Biomedical Innovation, Surgical Innovation, and Beyond

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Abstract

"There's a better way; find it" -Thomas Alva Edison

Some of the most remarkable human advances in the last hundred years have been health care related. Many of these advances have involved luck…the right people, the right circumstances. The Biodesign Innovation program at Stanford attempts to increase the probability that the right people and the right circumstances come together. There are several major and minor theses presented throughout this paper. The major thesis is that in today's medical world, clinical practice continues to become highly focused and at the same time, technology also is becoming more focused and complex. As a consequence, the innovation process (the chance that the right people are present at the right opportunity) is less efficient than it could or should be. Traditionally, little attention has been given to the process of innovation in general and specifically to the process within medicine. It is time to look at the innovation process and how structured programs can be devised to bring together unmet market needs, talented engineers, and creative individuals from the various medical surgical specialties to make innovation happen. One of the first university initiatives to address this issue has been the Biodesign Innovation program at Stanford University, run by Drs Paul Yock and Joshua Makower as a component of the multidisciplinary Bio-X center. This paper delineates an expansion of this program to the surgical disciplines, the Surgical Innovation program. A further extension is also in the works which expands the underlying principles of the Biodesign Innovation program to the traditional academic environment in which research projects, be they dissertation, post-doctoral projects, or undergraduate projects, are chosen using the needs assessment approach refined within the Biodesign Innovation program described below.

Introduction

"Only the answers change; the problems remain the same" -Sir William Osler

The program in Biodesign is part of a university-wide initiative in the biosciences at Stanford, called Bio-X. Biodesign has helped fund and develop a number of courses and other initiatives in the area of biomedical technology, invention, and implementation. The Innovation Program has been a central focus of this education effort. Modeled on the Pfresh Tech Program developed by Dr. Makower at Pfizer in the 1990s, the Innovation Program is structured around a dedicated fellowship in biomedical technology innovation and a two-term graduate course that exposes a large and multidisciplinary group of students to the process.

The central mission has been to create a process based approach to training innovators and leaders in innovation in the same way medical, law, and engineering schools train for their respective disciplines. Not surprisingly, the process of innovation is a unique animal, necessitating its own educational style and process.

In 2004-2005, the Innovation program has expanded, partnering with the Department of Surgery at Stanford to create the Surgical Innovation program. Further expansion in the next one to two years includes extension to the basic and applied research arena where a similar philosophy will be utilized to stimulate innovation in the basic engineering and biomedical science departments.

With the creation of the Surgical Innovation program, the structure of the Innovation Program has changed in some key respects. In 2005-2006, there will be two innovation fellowship teams, one in surgery and one in cardiovascular medicine. In subsequent years, new teams from different disciplines may be added (e.g., ENT, plastic surgery, opthamology). The surgery team will also include an engineer, typically a pre-doctoral bioengineering student. Another major change has been the addition of an optional second fellowship year. This second year, during which fellows will have the opportunity to pursue further development of a technology area chosen from the first year, provides more depth to the experience in each clinical area and stronger linkage to the clinical departments.

The first year continues to be organized in a similar way to the original innovation fellowship. This year looks in depth at needs finding as well as delineating the process for entering the clinic to find new needs. The first year also includes an all important boot camp, in which the fellow is exposed to many of the important concepts in the innovation process such as intellectual property consideration, project finance, company creation, etc.

The second year has a project focus and allows the fellow to tailor the curriculum to his or her career goals. The project is one chosen from the first year and it is expected that the non-clinical fellow (typically pre-doctoral) who paired with the clinician in the first year will commence his or her chosen research project on the basis of the needs finding process. Depending on the nature of the project, the experience of the fellow, and the future interests of the fellow, additional funding for the project may come from the NIH (in the form of SBIR or STTR), from private investors (in the form of sponsored research), or seed grants (such as from NCIIA, the Bio-X center, or entities such as the technology licensing office at Stanford).

The fellowship is really about the people and the team. A successful year is defined as one in which the team has devised at least one, and preferably several successful projects; depending on the nature of the project, projects may have been developed all the way to animals or remain at the napkin drawing phase. This success is considered directly related to the personality of the fellows and the team. Expanded more broadly, team dynamics are, in general, the key to success in multidisciplinary research.

Over the three years of the program so far, it has been found empirically that a team of four people is ideal for this type of program. In general, the team further divides into groups of two who then immerse themselves in the clinical setting, working side by side in the clinic with physicians and observing diseases and therapies in real time.

Interview process and team selection

"Getting good players is easy…gettin''em to play together is the hard part"
-Casey Stengel

The program begins with a very intense and careful selection process in which individuals are identified who not only show leadership potential but demonstrate specific character traits which have been found to lead to success within the innovation program. Such traits can be different from the academic skills often sought by degree programs, and include such characteristics as an ability to seek and accept new paradigms, an ability to work in a team environment, and an ability to quickly assimilate new technology in the context of clinical scenarios.

In addition to the individual, the team and the predicted interactions and synergies between the individuals is also very important. Predictably then, the characteristic which is of most concern is the ability of the candidate to work in a team. As will be further illustrated below, the structure of the program demands teamwork to be successful.

Combining one or more engineers with one or more clinicians has, in theory, seemed to be an optimal synergy. And historically, within the program and within several of the medical technology incubators in the area, this combination has proven to be a very successful one. There is great synergy between the knowledge of each individual; working closely together, the engineer can ask a question which challenges paradigms the clinician may have been taught. With the category of engineer and clinician, personalities need to be chosen wisely; for example, both parties need to have an open mind and an intellectual curiosity to break out of their paradigms.

Applicants should show some evidence that they can adapt to new paradigms and that they have the resourcefulness to find, synthesize, and apply new technologies and concepts quickly and broadly across different biomedical disciplines. One of the major theses of this paper is that technology is developing at a quick pace while physicians are becoming increasingly focused in their clinical practice. In order to increase the probability of the "aha moment" occurring, it will be necessary to further broaden one's horizons such that a greater knowledge base is attained. It is not expected that one individual can master a new technology in one year, but rather can that she or he can quickly grasp its salient features and apply it to the clinic.

In addition to letters of support and prior research experiences, the above skills are demonstrated in an intensive interview process. A great deal of time is spent crafting the interview questions to specifically allow for demonstration of these skills; questions are formulated based on a prior review of the application by the interviewer. This is perhaps another aspect in which the innovation program differs from many traditional academic programs, some of which do not even have an interview.

An example of an interview question is, "Describe a problem from daily life or otherwise which you've encountered over the past twenty-four hours." This could be something as simple as quickly removing frost from car windows. From there, the problem is quickly defined further and codified into a needs statement as described below. A ten minute brainstorming process ensues to assess creativity and ability to break paradigms.

The interview further questions and probes into prior innovative experiences the individual may have had; emphasis is placed on the degree of individual contribution to the process—"What challenge were you presented with that lead to the success of the project?" Further queries involve team experiences and forward thinking clinical scenarios which begin with a case vignette and then the question, "What do you see as the clinical problem, and what would the ideal technology look like which would solve this problem?"

Needs finding

"Creativity involves breaking out of established patterns in order to look at things in a different way" -Edward de Bono

Innovation fellows begin the year with an intensive boot camp, in which some of the key accessory ingredients for innovation are taught. Included are all-important issues such as patents and patenting (and, more basically, how to protect an idea), funding resources, regulatory pathways, and technology transfer. These issues are not typically taught in a formative way in the traditional academic setting (including business school!) As anyone involved with biomedical technology innovation knows, these issues can be more important than the technology itself. The boot camp in itself is almost an independent curriculum; its details are evolving as well. Experts on the issues are brought in for lectures, as are experienced start-up executives who understand the real-world impact of these issues.

Following the boot camp, a process called needs finding begins. The fellows, including at least one clinically trained person and at least one person trained in science or engineering, together undergo a clinical immersion in which they experience patient care first hand. The major motivation for this exercise is to allow the fellows to witness clinical procedures, techniques, and philosophy as currently practiced. The fellows are trained (part of the boot camp) to ask the why and how of the procedure, and then the what if. They are also trained to look for difficulties that physicians may be encountering…that is, particular obstacles or technicalities which could be modified or streamlined in some way.

Clinical needs are phrased into a simple statement. An example of a need statement may read something like "a need to restore blood flow in a chronically occluded blood vessel…." or "a need to quickly remove frost from all car windows without scraping."

The process of accumulating needs has in the past lasted approximately one to two months. In the surgery arm of the fellowship, however, the immersion lasts quite a bit longer in order to accommodate a set of rotations through the subspecialties such as ENT, plastic surgery, orthopedics, vascular surgery, minimal access surgery, and robotic surgery. The hypothesis for the number of rotations is that exposure to the various surgical fields will broaden one's horizons and allow the fellows to bring intellectual and technologic aspects, technology sharing, from other fields to the clinical need at hand.

An example which illustrates the power of technology sharing is that of radiofrequency (RF) energy; RF energy has been used for a long time (since 1926) in clinical surgery, utilizing alternating current flowing through tissues to vibrate molecules and generate heat. It was only recently that radiofrequency has been used for widely diverse diseases such as vertebral disk healing, uterine bleeding, and closure of defects in the heart. One could say that it took from 1926 to 1990 to really appreciate the utility of RF energy. Had there been an innovation fellow between Drs. Bovie and Cushing and the 21st century, it may not have taken sixty-five years.

The typical needs yield from the clinical immersion may be as high as two- to three-hundred clinical needs. The subsequent four to six weeks are spent sorting through the needs, ranking and characterizing them further. The ranking system continues to evolve. The current system involves four parameters: patient impact, provider impact, perceived technical feasibility, and scope of solution (incremental improvement, paradigm shift, etc.). These categories are judged on a scale of one to four and an average is taken. This past year the last variable was removed and there were two categories, incremental and paradigm shifting, each with a list of ranked needs. There is also a separate category for gut feeling, which is averaged as well. This is a subjective score by each member of the team, given after all the ranking is done. If the subjective score is substantially different from the average from the group, then the individual parameters are each reconsidered carefully. The subjective score was instituted as a check on the scoring process and as a way to tease out what is important, and perhaps which additional categories need to be added in order to create a more accurate ranking system.

Part of the ranking system is called needs validation—the fellows do not necessarily decide the rankings for each category on their own. Rather, they develop focused questions and circle back with the physicians in order to obtain an accurate rank. Going back to the need statement above, an example of a validation question may be "Does restoration of flow in fact provide any benefit, or has collateral flow already developed?" This question directly addresses the issue "What is the clinical utility if the need were to be solved?" It may seem obvious that restoring blood flow is a good thing (a lot of innovations fail because the need is not further interrogated beyond this point); on the other hand, if the blood is in fact restored, there may not be any further clinical benefit (collateral flow, etc). In the fellowship, such a question would be posed to clinicians and/or taken to the library for investigation. Answers are then plugged back into the needs database for re-calibration.

This time period is perhaps the most important part of the fellowship. It is here that the magnitude of the clinical problem is established. The clinical problems (all two- to three-hundred!) are discussed outside the clinic, in a quiet environment without distractions, among the fellows. This is perhaps the only such forum in history that has discussed so many clinical problems in such a short period of time with an eye toward technological solutions.

Brainstorming

"If at first the idea is not absurd, then there is no hope for it"-Albert Einstein

At this point, the fun really begins. Daily brainstorming sessions are followed with prototypes in the product realization laboratory. Paradigms are shattered (for better or worse); ideas are brought in from left field, right field, and the bleachers to solve problems; new pathophysiological paradigms are even invented. Of course, there are ideas which should stay in the bleachers, but once in a while, out pops a Fogarty catheter. It's actually quite a remarkable process; watching it leads one to think that the process may be quite useful in scientific research as well…indeed, this is another hypothesis in this paper and is a harbinger of where the program is headed.

Teaching component

"Creative thinking is not a talent, it is a skill that can be learnt. It empowers people by adding strength to their natural abilities…" -Edward de Bono

Having just gone through the process themselves, fellows now help teach an official Stanford course in which undergraduate and graduate students participate in a miniature fellowship. The part that is missing is the clinical immersion and needs identification period. Because of time constraints, the needs and clinical knowledge are transferred to the student teams; the teams either further characterize and validate the needs, or take them as presented.

Over a three month period, the student teams brainstorm, build prototypes, investigate patents, define markets, and write business plans for entry into the campus-wide business plan competition.

The innovation fellows supervise the process, answering questions, assisting with prototype design, and providing physician connections. In the course of teaching, the fellows solidify the process in their own minds. At the end of the course, the students present to a group which includes venture capitalists, industry veterans, and academicians. The fellows assist in building the story for these presentations which gives them experience for their own inevitable fundraising efforts. The course last year produced a dozen invention disclosures, at least two of which are proceeding to the patent phase and have received a great deal of industrial interest.

Prototype and design phase

This process is ongoing for the fellows from the brainstorming time to the end of the year, taking place concurrently with the teaching course in the middle of the year. The Bio-X facility at Stanford contains several prototyping facilities, as well as experienced technicians and faculty. Typically the top one or two ideas from the brainstorming period are chosen to further prototype, if amenable to prototype and if the idea can benefit from a prototype to illustrate or refine the concepts. Going back to the synergy in the team, typically at least one fellow is chosen who has extensive background in developing prototypes.

Externship

An externship period exists between the class and the final presentation period (two months) where fellows are placed in a work environment of interest to their future careers. In some cases, this involves a start-up company. In other cases, the externship involves further clinical exposure. In part, this phase is flexible, depending on the goals of the individual. A brief internship with the Food and Drug Administration has also been a path for the fellows. A stint with the FDA can be highly valuable for a fellow who plans to go on into product development. The regulatory paths for products can in some instances be the decisive factor in the financing of a project. Having seen the process first hand within the FDA can provide invaluable insight into the regulatory process.

Year 2

“What’s missing isn’t the ideas, it’s the will to execute them” -Seth Godin

The second year is, in part, optional. At the start of the biomedical innovation program in 2001, the fellowship was one year. As the program progressed, there was a certain attachment to the projects by the fellows which was evident in their reviews of the fellowship. Beginning with the Surgical Innovation program, the fellowship will have an optional second year. In this year, a project from the first year will be advanced through the prototype and seed funding phases if the fellow so desires. In part, the path of the fellow in the second year is dependent on his or her career plans and interests.

If the fellow desires to continue into a second year, the planning process will begin by the middle of the first year. As discussed above, part of the mission of the program is to educate the fellow with respect to the various funding mechanisms that exist, and these mechanisms will be accessed as the project is further planned. An actual five day seminar series is in the planning stage; this seminar series will feature experts in specific funding mechanism: NIH, SBIR/STTR, DARPA, NSF, Venture Community, and Corporate.

An additional highly compelling aspect of the second year is that the fellows will mentor the first year fellows in the process. Other options available for the fellows in the second year include a master's degree in bioengineering, work at a start-up company, etc. The myriad options available to fellows in the second year points to the breadth of experience obtained in the first year and the diversity of the fellows.

Fellowship outcomes

The one year fellowship, which has been in existence since 2001, has produced some remarkable results. Three companies—Acumen, Kerberos, and Neoguide—have been founded based on the needs finding process, and students from the fellowship have gone on to to take upper management roles in these companies. By way of example, Acumen Medical, founded by Chris Eversull and Nicholas Mourlas, has developed a novel catheter based method to enable a simplified implantation of pacemaker leads into the coronary sinus; FDA approval for their device is expected any day.

The clinical need around which Acumen was founded arose from direct observation of procedures in the interventional cardiology suite where Chris and Nicholas observed that cardiologists were struggling to cannulate the coronary sinus. Further discussion with the cardiologists validated the need, and the brainstorming and prototyping sessions produced the invention. The externship period allowed them to raise seed capital for the project.

Furthermore, there are at least five technologies actively engaged in the licensing process from Stanford. A sixth technology is about to become a company addressing the very large unmet needs related to aspiration pneumonia.

If not actively starting companies, former fellows are engaged in the early innovation process in one way or another. For example, Asha Nayak MD, PhD, is a senior project engineer at Medtronic Advanced Technologies, where she nurtures ideas and concepts through the proof of concept phase and on to clinical development. Daniel Francis is one of the first engineers at Cierra Medical, which is developing novel cardiovascular technologies. Aimee Angel is a venture associate at DeNovo ventures, where she specializes in early company formation and needs finding.

William Overall, Russell Woo, and Kelly Richardson are examples of fellows who continue to innovate and collaborate on multidisciplinary projects but who remain in the academic environment—William is a researcher at Stanford in the department of electrical engineering, Kelly is an electrophysiologist, and Russell is a surgical resident interested in pediatric surgery and robotics. These fellows, in particular, have provided insight into the expansion of the one year program to two years a to create a more academic track.

Conclusions

In summary, the innovation programs at Stanford University teach and develop unique ways of finding and approaching clinical problems in medicine and surgery. What began as a program for a few individuals to creatively explore their inventiveness in the cardiovascular sciences has evolved into a philosophy which transcends several fields of medicine. The next mission of the program leaders is to transfer the process to the surgical disciplines and to the more academic arenas so that students will choose projects which are firmly grounded in a clinical and/or market need. It is with this type of training that the multidisciplinary leaders of the future will be created.