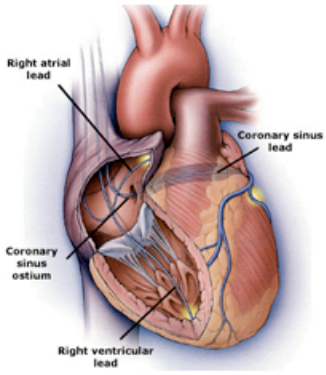
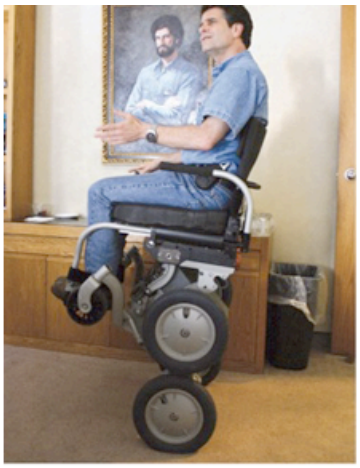
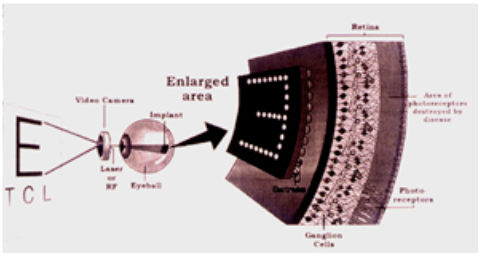
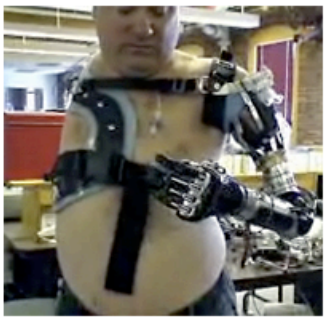
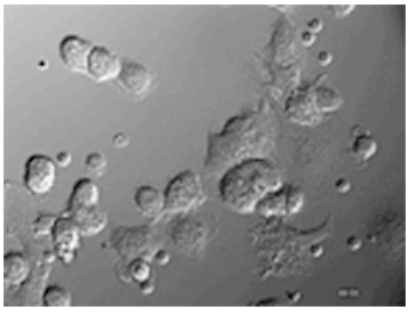
INTELLIGENT SYSTEMS AND THERAPIES
HOW ACCESSIBLE ARE THEY ?











Ethics 2241

N. Krishnamurthy and S. Jhunjhunwala
University of Pittsburgh, Fall 2009

INTELLIGENT SYSTEMS AND THERAPIES HOW ACCESSIBLE ARE THEY ?

Ethics 2241

N. Krishnamurthy and S. Jhunjhunwala
University of Pittsburgh, Fall 2009

Prelude

The IBOT came to our attention as one of the smart assistive technologies that is no longer available for paraplegics and other wheelchair users. Johnson & Johnson (J&J) as of January 2009, will no longer manufacture new IBOT's. It would also stop servicing the 1000 odd units as of 2013. Only six years ago the IBOT had got its FDA approval (August 2003) and it incorporated a number of different functions, including: a) Standard Function that provides mobility on smooth surfaces and inclines at home, work, and in other environments; b) Four wheel function that provides movement across obstacles, uneven terrain, curbs, grass, gravel, and other soft surfaces; c) Balance Function that provides mobility in a seated position at an elevated height; d) Stair Function that allows for ascent and descent of stairs, with or without assistance; and e) Remote Function that assists in the transportation of the product while unoccupied [1].

Given that the IBOT is an amazing product, it is a shame that it is no longer manufactured. The IBOT had retailed at $29,000 which many wheelchair users (blogs/forums) have indicated as beyond their reach if insurance does not cover for it. One can get a motorized wheel chair for costs ranging from two to eight thousand dollars, but smarter technologies like the IBOT cost way more due to the high lead time in development, and the costs thus incurred and royalties on the Intellectual Property (IP's) of the underlying technology. In 2007 the Centers for Medicare & Medicaid Services (CMS) issued an update classification [1] for the IBOT's 4-Wheel, Balance, Stair and Remote Functions as not meeting the definition of a Durable Medical Equipment (DME). This essentially meant that it would not pay for the features for which the IBOT was created. Subsequent to the CMS update, J&J decided to pull the plug on the IBOT as very few units were sold between 2007-08 to be able to viably manufacture and service this amazing product.

Motivating Question

A bioengineer is constantly creating novel devices and therapies (referred to as 'technology' from here on) to help people in different ways. Often a new technology that is developed to address a need can be prohibitively expensive. Does the use/benefit of a new technology justify any price put on that technology, or should principles such as just distribution of resources and the moral responsibility of ensuring that the general population reaps the benefits be applied while creating and marketing the technology? These are some of the questions that we will attempt to discuss in the form of two case studies.

Background – Current state of Prosthetics

The IBOT is only one of the many intelligent systems being developed for rehabilitation. Prosthesis, assistive technologies and rehabilitation systems are essential components in increasing the well-being of patients with a handicap or motor dysfunction due to injury or disease. The current survey of prosthetics does not include Cochlear Implant (CI) a device that transduces sound waves to electrical signals that directly stimulates the auditory nerve; nor does it include bone anchored and middle ear hearing aids, which were the first successful prosthetic devices implanted in humans in the 1950's. The survey also excludes the sophisticated cardiac rhythm management systems which are being developed currently, for we've had an opportunity to look at some aspects of this technology through the Telectronics J-Lead case from the Ethics 2241 course taught by Dr R. L. Pinkus at the University of Pittsburgh.

Though there are parallels between IBOT and the upper limb robotic prosthesis technologies (to be discussed later on), retinal implants and lower limb prosthesis are included in the background to bring out the issues involved in commercialization of assistive technology. The lessons learnt from functional electrical stimulation devices would be valuable in identifying end user needs to develop affordable technology that would ultimately lead to satisfactory adoption of technology, by patients requiring them.

Retinal implants:

Over 10 million people are legally blind (vision less than 20/200) because of photoreceptor loss at the retina (back of the eye), this loss could be due to degenerative retinal diseases such as Age-related Macular Degeneration (AMD) and Retinitus Pigmentosa (RP). Two groups one from North Carolina State University/Johns Hopkins University (NCSU/JHU) at the United States, and the other University of Melbourne/National ICT Australia Victoria Research Laboratory at Australia have developed a bionic eye for restoring vision that would allow discrimination of direction of motion (which would allow for mobility) and recognition of simple forms. Would this technology be affordable and mature to the point that the all cane users would switch to using the implants instead?

NCSU/JHU developed their retinal implant in conjunction with Second Sight LLC. The study of a retinal implant by M. Humayun et.al. [2] in a 76 year old male with X linked RP was done ten weeks after implant in his right eye (which had no vision for 50 years). 'Visual perception elicited by electrical stimulation of a single electrode produced a single spot and or with a black surrounding ring' [2]. Color percepts were often yellow and white, and occasionally red-orange spots. Size of the reported percept ranged from a match head to a quarter, depending on the strength of the applied stimulus current and its location matched the location of the stimulating electrode. Using a pattern of electrical stimulation of the retina, the subject was able to repeatedly report the order in which different electrodes were activated based on the location of the electrodes. Individual percepts when used in combination, the subject learnt to distinguish a ''direction'' that corresponded to the order of electrode activation.

Functional Electrical Stimulation (FES)

Orthosis and Prosthesis restores function for Lower and Upper limbs

The discovery by Luigi Galvani that charges applied to the spinal cord of a frog results in muscle contractions (1780) and experiments by Duchenne with Faraday's induction coil to help patients with paralysis regain muscle function (1840), ushered in the era of FES. Since then FES has been used to restore functions in spinal cord injury (SCI) and stroke patients with motor disabilities. Devices have been designed to facilitate tasks like walking, grasping objects with a hand, bladder control, ventilation and pain alleviation [4]. Vagus nerve cuff stimulation has been recently shown to pace the brain out of epilepsy, while deep brain stimulation is successful in treating parkinson and some focal dystonia patients, by removing the slowness in initiation, and amplitude of voluntary movements (Hypokinesia), and rigidity from co-contraction of opposing muscles [3 -5].

In the 90's (94-98), FES was clinically applied to restore lower extremity functions like standing up and walking. R J.Triolo et.al. at Case Western Reserve University/Veterans Affairs (CWRU/VA) did a long-term study of FES in thirteen SCI patients [7]. Prior to the surgery, the patients took a survey on their expectations and usage of the FES device, why they wanted the system, and if they understood the capabilities of the product. Eleven of these patients were interviewed after a year of implant surgery; nine of the implant recipients were using the neuroprosthesis regularly for standing and/or exercising at the time of the survey. Recipients noted improved health and a reduced incidence of pressure sores, leg spasms, and urinary tract infections. Subjects were moderately to very satisfied with the performance of the neuroprosthesis.

Despite the positive customer feedback in the Triolo et.al. study [7] and FDA approval of FES systems like Parastep(1994) and Freehand(1997) it is important to realize that rehabilitation of SCI patients to use FES is not easy, often the path to restoring mobility can be frustrating, involving 6-8hrs commitment in rehabilitation. Patients who were not up to this often give up using the system -- here in comes in the educational component in rehabilitation. The patient relearns the ability to take his first step or move his arm, like a child taking his first step, progresses in small increments to get acclimatized to his/her disability and in the use of the assistive device.

Patients, who did not understand the capabilities of the assistive technology, can cause themselves harm with improper usage of these systems. We found an adverse report (http://www.fda.gov) on the Parastep standing/walking system, based on a multicenter feedback study amongst patients. Unlike the Triolo study, this report concluded FES alone without an exoskeleton or brace is not safe for patients. Parastep costed $15,000. Most patients found using the system laborious, even after five months into rehab, in many centers patients gave up on the rehabilitation using FES. One center which started with 38 patients only 22 had limited success (7 poor or no walking, 8 walked a few steps, 7 had fair to good walking), while there was one patient who was able to walk 4000 feet.

Freehand FES system was an upper extremity neuromuscular stimulation device designed to restore hand grasp functions to manipulate objects. Freehand patients were a subset of SCI patients who had residual movement and intact motor neuron pathways to the distal extremities. Like the Parastep system, these devices used both intra and inter muscular stimulating electrodes which meant invasive lead placement surgery.

Lessons learnt from FES trials from the 90's

The lessons learnt from the FES clinical trials provided valuable information on gait analysis, and muscle synergies in effecting grasps. And has lead to development of orthosis and surface stimulating leads, used in devices like the Handmaster^{TM} which now cater to a broader patient population of stroke and SCI patients.

• Current lower limb prosthesis and orthosis

Passive variable damper knee - Rheo knee uses a clutch plate architecture and with a thin film of magneto fluid, to provide the compliance of an actual knee through a gait cycle. The passive Rheo knee costs the user a lot more effort to use. An actuator driven active orthosis that mimics the human reflex was designed to minimize usage effort. Energy harvested in other parts of the gait cycle was used to make the orthosis energy efficient. The orthosis could be driven by a 24W battery pack which weighed only 0.2kg (Dr. Hugh Herr's video talk [6]).

• Luke Arm - upper limb prosthesis

Luke arm is a modular arm that can be used with all levels of amputation (wrist, elbow and shoulder level). Prototype restores 14 degrees of freedom and provides haptic feedback on gripping pressure. It can take inputs from residual muscle and nerve activity and or arbitrary association of residual movements (shoulder, eye or pressure sensor on the foot) to manipulate a robotic arm to perform activities like, eating, chores around the house like using a drill etc. (Dean Kamen, the inventor of Segway and IBOT [6])

Understanding user needs:

The IBOT was born out of the needs expressed by wheelchair users to develop a chair that had functions of mobility at an elevated level, ability to negotiate uneven terrain, climb curbs/stairs and even provide a remote autopilot feature. These features were incorporated into a smart chair which was marketed as IBOT.

Surveys done by Kilgore et.al. [8] for para/tetraplegics and seminal survey undertaken by NIH DJ Atkins et.al 1996 [9] and a more recent survey in the Europian Union (EU) 2007 [10] were all

aimed at creating a database of users of prosthetic devices and to evaluate past use of prosthesis, preferences of the individuals to help determine the research direction that FES and prosthesis technology should take to have a meaningful impact in the lives of patients with motor disabilities. Despite the thirteen year gap between the Atkins et.al survey and the 2007 EU survey, the concerns and improvements suggested by the users has not changed, which is not surprising as the technology available for them has not improved much in the past decade either.

The development of upper-arm prosthesis for restoring grasping function in contrast to lower limb prosthesis has been characteristically slower. Even as pioneers in the field identified the complexity and control strategies to allow for multi-joint control without active intervention from the user as early as 1970 DC Simpson [11]. Only recently have research labs started to incorporate the extended proprioception (proprioception is the sixth sense or self awareness of body parts in space, and relation to other body parts) as a feedback mechanism to provide automated control of the robotic prosthetic arm.

The Atkins survey involved both a short survey (2477 users) and a long survery (1575 users - 1020 body powered users, 438 electric users, and 117 bilateral upper arm prosthesis users in the US). The ***users indicated improvements*** in currently available technology to allow for ***wrist movement, better control - requiring less visual attention, and ability to make coordinated motion of two joints.*** In terms of body comfort, all users suggested a need for better harness/glove and unobtrusive cabling and better batteries.

Forums and survey like these helped scientists to focus their research initiatives in providing ease of control/movement and greater degrees of movement freedom (wrist, shoulder, fingers etc.) as a priority, over and beyond the safety in use of the assistive technology, as expressed by users and not be driven by intriguing aspects of currently available technology.

Case Study: Upper Limb Prosthesis

The IBOT and current upper limb prosthesis technology have a lot of parallels. Both systems are technologically complex and both have been developed with costs over $50 million, in prototype development. While the IBOT was developed by DEKA using funds from the healthcare giant J&J. The luke arm was developed by DEKA through an $18.1 million grant from DARPA's Revolutionizing Prosthetics 2007 program. In addition DARPA has awarded $30.4 million to the Applied Physics Laboratory (APL) of Johns Hopkins University, from its Revolutionizing Prosthetics 2009 program, for developing a mechanical arm that closely mimics the properties and sensory perception of a biological limb. JHU recently delivered its first prototype (built like the Luke arm) to use of residual nerves to control the robotic arm. Knowing the fate of the IBOT, and working in a lab with an interest in neuralprosthesis, the dilemma's that come to my mind are:

1. Will the Luke arm or the current upper arm developed by APL-JHU be affordable and available to the general population?

2. What are the roles of the manufacturer, the engineer, and the government, to ensure that technological solutions to problems, ultimately reaches the intended population?
3. When does the researcher draw the line in developing novel technology that is currently very expensive and/or divert resources to other pressing needs?

Case Analysis

Known Facts

- "450,000 people in the United States have sustained traumatic spinal cord injuries, with more than 12,000 new cases of SCI emerging in the U.S. every year" [26]. According to the National Stroke Association, the total cost of stroke to the United States is about $43 billion a year. Stroke and traumatic injury are only a small fraction of the patients with motor disabilities. Degenerative diseases like Duchenne' s muscular dystrophy, ALS, Parkinson's disease and other motor disorders like Cerebral Palsy, and Dystonia are examples of other major medical conditions that cause movement dysfunction.

- FES, Orthotic Prosthesis and Exoskeleton/Braces and Wheelchairs have been designed to improve the quality of life of patients with motor disability. The assistive technology provides independence and a sense of self reliance to the user to carry out tasks like standing, walking and grasping. The use of these devices have also shown to improve the health condition of the patients, they have lesser incidence of urinary tract infection and pressure sores [7].

- The current DARPA arm is being designed from the identified user needs for wrist movements, better control (requiring less visual attention) and ability to make coordinated motion of two joints, better comfort of harness/glove and a lighter prosthesis (Atkins survey [9]).

- In 2003, the average price Medicaid paid for a prosthetic arm was $3,645, while a computerized prosthetic arm costs from $10,000 to $12,000 (this estimate is based on currently available myoelectric prosthesis). Applying a 4.5% inflation factor, the average price Medicaid will pay in 2006 for a prosthetic arm of $4,160. A computerized prosthetic arm will cost from $11,412 to $13,694 [27].

- The Luke arm with its 12 processors and 14 actuators will cost a lot more than the currently available myoelectric prosthesis. A conservative estimate would be three times the 2006 estimate, i.e. it would cost between $ 30,000 to $39,000 per prosthesis. The IBOT which retailed in the similar range has been pulled off the market due to a lack of demand by J & J.

Key Question

Can the DARPA arm be produced at an affordable price ? How can the government intervene to make this possible?

Case Resolution

Role morality of a Bioengineer

Harris et.al [25] define the role of a bioengineer in terms of the "***code of professional responsibility***". The codes of ethics for engineers has in it the ***core value of safety***, focusing on ***beneficence*** *or doing good*, and ***non-maleficence*** *or do no harm*. In order to perform their professional role, engineers commonly **use a problem-solving framework**, which involves developing a technology through iterative steps: 1) Problem definition- user need identification. 2) Articulation of measures of effectiveness of solutions 3) Identification of solutions to problems. 4) Weighting solutions - through risk/benefit analysis. 5) Selection of a solution. 6) Improvement by obtaining feedback from enduser and repeating steps 1 through 5 [12] .

The IBOT and the Luke arm were developed using a similar problem-solving framework. User needs were identified, technological solutions were evaluated for performance, and every alternative was compared and contrasted to arrive at the end product.

Role morality of a Manufacturer

In addition to developing new innovative technology the scientist/engineer has a moral obligation to be involved in transfer of technology (transition of a proof of concept to make a technology robust and reliable to be able to manufacture in mass for clinical use). The role of an engineer as technology transfer agent is often tricky, as he has to work with multiple organizations like insurance providers, suppliers, distributors, physicians and patients, regulatory organizations like FDA and other government offices like the patent office to ensure that the technology/product reaches the patient/end-user.

The manufacturing engineer as an agent of transfer of technology strives to economize, and cater to individual needs of the customer. The Luke arm was developed as a "proof of concept" in mimicking the functional capabilities of a biological arm, and no expense was spared it took $18 millions to develop it. To make this technology clinically available one needs to look at features that are critical to retain, and make a stripped down version, that can produced in mass at an affordable price. A **cost-benefit analysis** of the functional capabilities of the robotic arm would

enable the engineer to create a custom-fit a solution which in addition to meeting the needs of the user would also reduce cost of the solution by supporting only features requested by the end-user.

For instance the end-user could foresee a reduction in the number of actuators by choosing to use basic wrist function with three robotic fingers in comparison to the full fledged 14 degrees of freedom provided by the Luke arm.

Responsibility of Society/Government

The IBOT wheelchairs are no longer available in the market. The CMS (government), the manufacturer (J&J), and society at large, have each contributed to get to this wasteful situation. Years of development time and millions of dollars spent in research has gone to waste because the technology is no longer in use. This case also raises an alarm over the viability of the DARPA arm being developed at an expense of $50 millions.

Medicaid/Medicare reimbursements in any society often boil down to rationing the available funds among competing needs. A national survey of children with special health care needs carried out in 1999 [13] indicates the prevalence of unmet needs in children with special needs, the table below captures the essence of the problem: **rationing healthcare leads to " prevalence of unmet needs**". Data from Table 2 of [13]

Prevalence of unmet need	Unmet Need for Therapy Services (n = 8291)	Unmet Need for Eye glasses or Vision Care (n = 13 360)	Unmet Need for Hearing Aids or Hearing Care (n = 2343)	Unmet Need for Communication Aids or Devices (n = 743)	Unmet Need for Mobility Aids or Devices (n = 1644)
% unmet need	11.1	5.8	9.2	24.7	9

Larry Churchill in his book "Rationing Healthcare in America" used eight rules of social justice to weigh the competing demands and ration the finite resources amongst them. Society has a moral obligation to honor longstanding obligations to the physically handicapped. The user survey in 1996 and the more recently in 2007, both indicate that the technology available for patients with motor disabilities has not improved much in the past decade.

The government must clearly do more than just fund research teams in developing technology. It must ensure that technology gets transferred, and manufacturers can produce the products viably. The goverment can provide reimbursement through medicare on the principle of **restorative**

justice, for ignoring the needs of the physically handicapped for so long, and thus aid in the sustainability of the developed technology.

Most smart devices are expensive due to multiple Intellectual Properties (IP's) or patents associated with them. While IP's foster innovation by providing incentive to innovators, in cases like the IBOT where technology becomes unusable, the government must intervene and **procure the IP** and subsidize its subsequent use, or the state could **appropriate the IP** by exercising its "**eminent domain "** (Is the power of the federal or state government to take private property for a public purpose, even if the property owner objects).

The NIH and the US government are aware of the legal complications associated with IP, and have taken proactive measures by issuing guidelines for the application and issuance of IP in the field of Human Genome and Genetics in 2004 [28]. This is an example of how a government can do more to preempt legal deadlocks due to patents and IP. This woud ensure that treatments and therapies can be developed for gene linked diseases, in a timely manner without legal battles over patents. Similar steps need to be taken in other fields as well.

Background – Tolerogenic Cell Therapy

What medical treatment is commonly prescribed to patients who have a tissue or organ that has lost its ability to function properly? More often than not, the only treatment option for such patients is transplantation of that tissue or organ. Transplantation in the field of medicine, as its name suggests, is defined as the transfer of tissue or organs from one individual to another [14, 15]. The transplanted tissue or organ takes over the function that is lost in the patient receiving the transplant, thereby curing the patient of that particular problem. But in doing so a slew of other problems are generated, which combined together can be expressed as the phenomenon of "rejection". Janeway et. al. and Lechler et. al. describe rejection as the process by which the immune system recognizes the transplant as "foreign" and initiates adverse responses against it[16, 17]. The process of rejection causes cell death and necrosis of blood vessels in the transplanted organ, and hence the organ stops functioning normally, which can ultimately be fatal.

The process of transplant rejection can be slowed by suppressing the immune system. Immunosuppressive drugs are commonly prescribed to transplant patients to achieve this goal. Although these drugs help to prevent the process of rejection, they are associated with multiple negative side effects such as, damage to the kidney and liver, increased risk of microbial infections and a greater chance of malignancies [18, 19]. Currently, even though these side effects exist, immunosuppressive drugs are prescribed to transplant patients as researchers are yet to discover a better treatment to manage/prevent the process of rejection.

Over the past few years a new concept to prevent rejection has been brought forth – the generation and use of tolerogenic cells [20-22]. Tolerogenic cells can crudely be defined as those cells of the immune system that play a role in regulating immune responses usually after external manipulation (the immune system contains cells that can regulate other immune cells to prevent self-tissue damage, but external manipulation is required in order to prevent damage of transplanted tissue). As their definition suggests, these cells have a unique property of being able to modulate the immune system in order to prevent adverse immune responses against specific cells, tissues or organs. Researchers across the country are working towards harnessing the potential of these cells as it is widely believed that advances in research on tolerogenic cells will eventually lead to the development of a cell-therapeutic that can prevent the process of transplant rejection.

One of the disadvantages of using cell-therapeutics is that they are expensive. The average cost for a single cellular-therapeutic injection can be roughly $15,000 (current cost estimates based on interviews with Dr. Angus Thomson and Dr. Theresa Whiteside). This amount is for minimally manipulated cells, and in general the cost increases exponentially with each additional manipulation step. Given the high cost and complexity of obtaining such cells, many cell-therapeutic critics believe that such a technology can never be widely commercialized.

Case study: Cell Therapy

Mike, a federally funded researcher at the University of Pittsburgh, has been working towards developing platform technologies that will promote production of tolerogenic cells outside the body, which if infused into patients can help prevent rejection of transplants. Based on a number years of research he has identified a set of conditions to culture immune cells that will enhance the generation and expansion of tolerogenic cells. These conditions involve the use of 5 different growth factors and 3 different small-molecular drugs, all of which are expensive. Further, under these conditions he has to culture these cells for a total of 3 weeks, while he normally cultures them for only 1 week. Mike understands that the new process he has come up with works out to be extremely expensive (price of a cellular therapeutic produced using minimum manipulation is about $10,000-15,000, while given the number of manipulation steps in the new therapeutic under development, he estimates it would cost more than $50,000), but it has the potential to be developed into a cure for the problem of rejection. He has the money in his lab to continue research on testing these culture conditions and developing a new cell-therapeutic, but is worried about the economic feasibility of the therapeutic in the clinic. He feels that given the high price, the cell-therapeutic he is developing can be afforded by a select few. He has recently heard about the fate of IBOT wheelchair, and hence fears that the therapeutic under development may meet the same fate. This puts him in a dilemma –

1) Should he continue his current research to establish whether the new culture conditions would lead to generation of tolerogenic cells even though it may never be used in the clinic?

2) Should he try to focus his research on reducing the number of growth factors and drugs required, or to look for cheaper alternatives?

3) As a publicly-funded researcher is it his responsibility to develop technology that can be afforded by the general masses, or is towards doing novel research and develop cutting edge technology?

Case Analysis

In order to understand if others have faced similar dilemmas, Mike does a literature search on case studies in ethics that deal with the same problem. He finds an article by David Merryman[23] that discusses the ethical issues involved with the development and distribution of costly technology. One of the prominent ethical theories used in this case study was **utilitarianism** (*defined generally as the "greatest amount of good or happiness" by John Stuart Mill[24] and later by Harris et. al.[25]*) - he decides to use this as the primary theory to analyze his dilemmas.

To perform an ethical analysis he begins by summarizing the information known about this case.

- Rejection of transplants is a significant medical problem leading to loss of a large number of human lives.
- Currently, rejection is prevented temporarily by using immunosuppressive drugs.
- Immunosuppressive drugs need to be taken through the lifetime of the patient, and long term use of these drugs can have many adverse side effects such as kidney and liver damage, increased chances of infections and increased risk of tumors.
- Tolerogenic cell therapy is an attractive alternative as it can prevent rejection and improve quality of life of patients while not having any of the side-effects of immunosuppressive drugs.
- He has identified 5 growth factors and 3 drugs (cocktail) that together can promote development of tolerogenic cells.
- His research indicates that the cells need to be grown in this cocktail for 3 weeks
- Current cell therapeutics in clinical trials, developed with minimal manipulation cost about $10,000-15,000/ patient (for 3-4 injections).
- The cost of cellular therapeutics increases exponentially with each additional manipulation step.
- He is unsure as to what the price of this new therapeutic could be, but estimates it to be over $50,000/patient.

He has recently heard about the IBOT wheelchair, the price of this technology and its fate in the market. Mike is also aware of the fact that transplants are regularly performed at different hospitals throughout the country, and that these operations are extremely expensive (in the order of $100,000) but still covered by the insurance companies. Hence, he decides to use the situation of transplants being covered by insurance while the IBOT not being covered as benchmark cases to analyze his dilemma with regard to the cost of tolerogenic cell therapy and its feasibility in the clinic. Since the most important dilemma he faces revolves around the cost of a technology versus the benefits associated with it, he decides to perform a **cost-benefit analysis** (*defined as weighing the cost associated with an action versus the benefit associated with it, and arriving at a decision based on whether the cost outweighs the benefit and hence not performing the action or the vice-versa[25]*).

To perform a logical, scientific and sound cost-benefit analysis he decides to make use of the **line drawing technique** (*comparing a particular dilemma to different questions each of which have a definite positive and negative paradigm*[25]) to help him analyze his case in the context of the two benchmark cases.

Line drawing assessment for tolerogenic cell therapy case:

Question	**Positive**		**Negative**
Would this technology/treatment help reduce fatalities?	Life saving	----X----------	Not life saving
Would this technology improve quality of life?	Yes – vastly improve quality of life	--------X----------	No improvement in quality of life from current condition
How many patients will benefit from this technology?	Large numbers	----------X----------	Small numbers
How expensive will this technology/treatment be?	Low cost	----------X--	High cost
How accessible (in terms of ease of manufacture and distribution) will this technology be (market economics)	Can be produced and distributed in high numbers	----------X	Can be produced and distributed in very small numbers

He identifies the costs associated with tolerogenic cell therapy as the price and accessibility of the technology, while the benefits are saving a life, improving quality of life, and affecting a

large number of patients. To assign a quantitative value to each of these questions, he decides to apply the same line drawing to the two paradigm cases.

Line drawing assessment for transplants:

Question	Positive		Negative
Would this technology/treatment help reduce fatalities?	Life saving	X----------	Not life saving
Would this technology improve quality of life?	Yes – vastly improve quality of life	----------X----------	No improvement in quality of life from current condition
How many patients will benefit from this technology?	Large numbers	----------X----------	Small numbers
How expensive will this technology/treatment be?	Low cost	----------X	High cost
How accessible (in terms of ease of manufacture and distribution) will this technology be (market economics)	Can be produced and distributed in high numbers	----------X	Can be produced and distributed in very small numbers

Line drawing assessment for IBOT wheelchair:

Question	Positive		Negative
Would this technology/treatment help reduce fatalities?	Life saving	----------X	Not life saving
Would this technology improve quality of life?	Yes – vastly improve quality of life	X----------	No improvement in quality of life from current condition
How many patients will benefit from this technology?	Large numbers	----------X----------	Small numbers
How expensive will this technology/treatment be?	Low cost	----------X------	High cost

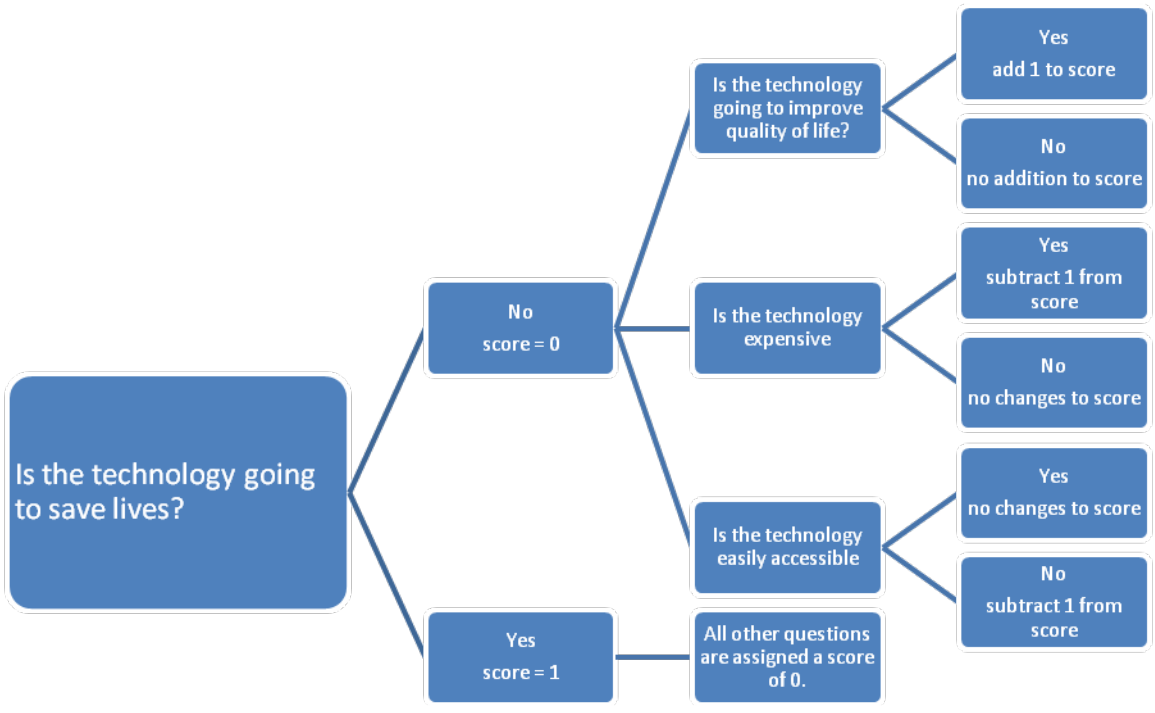
How accessible (in terms of ease of manufacture and distribution) will this technology be (market economics)	Can be produced and distributed in high numbers	------X----------	Can be produced and distributed in very small numbers

From the line drawing assessment of the two paradigm cases and the fact that transplants are covered by insurance while the IBOT wheelchair was not, Mike feels that the following conclusions can be drawn:

- Life saving technology has a much greater value than technology that improves quality of life (without receiving the transplant the patient would die, in comparison to not having an assistive technology would lead to the patient not being able to perform some daily tasks, none of which are required for survival in today's world)
- Cost and ease of availability of technology do not matter if the technology is going to save lives, but do matter if the technology is only going to improve the quality of life.

Based on these conclusions, he feels that each of the cost-associated or benefit-associated questions cannot be assigned an independent value (independent weightage). Since the questions are dependent on each other (hierarchical dependence), he uses a decision tree to assign a value to the questions. Also, he decides to assign a value of either 1 or 0 (positive for benefit, and negative value for cost) as monetary values are difficult to assign to each of these questions and it is easier to state whether a question plays a role in the decision making process or not. Hence a value of 1 would imply that the question plays a role, and a value of 0 would mean it does not.

Decision tree:



Using this scoring scheme, it can be determined that the cost-benefit score for transplants is 1, while the score for the IBOT wheelchair is 0. According to this scheme, this would imply that in the case of transplants the benefits outweigh the costs and hence they are covered by insurance, while in the case of IBOT wheelchair the benefits do not outweigh the costs and hence it is not covered by the insurance. Also, using the same scheme the cost-benefit score for tolerogenic cell therapy is 1.

This ethical analysis bring to the forefront a concept of what is acceptable in our society, which is also a reflection of our culture – *there is no price associated with saving a life, or put in other words 'a life must be saved at all costs'*. If this statement is applied universally, then it would be justified to go ahead with research on the development of tolerogenic cells, to save lives at any cost (applying the concept of **universalizability**).

Mike also took the opinions of two experts in the field of transplantation and cell therapy (Dr. Angus W. Thomson, *Distinguished Professor of Surgery, Professor of Immunology, Professor of Microbiology & Molecular Genetics, Professor of Clinical & Translational Research, University of Pittsburgh School of Medicine, Thomas E. Starzl Transplantation Institute,* and Dr. Theresa L. Whiteside, *Professor of Pathology, Immunology and Otolaryngology*, *Director, Immunologic Monitoring and Cellular Products Lab. Hillman Cancer Center, University of Pittsburgh*) to help him resolve his dilemma. He believes that their **professional knowledge** will provide a better insight into his dilemma. A key fact that was brought forth based on his meeting with both of these faculty members was that contrary to popular belief, '*cell therapy is not much more expensive in comparison to traditional therapies*'. The costs of cell therapy are about the same as or at times even lower than the cost of conventional treatments. For example the cost of traditional cancer therapy (chemotherapy and radiation) can amount to a total of over $10,000-15,000 per course of treatment (about the same cost of a dendritic cell based therapy, as pointed out in the background section). Similarly, the annual cost of immunosuppressive drugs prescribed to transplant recipients is around $10,000. When added over a lifetime this cost usually is around the order of $100,000. This cost will be equal to or greater than the tolerogenic cell therapy that Mike is developing.

Further, Dr. Angus Thomson pointed out that the primary role of a scientist (be it a bioengineer, a biologist, a chemist etc.) is to increase the knowledge base and create novel technology – **role morality** *("obligations associated with profession" – Dr. Rosa Lynn Pinkus glossary of concepts in ethics*). If possible, it is important to keep the possible application, affordability and distribution of the novel technology in mind too.

Based on this knowledge and the ethical analysis that he performed earlier, it was clear to Mike that research involving generation of tolerogenic cells should be continued. Additionally, if he has the time and resources he should definitely attempt to reduce the cost of the technology he is developing.

Dr. Pearlman's comments "I agree there is a stark difference between how life-saving vs. non-life saving treatments are funded. An additional facet to investigate is why the c-leg, which costs nearly as much as an ibot, would be funded w/o much trouble. I expect also that the DARPA arm will see far fewer barriers to CMS funding than the IBOT. We attribute these differences to social norms related to trying to restore function, or 'fix' or 'cure' the problem. With wheelchairs, like the IBOT, many (including, we believe, policy makers) cannot see it as a 'cure' so it becomes less important (less funding). Instead of trying to optimize quality of life for individuals with spinal cord injury by funding these devices, a policy maker may think it is more important to fund research to find a cure for spinal cord injury..."

Acknowledgement

We would like to thank Dr. Angus W. Thomson and Dr. Theresa L. Whiteside for graciously agreeing to meet with us and patiently answer our questions.

We would also like to thank Dr. Rory A Cooper Director and Dr. Jonathan Pearlman Associate Director of the Human Engineering Research Labs, VA Pittsburgh, for taking time despite their busy schedule to respond to our queries on the IBOT case via email.

References

1. RCN65- CMS revision - Pub 100-03 Medicare National Coverage Determinations, 2006
2. Visual perception in a blind subject with a chronic microelectronic retinal prosthesis, Vision Research, Volume 43, Issue 24, Pages 2573-2581, Mark S. Humayun, James D. Weiland, Gildo Y. Fujii, Robert Greenberg, Richard Williamson, Jim Little, Brian Mech, Valerie Cimmarusti, Gretchen Van Boemel, Gislin Dagnelie, Eugene de Juan Jr., November 2003
3. An introduction to rehabilitation engineering, Edited by Rory A Cooper, Hisaichi Ohnabe and Douglas A Hobson, Taylor & Francis, 2007
4. Articles from Volume 38 Number 6 issue, Pages 601-655, Journal of Rehabilitation Researd & Development, 2001
5. Shattered Nerves - How science is solving modern medicines most perplexing problem, Victor D Chase, The Johns Hopkins University Press 2006.
6. Videos from http://www.youtube.com
7. Long-term user perceptions of an implanted neuroprosthesis for exercise, standing, and transfers after spinal cord injury, Sanjeev Agarwal, MD; Ronald J. Triolo, PhD; Rudi Kobetic, MS; Michael Miller, MS; Carol Bieri, MS, PT; Sahana Kukke, MS; Lori Rohde, MS, PT; John A. Davis, Jr., MD, Journal of Rehabilitation Research and DevelopmentVol. 40, No. 3, Pages 241–252, May/June 2003

8. Neuroprosthesis consumers' forum: Consumer priorities for research directions, Kevin L. Kilgore, PhD; Marcia Scherer, PhD, MPH; Rod Bobblitt; Jocelyn Dettloff; David M. Dombrowski;Nicholas Godbold; James W. Jatich; Robert Morris; Jennifer S. Penko; Eric S. Schremp; Lisa A. Cash, Journal of Rehabilitation Research and Development Vol. 38 No. 6, Pages 655–660, November/December 2001

9. Epidemiologic Overview of Individuals with Upper-Limb Loss and Their Reported Research Priorities, Atkins, Diane J.; Heard, Denise C Y; Donovan, William H., JPO Journal of Prosthetics & Orthotics. 8(1):2-11, Winter 1996

10. Survey of Upper-Extremity Prosthesis Users in Swedenand the United Kingdom, Peter J. Kyberd, PhD, Constanze Wartenberg, PhD, Leif Sandsjo¨ , PhD, Stewe Jo¨ nsson, CPO, David Gow, BSc, Joakim Frid, MSc, Christian Almstro¨m, PhD, Lena Sperling, PhD, JPO Journal of Prosthetics & Orthotics. Volume 19 • Number 2 • 2007

11. The choice of control system for the multimovement prosthesis: extended physiological proprioception, DC Simpson… - The control of upper-extremity prostheses and orthoses, 1973

12. Innovation and Change in Medical Technology: Interactions Between Physicians and Engineers Henry R. Piehler aMaterials Science and Engineering, Biomedical Engineering, and Engineering & Public Policy Carnegie Mellon University, Pittsburgh, PA

13. Unmet Need for Therapy Services, Assistive Devices, and Related Services: Data From the National Survey of Children With Special Health Care Needs, Stacey C. Dusing, PT, MS; Asheley Cockrell Skinner, BA; Michelle L. Mayer, PhD, MPH, RN, Ambulatory Pediatric Association, Volume 4, Number 5, September–October 2004.

14. Merriam-Webster Online. http://www.merriam-webster.com/dictionary/transplant. [cited 3-30-2009].

15. The Free Dictionary. http://www.thefreedictionary.com/transplant. [cited 3-30-2009].

16. C.A. Janeway, P. Travers, M. Walport, M.J. Shlomchik. Immunobiology. 6th ed. New York and London: Garland Science (Taylor and Francis group), 2005.

17. Organ Transplantation - How much of the promise has been realized? R.I. Lechler, M. Sykes, A.W. Thomson, L.A. Turka. Nature Medicine 2005;11(6):605-613.

18. Cardiovascular Risk Estimates and Risk Factors in Renal Transplant Recipients. B.K. Krämer, C. Böger, B. Krüger, J. Marienhagen, M. Pietrzyk, A. Obed, et al. Transplantation Proceedings 2005; 37:1868-1870.

19. The therapeutic prescription for the organ transplant recipient: the linkage of imunosuppression and antimicrobial strategies. R.H. Rubin, T. Ikonen, J.F. Gummert, Morris RE. Transplant Infectious Diseases 1999; 1:29-39.

20. Tolerogenic dendritic cells and the quest for transplant tolerance. A.E. Morelli, A.W. Thomson. Nat Rev Immunol 2007; 7(8):610-621.

21. What does the future hold for cell-based tolerogenic therapy? J.A. Bluestone, A.W. Thomson, E.M. Shevach, H.L. Weiner. Nat Rev Immunol 2007;7(8):650-654.

22. Tolerogenic Dendritic Cells. R.M. Steinman, D. Hawiger, M.C. Nussenzweig.Annu Rev Immunol 2003; 21:685-711.

23. Development of a Tissue Engineered Heart Valve for Pediatrics: A Case Study in Bioengineering Ethics. W.D. Merryman. Soc Eng Ethics 2008; 14:93-101.

24. Utilitarianism. John Stuart Mill. 1863 [cited 4/12/2009]; Available from: http://www.utilitarianism.com/mill2.htm

25. Methods for Moral Problem Solving. Engineering Ethics: Concepts and Cases. C.E. Harris Jr., M.S. Pritchard, M.J. Rabins. 2nd ed: Wadsworth, 2000.

26. http://www.christopherreeve.org/ [cited 4-12-2009]

27. COMMITTEE ON LEGISLATIVERESEARCH OVERSIGHT DIVISION FISCAL NOTE ... January 13, 2005.

28. INTELLECTUAL PROPERTY RIGHTS IN GENETICS AND GENOMICS http://grants.nih.gov/grants/guide/rfa-files/RFA-HG-04-004.html