4.5 Concept Exploration and Testing

INTRODUCTION

If "a picture is worth a thousand words," then in the medtech field, "a prototype is worth a thousand pictures." Fundamentally, there is no substitute for taking all of the conceptual, abstract thinking that has been performed to date and giving it a physical or functional form. Simple concepts can be fraught with problems or result in elegant, effective solutions. Complex ideas can lead to revolutionary results or be impossible to achieve. The only way to find out is to start more deeply exploring concepts through techniques such as prototyping.

The goal of concept exploration is to translate a promising concept from an idea into a rudimentary design, and then into a working form, in order to answer important technical questions. Concept exploration can be thought of as the beginning of the research and development (R&D) process – since it is an essential step through which the innovator learns about functionality, gathers preliminary feedback from target users, and tests features that can only be understood and proven through the manifestation of the design.

One of the most important techniques used in concept exploration is prototyping, which is the process of creating early, experimental versions of a product. Prototyping plays a role at multiple stages of the biodesign innovation process. During ideation, the use of crude props to communicate ideas is one form of prototyping. Later, during concept screening, prototyping can be used as a mechanism for quickly and inexpensively evaluating multiple solution ideas against specific design criteria before deciding on a final concept. As innovators move forward, their technical requirements, designs, and models become more advanced. The more robust prototypes that result are used to refine product functionality and features through some combination of user, bench, simulated use, and tissue testing. As these tests are completed, successful prototypes begin to more comprehensively meet important design requirements and innovators begin to transition from prototyping to R&D (or product development).

Importantly, this chapter does not provide innovators with detailed instruction on how to construct different types of prototypes (Some preliminary information on this topic is

OBJECTIVES

- Understand how concept exploration is facilitated by techniques such as prototyping and supported by the testing modalities outlined in the biodesign testing continuum.
- Learn guidelines for prototyping, a key technique used in concept exploration, and what questions can be addressed through this approach.
- Become familiar with how to use prototyping in different engineering disciplines, including how to translate concepts into functional blocks.
- Understand how to use prototyping to create design requirements and generate high-level technical specifications related to product feasibility.
- Appreciate how to employ user, bench, simulated use, and tissue testing to transform a concept into increasingly advanced prototypes as the biodesign innovation process progresses.
- Recognize how to use concept exploration as a screen for prioritizing concepts.

provided in online Appendices 4.5.1, 4.5.2, 4.5.3, and 4.5.4). Instead, it outlines an approach innovators can follow to maximize the effectiveness of their concept exploration and testing efforts.


See ebiodesign.org for featured videos on concept exploration and testing.

CONCEPT EXPLORATION AND TESTING FUNDAMENTALS

Initial concept selection helps innovators narrow their focus from hundreds of **concepts** to a few (see chapter 3.2). In contrast, exploring concepts through prototyping may lead innovators to broaden their focus again as they explore dozens of different ways to technically realize the few concepts under consideration. Subsequently, by employing various testing approaches, innovators once again narrow in on the most promising solutions. However, all of these activities have the same goal: to provide additional data that eventually enables the innovators to choose a final concept and a single way of addressing an important **need**.

In determining which activities to undertake during concept exploration and which questions to answer through prototyping, innovators should strategically prioritize which elements of a concept present the greatest risk to the technical viability of an idea and thus need to be addressed early on. For instance, if a concept revolves around using a certain material in a truly novel way, innovators may seek to prove during concept exploration that the material will perform as hypothesized. If the answer to a limited prototyping experiment (**bench** or tissue test) suggests that the material could be successfully utilized in the intended way, this information helps mitigate significant risk in terms of the concept's feasibility. As risks are mitigated, innovators are able to attract increased interest in their solutions (see 5.2 R&D Strategy and 6.3 Funding Approaches). Accordingly, they should be thoughtful about how they prioritize their work.

At a more tactical level, concept exploration and the testing of the resulting **prototypes** represent the earliest parts of the R&D process. The biodesign testing continuum, shown in Figure 4.5.1, provides a complete overview of the progressively detailed and rigorous tests that are performed as early prototypes are transformed into full-fledged products. However, innovators typically rely on **user**, bench, tissue, and simulated use tests during concept exploration (although this varies based on the type of project and critical risks to be addressed). The later stages of this diagram – from live animal and cadaver testing through **clinical trials** – will be covered in 5.2 R&D Strategy and 5.3 Clinical Strategy.

Guidelines for effective prototyping

Early-stage prototyping is a creative exercise that can be energizing as well as highly informative. The approach described in this section applies to developing all types of prototypes, from mechanical solutions to those based on biomaterials science, electrical engineering, or computer science. As shown in Figure 4.5.2, some prototypes are quick, easy, and inexpensive to develop, while others are more complex, costly, and time-consuming. This is determined primarily by the stage in the biodesign innovation process and the objectives the innovator is seeking to address.

Prototyping is highly iterative, with each successive prototype built to answer questions that arise from the performance successes and deficiencies of previous versions. One way to effectively prototype in an iterative and focused manner is to break a concept down into smaller blocks that correspond to its different functions. Rather than prototyping the whole concept at once, the innovator focuses on proving the feasibility of smaller, essential components before testing them as a system. For example, in developing a new intravascular drug-eluting stent that elutes a commercially available drug over a longer period of time, innovators might explore a block focused on the polymer or mechanism used to allow for longer elution time (a biomaterials science and/or chemical engineering block), one focused on the mechanical properties of the stent itself so that it is

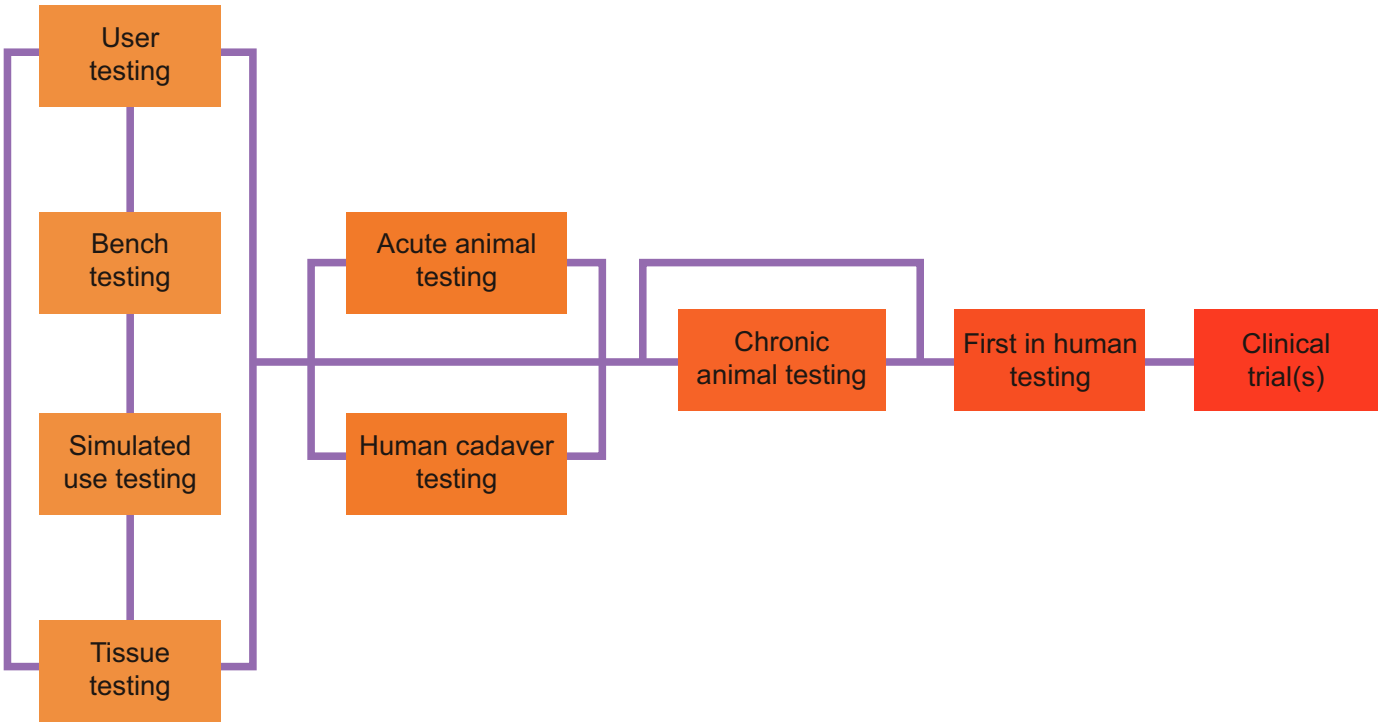

FIGURE 4.5.1
The biodesign testing continuum represents points of evaluation and feedback as innovators move from prototype to product. Note that not all tests are required as part of every project. The specifications undertaken should be based on the characteristics of the product.

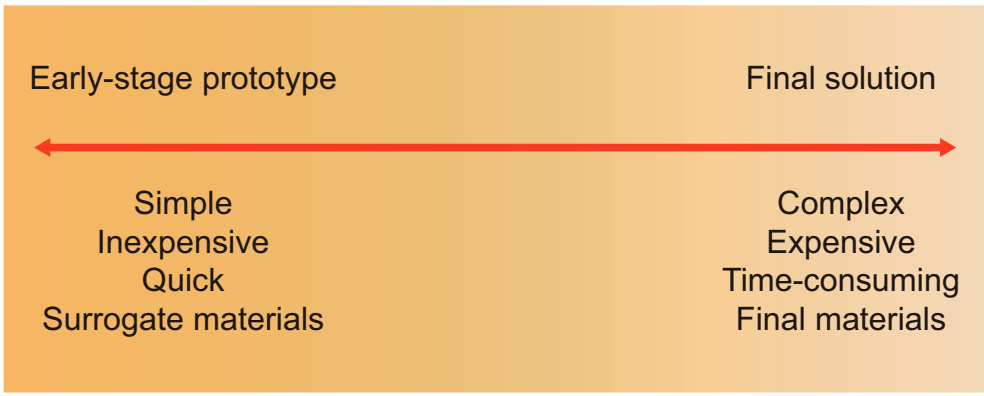

FIGURE 4.5.2
Different types of prototypes can be used to accomplish different objectives at varying stages of the biodesign innovation process.

well-seated within a vessel (a biomaterials science and/or mechanical engineering block), and another looking at the collapsed shape and pattern of the stent to allow for delivery (a mechanical engineering block). They then might tackle each block separately or in parallel, with several different prototyping exercises early in concept exploration to prove the feasibility of each element and/or uncover new issues that need to be addressed. This approach makes it easier for the innovators to define highly specific objectives for each preliminary prototype, and it also helps them determine which aspects of a concept are truly novel and, therefore, may represent the greatest risks that need to be mitigated. Additionally, for large-scale concepts (e.g., a new type of X-ray scanner), smaller blocks may be all that can be prototyped at an early stage of the project.

Through the creation of an iterative series of prototypes, innovators refine their understanding of how

the concept will work and gain an appreciation of issues related to the technical feasibility of the concept. As the smaller functional blocks are successfully prototyped, innovators can then start to put them together to understand how the solutions to the various blocks work together. As this process unfolds, they will identify some of the key design requirements that are most likely to satisfy the need in the user's mind. In response, they can continue to iterate on the prototypes until the solution adequately addresses the underlying need.

To take this approach to prototyping, innovators should follow the guidelines outlined below:

- Clearly identify the questions to be addressed through prototyping, focusing on the issues that – if answered with a prototype – will mitigate significant risks.
- Recognize that different types of prototypes may be necessary to address different questions.
- Isolate the most important functional blocks of a solution that need to be explored.
- Understand what is known about each functional block and what must be learned or proven.
- Use what is learned through prototyping to define more detailed design requirements and technical specifications.

To help illustrate these guidelines, an example of innovators working on a solution to the need for *a way to prevent strokes in patients with atrial fibrillation caused by left atrial appendage (LAA) thrombus* is followed throughout the chapter. As described in 2.2 Existing Solutions, the LAA is a small, pouch-like structure attached to the left atrium of the heart in which blood can coagulate to form clots, or thrombi, in patients with an abnormal heart rhythm (such as atrial fibrillation). These clots can dislodge and travel to the brain where they have the potential to create a blockage in an artery, leading to a stroke. In this example, the innovators are focused on the concept of preventing LAA thrombus by filling the LAA with a material that can be delivered in liquid form after which it will transform into a more solid consistency to eliminate the space where thrombi can form.

Identify the questions to be addressed

When innovators prepare to develop a prototype, their first challenge is to define the specific question or issue to address throughout the prototyping process. Clearly articulating this for each prototype helps to identify what critical elements of the concept should be included in the model. Including "extra" or extraneous features in a model complicates the end results, distracts from testing issues on the critical path, and can unnecessarily increase the time and cost required to build a model. The point is to construct the simplest model possible that will adequately address the key question or issue.

One of the most critical issues that often needs to be addressed during the concept exploration process is whether or not a concept is technically feasible. Most early prototyping work is focused exclusively on proving the technical feasibility of an idea. For instance, it is important to determine whether or not the invention will work with living anatomy. To answer this question, a crude mock-up in conjunction with an animal tissue test could be used to demonstrate that the basic approach is feasible. In the LAA example, the heart could be accessed by means of an existing device, such as a catheter. With only minor modifications, it could be used to inject dye into the LAA of a cow's heart to demonstrate that the general approach of filling the LAA with liquid is feasible. While the functionality of this preliminary model is severely limited, the innovator is able to learn that it is possible to fill the LAA with liquid, and is not distracted by other features that were not necessary to answer this question.

As prototyping progresses, other questions beyond technical feasibility become increasingly important. Prototyping can be equally effective in resolving these issues. A sample of the many different types of questions prototyping can be used to answer is shown in Table 4.5.1.

Continuing with the LAA example, the innovators might want to answer questions about what components are required to make the concept feasible. The crude catheter and cow's heart could be used to try various materials that start as liquids and then solidify, in order to find one that might work. Next, they could seek to demonstrate to key **stakeholders** that this can be done in

Table 4.5.1 There are many different and important questions that can be answered through prototyping.

Issue	Process for resolving issue	Related chapters
Will the concept work? Is it technically feasible and will the product function as designed?	Understand the underlying fundamentals of the clinical problem and then build the prototype and test it.	2.1 Disease State Fundamentals 5.2 R&D Strategy 5.3 Clinical Strategy
Is the innovation novel and unobvious? Can it be patented?	Having sketches and/or prototypes of the idea will help to define the claims of the invention.	4.1 Intellectual Property Basics 5.1 IP Strategy
Will customers adopt and use the product?	Take the prototype to thought leaders and target users in the market. Let them touch and feel it to provide feedback and confirm their interest.	5.3 Clinical Strategy 5.7 Marketing and Stakeholder Strategy
Can it be manufactured?	The development of sketches and/or CAD drawings will help determine manufacturability. It can also be helpful to find precedents and reverse-engineer them. Discuss the prototype with materials and manufacturing vendors to understand their input, ideas, and concerns.	5.2 R&D Strategy
Can it be offered at a price that supports a clear **value proposition** and a sustainable business?	Use vendor estimates/quotes (volume and price) to understand what is the realistic cost to produce the product. That information can then be used to estimate pricing relative to the product's value proposition and the price of competitive offerings. It can also help determine whether the innovators can sustain a reasonable business based on the expected selling price.	5.2 R&D Strategy 5.7 Marketing and Stakeholder Strategy 6.1 Operating Plan and Financial Model
When can it be made available?	Use vendor estimates/quotes (volume and time frame) to develop a project plan that estimates when it is realistic to expect a finished product. Consider hiring a consultant to assist with this exercise.	5.2 R&D Strategy 6.1 Operating Plan and Financial Model

a live animal. They may further develop or modify a catheter, then deliver the previously identified material in an animal study, and later study its pathology post-mortem. Finally, the innovators may want to translate their design and everything that has been learned about the technical specifications to a human scenario, which would include additional design requirements. They also might need to do additional research and make more modifications to the design to ensure that the catheter and material are inert and will not have side effects in the human bloodstream.

As shown by this example, the question or issues that prototyping can address evolve as the design progresses. Each prototype is built on the learnings from previous models. In this fashion, prototyping and its associated questions and issues are highly iterative,

FIGURE 4.5.3
A display of the prototype iterations, from an early works-like prototype (top left) to current day product (bottom right) (courtesy of Miret Surgical Inc.).

similar to much of the biodesign innovation process (see Figure 4.5.3).

Choose the best type of prototype

To answer specific questions or issues that are identified as being important during prototyping, innovators can expect to use a combination of the following types of models:

- **Works-like model** – Demonstrates how the device works. It may not look or feel quite right, but it can be used to demonstrate basic technical feasibility, assess whether the customer would be interested in a device that works in this new way, and/or gather feedback about what they like and/or don't like about the functional aspects of the solution. The bulk of prototyping often is performed using works-like models. Works-like models can apply to mechanical concepts, software programs, applications, or most other types of concepts that have a specific function that needs to be tested.
- **Feels-like model** – Something made of the final material or a surrogate material to demonstrate ergonomics, grip, weight, size, and other tactical factors (e.g., surgical tools). Three-dimensional (3D) printing technologies and other rapid prototyping techniques may be used to create feels-like models, particularly to represent the more physically structured and solid elements of a concept. These models can serve as an important input into human factors considerations. For this reason, they are often used in the early stages of developing wearable technologies as they can be helpful in gathering feedback about **user experience** as it relates to form or design. (See online Appendix 4.5.1 for more information about 3D printing.)
- **Is-like model** – A prototype that performs the desired function and works as intended. An is-like model may not resemble the final form, but could be used clinically. Depending on the nature of the device and the likely regulatory requirements, these models might be used in animal or possibly early human

testing. They are often used to transition from design into human testing and manufacturing. For software solutions, an is-like model may represent alpha or beta versions of the software in which the code is functional, but it is still undergoing internal and/or external testing and is not yet ready for general release. These models are also very useful for gathering user experience feedback.

- **Looks-like model** – What the device will look like in terms of its shape, color, size, and/or packaging. Though this is important closer to the end of development when user feedback and marketing decisions are made, a crude looks-like model may be useful earlier to help communicate to others what the innovators are trying to achieve. With 3D printing becoming more accessible and affordable, innovators can more readily produce sophisticated and "finished-looking" looks-like models. These models can be excellent communication tools to a wide variety of stakeholders, including investors and customers. For software applications, innovators can use mocked-up screenshots to gather feedback about the user interface and design for software and applications.
- **Looks-like/is-like model** – A combination of the previous two models. This type of model both functions as and looks like the final device. This step may be undertaken by manufacturing as the is-like model is modified to incorporate the looks-like elements during the technology transfer process from design to manufacturing. This more robust model is a natural candidate to best understand user experience with the product and applies equally well to a range of products from software and applications to mechanical solutions.

Again, it is generally most effective to start with simple works-like prototypes that *only* convey basic information about the concept and are narrowly focused on answering a single, specific question. In the LAA example, the innovators' first step was simply to determine if the LAA could be accessed and filled with liquid. The exact shape, size, weight, look and feel, and complete functionality of the device were irrelevant to answering this basic question. As a result, a simple works-like model was not only appropriate, but relatively easy and inexpensive to construct. It also did not introduce unnecessary complexity into the process of answering the relatively simple question the prototype was designed to address.

The more questions a single prototype seeks to answer, the more risk an innovator faces in understanding the results of the model (i.e., the specific cause of a particular technical problem). This is not to say that advanced prototypes that represent more finalized designs should be avoided. On the contrary, they are essential to proving the total concept. However, they should be built in such a way that they represent the summation of all the work done to date (and all the questions that have been answered by previous prototypes). In this way, advanced prototypes can still be built to answer a single question – it may just be a higher-order inquiry, such as "Will the model work in a living system?"

Before attempting to build complex prototypes, it is essential for innovators to have a deep understanding of how similar solutions currently available in the market function and what their strong and weak points are in terms of design, interface, and user experience. Often referred to as "reverse engineering," the idea of disassembling and analyzing existing products or devices can be helpful in making the prototyping process more efficient and giving innovators a foundational understanding of what does and does not work well within existing solutions. However, it can be dangerous if innovators start to anchor on the "current state" and adopt unnecessary constraints dictated by the existing technology.

Just as developing a prototype that is unnecessarily complex can be distracting to the innovators, it can also be distracting to users when asked to give their feedback. For example, if an early works-like prototype looks too much like a finished product, users may concentrate on how the device looks and feels instead of focusing on critical issues related to its fundamental functionality. The level of the prototype must match the question or issue being considered and only incorporate as much complexity as is needed to find this answer. Crude prototypes, using common materials, can provide a

highly time- and cost-effective mechanism for testing the basic functionality of a device. Some examples of rudimentary, but effective prototypes are shown in Figure 4.5.4.

The Oculeve example further demonstrates how different types of prototypes can be used to answer different questions and the value that rough, "low tech" models can provide.

FIGURE 4.5.4
Clockwise from top left to center: an electrical engineering breadboard (iRhythm Technologies); a rough prototype of a device to constrict a body passage and the mold that was used to cast it (Jeremy Koehler); a prototype pump and vacuum system (Calcula Technologies); an early model for a neonatal hearing screening device (Sohum Innovation Lab); and a rough functional prototype for an intravascular tool (InterVene Inc.).

FROM THE FIELD OCULEVE

Using early models to test technical feasibility and likelihood of adoption

Several years ago, a team in the Stanford Biodesign program began pursuing a way to treat chronic dry eye disease that would be more effective than the prescription eye drops (topical cyclosporine) that are the current **standard of care**. Dry eye disease (DED) is caused by insufficient tear film on the eye, either because the lacrimal gland does not produce enough tears, or because the tears evaporate too quickly from the eye's surface.[1] Without a stable protective tear film, the surface of the eye becomes inflamed, causing patients to experience painful dryness, burning or grittiness, and impaired vision.[2] An estimated 20 million Americans are affected by dry eye disease, with 1.6 million suffering from a form of DED that is severe enough to be debilitating.[3]

As the team vetted the dry eye need, member Michael Ackermann began mulling over ideas for a solution. Ackermann, an electrical engineer who had previously worked for Boston Scientific on neurostimulation devices, believed that this approach might provide an answer to the dry eye problem. "The lacrimal gland, which is innervated by a parasympathetic nerve, produces tears when stimulated by this nerve. So, by delivering stimulation pulses to activate the nerve, we could potentially activate the downstream organ," he explained.[4] Although the idea resonated with the team almost immediately, Ackermann noted that, "True to the process, we didn't chase it down too quickly. We went through the steps in the biodesign innovation process, but as the dry eye need became increasingly compelling, this solution idea kept resurfacing and withstanding the various trials we put it through."

Taking the neurostimulation idea forward into concept exploration and testing, the team began grappling with how to prototype a solution. "It was an interesting phase for us," recalled Ackermann. "The downside of neurostimulation is that it requires a really sophisticated device, so it is hard to build exactly what you want and go and get feedback with it." Faced with this challenge, the team focused on the most pressing questions they had to answer. "We needed to know two things – one, would electrical stimulation produce lacrimation, and two, would the doctors and patients be willing to use it," said Ackermann. Accordingly, they decided to focus on two primary types of prototypes: "looks-like" and "works-like" models.

The looks-like prototypes would be used to gather user feedback and address the adoption question. These "low resolution models," made initially from Play-Doh and cardboard, were used as a visual tool to help explain the concept to doctors and gauge their interest. "The first looks-like prototype was for a device that would be implanted in the chest with a lead up to the ocular orbit," Ackermann described. "The second iteration resembled a cochlear implant with a lead that would go over the ear." Both versions garnered mostly negative feedback from physicians, sending the team back to the design table. For the next version, Ackermann and colleagues evolved their concept significantly, designing a tiny device that could be placed directly into the orbit. "Our first intraorbital prototype, which looks much like the device we have now, was made out of a piece of plastic cut from the packaging of a handtool, and a little piece of modeling clay to simulate the titanium can portion of it," he remembered (see Figure 4.5.5). "This time, the feedback we got was, 'Yes, if you have something that kind of looks like this and it works, then that would be something we'd be excited about.'" Encouraged, the team began testing the looks-like prototype on cadavers in Stanford's anatomy lab to "start getting some sense of how the surgical procedure would work, and how the device would fit in with the orbital anatomy," he said.

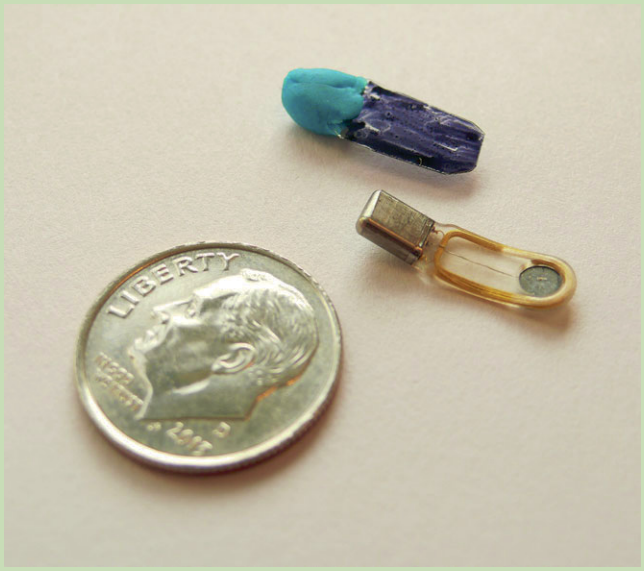

FIGURE 4.5.5
One of Oculeve's look-like prototypes alongside the near-final version of its intraorbital implant (courtesy of Oculeve).

In parallel, Ackermann and his teammates began to develop a works-like prototype to test the concept of electrical stimulation of the lacrimal gland to increase tear production. "We started with a clinical stimulator that was used to identify nerves in anesthesiology for nerve blocks, and we attached some percutaneous fine wires electrodes to it," said Ackermann. Although the prototype "looked nothing like our final product," it replicated the mechanism of action accurately enough for the team to put the prototype through successful bench and animal testing. "The neurostimulator we used was an **FDA**-cleared, off-the-shelf product, but we did confirmatory testing anyway to be extra careful before considering human use," stated Ackermann. For example, in one of its animal tests, the team delivered a 10× dose of stimulation to rabbits and then studied the histology to confirm the safety of the treatment, as well as its efficacy. "We also performed a thorough risk analysis to be sure we had considered and mitigated all of the significant risks we could encounter in the clinic," he added.

Reflecting on the team's early prototyping and testing experience, Ackermann commented that, "Both types of prototypes really pushed us along." He also credited "an extraordinary team of advisors" that included Daniel Palanker, Associate Professor in the Department of Ophthalmology, Stanford School of Medicine, and Mark Blumenkranz, Professor of Ophthalmology at the Stanford University Medical Center. "These guys are savvy, with great reputations and experience. Their feedback and advice as field experts was instrumental in helping us shape the concept," he emphasized. Finally, Ackermann stressed the importance of using rough prototypes to quickly begin figuring out what works. "You can learn a lot by using surrogate devices and early prototypes that execute on the concept, or parts of the concept," he said. The information gathered through concept exploration and testing positioned the team to begin thinking about more robust R&D and clinical strategies to bring the idea forward. (See 5.2 R&D Strategy for more information about this project, which would eventually lead Ackermann and his colleagues to found a company called Oculeve, Inc.)

Identifying the functional blocks of a solution

When the initial questions or issues the innovators want to answer are too broad to be easily addressed with a single series of prototypes, they are encouraged to divide the concept into "functional blocks." The original **need criteria**, along with more specific functional design requirements that may have emerged through the analysis performed in chapters 4.1, 4.2, 4.3, and 4.4 can be used to establish the boundaries for the blocks. Each block should represent one aspect of the concept that can be prototyped and is usually tied to a distinct engineering discipline based on its characteristics. Some common examples of the engineering disciplines addressed by different functional blocks include mechanical engineering, biomaterials science, electrical engineering, and computer science/software engineering.

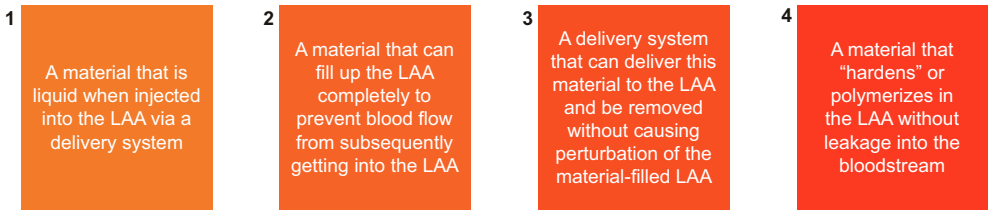

FIGURE 4.5.6
The primary functional blocks related to the LAA example.

Once the relevant functional blocks for a concept are defined, innovators can prototype each one independently, based on which questions they seek to answer, before bringing the blocks together to prototype the concept as a whole. Importantly, the key elements that could demonstrate the viability of an idea may be represented by only a few blocks (or sometimes a single one).

The primary functional blocks for a prototype for the LAA example might include those shown in Figure 4.5.6. As these blocks demonstrate, the original concept has a mechanical engineering component (#3) and biomaterials science components (#1, 2, and 4). While some concepts reflect a "pure" solution within a single engineering discipline, it is not unusual for innovative concepts to combine different types of engineering science. Instead of breaking down the issues related to biomaterials science into several blocks, another approach might be to classify all of the blocks related to material into a single block with multiple properties. While this may be appealing if the blocks are closely related, by breaking the concept into a more granular level of detail, with multiple blocks for a given engineering discipline, the innovators can more easily determine which of these smaller blocks should be prototyped first, based on what might be novel and what represents the highest degree of risk that needs to be addressed. As the innovator learns about what blocks can be addressed with readily applicable existing solutions, there is no harm in combining them if it makes sense.

The emergence of combination products, such as the drug-eluting stent or biologic coated stent for treatment of coronary artery disease, now demands even more sophisticated prototyping. These new devices often have even more complex functional blocks that can interact with each other in complicated and unpredictable ways. Biologic and pharmacologic blocks add other mechanisms of action to consider that may be mechanical, electrical, or chemical in nature. In this case, expertise in pharmacology and molecular biology would be essential to the prototyping team. In addition, lab resources for both macro and microscopic evaluation of mechanisms would be required. This may not only involve cell and tissue culture facilities, but also new technologies to measure these mechanisms, such as small and large animal imaging.

Understand what is known

Once the functional blocks of a concept have been defined, innovators can evaluate what is already known about each one. This is essential since it helps determine which blocks to focus on first, in order to address the ones that represent the greatest risk. Having a thorough understanding of how similar and competitive solutions function can also help innovators identify which functional blocks are truly novel and which might already have reasonable solutions that can be leveraged to make a concept work. In some cases, many elements of a solution concept may already be well understood, while just one or two aspects still need to be proven through prototype development. For instance, in the LAA example, the innovators can potentially leverage available catheter-based delivery systems, which provide a well-understood mechanism for reaching the heart and are acceptable to certain stakeholders such as cardiologists. Much greater uncertainty exists around the material for filling the LAA and its interaction with the heart. As a result, the innovators might decide to focus their earliest prototyping efforts on the biomaterials science functional blocks #1, #2, and/or #4 before moving on to #3.

Examining the functional blocks further, the innovators may also discover that there are existing materials

that can fill an anatomical space (such as the LAA) and be delivered in a liquid form via a catheter. In contrast, they may be uncertain about the existence of materials that can polymerize while in contact with the bloodstream. In this case, they could choose to focus on this latter functional block first to ensure that unknown can be resolved before investing significant time in other areas. Note that under these circumstances, it makes sense for the innovators to divide the biomaterials science aspects of the solution into different functional blocks, rather than considering them all together since many more unknowns exist in this one area versus the others.

Define more detailed design requirements and technical specifications

Just as breaking a solution concept into functional blocks can simplify how to approach the prototyping process, it can also aid with defining more precise design requirements and technical specifications. Once the original need criteria (which are usually fairly high-level) have been considered, additional criteria, relevant to each of the functional blocks, can be defined based on what has been learned to date. For instance, in the LAA example, a more precise design requirement for block #3 is that a catheter-based delivery system should be less than 8 French[5] in diameter and steerable to deliver the chosen material to the LAA. This is based on the determination that cardiologists, not cardiac surgeons, would probably perform the procedure and would prefer a method and tools similar to what they already use. Such specifics can be used at this point to guide prototype development along a pathway that takes into account relevant outside factors. At the same time, detailed design requirements help further define the questions that should be answered through each successive prototyping exercise.

Once a concept or a key element of a concept has been given a working form, it is easier for innovators to solicit specific input to guide improvements affecting the usefulness and marketability of the idea. Real users – members of the target audience for a device – play an important role in directing prototype development as they can identify detailed design requirements that may be unknown to the innovators. Sometime the term "design requirements" is interchanged with "**user requirements**," which emphasizes the importance of the user in generating this information. Users can also raise issues and risks to which the innovators have become "blind" due to their deep involvement with the concept.

Having a crude prototype that meets the need criteria and some basic design requirements of key functional blocks (as understood by the innovators) is the easiest way to start the process of gathering more detailed information. Going back to the LAA example, the innovators can gain important input by showing users a model based on a standard cardiology catheter, a substance such as glue, and a cow's heart. In this scenario, the innovators could demonstrate how the glue can be introduced via the catheter to fill the LAA, after which it polymerizes and hardens within one hour. The cardiologist might then point out, for instance, that the glue would need to polymerize in less than 20 minutes, as one hour could be too long to keep a catheter in the left atrium. Accordingly, the next prototype in the series would have a goal to address this more refined design requirement. Consulting with multiple users can help the innovator avoid the **biases** of any single individual.

Through the process of developing increasingly detailed prototypes and refining design requirements, innovators will naturally develop an appreciation of key technical specifications. Technical specifications represent the important engineering parameters that a solution must satisfy in order to meet the need and important design requirements, provided that these requirements are within the bounds of technical feasibility. Stated another way, technical specifications capture and explain how a solution must function. These specifications typically focus on technical features (e.g., what loads the device must tolerate, what material a device must be made of, how durable it must be, what level of encryption is needed), but may also address "softer" attributes desired by the user which are related to device functionality (e.g., compatibility with other devices, how it is operated, ergonomic features). All such specifications warrant careful consideration during device design as they will likely impact R&D and product development activities later in the biodesign innovation process.

Technical specifications can also emerge from the successes and failures that the innovator experiences in developing different prototypes. The LAA example can once again be used to illustrate this point. Prototyping in a live animal may show the innovator that a catheter has to have a certain rigidity so that it does not collapse as it is inserted into a blood vessel. Through trial and error, the innovators would gradually come to understand the appropriate load factor that it has to withstand. Once this determination is made, this specification would be considered essential for the solution to be technically feasible.

While little emphasis is placed on rationalizing design requirements and technical specifications early in the biodesign innovation process, innovators must begin to acknowledge necessary trade-offs between these parameters as design and development progresses. For example, users might want a device that has many technically complex features but also is miniature in size. When a design is initiated, they may be faced with limits on the degree of miniaturization that is possible while meeting the requirements for technically complex features. If the innovators do not have a clear sense of which requirements are most critical, more user input may be needed to help balance these requirements against relevant technical specifications. Alternatively, multiple designs can be created to emphasize different combinations of key requirements. Target users can then be asked to respond to the specific designs instead of helping to prioritize requirements in the abstract – an exercise that many individuals find more challenging. Regardless of which approach is chosen, innovators must carefully monitor the interplay between design requirements and technical specifications to ensure that a solution can be feasibly engineered.

One approach that can be useful in prioritizing and rationalizing the technical specifications that lead to product features is called Kano model analysis. Innovators can use this method to systematically make feature-level decisions (whether or not to include a single feature in a new product) or to identify an optimal mix of features that generates the most excitement with users and is recognized by key stakeholders to offer real **value**.[6] More information about Kano analysis is provided in the User Testing section of this chapter.

Timing of prototyping

While there is not necessarily a "right" time to start prototyping, many experts encourage innovators to begin as early as possible so that they learn from the process and apply that learning to iterative design and development. If there is a question that engaging in prototyping can answer, that exploration is usually a worthwhile effort. As Tom Kelley, general manager of design firm IDEO, explained:[7]

> *Quick prototyping is about acting before you've got the answers, about taking chances, stumbling a little, but then making it right. Living, moving prototypes can help shape your ideas. When you're creating something new to the world, you can't look over your shoulder to see what your competitors are doing; you have to find another source of inspiration. Once you start drawing or making things, you open up new possibilities of discovery [by] doodling, drawing, [and] modeling. Sketch ideas and make things, and you're likely to encourage accidental discoveries. At the most fundamental level, what we're talking about is play, about exploring borders.*

The downside of prototyping too early in the biodesign innovation process is that innovators can get swept up in creating a working model before they are certain that the solution meets key need criteria and/or design requirements. Another pitfall is becoming committed to a concept once it takes a working form, despite fundamental flaws that may affect the technically feasible of a final product. Issues such as these may lead innovators to invest money and to spend days, weeks, or months defining and refining a concept that may ultimately be inadequate to satisfy the underlying need (see the OneBreath example in 4.6 Final Concept Selection). Innovators must make a careful judgment about the ideal time for initiating (and sustaining) prototype development, since there are many pros and cons (see Table 4.5.2).

Table 4.5.2 Advantages and disadvantages of working with early models as part of the prototyping.

Advantages of early working models	Disadvantages of early working models
• Flexible; can be relatively easily changed. • Relatively inexpensive (compared to later prototypes). • Can help identify critical design requirements from users early on and incrementally throughout the development cycle. • May provide the proof of concept necessary to attract funding. • Can demonstrate key technical challenges and issues regarding feasibility. • Can help give users an idea of what the final product will look like and how it will operate. • Can encourage active engagement in the development process by users. • Can motivate the innovator(s) and drive an increase in product development speed.	• User needs and design requirements may not yet be adequately understood, rationalized, and reflected in the designs. • Early designs may not adequately address user expectations and may, therefore, disappoint the target audience. • The innovator may become prematurely attached to certain aspects of an early prototype that are counterproductive to upstream (user requirements) or downstream (technical feasibility and manufacturing) considerations. • The innovator might waste time and money prematurely prototyping an incomplete or flawed design.

Concept exploration as part of the biodesign testing continuum

As described earlier, concept exploration is a key early component in the larger R&D effort. In particular, prototypes are used to gather user feedback and prove the technical feasibility of certain concepts through various types of early testing. These testing modalities, as shown in Figure 4.5.7 (excerpted from the biodesign testing continuum), are important to understand as part of concept exploration.

User, bench, simulated use, and tissue tests are usually undertaken multiple times throughout the iterative design process. Live animal testing, cadaver testing, and human testing are frequently performed during the later stages of the biodesign innovation process when more advanced works-like and is-like models are available (see 5.2 R&D Strategy and 5.3 Clinical Strategy). Throughout the testing continuum, the innovator continues to collect information about key design requirements and understand increasingly important technical specifications. Key considerations for user, bench, simulated use, and tissue testing are outlined below.

User testing

User testing involves evaluating a concept by testing it with users to gather their input and observe their interactions with it. At first, this activity may involve showing target users drawings or storyboards of a solution idea and asking for their feedback. Next, it may involve showing users works-like, looks-like, or is-like models to observe their informal reactions and interactions. Over time, it may evolve to be more rigorous, relying on techniques such as usability testing to systematically gather qualitative and quantitative data under controlled circumstances. In a usability test, users are given a relatively advanced prototype and observed interacting with the technology or device to determine how well it meets key requirements and technical specifications. Innovators are unlikely to perform robust usability tests during preliminary concept exploration, but it is a useful method to consider as R&D progresses.

As mentioned, Kano model analysis is another valuable tool for systematically gathering and acting on user feedback. This approach enhances the early work innovators performed in defining need criteria by

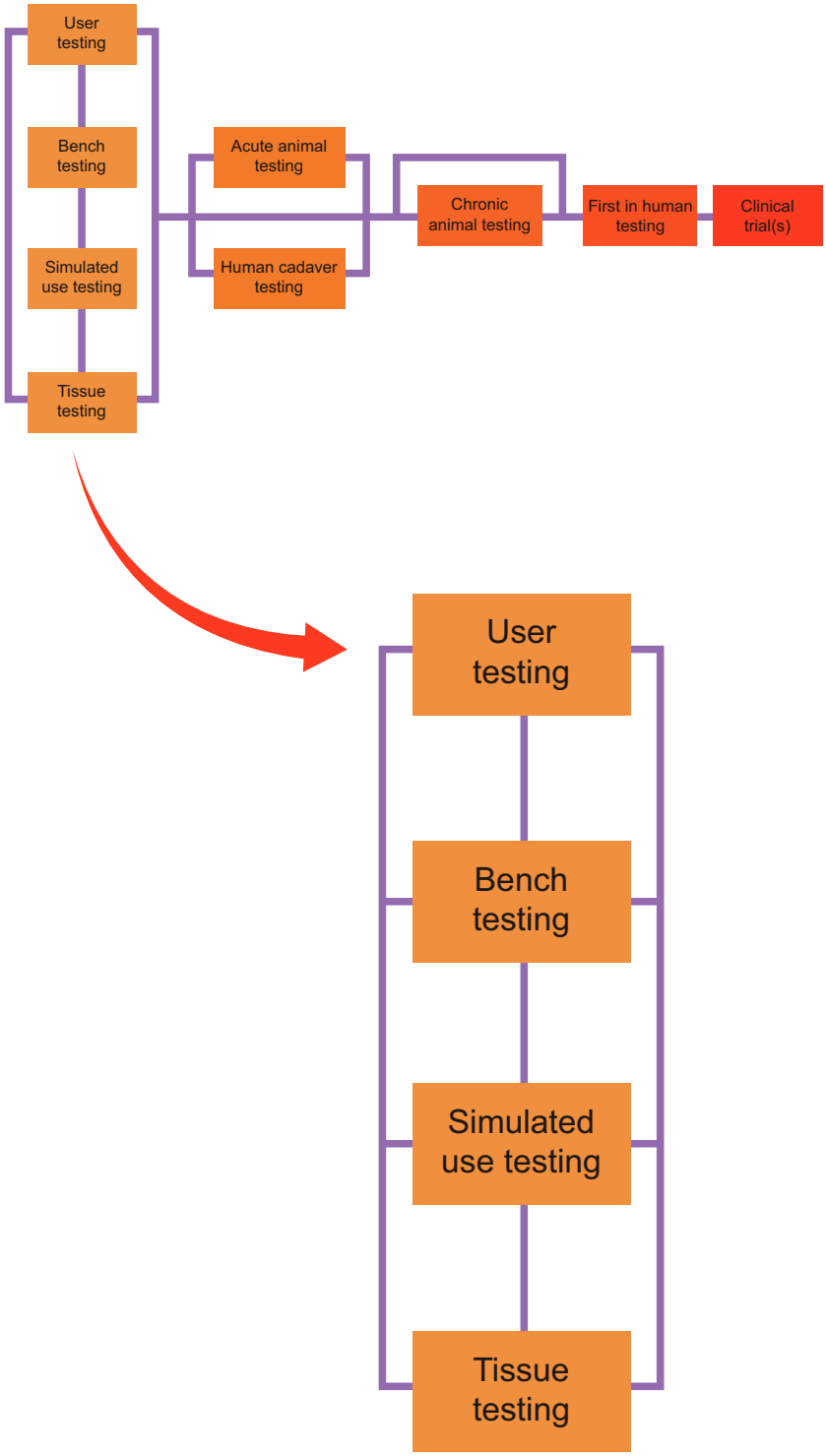

FIGURE 4.5.7
A combination of user, bench, simulated use, and/or tissue tests can enable innovators to effectively evaluate their early prototypes.

providing a framework to put features into four key categories:[8]

1. **Must-haves** – The features that are most critical to customers.
2. **Dissatisfiers or must-not-haves** – The features that would turn people off and drive them away.
3. **Yielders of indifference** – The features that cause a "who cares?" reaction.
4. **Exciters** – The features that delight users, provide unexpected excitement, and contribute to a high level of satisfaction and perceived value.

To classify features according to this construct, innovators use a prototype or model to show users a series of features. For each one, they should ask the users to answer a "functional" and a "dysfunctional" question, such as:[9]

- How would you feel if the new device offered this feature as part of its design?
- How would you feel if the new device did NOT offer this feature as part of its design?

For both questions, users are asked to choose from the following responses:[10]

- It would excite me to have it that way.
- I would require it to be that way.
- It does not matter to me if it were that way or not.
- I wouldn't like it, but I could live with it that way.
- I would not accept it to be that way.

Once the results are gathered, the Kano technique outlines an approach for analyzing the data to understand user priorities and preferences related to specific features, as well for determining an optimal mix of product features. See the Getting Started section for references on Kano Analysis.

Before innovators are ready to engage in formal user testing methods such as usability testing and Kano model analysis, they can still gather useful user input by following some general guidelines:

- **Gather user experience feedback by asking users open-ended questions** – What do they think of this? What could be better? Why don't they like it? Is the reason they do not like it functional, design-related, or practical in nature?
- **Understand user interface and experience issues by observing users as they handle and use the prototype** – What features give them the greatest difficulty as they use it on the bench or in animals (e.g., for a mechanically oriented solution) or interact with it in their typical surroundings (e.g., for an application or software program)? What seems to attract or appeal to them?
- **Gather design input by asking users to imagine using the device in a clinical setting** – If it is not possible to directly observe users trying the device or technology (i.e., due to privacy or regulatory constraints) or it is too early in development to provide them with an advanced model, ask them about the other factors that must be considered in designing the device to integrate it into an operating room, physician's office, catheterization laboratory, healthcare system, etc. Are there other equipment/environment considerations that affect its use? For software and applications, are there compatibility or integration issues that need to be incorporated?

While it is unlikely that all of the feedback gathered from multiple users will be consistent, the opportunity to consider a wide range of opinions can reveal the full spectrum of strengths and deficiencies associated with a prototype. The innovators will then have to determine, based on their own observations, what user feedback to act on, as well as which elements of the prototype to further refine or modify, and which ones to accept.

The Vynca story highlights the importance of gathering user input often and early. Though important across the whole range of biomedical technologies, it can be useful (and relatively easy) to get early input for consumer-oriented products such as software or mobile health applications.

FROM THE FIELD VYNCA

The importance of understanding users and user testing

Rush Bartlett, Ryan Van Wert, and Frank Wang of the Vynca team knew as they launched Vynca that one of the most important elements of developing any **medtech** solution – especially a software-based offering – is making sure it is tailored to the needs of the most essential and influential end users. As they set out to address problems surrounding end-of-life physician orders for resuscitation, they identified numerous users (or stakeholders) to consider. "Stakeholder analysis was the single most important factor that we looked at," said Bartlett. While patients, physicians, nurses, nursing home and hospital administrators, dispatch center personnel, and hospital IT staff were all key audiences that could affect the adoption of a new solution in the space, they prioritized physicians and hospital IT staff as being most central to accepting or resisting whatever they designed.

When conducting clinical observations in pulmonary and critical care medicine as Biodesign fellows, Bartlett and Van Wert were drawn to problems related to acute resuscitation orders and related end-of-life issues. Within the span of a week, they encountered two different cases where elderly patients were put on life support despite having previously filled out a Physician Orders for Life-Sustaining Treatment (POLST) form that clearly specified their wishes to avoid such an intervention. POLST forms are widely accepted in the medical community, but the challenge is ensuring that physicians have reliable and timely access to the information. This is particularly important because the vast majority of patients with terminal illnesses do not want aggressive care at the end of life, but physicians are obligated to provide this care unless instructed otherwise.

In one case, the patient had a POLST form with him (indicating that he did not desire to be put on life support) when he was transported to the hospital, but it was left behind in the ambulance. Unable to speak for himself, the patient was placed on a ventilator and transferred to the intensive care unit. When the team was validating the need through further observations in the emergency department, the members realized that the POLST form, as with other paper documents, is given to the registration clerk and sent to the hospital's central document management center where it is manually scanned, labeled, and uploaded to the electronic medical record (EMR). This process typically takes one to two days. In effect, the existing workflow for POLST in the emergency department precluded the treating physician from viewing the form to make critical management decisions. Bartlett and Van Wert's physician advisor, Dr. Allen Namath, a critical care specialist, had encountered the problem of recording and acting on patient's wishes on numerous occasions. As a pulmonologist and an intensivist, Namath had the unique perspective of seeing both sides of the problem. He had traditionally filled out POLST forms in his pulmonary clinic, but would unexpectedly see some of the same patients who clearly indicated they never wanted to be placed in the ICU appear there during his ICU shifts. "Very quickly, this need filtered to the top of our list based on patient impact and high cost to the system," explained Van Wert. "One-third of the Medicare budget in the US is spent on patients during their last year of life, much of it for care that patients do not want to receive in the first place." Accordingly, they decided to focus on the need for *a way to rapidly transmit POLST form information to any part of the healthcare setting*.

The team brainstormed a wide variety of concepts for capturing and transmitting end-of-life treatment wishes. However, said Bartlett, "We realized that the POLST form was well accepted and backed by two decades of clinical literature." For this reason, the members decided to first focus on making the form easier to complete in a digital format with added features that would improve

security, assist with patient education, and make the captured information more accurate in terms of reflecting patient preferences. The second critical step was then to innovate ways to make the information rapidly accessible to any healthcare providers in any setting.

Physicians were a top-priority user group because they played a central role in completing the forms during an office or hospital visit with the patient. They were also the ones who needed to access the information on a just-in-time basis when administering care. Additionally, as Van Wert noted, “Having a clinical champion is always essential to drive adoption of a new technology in a health system.” With this audience in mind, the team defined a series of user requirements that would serve as the basis for its solution, including eliminating paper, integrating the solution with EMR systems, and making the POLST information available via a single click. “I have seen a lot of suboptimal hospital IT software,” said Van Wert. “Every extra mouse click and every extra login adds a lot of time to the physician’s day, especially when they’re doing activities that are repeated over and over again. We were committed to putting ourselves in the healthcare provider’s shoes as we built the system because we realized this would be a key driver to adoption.”

At this point, the team was ready to begin prototyping. “One attractive thing about software-based solutions is the speed with which they can be prototyped and tested,” Bartlett stated. “Relative to traditional medical devices, it’s easy to create different types of prototypes of software products to demonstrate them to potential customers and gather more information about what they’re looking for in terms of usability.”

The team’s prototyping approach was based on the development of a series of increasingly robust models. The members began by drawing the workflow of the website with pen and paper under different use case scenarios. Based on preliminary feedback on these mock-ups, they created diagrams and slides with more detail, which they sent out for feedback from a larger group (see Figure 4.5.8). Next, they developed an online

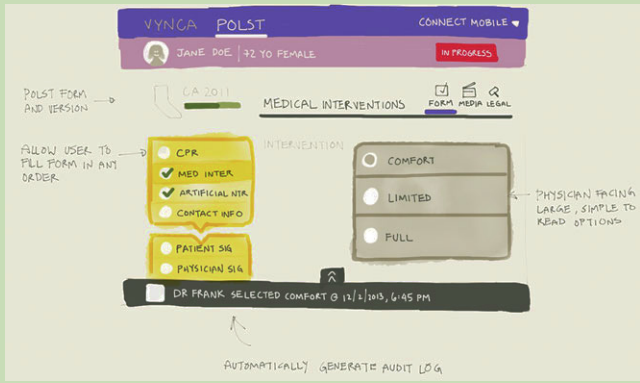

FIGURE 4.5.8
A wireframe sketch of the preliminary website concept that the Vynca team used to gather feedback from users (courtesy of Vynca).

looks-like model that appeared on the screen as it would, but did not have active functionality. Finally they created a “bare bones” but functional website (a looks-like/is-like model) which they used to gather critical input from a wider audience. “Having a functional prototype to show to potential customers was very powerful,” Wang said. “We didn’t want to build the solid, **HIPAA** compliant, robustly scalable, final site until we were sure. You only want to do that once.”

With each model (see Figure 4.5.9), the team gathered increasingly detailed feedback from an expanding group of physician users. They shared the initial drawings within the team and with their close physician advisors. They showed the subsequent storyboard slides and the looks-like model to a slightly larger group of physicians in their network. By the time the looks-like/is-like model was ready, they developed an online user survey to send to an expanded group of doctors that represented potential users of the POLST form. Importantly, when gathering each round of feedback, Bartlett, Van Wert, and Wang made a concerted effort to sit down with the physicians, observe them as they interacted with the prototypes, and ask open-ended questions about how they could imagine the system fitting in with their day-to-day work flow. Although the team members were eager to get input from anyone who would talk with them, Bartlett commented that not all user feedback is equally valuable

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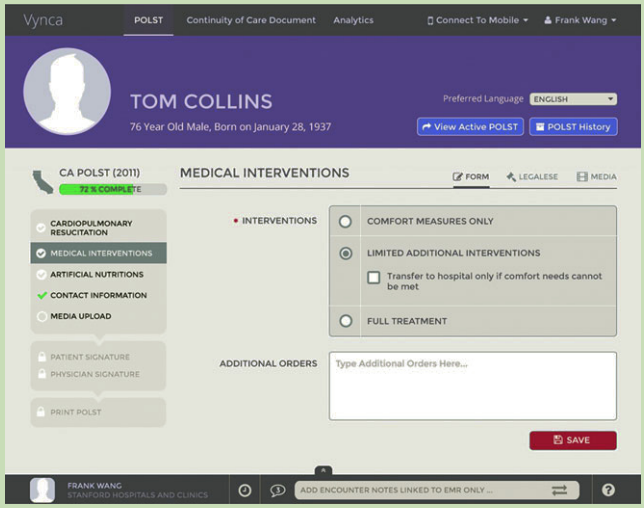

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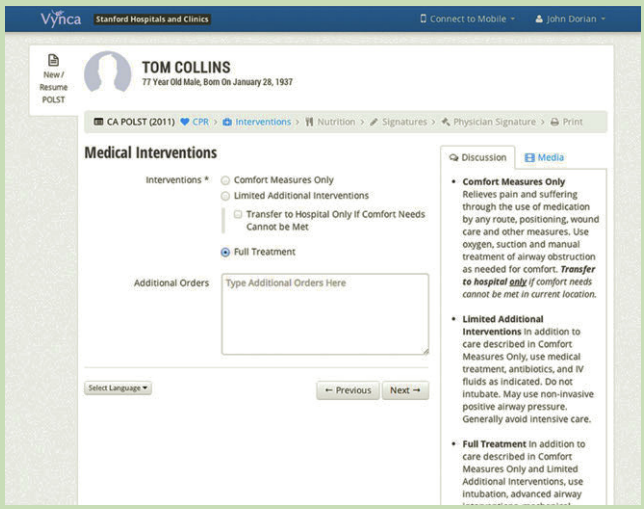

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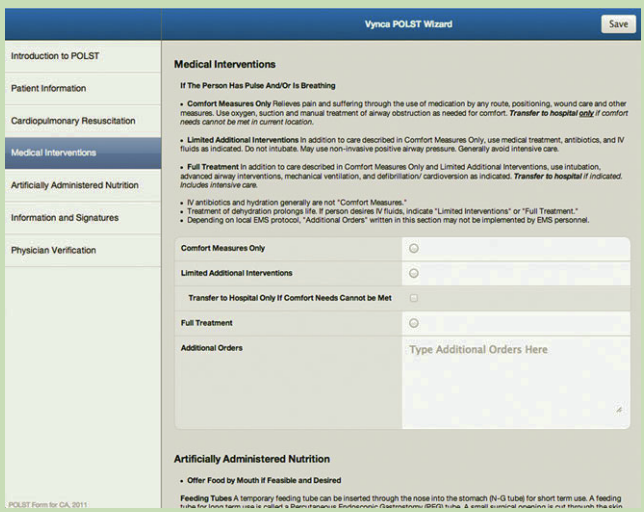

and innovators should be somewhat selective in terms of who they approach. “Make sure you’re getting the right users because not all feedback you receive is going to be relevant. Sometimes you have to ignore input or take some of it with a grain of salt. Make sure you connect with high-quality users that are directly in the line of fire, so to speak. They’ll give you the highest impact feedback. If you send a random email to the followers of a blog, a lot of the feedback is going to be garbage and it’s going to dilute your signal.” For this reason, Bartlett and his colleagues invested significant time in cultivating relationships with leaders in the palliative care field.

As the team began to deeply understand the requirements of the physicians users of their solution, they also started exploring what it would take to get hospital IT departments to adopt it. “There was a lot of pounding the pavement and getting people to talk to us,” said Bartlett. The team used its Stanford affiliation to connect with members of the hospital’s IT department. “We asked them, ‘What would you be looking for in a solution as an IT director?” noted Van Wert. “IT departments are often negative stakeholders in this process. They sometimes lobby against changes because those changes expose them to risk. Further, they see so many new tools that people want to integrate with the hospital EMR system, but they’re not necessarily exposed to the clinical needs behind them. As a result, they’re unable to judge the merits of the solutions except by how it increases their risk exposure,” explained Bartlett. Accordingly, the team committed itself to differentiating its software by ensuring that its implementation would be as minimally disruptive as possible. The members also took the time to explain the need and garner wide support for the new system across the hospital system.

Elaborating on this approach, Bartlett said, “By working with IT department to ease integration challenges, innovators can mitigate adoption risk.” In the process,

FIGURE 4.5.9

These screenshots show how the Vynca website progressively changed with feedback from key stakeholders (courtesy of Vynca).

these conversations helped the team uncovered additional technical and user requirements, especially around HIPAA compliance, privacy, and security issues. To augment this information, said Wang, "We learned a lot from looking at how other third-party tools available in the market integrate with the EMR system."

In 2014, the team, which adopted the name Vynca, was on the cusp of launching an e-POLST project **pilot** with a prestigious academic hospital. This particular institution was an early pioneer in POLST management in the United States and remains a national leader. Through the pilot, Vynca will be able to test a fully functional, cloud-based, HIPAA compliant version of its software and gather additional user feedback on a large-scale basis. The hospital is also helping the team build connections to other potential hospital customers by leveraging its record of leadership and advocacy in POLST management.

Bench and simulated use testing

Bench testing refers to the testing of materials, methods, or functionality in a small-scale, controlled environment, such as on a laboratory workbench. These early tests typically serve to help identify key elements of a design in terms of materials or functionality. This allows the innovator to make optimal choices about how to build more robust prototypes for later stages of testing. In bench tests, individual components or subassemblies are put into a test loop where all of the associated variables can be independently controlled, measured, and recorded.[11] Bench tests should be designed as simply as possible. For example, for a catheter device with an articulating arm and handle mechanism, the innovator should test the arm mechanism independently of catheter tracking or lubricity to ensure that each of the individual features works independently. This makes it easier to understand the test results when combinations of features are eventually tested together.

In simulated use testing, various features or functions of the prototype are tested as a system on an anatomical model or proxy. Device characteristics and design parameters can be tested in a predictable and reproducible manner to demonstrate actual performance. For instance, a bench top simulated use system that mimics physiological hemodynamics and vascular anatomy can be used to test and refine a vascular implant prototype before going into expensive animal studies. For some devices, simulated use testing can help fulfill validation testing requirements of the FDA or other regulatory agencies.

When developing bench tests or simulated use experiments, innovators should use simple methods and generic materials or machines (tensile testers, weights, levers, calipers, etc.). They should test in real tissue later in the testing continuum, as many less-costly surrogates are readily available to refine and develop prototypes to a point where the design has a better chance of working in real tissue. During preliminary tests, materials that can provide a substitute for tissue include silicone, chamois, nylon, sponge, foam, or ceramic pieces (for bone).

Niveus Medical, a company started by Stanford Biodesign fellow Brian Fahey, employed simulated use testing to gain valuable feedback on the design and functionality of early prototypes. The company created a novel muscle-stimulation solution to address the problem of weakness, debilitation, and muscle atrophy in patients facing extended periods of immobilization or bed rest. In designing a solution, the team had a series of human factors issues to explore. Some of these dealt with the interaction between the device and patient since the solution included a component affixed directly to the skin. Others dealt with the workflow of the nurses who would equip patients with the device and monitor its usage. Early in the concept generation and screening stages of the innovation process, the Niveus team recognized that the product had to be designed to fit into the complicated and hectic environment found in hospital settings. "Any solution that was viable had to be very easy, quick to deploy, and intuitive to use, with limited training required," Fahey explained.

To address these human factors, the Niveus team created a looks-like prototype, which consisted of a disposable electrode pad, a connection cable, and a mock generator. Then, the engineers set up two different types

of simulated use tests. First, they used mannequins to explore different human factors related to fit, sizing, and placement on the skin. Second, they set up focus groups of 8–10 nurses, who were asked to use the looks-like prototypes on mannequins lying on beds with only limited instruction. "So we didn't just prototype the product, we prototyped the workflow," said Fahey. The team observed the nurses through the end-to-end process of finding the product on a shelf, opening the package, interacting with the product components, placing the pad on the mannequin, connecting it to the generator, and then removing the system. "Testing the entire workflow allowed us to validate several assumptions and learn some new things as well," he commented. For instance, the team noticed that different nurses placed the generator component in different parts of the room, which meant that the connecting cable had to be flexible and long enough to accommodate the different use cases. As a result of this insight, the engineers ended up redesigning the connecting cable and changing the position of where it interfaced with the disposable pad. Fahey also stressed the importance observing how users "naturally do things" with the product, such as how they might bend or break it, so that the team can design around possible failure modes of the device. "It is always good to know your limitations early on," he noted.

As a rule, innovators should use tests consistent with the stage of prototyping that is being undertaken. As the prototypes and models grow more sophisticated (through design evolution) and risks are retired, tests can become more complex such that they begin to more closely resemble actual use. Eventually (and often rapidly), the design gets to a point where tissue testing is required to generate the next set of design requirements.

Tissue testing

Tissue testing is an essential component of medical device prototyping for certain types of products that should be undertaken after a concept has been proven in simpler tests. This is not to say that tissue testing cannot be undertaken earlier, but by answering many of the straightforward questions through bench and simulated use testing, results are less likely to be confounded by non-critical data. Innovators can quickly evaluate a device's mechanism of action using animal tissue available from the local grocery store or butcher – for example, substituting the skin on chicken feet to emulate human skin when testing the ability of a new suturing device to penetrate tissue. Electrical mechanisms may be evaluated in much the same way. For instance, a skinless chicken breast can be used to assess the ability of a new ablation catheter energy source to create tissue injury. With chemical mechanisms, a similar approach can be used. As shown in the LAA example, developing a glue that would adhere to the endocardial (inside) surface of the heart is critical. For a preliminary tissue test, an inexpensive cut of beef could be used to evaluate the interaction between the glue and the tissue.

Although mechanisms of action can often be evaluated using simple, widely available animal tissue (like beef tongue, steak, gelatin, or poultry), device feasibility must almost always be confirmed using animal or cadaver tissue that is more representative of the anatomical or physiologic properties that the device intends to address. For example, swine and sheep organs can be obtained from many commercial slaughter houses. These tissues can be shipped fresh or be frozen for later use. When using animal organs or body parts, the innovator's goal is usually to assess the basic functionality of the prototype. While animal parts are good substitutes for many (but not all) prototyping projects, human tissue testing will eventually become essential for products that interact with the human body. Human tissue can be drastically different from animal anatomy for certain organ systems, so more advanced tests are necessary to evaluate a device. In an effort to better understand the size, shape, and contour of the space in which a device needs to operate before a human tissue test is designed, an innovator may find that a trip to an anatomy lab is invaluable. Additionally, with proper licensing and disclosure of intent, human cadaver tissue can be obtained from commercial sources (note that when working with human tissue, proper lab facilities and processes for its safe use and disposal are essential). See 5.3 Clinical Strategy for more information.

Keep in mind that dead tissue has obvious limitations compared to living tissue. However, for purposes of initial anatomical and physiologic properties, it is a good place to start. Once live tissue fed, by oxygenated blood, at body temperature, and with certain intact anatomical

relationships is required, then tissue testing may not be adequate. Importantly even with dead animal tissue, there are certain guidelines that need to be followed with respect to proper handling and disposal. For instance, universities and other laboratory facilities typically recommend that innovators wear closed toe shoes, a lab coat or disposable gown, gloves, and potentially eye and/or mouth protection when working with tissue samples.

In-house versus outsourced prototype development

When innovators or companies are ready to begin prototyping, they must decide whether prototypes will be developed in-house or by a third party that specializes in prototype development. This decision depends in large part on the nature of the concept, the cost-efficiency of each approach, and the skills and resources of the team. While third parties can provide access to vast experience and specialized equipment and materials, a team may give up an important learning opportunity if it decides to outsource the development of its prototypes. However, this may be essential for more complicated and sophisticated projects. Innovators, especially relatively inexperienced ones, are encouraged to entrust at least some portion of their prototyping efforts to the company's in-house engineering team to capitalize on the invaluable learning that can take place. The advantages and disadvantages of these two different approaches are summarized in Table 4.5.3. These principles apply across project types, from mechanical engineering solutions to software.

Table 4.5.3 Advantages and disadvantages of in-house versus outsourced prototyping.

	In-house prototyping	Outsourced prototyping
Advantages	• Hands-on prototyping experience contributes to the expertise of in-house engineers. • Company engineers directly learn what works and what does not and can apply those learnings directly to the design to test changes or add/delete features. • Direct prototyping experience allows the iteration process to occur faster. • In-house prototyping can save a great deal of time if the design proves to be not feasible. • Overall, in-house prototyping is usually cheaper than outsourcing (except for complex processes and custom parts). • Intellectual property and proprietary information about what may or may not work can be captured. This information may be used to block competitors.	• Outside specialists possess high levels of expertise on specific processes and equipment. • Outside shops have developed many prototypes for other companies and can offer invaluable advice and design assistance, especially in the prototyping of non-critical, proven components. • In some cases, outsourcing can be less expensive than purchasing the required equipment (and undergoing training) in-house.
Disadvantages	• Some equipment may be too costly for a small start-up to purchase. • Some processes may require expertise that is not available in-house. • The team typically cannot be built up quickly or scaled down easily based on prototyping needs, which may have significant time and money implications.	• Outsourcing can often take more time since the shop has to meet the needs of multiple customers. • An outside shop does not possess unique or vast knowledge about the innovation. • Issues related to intellectual property must be managed carefully in every outsourcing deal. • Design iterations and risk retirement can take longer. • Outsourcing can be costlier than in-house prototyping, especially for simple designs.

Whenever possible, innovators should make an effort to establish a basic prototyping lab of their own to perform early prototyping activities. Depending on the project, this may include tools, materials, computing resources, and software to create mechanical, electrical, material, and software models, or prototypes that combine these different disciplines. Then, as the complexity of the models increases and more specialized equipment and materials are required, specific steps or prototypes can be outsourced on an as-needed basis. This hybrid approach is often the most sensible and affordable way for a lone innovator or young start-up company to proceed. However, there are also times when innovators might choose to establish a more comprehensive prototyping facility. For example, Perclose, a pioneer in the femoral vascular closure space, took this approach and gained vast efficiencies in its design cycle, thereby realizing a significant return on its investment. In this scenario, the cost of setting up the prototyping lab was built into the initial financial model (see 6.1 Operating Plan and Financial Model).

The Evalve story below highlights the advantages that can be realized through in-house prototyping and also demonstrates how one company followed the guidelines outlined in this chapter.

FROM THE FIELD EVALVE, INC.

Understanding prototyping as part of the biodesign innovation process

Evalve, Inc. was founded to develop percutaneously delivered devices and tools for repairing the mitral valve, one of the heart's four valves.[12] Mitral valve regurgitation (MR) occurs when the valve's leaflets or flaps do not close completely, resulting in the backflow of blood from the left ventricle into the left atrium and into the lungs, dilation of the left atrium, and the eventual enlargement of the left ventricle. A minor amount of MR occurs in as much as 70 percent of adults.[13] Significant (moderate to severe) MR is much less common, affecting roughly 4 million people in the US.[14] Despite the significant sequelae of untreated mitral valve regurgitation, which can include atrial fibrillation, heart muscle dysfunction, congestive heart failure, and an increased risk of sudden death, just 50,000 individuals undergo surgery in the US each year to correct the problem.[15] Three to four times that number of patients experience symptoms and complications serious enough to warrant the traditional therapy used to treat MR – open heart surgery – but do not receive the procedure, either because they are too sick for heart surgery or are in a position of "watchful waiting." Evalve's founder, Dr. Fred St. Goar, a Stanford-trained interventional cardiologist, was familiar with the **morbidity** associated with open heart surgery and saw a market opportunity for a less invasive solution. After **brainstorming** several different approaches focused on suturing the valve leaflets, St. Goar and other Evalve team members, including vice president of R&D Troy Thornton, hit on the idea of a clip that would stabilize the leaflets and also hold part of the valve closed, allowing the leaflets to function properly.

Evalve's small team of engineers and technicians began building prototypes early in the development process. First, they made rudimentary sketches by hand. Then, technicians and engineers developed crude prototypes in ones and twos in Evalve's lab, using pig hearts from a local butcher to experiment on. According to Thornton, "Eliminating options is an important part of prototyping," and simple experiments with early prototypes were used to rule out certain concepts and ideas that might have consumed significant time and money down the road. Additionally, even though they started working with pig hearts, the team recognized the need to understand the disease in humans as quickly in the process as possible. Many development paths that may seem promising early on can be derailed by the unique intricacies of the human anatomy. "We sent a few of the engineers out to the

pathology lab to look at human hearts that have mitral valve disease," said Thornton. "That was enlightening and important. Surgeons can tell you what it looks like and you can see pictures in a book, but seeing the problem in person is quite different." With a strong first-hand understanding of the disease in humans, the team was able to be more efficient in its approach to prototype development, relatively quickly eliminating paths that proved not to be fruitful.

As Evalve pushed ahead, it discovered that there was too much prototyping and testing for a single engineering team to handle. In addition to the clip, Evalve needed to develop a guiding system and a clip delivery device, so it developed three engineering groups to help break down the problem into smaller, more manageable pieces. "From a conceptual standpoint, we realized that the project was too big to tackle all at once," recalled Thornton. "Breaking the product into manageable chunks became critical for a complex project like this." One team, which was focused exclusively on the guiding system, spent many months developing different designs and conducting animal studies just to isolate and understand the functionality required to address this variable. Another team worked on the clip delivery catheter that would be able to actuate the clip once inside the heart. That left one additional engineering group to focus solely on designing the best clip they could to hold the mitral valve leaflets closed and restore normal heart function. While breaking into separate teams was effective in terms of advancing Evalve's understanding of the device's core components, it required a certain amount of additional coordination. "Everything has to come together," said Thornton. "All three engineering teams have to talk to each other constantly. They have to communicate well because if somebody changes something on part A, it could affect system B or C." Due to the interdependencies of the different components, each team also needed to maintain and document specific design requirements for their components to keep the effort synchronized. Adjustments to resources had to be made at various times during the project to assure that all three teams could move forward at the same fast pace. Despite these challenges, however, the narrower focus of each of the engineering teams allowed Evalve to innovate much faster and more efficiently than when they were a single working group.

Another important input to Evalve's prototyping efforts was the collection of physician feedback as early and often as possible. St. Goar said, "The downfall of more than a few companies has been getting an idea and then having a group of engineers go off to create something very elegant, very sophisticated, and very complex that the physicians just can't imagine using in clinical practice." For Evalve, the downside of physicians potentially being turned off by flaws in early, crude designs was far outweighed by the upside of having their input to take into account in the design process. Having users who were able to be involved all the way through the process, looking at many versions of prototypes and speaking to the positives and negatives of different design features was especially critical. In addition, although the new, less invasive procedure would ultimately be performed by interventional cardiologists out of the catheterization laboratory, St. Goar and Thornton made a point of involving surgeons in their prototyping work. St. Goar explained, "We were trying to match what the surgeons did. If we simply addressed the need from an interventional cardiologist perspective, we might miss the therapeutic mandate. The surgeons knew what needed to be accomplished, and we certainly didn't want to lower their clinical standards. Having surgical input early on was invaluable."

Eventually, after its engineering workstreams started coming together, Evalve had to make the decision about when to begin testing in humans. "There is a little bit of a leap of faith that's required," St. Goar said. "You've got to bite the bullet and say, 'Okay, this is it, we're going to go.' But that's not always easy to do." For Evalve, having positive, longer-term results from animal tests

was one factor that helped the team make this decision. It was also important that the design had been shown to meet its critical design requirements. Additionally, executive management played a key role. "Our President and CEO, Ferolyn Powell was very helpful. An engineer by training, Ferolyn had been intimately involved in the development of the technology which allowed her to fully comprehend the risks," said St. Goar. In this case, the board of directors also weighed in. Thornton remembers one director saying, "You can do all the animal studies you want, but you're not going to learn a damn thing until you get into people. You could spend another six months refining this thing, but it's time to move forward."

This decision was closely related to a development challenge that many inventors and companies struggle with: **design creep**, or the tendency for engineers to spend too much time changing minor aspects of a design or prototype that are unlikely to affect the overall performance of the device. Clearly defining what the "must-haves" versus the "nice-to-haves" are for a device is one strategy that inventors often use to keep the iteration process under control and avoid design creep. Fully satisfying the must-have requirements should be a signal to the team to take the next step forward. According to St. Goar and Thornton, the FDA has particularly strict rules regarding design changes that occur after human trials are initiated, especially for a permanent implant, so design creep can be highly problematic for firms at this stage. "There are always ways to make a device better than it is today, but you really have to be committed, once the decision is made to move into human studies, to stick with your design," said St. Goar.

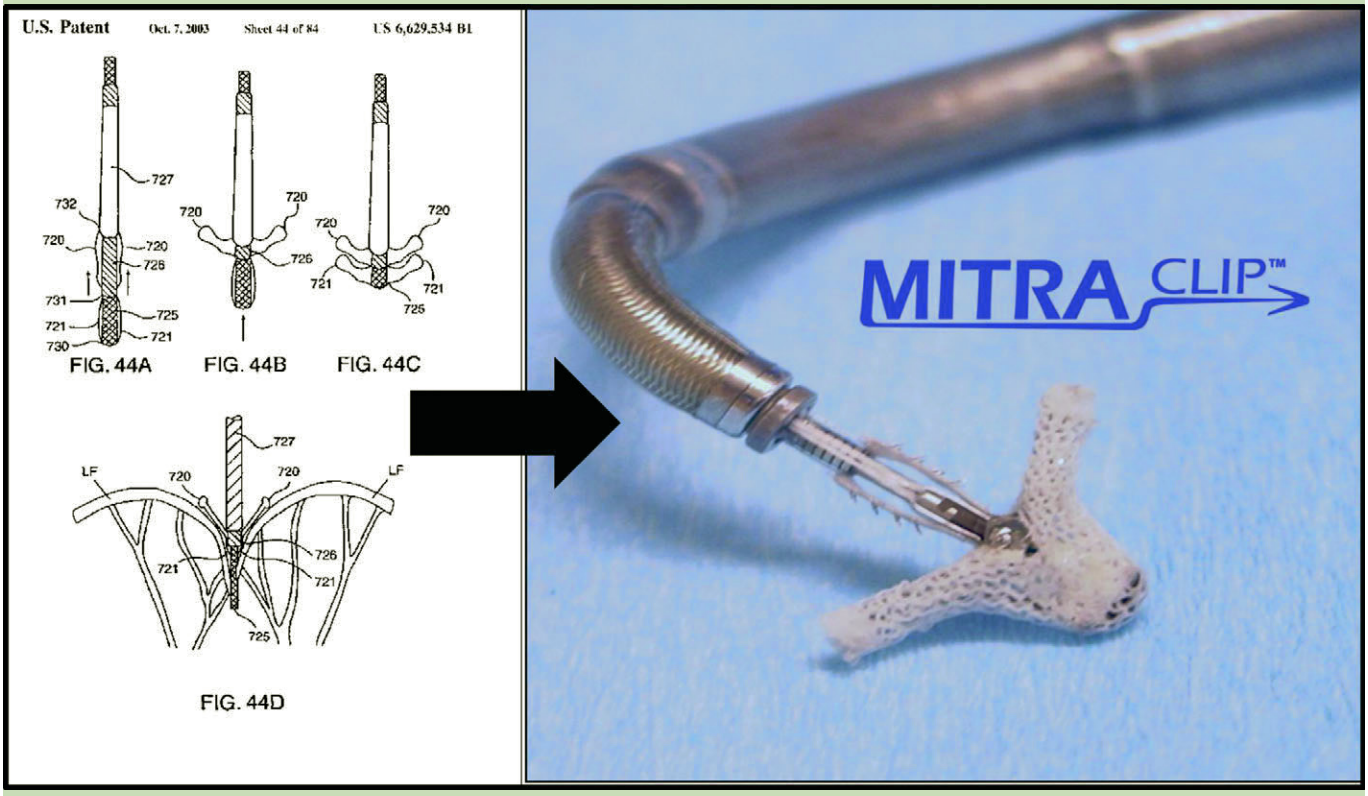

FIGURE 4.5.10
From the early design captured in a patent drawing to the finished product, the Mitra Clip evolved significantly over time (courtesy of Evalve, Inc.).

Although Evalve developed its prototypes in-house, the company also worked with an outside consultant with experience in medical device design, development, and manufacturing. "I think there's sometimes a little hesitancy on the part of the engineers to bring in an outside consultant," said Thornton, "but you've just got to get over it and say, 'Hey, maybe we've got something to learn from somebody else.'" He continued, "We brought in the consultant to work with our top three engineers who were working on the clip design to help them refine it. We used him extensively for brainstorming and developing ideas. He had years and years of experience and knew these specialized vendors who could do micro stamping processes, which we really needed but none of us had known about before. Bringing in outside expertise at the right time in the project can be a pretty critical step."

When offering advice to other inventors and companies, both Thornton and St. Goar stress perseverance as being essential to prototyping, as well as the larger biodesign innovation process. In the case of Evalve, as Thornton described, "There were a couple years of trial and error before it really took off." St. Goar added that patience also comes in handy. "We spent a period of time trying a number of different approaches, none of which looked anything at all like where we eventually ended up," he said (see Figure 4.5.10).

Evalve received a **CE mark** for the Mitra Clip in 2008. A year later, the company was acquired by Abbott Vascular. In 2013, the device received premarket approval by the FDA for use in patients with significant symptomatic degenerative MR who are at prohibitive risk for mitral valve surgery.[16]

Tips for effective concept exploration

As innovators gain experience with prototyping and testing, they build confidence and become increasingly effective in designing and developing models. Those without vast experience, however, will be well served to consider the following advice as they get started:

- **Consider multiple factors** – While exploring concepts, be sure to think about the function, form, material, manufacturing, cost, and feasibility of a prospective device or software solution.
- **Understand how competitive solutions work** – One of the best things to do early in the concept exploration process is to try to obtain examples of similar or competitive devices or solutions to understand how they work and what is good or bad about their design, user interface, or technical underpinnings. Having this knowledge can go a long way in making the concept exploration process more efficient. Just be careful not to anchor on the approaches employed by existing technologies.
- **Play with scale** – When prototyping small devices, consider scaling up 5× to l0× to make the initial exploration process easier during preliminary experiments. Look at things (especially moving parts) under a microscope to be certain to achieve a detailed understanding of how they function. Just remember that it will be necessary to find solutions that can be replicated at the size appropriate for their actual use.
- **Iterate** – Anticipate that concept exploration and specific prototyping exercises and tests will require multiple iterations and plenty of trial and error. Keep ample resources/materials on hand for practicing and correcting mistakes.
- **Consider the effects of reuse** – Construct reusable prototypes and test them for degradation with time and repeated use. Consider computer modeling and/or the use of specialized testing machinery to subject prototype devices to repeated physiologic loads. This process (and the associated test data) is often required for regulatory submissions. For example, devices implanted into the vasculature must endure

tens of thousands of simulated heartbeats without failure or breakdown. Some computer models are commercially available to test this. Others are being developed for specific disease or device applications.

- **Take pictures** – Photograph everything! A great deal can be learned from understanding and keeping a record of how each prototype has progressed based on lessons learned from earlier models. This also serves as compelling history for the company and customers as the product is introduced into the market and the company's story evolves.
- **Save all work** – Keep all prototypes as a physical record of development.
- **Maintain detailed notes** – Keep detailed notes (measurements, techniques, materials, etc.) regarding exactly how the first prototype was constructed so that the process can be replicated. Use a disciplined version control system for all drawings so that the design can be replicated later, as needed.
- **Be cautious regarding confidentiality** – Because there may be a significant amount of invention that occurs during prototyping, be sure to contract with a consultants who agree to relinquish all rights to any intellectual property generated from the design process. Protect all technology that is developed as a result of the prototyping process. Non-disclosure agreements should be signed with any contract suppliers/shops used (see 4.1 Intellectual Property Basics).

For more information and tips for prototyping specifically in the disciplines of mechanical, biomaterials science, electrical engineering, and computer science/software, see online Appendices 4.5.1, 4.5.2, 4.5.3, and 4.5.4.

Online Resources

Visit www.ebiodesign.org/4.5 for more content, including:

Activities and links for "Getting Started"

- Identify the questions or issues to be addressed through concept exploration
- Design the minimal model needed to answer those questions
- Identify and prioritize functional blocks
- Build the model
- Test/refine prototypes to develop design requirements and technical specifications

Videos on concept exploration and testing

Appendices that include reading lists and additional guidance on building:

- Mechanical device prototypes
- Biomaterials-focused prototypes
- Electrical prototypes
- Application and software prototypes

CREDITS

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