writing group to review new evidence and update the ACC/AHA/SCAI 2005 guideline update for percutaneous coronary intervention, writing on behalf of the 2005 writing committee. *Circulation*. 2008; 117(2):261.

⁹⁴ Leon M, Smith C, Mack M, et al. Transcatheter aortic-valve implantation for aortic stenosis in patients who cannot undergo surgery. *N Engl J Med*. 2010; 363(17):1597-1607.

⁹⁵ Cohn LH. *Cardiac Surgery in the Adult*. McGraw-Hill Medical Publishing, 2008.

⁹⁶ Frost and Sullivan. Feb. 2009. Cardiovascular Business Digest - U.S. Heart Valve Market. Available from: <http://www.frost.com>

⁹⁷ Mack MJ. Does transcatheter aortic valve implantation mean the end of surgical aortic valve replacement? *Texas Heart Institute Journal*. 2010; 37(6):658.

⁹⁸ Vahanian A, Alfieri O, Al-Attar N, et al. Transcatheter valve implantation for patients with aortic stenosis: A position statement from the European association of cardio-thoracic surgery (EACTS) and the European society of cardiology (ESC), in collaboration with the European association of percutaneous cardiovascular interventions (EAPCI). *Eur Heart J*. 2008; 29(11):1463.

Hypothesis 4:

Disruptive innovation always represents a lower margin business opportunity relative to traditional products.

Profitability of Disruptive Innovation to Incumbent Firms:

The Christensen model of disruptive innovation requires that these technologies be lower cost and lower margin than traditional technologies. The implication of this dynamic is that incumbent organizations are reticent to invest in disruptive technologies because the combination of lower margins, and initial ill-defined markets, discussed above, represent less profitable business opportunities relative to their traditional products. Therefore, invoking the theory of *resource dependence* it is argued that incumbent organizational structures are incapable of developing disruptive innovations because continued rational decision making will divert resources away from disruptive projects that rationally appear to promise lower profits, and towards sustaining innovations that appear to promise higher margins and profits.

The implication of this theory is that disruptive technology must be commercialized through an independent organizational structure. Often that means development by a new entrant to the market, but it may also mean a resource independent organization within the incumbent enterprise.

Within the interventional medical device industry however, the cost of a product is not a major driver of value relative to the device's clinical utility. Furthermore, an intermediary agent, specifically the surgeon, exists between the manufacturer and the end user. This intermediary agent does not bear the cost of the product decision and therefore a moral hazard is created, which dilutes the effect of price on the overall value proposition. It therefore is hypothesized that disruptive innovation within the interventional medical device industry may exist at more profitable levels than incumbent technology. The implication of this hypothesis being that contrary to previously examined industries, incentives exist for the development and commercialization of disruptive innovation by incumbent firms.

This hypothesis will be tested through determination and examination of the pricing of tissue valves relative to mechanical valves, and transcatheter valves relative to surgically implanted valves. In addition, changes in systemic procedural costs will be evaluated during each technological iteration.

Tissue Valve Pricing Relative to Mechanical Valves:

Through examination of historical literature and recent market research reports it is possible to reconstruct the approximate pricing for tissue and mechanical valves at multiple periods in time. Pricing data for mechanical and tissue valves exists for 1984 and for present day.

The cost of a mechanical valve varied based on the valve design. For an “aortic caged ball” valve design, specifically the Starr-Edwards Model 1200/1260 the list price in 1984 was \$1,700. The “aortic tilting convexoconcave disc valve”, specifically the model manufactured by Bjork-Shiley cost \$2,100. The “aortic bileaflet”, which became the dominant mechanical valve design, manufactured by St. Jude Medical was sold at a list price of \$2,095 in 1985.

The dominant tissue valve design in 1985 was the “Carpentier-Edwards Bioprosthesis”, which sold with a list price of \$1,875 in 1984. A summary table of this pricing data is presented below.

Valve Design	Valve Type	Manufacturer	List Price	2005 Inflation Adjusted Price
Aortic Caged Ball	Mechanical	Edwards	\$1,700	\$3,180
Aortic Tilting Convexoconcave Disc	Mechanical	Bjork-Shiley	\$2,100	\$3,792
Aortic Bileaflet	Mechanical	St. Jude Medical	\$2,095	\$3,783
Carpentier-Edwards Bioprosthesis	Tissue (Porcine)	Edwards	\$1,875	\$3,508

Table 1: Reference prices for mechanical and tissue valves in 1984/85 and inflation adjusted to 2005 dollars.^{99,100}

By 2005, the aortic bileaflet mechanical valve and the Carpentier-Edwards tissue valve each became widely accepted as a dominant design. An evaluation of pricing for these two valves in 2005 shows an average selling price of \$4,427 for a mechanical valve and \$4,929 for a tissue valve.¹⁰¹

Valve Type	Average Selling Price
Mechanical	\$4,427
Tissue	\$4,929

Table 2: Average selling prices of tissue and mechanical valves in 2005.¹⁰²

While the manufacturing costs for tissue versus mechanical valves are not readily available, it has been estimated by expert opinion that manufacturing cost are likely to be comparable across mechanical and tissue valve technologies.¹⁰³

The preceding data illustrate a number of interesting points. First, in the early years of tissue valve development, the product was sold for roughly 10% below the price of a bileaflet mechanical valve. However, tissue valves also sold for roughly 10% more than aortic caged ball valve. It is also worth noting that Edwards was manufacturing both the aortic caged ball valve and the tissue valve in 1984 and the tissue valve was being sold at a higher price, and therefore represented a potentially more profitable product line than their traditional caged ball valve.

Furthermore, it is interesting to note that prices for valves have risen faster than the rate of inflation, and that tissue valves are now sold for higher prices than mechanical valves. The reasons for this change in relative pricing may be due to multiple factors. First, as previously described, the performance characteristics of tissue valves were not fully understood in the mid-1980 and therefore the product may have needed to sell at a discount to mechanical valves due to this unknown characteristic. Secondly, the pricing may be a function of the rate of sustaining innovation in both mechanical and bioprosthetic valves. By 1984 mechanical valves had progressed through multiple rounds of sustaining innovation, as evidenced by the multiple valve designs and variety of manufacturing materials applied to these core designs. However, tissue valves had not yet progressed through this period of sustaining innovation. Specifically, through the 1990s as more was learned about the physiology of calcification and valve degradation, a variety of design solutions emerged to address these issues. Among the sustaining innovations in valve technology were the shift to bovine pericardium from porcine pericardium, and modifications in the chemical preservation of valves to slow the calcification process.

For Edwards the pursuit of tissue valves represented a rationally profitable business opportunity as evidenced by the higher price they were able to charge relative to their caged ball valve. Additionally, the increase in tissue valve prices over time, relative to mechanical valve prices, is further support for the notion that tissue valves represented a profitable business opportunity for industry incumbents. Therefore the hypothesis that, *“Disruptive innovation always represents a lower margin business opportunity relative to traditional products”* may be rejected.

Throughout the development of mechanical and tissue valves, the general surgical procedure was not significantly affected by these technological changes. Therefore, it is also reasonably assumed that the procedural costs were not significantly affected by the emergence of tissue valves and their subsequent sustained innovation. However, it is worth understanding whether this dynamic is different for technology that requires significant changes in the surgical process.

Transcatheter Valve Pricing Relative to Surgical Implantation:

The emergence of transcatheter technology represents a complex and expensive deviation from traditionally implanted surgical valves. In the examination of cost and price, however, it is essential that both the cost of the device and the cost of the surgical procedure be evaluated. In the circumstances of transcatheter valve technology it would be expected that both costs would change dramatically.

An evaluation of the cost effectiveness of TAVI was recently undertaken by Dr. Matthew Reynolds, and the results presented at the 2011 meeting of the American Heart Association.¹⁰⁴ This study includes estimated costs for both the commercial price of the Edwards SAPIEN transcatheter valve, as well as an estimate of overall procedure related costs. With regard to the price of the transcatheter device, the estimated commercial price is \$30,000. The estimated costs associated with the patient admission are \$78,540.

With regard to the device costs it is clearly evident that TAVI technology represents a significantly more costly device than surgically implanted tissue valves, which were previously shown to cost approximately \$4,929. While the precise manufacturing cost for TAVI technology is not available, assumptions regarding the gross margins are possible through evaluation of financial statements and SEC filings from Edwards. Specifically, these filings show that as the TAVI volume grows, so has Edwards' overall gross margin. Furthermore, management attributed the improvement in gross margin to an improved product mix.¹⁰⁵ Therefore, it can be reasonably assumed that the increased TAVI sales in this quarter contributed to improved corporate margins. These results imply that the TAVI technology represents a profitable business opportunity for this incumbent manufacturer due to both improved gross margins and higher selling prices. The higher selling prices are related to the manufacturer's ability to capture the value they create in disrupting ancillary procedural expenses and, as with most medical devices, are not driven by the costs of production.

Given these results the hypothesis that, *"Disruptive innovation always represents a lower margin business opportunity relative to traditional products"* may be rejected.

The analysis of device costs looks exclusively at the perspective of the medical device manufacturer; however, it is also important to evaluate the cost and pricing structure for the care provider. The estimate of procedural costs using TAVI is \$78,540, as previously mentioned. However, the mean inpatient charges for a traditional surgical intervention are estimated at \$135,000.¹⁰⁶

An interesting dynamic appears to exist for this disruptive innovation, wherein the innovation represents a profitable business opportunity for the innovator, but use of the technology may represent a less profitable business opportunity for the end user, specifically the hospital system. In a non-medical environment one would expect this type of device to lack an incentive for adoption because the end user would have no rational reason to shift to a less profitable product or process. However, in the medical system the procedural decisions are driven by clinical necessity and clinical outcomes as opposed to profitability. Furthermore, the physician intermediary is intentionally insulated from the

impact of these procedural decisions through a dual reimbursement structure that reimburses the facility separately from the physician. Therefore the physician would ideally not have a financial incentive to recommend one procedure over another, and would be guided exclusively by clinical data.

In this circumstance a relevant question is, "*what is being disrupted*" and how does the answer affect the market dynamics and incentives for incumbent firms to innovate. Using the current example of TAVI it may be argued that the device is more disruptive to sophisticated surgical skill, than it is to surgically implanted valves. While the end result would be disruption of both surgical skill and the surgical product, the dynamics of price can be speculated to result from this disruption of surgical skill. Specifically TAVI promises to create enormous value, both by expanding valvular repair into newly indicated populations, and by removing the complexities and cost associated with open-chest surgery. By disrupting the need for cardio-pulmonary bypass, a sternotomy, the surgical setting, and even the extended training associated with a cardio-thoracic surgeon the manufacturers of transcatheter valves are able to capture the enormous value created by this technology. Therefore, even though transcatheter technology is disruptive to an incumbent firm's traditional surgically implanted product lines, the transcatheter technology represents a highly profitable business opportunity due to the captured value from disrupting surgical skill and reducing procedural complexity.

Conclusions:

To evaluate the hypothesis that disruptive innovations do not represent profitable business opportunities to incumbent organizations an evaluation of pricing and estimated margins was undertaken for mechanical, tissue, and transcatheter valves. The results of this analysis demonstrated that each disruptive iteration appeared to represent a profitable business opportunity for an incumbent firm. We are therefore able to reject the hypothesis that, *“Disruptive innovation always represents a lower margin business opportunity relative to traditional products”*.

However, the analysis of tissue valves disrupting mechanical valves represents a unique dynamic relative to the analysis of TAVI disrupting surgical valves. In the case of tissue valves, the product was directly disruptive to another incumbent product; but in the case of TAVI the product promises to be disruptive to both an incumbent product and surgical complexity.

The development of tissue valves represented a profitable business opportunity for Edwards as evidenced by the increase in price over their existing mechanical valve technology. The technology represented an improvement in ancillary performance that was known to have value in defined patient populations. Furthermore the lower traditional structural performance was only relevant in younger patients whose expected longevity was longer than that of the tissue valve. While this performance metric initially limited the market size for tissue valves, it did not limit the value proposition for older patients, whose life expectancy was less than that of the expected valve durability. Therefore in this initial population the tissue valve technology offered additional value, which could be captured by the manufacturer. Also, as sustaining innovations took place on tissue valve technology, and the technology became applicable to younger patients, the manufacturer was able to continue capturing that value, as evidenced though the rise in tissue valve prices past the price of mechanical valves.

Even though tissue valve technology is beginning to disrupt mechanical valve technology it still represented a profitable business for incumbent firms who were rationally incentivized to enter this market and pursue long-term investment in sustaining innovations related to tissue valve technology.

In contrast, the dynamics of TAVI represent a different disruptive circumstance. Were TAVI to be evaluated at a system wide level, as opposed to solely from the perspective of the medical device manufacturer, then it may adhere more closely to the characteristics enumerated by Christensen. Specifically, the effect of TAVI on the system is likely to reduce healthcare costs given the prior estimates of procedural charges. However, this assumes that TAVI technology will continue to progress and will eventually be indicated for use in patients who are surgical candidates. In the short term the impact of expanding therapy to a wider patient population may result in higher total healthcare costs. The hospitals may benefit because they will continue to perform surgical procedures on patients who are surgical candidates, but they will also now be able to perform TAVI on patients who are not surgical candidates. However, if a time comes when surgical candidates can be treated with TAVI, then hospitals will be forced to transition from a more profitable surgical procedure to a less profitable interventional procedure.

The dynamics facing TAVI are similar to that of angioplasty and stenting, which created a similar disruptive dynamic for coronary artery bypass grafting (CABG). The impact of innovation on overall spending, and clinical outcomes, has been examined by Dr. David Cutler and Dr. Mark McClellan. In the case of treatment for heart attacks they show that spending levels increased due to technological innovation, but more as a result of treatment rates than increases in price.¹⁰⁷ These technological innovations were primarily tools and techniques for performing angioplasty or stenting, which led to more patients being eligible for intervention following a heart attack. The authors of this study go on to demonstrate that the associated costs of this procedure are more than compensated for by the net benefit to society achieved by expanding treatment rates. From a system wide perspective this dynamic is similar to that described by Christensen. Interventional techniques are cheaper and easier than surgical techniques and therefore allow more patients to receive therapy.

However, the inconsistency with Christensen's theory arises when evaluating solely from the perspective of the medical device manufacturer. As described above, the manufacturer has incentives to pursue disruptive innovation in this industry that are unique to the healthcare space. In particular, incumbent firms are able to pursue disruptive innovations because the most significant component of what they are disrupting is not their traditional product. More often it is disruption of surgical skill or another high cost procedural component. By disrupting these procedural expenses medical device manufacturers are able to capture a larger component of the value they create and therefore the innovations they release can be priced at levels higher than their traditional products. Given that medical device innovators often disrupt procedures more than technologies; they may be more accurately characterized within Christensen's model as "new-entrants" as opposed to "incumbents". This dynamic creates a rational incentive for these medical device manufacturers to pursue disruptive innovation.

⁹⁹ Morse D, Steiner RM, Fernandez J. Guide to prosthetic cardiac valves. 1985.

¹⁰⁰ Inflation calculations based on consumer price index changes. Available from:
<http://www.westegg.com/inflation/>

¹⁰¹ Frost and Sullivan. Feb. 2009. Cardiovascular Business Digest - U.S. Heart Valve Market. Available from:
<http://www.frost.com>

¹⁰² Frost and Sullivan. Feb. 2009. Cardiovascular Business Digest - U.S. Heart Valve Market. Available from:
<http://www.frost.com>

¹⁰³ Schoen, FJ. Personal communication. April 2011

¹⁰⁴ Matthew R. Reynolds, M.D., M.Sc., On Behalf of the PARTNER Investigators, Lifetime Cost Effectiveness of Transcatheter Aortic Valve Replacement Compared with Standard Care Among Inoperable Patients with Severe Aortic Stenosis: Results from the PARTNER Trial (Cohort B)

¹⁰⁵ Edwards Lifesciences. May 9, 2011. Form 10-Q

¹⁰⁶ Frost and Sullivan. Oct. 2009. The next major medical device blockbuster: Transcatheter valves Available from:
<http://www.frost.com>

¹⁰⁷ Cutler DM, McClellan M. Is technological change in medicine worth it? Health Aff. 2001; 20(5):11.

Discussion

Summary of Findings:

The motivating and overriding question addressed in this thesis is whether the interventional medical device industry has unique characteristics of disruptive innovation. The unique regulatory requirements and economic structure within the healthcare industry provide a rational basis for exploring this question in greater detail. This thesis sought to evaluate this question using the model of disruptive innovation established by Clayton Christensen in "*The Innovator's Dilemma*" and applied core tenants of this model to the market for prosthetic heart valves. Four specific hypotheses were generated; data was prospectively gathered to evaluate these hypotheses; and the hypotheses were evaluated on the basis of this data.

The hypotheses were:

1. **H₀:** Disruptive innovation in the interventional medical device industry will always have inferior traditional performance and higher ancillary performance than incumbent technology.
2. **H₀:** Disruptive innovation in the interventional medical device industry will always be rejected by leading customers.
3. **H₀:** Disruptive innovation in the interventional medical device industry is always first commercialized in a small or insignificant market.
4. **H₀:** Disruptive innovation always represents a lower margin business opportunity relative to traditional products.

The conclusions reached with regard to each hypothesis are as follows:

1. Disruptive innovation in the medical device industry *does not* always emerge with inferior traditional performance. Therefore the hypothesis of inferior traditional performance can be ***rejected***.

In considering the characteristics of performance it was illustrated that tissue valves have in fact held quite close to traditional characteristics of disruptive innovation. They initially had inferior durability but higher ancillary performance in the form of thromboembolic risk. Furthermore, with continued sustaining innovation tissue valves are beginning to disrupt larger segments of the mechanical valve market. However, as previously noted, tissue valves were introduced prior to the rigorous regulatory requirements that now govern the market entry of new valve technology. Given this dynamic the evaluation of TAVI is more relevant for examination of performance characteristics currently necessary for disruptive innovation to reach the market. As elucidated above, TAVI technology represents comparable outcomes in the traditional performance metrics of mortality and thromboembolic risk. However, TAVI also represents an improvement in the ancillary performance characteristics of patient comfort and ease of implantation.

2. Leading customers were supportive, if skeptical, of tissue valve development. Therefore the hypothesis of rejection by leading customers can be **rejected**.

The question of leading customer's support for disruptive technology was a nuanced evaluation. In the case of transcatheter technology it is apparent that leading customers did not significantly contribute to technological development, and also will be mostly unable to use this innovation as it shifts procedures from a surgical to an interventional setting. However, the level of support, or rejection, of tissue valves among cardiac surgeons is less clearly defined. This technology was developed by leading cardiothoracic surgeons and fit within the constraints of the existing surgical procedure. Despite enthusiastic utilization by these innovators, their colleagues voiced apprehension and skepticism regarding the technology. In parsing this conflict it was apparent that even though leading customers were skeptical of the initial performance characteristics of tissue valve technology they also understand and appreciated the potential value that could be generated through the ancillary performance. It is this combination of development by a leading customer, ability to be used by leading customers, and appreciation of value among leading customers that led to a rejection of this hypothesis. Furthermore, one could extrapolate these results to suggest that leading customers are likely to reject innovations that are disruptive to their primary business model or skill set. In the case of tissue valves the device was accepted by the community because it could be readily integrated into their practice; however TAVI represents a significant disruptive threat to the value proposition of a cardiothoracic surgeon, specifically his/her surgical training, and therefore is rejected by these customers.

3. The market for transcatheter technology was shown to be significant, and therefore the hypothesis that disruptive innovation must start in an insignificant market can be **rejected**.

Evaluation of the market size for disruptive technology also presented interesting dynamics that differed between the introduction of tissue valves and the introduction of transcatheter valves. In the case of tissue valves the market may have initially been estimated as all patients needing valvular replacement. However, it was soon realized that the lower durability of tissue valves would limit this technology to patients in whom longevity was less than expected valve durability. This would appear to limit the innovation to a small or insignificant market, although incentives also appeared to exist for incumbents to invest in this technology. This incentive may have been due to an ability to analyze a market that did not yet exist, specifically the market for tissue valves in younger patient populations. Analysis of the market size for transcatheter technology initially appeared to be similarly limited to high-risk or non-surgical patients. However further research demonstrated that this market was in fact quite large, well defined, and represents a significant opportunity for growth among incumbent firms. Therefore on the basis of the initial size of the transcatheter market this hypothesis was rejected.

4. Margins for both tissue valves and for transcatheter technology were shown to be either the same or higher than traditional technology. Therefore the hypothesis that disruptive innovation begins in lower margin businesses can be **rejected**.

Evaluation of the margins for tissue valves and for transcatheter valves provided similar conclusions, although each analysis elucidated unique dynamics for the corresponding innovation. Both tissue and transcatheter technologies represented either similar or higher margin business opportunities. Both markets also appear to incentivize innovation by an incumbent firm. However, the dynamics of what each product disrupts, and the timeline for disruption is unique in each circumstance. In the case of tissue valves, the product was eventually disruptive to mechanical valves and this disruption took place over nearly 20 years of sustained innovation. In the case of transcatheter technology, the product is disruptive to both an incumbent product but also disrupts the need for advanced surgical skill and associated surgical complexity. It appears that due to the disruption of surgical skill this product is capable of much higher pricing and therefore able to capture value from disrupting a secondary process in addition to their incumbent product. The implications of this dynamic will be discussed further in the subsequent section.

The conclusions above should not be interpreted to mean that disruptive innovation in the medical device industry *always* runs contrary to the traditional characteristics of disruptive innovation. Rather these conclusions should inform decision making by creating awareness that the medical device industry does not strictly adhere to traditional characteristics in all instances. For each of these hypotheses the conclusions were generally split between the two evaluated technological discontinuities, however this splitting was not uniform across hypotheses.

Implications:

The conclusions of this work have implication for the strategic decision making of various medical device stakeholders. Among those stakeholders are regulatory officials, healthcare policy officials, industry management, and technology transfer offices.

Regulatory officials have placed significant emphasis on creating incentives and monitoring the innovative process for medical devices.¹⁰⁸ These regulatory officials recognize that medical device innovation can positively impact the outcomes of patients worldwide.¹⁰⁹ However, the structure within which medical device innovation must take place is unique given the need to confirm safety and efficacy of technology prior to market introduction, and the limitations placed on indicated marketed uses for such technology. This dynamic changes the characteristics of disruptive device innovation as it prohibits market experimentation with novel technology. Furthermore, the current regulatory structure does not appear to have a robust process for dealing with tradeoffs between traditional and ancillary performance. In contrast to traditional examples of disruptive innovation where technologies enter the market with lower traditional performance and higher ancillary performance, medical device technology must have at least comparable traditional performance and higher ancillary performance to satisfy regulatory requirements. Regulators are faced with a difficult balance between protecting public safety and providing a pathway for approval of technology with challenging trade-offs in performance. Understanding these performance trade-offs is important in ensuring that disruptive innovations reach the market in a competitive structure that allows the application of technology to appropriate patients and provides competitive incentives for investment in sustaining innovations.

Important implications also exist for healthcare policy stakeholders. The traditional forces of disruptive innovation have been shown to be powerful forces in lowering costs and increasing utilization of a product. Given the current focus on healthcare costs it is important to understand how these disruptive forces could be applied to medical technology. The findings of this thesis imply that incentives do exist for incumbent firms to pursue disruptive innovation. However, the technologies may be disruptive to surgical procedures more than incumbent technology. When this is the case, the technology may be able to capture the value of this disruption through higher prices and margins. The role of perspective is also important because while device manufacturers are incentivized to disrupt complex surgical procedures they may still not be incentivized to directly disrupt their own products. Additionally, the impact of cost in making product choices is muted through the use of a physician agent who is separately compensated for their services. This again represents a challenging balance between removing financial bias in clinical decisions and providing an incentive for medical device manufacturers to focus on lower cost disruptions to existing products as opposed to higher cost disruptions to surgical processes.

With regard to industry management the question of “*what is being disrupted*” is of paramount importance. In situations where a high cost and complex procedure can be replaced by a lower cost procedure using medical technology it is likely that the manufacturer of that technology will be capable of capturing the value created through higher prices for their technology. In these situations the manufacturer will be incentivized to innovate within this space in a manner that is atypical of traditional disruptive innovations. Specifically, resources will be expected to rationally flow to the disruptive technology because it represents a profitable business opportunity. Furthermore, the ability to use epidemiological data to prospectively analyze markets, combined with an ability to prospectively understand the key clinical drivers of value, allow incumbent organizations to pursue a rational decision making process that would be expected to result in investment in promising disruptive innovations. Some specific implications of this dynamic are the expectation that these types of disruptive innovation would be pursued early by industry incumbents and that these projects are likely to be successful within existing organizational structures. Invoking the theory of *resource dependence*, projects that represent profitable opportunities are likely to receive greater resources in a well-functioning organization. Therefore, it is important for industry management to understand precisely what is being disrupted by a potential technology. In the case where ancillary services or products are disrupted, and the innovator can capture the created value, they may follow the characteristics of a new entrant more than an incumbent firm.

As technology transfer offices evaluate potential licensees for their intellectual property a key objective is to ensure that the technology is developed and commercialized. First, the office should determine whether the technology is sustaining or disruptive in nature. If the product is a sustaining innovation then the office would be well served to license to an industry incumbent as incumbents have a long history of successful development of sustaining innovations. However, if the technology is a disruptive innovation then the subsequent question of “*what is being disrupted*” must be asked. Using traditional theories of disruptive innovation these technologies would need to be commercialized using an organizational structure that is independent of an incumbent firm. By asking the question of what is

being disrupted, licensing offices may find that in addition to disrupting a product, the technology is also disruptive to either surgical skill or procedural overhead of another kind. As illustrated through the analysis of transcatheter technology, in these instances the product may represent a profitable opportunity for incumbent firms who would be rationally incentivized to commercialize this disruptive technology. Therefore for this subset of disruptive technologies, incumbent firms with a track record of success may represent a preferable licensee, as opposed to licensing to a new entrant as would be indicated through traditional models of disruptive innovation.

Hypothetical Disruptive Effects of TAVI:

While TAVI technology is widely perceived as a potent disruptor to surgical procedures, the primary clinical trials to date have focused on non-operative or high-risk surgical candidates. This initial patient pool, by design, is therefore focused specifically on patients for whom surgical techniques are not a preferred option. Were the technology to remain focused exclusively on this patient subset then it would not generally compete with the surgical procedure. Therefore one could retrospectively object to the classification of TAVI as a disruptive innovation based on its limited impact to incumbent procedural techniques. The initial clinical testing of TAVI in a cohort of patients with significant unmet clinical needs allows for the determination of clinical performance outcomes in a way that would not be possible if TAVI were immediately positioned against prime surgical candidates. The ancillary performance of TAVI provides for its use in an untreated segment of the market, which allows experience to be gained that may provide for expansion of clinical indications that eventually disrupt the current surgical therapy guidelines.

Hypothesizing about the future success and broad applicability of TAVI techniques and technology leads to two potential outcomes. As clinical studies on TAVI technology expand to include patients who are surgical candidates, these trials may find the technology to be either non-inferior, or inferior to current surgical techniques. Each finding would have implications on the long-term incentives for continued development of this technology's disruptive potential.

In the case where a hypothesized clinical trial were to find TAVI to be non-inferior to surgical techniques one would expect to see rapid widespread adoption of TAVI technology, with corresponding disruption of surgical procedures. This clinical result would likely shift the mode of competition from that of a symbiotic relationship to that of direct competition. In the initial symbiotic state the two procedure types, TAVI and surgical, treat distinct patient populations and therefore are not capable of shifting volume between the two procedures. In addition the increased awareness of therapy options may increase the number of patients who are screened and therefore could contribute to volume increases in both patient populations. However, if TAVI were proven to be a clinically non-inferior substitute for surgery then the ancillary benefits of TAVI would likely cause it to be a preferred option among clinicians and patients.

In the hypothetical case where TAVI technology is demonstrated to be inferior to surgical techniques we could envision two immediate implications. The likelihood of the immediate reaction is dependent upon the degree of inferiority of TAVI relative to the surgical procedure. Given the ancillary benefits of TAVI,

patients and clinicians may be willing to accept decreased performance along certain clinical metrics. For instance if a clinical trial were to determine slightly higher rates of stroke for TAVI patients over a multi-year horizon, relative to surgical patients, then patients and clinicians would weigh that inferiority against the potential psychological benefits of a minimally invasive procedure. Within this assessment surgical procedures may demonstrate “over-performance” in terms of stroke reduction, which would be revealed by a patient’s willingness to accept a higher stroke risk in exchange for the benefits of percutaneous technology. In this instance the ability for TAVI to disrupt surgical procedures would also depend on the assessment of third-party payers, specifically insurance providers. A study demonstrating clinical inferiority could result in insurers refusing to pay for TAVI therapy. In this case adoption would be severely restricted until TAVI were to demonstrate either non-inferiority or superiority to surgical techniques.

It also may be true in this hypothetical situation that patients and clinicians determine the inferiority of TAVI outweighs its ancillary benefits and therefore surgical techniques remain a preferred therapy. In this instance, or in the instance where payers reject the technology’s performance, one would expect the manufacturer to assess the market opportunity for disrupting the surgical technique. If this opportunity were attractive, which in this case it appears to be, then one would expect the manufacturer to invest in sustaining innovation until the performance of TAVI is comparable to the performance of a surgical procedure.

In evaluating and hypothesizing whether TAVI will disrupt surgical procedures, and if so how quickly that disruption will take place, it is necessary to speculate as to the long-term performance of this technology. In the case of tissue valve technology, the developmental timeline spanned decades before tissue valves began their disruptive march, which is apparent through the steadily increasing ratio of tissue to mechanical valve utilization. TAVI may also span an extended timeline before disrupting surgical techniques and an assessment of that timeline would be dependent upon TAVI’s initial level of performance, which has yet to be determined in a low-risk surgical cohort. However, despite this starting level of performance it is clear that TAVI technology offers ancillary benefits that cannot be matched through a surgical procedure. It is this capacity for ancillary performance, and corresponding shift in value proposition, that makes TAVI a disruptive technology. With continued sustaining innovation one would expect the level of TAVI’s traditional clinical performance to rise and, over some length of time, become comparable to that of surgical techniques. Once comparable traditional performance is reached, the ancillary benefits of TAVI technology would be expected to cause rapid disruption of the traditional surgical market. Therefore the long-term impact of TAVI technology is hypothesized to be disruptive to surgical procedures. However, the requisite timeline is dependent upon the initial level of performance and rate of subsequent sustaining innovation.

Study Limitations and Applicability of Findings:

The preceding study is limited in scope and applicability of the findings. The conclusions are limited to the interventional medical device industry and given the previously discussed regulatory and economic characteristics may not be applicable beyond the medical device space. Furthermore, the conclusions are based upon a case study of one technology and therefore do not represent a statistically significant

sampling of data. Additionally, the long time horizon of innovation that is evaluated also coincides with changes in regulatory and economic structure within the medical device industry, which may impact results.

Despite these limitations, the results are believed to provide an informed basis for continued research into disruptive innovation specific to the interventional medical device industry. The complexities of innovating within this industry and the reliance upon enabling clinical science create extended innovation life cycles and thereby necessitate the examination of innovation across periods of time that may include changes to regulatory or economic structure. Furthermore, there are a limited number of medical device technologies that are supported by the detailed historical perspective that exists within the heart valve industry. Additionally, for medical technologies that do have a long history of innovation, the clinical variability between anatomic or pathologic idiosyncrasies would create challenges in aggregating findings and drawing conclusions across a statistically significant number of case studies.

Another challenge is the ability to prospectively identify what technology represents a “disruptive” versus a “sustaining” innovation. The perspective of this thesis was that a disruptive technology be defined by its ability to dramatically change the basis of competition. However, others may argue that disruptive innovation should in fact be defined by the characteristics that were tested in the preceding hypotheses. If one were to argue that consideration as a disruptive technology required adherence to the four characteristics previously delineated then the results of this thesis would be invalidated. However, the use of such an argument would appear to be a self-sustaining claim that relies upon semantic nuance to retrospectively force adherence to the traditional model of disruptive innovation. While the proper categorization of the technologies evaluated within the thesis could be subject to debate, it is believed that they both satisfy the criteria for disruptive innovations based on the ways in which they dramatically shifted the basis of competition and value proposition.

Furthermore, this thesis evaluates the perspective of the medical device manufacturer, but does not deeply examine the effects of disruptive medical device innovations on the overall healthcare system, or on the provider of health care, being the physician or hospital. Evaluation of innovation from a systemic viewpoint may result in different conclusions than those presented here as the question of “*what is being disrupted*” may lose significance when the effect of innovation on all stakeholders is evaluated.

Another area of consideration, which is not assessed within this study, is the market for medical devices outside of the United States (US). Specifically emerging markets such as China, India, and Brazil are beginning to grow and contribute more heavily to the earnings of large medical device manufacturers. The dynamics of healthcare delivery within these environments is different from the US model in a number of ways that may affect the applicability of Christenson’s model of disruptive innovation. First, consumers are responsible for a larger portion of the costs of care that they receive. Therefore these markets place a stronger weighting on the costs of care when assessing the overall value proposition for a given therapy. This may create an opportunity for the development and introduction of less costly, and possibly lower performing, device technology within these markets. Secondly, the number of

subspecialty trained surgeons in these geographies is limited. This creates a stronger need for devices that are disruptive to the need for costly surgical training. This training is costly in terms of both the time and energy required to receive the training as well as ancillary surgical costs related to that specialist providing therapy. For example, one could envision the TAVI technology being more readily adopted in geographies where cardiothoracic surgeons are not present but interventional cardiologists do exist. This dynamic is hypothesized due to both the lower total costs associated with a percutaneous intervention as well as the decreased level of training necessary to successfully complete the procedure; however, the ability to perform TAVI would also be predicated upon access to enabling technology such as fluoroscopic imaging.

Additional research would be warranted regarding the applicability of disruptive innovation to emerging markets. Interesting hypothesis could evaluate whether low cost solutions that reduce the need for high cost surgical skill are demanded within these markets. Subsequently one could ask whether the development and use of these low cost solutions could spur future adoption within the US market after sustaining innovations have increased the performance to a level of non-inferiority with current techniques. This dynamic could challenge the current focus of innovation wherein solutions are developed for the US or European market with performance requirements dominating the impact of cost within the market's assessment of value.

Further Areas of Study:

The premise of this study was limited to interventional medical devices. However, it would be reasonable to ask similar questions regarding the characteristics of innovation in the context of other types of medical devices or within the healthcare system more broadly. Some of this work has already been undertaken.¹¹⁰ Despite this existing body of work additional clarification would be useful for non-interventional medical devices such as imaging equipment or other technologies with large associated capital costs. Furthermore the dynamic of competition that exists between hospital systems would be interesting to explore. Specifically in the context of high capital cost medical device innovations it could be speculated that health care systems will be incentivized to acquire excess capacity with these technologies as they seek to compete against neighboring health care systems. This may create dynamics for innovating high cost equipment with relatively low marginal benefit. This dynamic would be worthy of additional research and is beyond the scope of the questions asked within this thesis.

This particular study could be expanded to deal with the emerging technologies for percutaneous mitral valve repair and compare those technologies to traditional methods of surgical repair. The technology and surgical procedures associated with mitral valve repair are sufficiently different from aortic valve replacement as to prohibit their inclusion in this analysis. Additional technologies that would be worthy of evaluation include laparoscopic surgery, angioplasty, or the implantable pacemaker or defibrillator market. Each of these technologies represents a dynamic where the basis of competition was shifted over time and each technology generally progressed along a trajectory from more to less invasive procedures. It would be hypothesized that these industries would exhibit similar characteristics of innovation to those of the prosthetic valve industry, but additional research is warranted to explore the dynamics of innovation for these distinct technologies.

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