

Innovation and Translation Efforts in Wireless Medical Connectivity, Telemedicine and eMedicine: A Story from the RFID Center of Excellence at the University of Pittsburgh

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Abstract

Translational research has recently been rediscovered as one of the basic tenants of engineering. Although many people have numerous ideas of how to accomplish this successfully, the fundamental method is to provide an innovative and creative environment. The University of Pittsburgh has been accomplishing this goal through a variety of methodologies. The contents of this paper are exemplary of what can be achieved through the interaction of students, staff, faculty and, in one example, high school teachers. While the projects completed within the groups involved in this paper have spanned other areas, the focus of this paper is on the biomedical devices, that is, towards improving and maintaining health in a variety of areas. The spirit of the translational research is discovery, invention, intellectual property protection, and the creation of value through the spinning off of companies while providing better health care and creating jobs. All but one of these projects involve wireless radio frequency energy for delivery. The remaining device can be wirelessly connected for data collection.

Keywords: Translation research, University of Pittsburgh, roborat, wireless deep brain stimulation, vagus nerve stimulation, electroporation device, wireless Doppler, programmable pulse oximetry, implantable RFID tags, implantable blood flow monitor.

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1 Introduction

The dividing line between basic research and research that can be easily translated into value has always been difficult and somewhat controversial. We assume engineering schools are traditionally more on the translational side but not completely as have been the discussions (mostly friendly) involving Engineering and Engineering Science. More recently, the interpretation of value has extended the translational domain due to the medical value of many engineering developments.

The innovation and translation efforts are embedded in the core of our research culture at the Swanson School of Engineering and the School of Medicine at the University of Pittsburgh. In FY2012, there were 310 invention disclosures to the Office of Technology Management (OTM) for commercial consideration, which represents a 21 % increase from previous year and a 319 % increase over invention disclosure submissions in 2003. In 2003, the University of Pittsburgh researchers submitted only 74 invention disclosures, which sparked a strategic shift at OTM aimed at attracting more innovators and actively engaging them in the innovation commercialization process at the University of Pittsburgh. Overall, there were 1,290 invention disclosures over the past five years. The University's patent portfolio continued to grow substantially in FY2012. The U.S. Patent and Trademark Office awarded the University of Pittsburgh and its innovators 49 new U.S. patents in FY2012, representing a 32.4 % increase from FY2011.

OTM's ultimate goal is to move as many innovations as possible into the commercial marketplace, which led to the execution of 132 technology licenses or options to commercial partners in FY2012. This represents a 26 % increase from FY2011. Total revenue for FY2012 rose to nearly \$6.8 million, up more than 10.2 percent from FY 2011. Total revenue includes licensing revenue, equity sales, and legal fee reimbursement from licensees. Due to higher number of "platform" innovations developed at the University of Pittsburgh accompanied by more concentrated effort by OTM and the Office of Economic Development (OED) to promote and facilitate start-up activities, the university had nine start-ups this past year. Success was driven, in part, by a combination that included OTM licensing managers and executives in residence, OEDs development and implementation of the new Pitt Ventures initiative and start-up process, and a growing number of innovations with more than one potentially profitable commercial application. Last, but not least, the University of Pittsburgh is also a home to one of the six national Coulter Translational Research Partners II Programs, which is accompanied by a \$3.54 million five-year grant from the Wallace H. Coulter Foundation.

This thriving innovation environment is well suited for the RFID (Radio Frequency Identifica-

tion) Center of Excellence at the University of Pittsburgh, which was formed in 2005. The mission at the center is to be a unique workforce, rooted in a research and learning environment that is strongly connected with industry. The RFID Center of Excellence and the earlier Swanson Center for Product Innovation have spawned numerous spin off companies and licensed technologies where the focus has shifted to biomedical applications. The spirit of the research environment has always been in concert with both Wallace H. Coulter and Jerome H. Lemelson thus focusing on research and technology that translates to generating value and jobs with the more recent emphasis on biomedical applications.

This paper illustrates the range of products and technologies that have been translated into seven companies and numerous patents that have been licensed to these and other companies to create value through innovation in American industry.

The projects of the Center have won dozens of awards for both faculty and students over the years with more than 25 named student inventors on US Patents. The student experience is one of the most important issues for an educational research center. The projects covered in this paper have made it possible for students to interact directly with clinicians in both engineering and medical environments. These experiences have covered both translating medical problems into technical solutions and taking part in numerous clinical trials involving animals (mice, Sprague Dawley rats and swine) and cadavers. Needless to state, all projects described in this manuscript had the necessary approvals from either the Institutional Review Board or the Institutional Animal Care and Use Committee, if needed.

2 Our innovation efforts

2.1 Robo-Rat

Bell's palsy (damage or injury of the seventh cranial nerve) can cause facial paralysis on one side of the face [1]. Such facial paralysis can cause visible defects such as sagging of the cheek and mouth, loss of blink, which raises severe health concerns [2]. For example, the inability to blink means that the eye will not be properly lubricated or protected from debris [1]. Besides the Bell's palsy, other causes of facial nerve damage include tumor, trauma, infection, and generalized polyneuritis [1]. Most of the treatments for facial nerve paralysis only provide temporary protection to the corneal surface without restoring defects such as the loss of blink (e.g., [3], [4], [5]). Specifically, previous contributions showed that electrotherapy is beneficial for restoring facial control and lessens

synkinesis [6], [7].

The University of Pittsburgh originally began this work under the project title Blink Right. In conjunction with the RFID Center, the ophthalmology department at the University of Pittsburgh targeted ameliorating those suffering with the condition by stimulating the muscles associated with blinking the eye on the affected side. This was accomplished by detecting a patient's blink on the unaffected side and then stimulating the muscles required to perform the blinking function on the side affected with the Bell's palsy. To demonstrate the capability to stimulate muscles simultaneously and remotely, the Sprague Dawley rats were chosen. The mechanical movement of one rat's leg produced a simultaneous and remote stimulation in the same leg on the remote rat.

One rat's functional leg was outfitted with a probe, which feeds into a processing chain of analog and digital electronics that detect the probed nerve's electrical activity generated by mechanically stimulating the functional leg. The post-processed nerve signal is transmitted via wireless radio transmitter. On a second rat with a de-nervated leg, the transmitted wireless signal is detected by a wireless radio receiver which feeds into a processing chain of analog and digital electronics which generate the stimulation signal. The stimulation signal is applied to the de-nervated rat's leg to generate a contraction [1]. Thus, move one rat leg and the leg of the second rat moves with only a wireless radio frequency connection between the two - hence the name Robo-Rat. A few of the animal trials photos are shown in Figure 1.

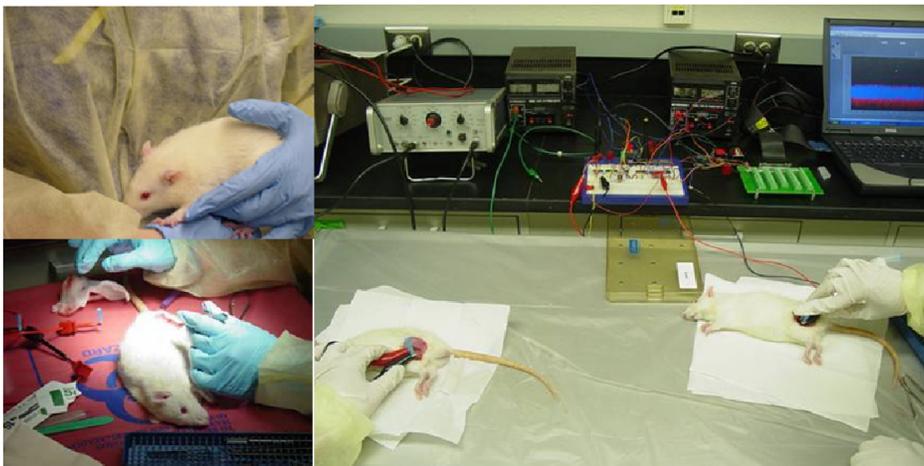


Figure 1: Roborat in action

Several *in vivo* experiments were conducted involving the gastrocnemius leg muscles of our rats. These experiments established (1) the magnitude of the stimulation signals required to generate contraction in the de-nervated gastrocnemius leg muscle, (2) the magnitude of the electrical output

from functional gastrocnemius that could be sensed resulting from mechanical stimulation, and (3) real-time remote stimulation of a de-nervated rat's gastrocnemius leg muscle actuated by the mechanical stimulation of a separate rat's functional gastrocnemius leg muscle.

These experiments have shown that we can utilize radio-frequency sensors to initiate functional electrical stimulation of a denervated muscle from a normally functioning muscle. Our results showed that to produce a sufficient contraction, higher stimulation voltages were required with longer pulse widths, which can be attributed to fatigue of the individual muscle fibers. The experimental results showed that 1V-2V stimulation voltages for 10 milliseconds were sufficient to produce sufficient contraction without histopathologic damage to the tissue. The location of the probe also played a role in the detection of voltage levels. Additional promising applications of this system exist, not just in otolaryngology and neurology but also in rehabilitation.

Graduate students in the Department of Electrical and Computer Engineering at the University of Pittsburgh developed this technology. The Blink Right technology was licensed to a San Francisco-based company, the same company that purchased licensing for Wireless Deep Brain Stimulator from the university (described in the next section). This technology was one of the many technologies that stemmed from the RFID Center's generation of intellectual property in the realms of wireless energy harvesting, low power devices, and wireless communication through tissue.

2.2 Wireless Deep Brain Stimulation

Parkinsons disease is a neurodegenerative disorder, and its symptoms include stiffness, slowness of movement, and resting tremor [8], [9]. Other common symptoms include depression and dementia [10], [9]. Various treatments exist for Parkinsons disease, including numerous drugs (e.g., [11]) and deep brain stimulation (DBS) (e.g., [12]). DBS usually involves surgery to implant a probe into the brain and its corresponding controller into the body (e.g., [13], [14]). DBS is mainly used for Parkinsons disease, but it can also be used to treat other diseases, such as Huntingtons disease (e.g., [15]), dystonia (e.g., [16]), and epilepsy (e.g., [17]). Both biological tests and computer simulations support the idea that stimulation regulates neurons, improving data propagation over the irregular neuronal activity present before DBS.

However, DBS devices can be cumbersome. First, they require a large implanted battery, which have a limited life. Second, a control pack needs to be implanted in the chest. Such a pack would then have subcutaneous wires threaded up through the neck to the top of the skull. These implanted

devices and wires can cause irritation and infection leading to removal of the device in some cases. All of these drawbacks lead to device replacement surgeries every three to five years.

These drawbacks led the RFID Center of Excellence to design and test a small remotely powered device capable of driving a DBS probe from directly under the scalp as shown in Figure 2. The device is remotely powered via inductive coupling, consuming just over 10 joules per day. A 1.2-in. square printed circuit board with maximum thickness of 0.25 inches is used to fit the implantable circuitry. Our results showed that we can power and program the device through air, porcine skin and a cadaver scalp. Additionally, the power transmitting coil can be driven via a small, cheap and easily replaceable external battery pack. A model has been made to demonstrate a feasible realization of the entire device which is both functional and aesthetically pleasing.

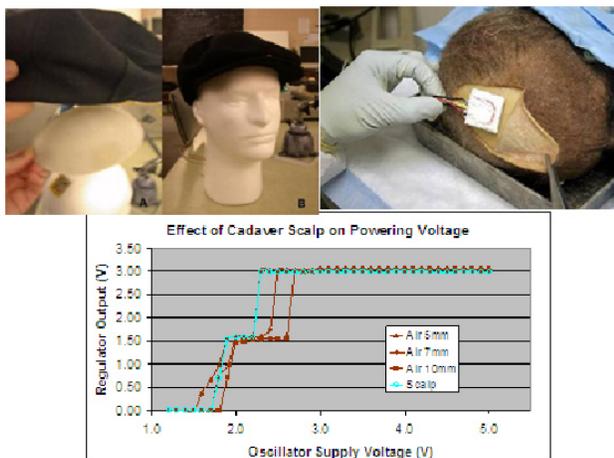


Figure 2: Wireless deep brain stimulation.

The wireless DBS began when a San Francisco-based company worked with the RFID Center of Excellence to develop a new technology which targeted reducing the infection rates associated with the use of wired DBS devices. The wireless DBS could run on power supplied by batteries and supercapacitors for several days before needing to be recharged, and the recharging unit was affixed at the end of the patient's bed to provide an easy mode of recharging while the patient slept. The RFID Center developed the wireless DBS and the University of Pittsburgh licensed the technology to the San Francisco-based company. After the company ran into financial hardship, the license for the wireless DBS reverted back to the University.

Later on, the same company worked with the RFID Center to expand the wireless DBS technology to source it's power from local wireless radio stations. These technologies have since garnered interest from several companies. Both graduate and undergraduate students of the department of Electrical and Computer Engineering at the University of Pittsburgh were responsible for developing these technologies, with many of the milestones in the development of the projects coming from undergraduate senior design projects.

2.3 Vagus Nerve Stimulation

The deep brain stimulation concept was modified to provide stimulation to the vagus nerve which is used to offset a seizure for patients with epilepsy. Shown in the figure below is the wired version of the stimulator. In the wireless version, the stimulator is implanted in the neck with electronics while the recharging (powering) circuitry is located in the patient's collar. Such a device would require a large battery and a control pack to be implanted in the patient's body. Subcutaneous wires would be running through. All these pieces represent a source of irritation and infection, and as such could potentially require the patient to take antibiotics or to have the device removed. Needless to say, the device is affected by magnetic interferences and a limited battery life, which can require another surgery to replace the device. Therefore, it is desired to stimulate vagus nerve but without the aforementioned shortcomings.

Sponsored by the National Science Foundation, a team of researchers from the University of Pittsburgh partnered with a number of high school teachers to develop an implantable device that would address the issues outlined above. The implanted device provides a method of electrically stimulating the vagus nerve of a patient through the generation of current pulses through one or more probes implanted in the body of the patient. The implantable device also includes control circuitry electrically connected to the probe(s) that is structured to generate the current pulses. The power circuitry of the implant was designed to eliminate the need for a battery and consequently the issues that go along with battery usage. The implant can receive energy from a far-field source (e.g., a local radio station). The received energy is converted into a DC power signal by the power circuitry that also provides this DC power to the control circuitry. Thus, by creating a passively powered and implantable device, issues such as transcutaneous wires as well as limited lifetime battery supplies are eliminated. The unique expertise of the RFID Center of Excellence in the area of wireless communications and energy harvesting made it a clear choice of partnership for the high school teachers who designed this device over a summer program.



Figure 3: Vagus nerve stimulation.

2.4 Mass Immunization Device

Naked plasmid DNA (pDNA) is the simplest and safest gene delivery system and is primarily used for genetic immunization studies [18]. Gene delivery *in vivo* using electroporation is an alternative approach [19], where naked DNA injection is combined with a pulsed electric-field treatment. In electroporation, it is assumed that cell membranes are equivalent to an electrical capacitor [20], and the lipidic membrane acts as a dielectric element. By applying an electric field to cells, we introduce structural defects in the cell structure permitting the transit diffusion of nucleic acids [21], [20]. The membrane permeability increases due to the electric pulses, which represents the first step in the electro-gene transfer. Next, molecules are diffused through the membrane [21]. The advantage of electroporation is that its transfection efficiency is significantly greater than that of naked DNA injection and has reduced inter-individual variability [22]. Electroporation based *in vivo* gene transfer has been used for introducing DNA into rat hepatocellular carcinomas, mouse testes, hepatocytes, skeletal muscle, melanoma, lung, skin, and rat skeletal muscle for correcting anemia of renal failure (e.g., [18], [23], [24]).



Figure 4: A device for electroporation.

The genesis of this technology began when the pharmacology department at the University of Pittsburgh received a contract to develop treatments to contain or manage epidemics caused by infectious agents. The project started with the pharmacology department studying methods of electro-gene transfer for genetic immunization and gene therapy. The Department of Electrical and Computer Engineering at the University of Pittsburgh was responsible for developing the associated hardware and electronics necessary to deliver the immunizations in a safe and repeatable manner in an epidemic scenario.

The Swanson Center for Product Innovation, and later on the RFID Center of Excellence,

has designed a device that by alternating the polarity of the applied electric field elucidates the mechanism of *in vivo* electro-gene transfer as shown in Figure 4. In other words, DNA is forced into the cells at the anode during the first pulse. DNA is forced back to the cathode when the polarity is reversed during the second pulse. This process is continuously repeated. Our results, described in [18], enabled us to have better understanding of electro-gene transfer, that can allow us to propose more efficient conditions for *in vivo* electroporation.

2.5 “Smart” Pill Dispenser

Medication adherence is essential to the effective treatment of serious and chronic illnesses. In today’s settings, the patient is primarily responsible for following his or her medication regime (e.g., [25], [26]). Treatments for chronic diseases especially rely on effective adherence, and missing a scheduled dose can negatively impact the treatment plan. During clinical drug trials, for example, researchers are attempting to understand the effectiveness and side effects of potential treatments. These drug trials must be controlled and consistent in order to accurately represent the positive and negative effects of the proposed drug, and to provide an adequate understanding of the drug effects before the drug is released to the general public. Given that medication doses can be missed or accidentally taken multiple times, healthcare providers and researchers desire a reliable method of verifying that prescribed treatment plans are being followed by patients and/or study participants (e.g., [27], [28]). While self-reporting is the most common and sometimes the only feasible method, its accuracy depends on the patient’s memory and reliability. Medication adherence becomes especially problematic with age (e.g., [29]).

Therefore, there is a need for technologies that aid patients in remembering doses and recording adherence for medical records. These technologies are important not only for extending and improving the lives of patients, but also for enabling improvement of treatment plans based on accurate logs of medication use. By improving adherence, medical resources can be more efficiently allocated by eliminating the wasted resources resulting from inconsistent treatment plans [26]. The RFID Center of Excellence has been increasingly involved in such medical and biomedical solutions. The proximity of the university to medical centers enables the identification of relevant problems, such as medication adherence, and development of applicable solutions. As such, design work in our center often involves consideration of human factors in addition to basic functionality.

To address the issues surrounding medication adherence, a “smart” pill box was developed in the RFID Center of Excellence. The pill box keeps a time record of when a patient removes each

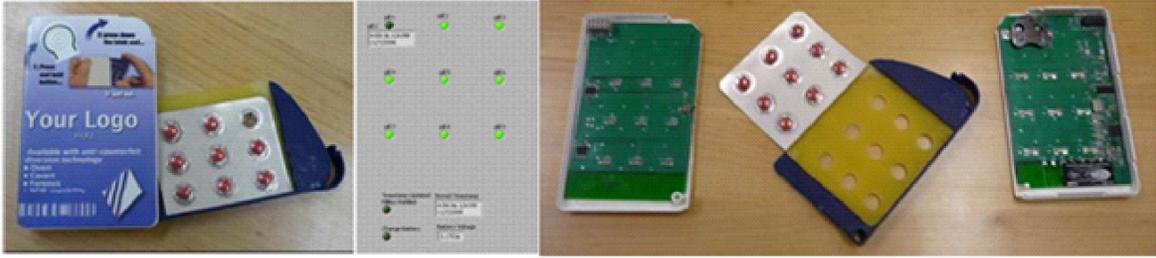


Figure 5: A “smart” pill box.

pill from the box as well as which pills are removed. The device then wirelessly communicates the recorded data when the box is in range of an associated receiving station (server). The device was designed around a typical blister pack, as shown in Figure 5, and was successfully integrated with a commercial off the shelf pill dispensing box manufactured by West Pharmaceutical. The device functions with common blister pack pill packages to increase the likelihood of adoption due to ease of handling by the pharmacy and ease of use by the patients. The pill detection method was implemented in a compact form factor that can easily be expanded and configured to other blister pack dimensions.

A graphic user interface (GUI) was also developed in the RFID Center of Excellence, to display information received from the pill box. The image in Figure 5 with the green indicator lights is a screenshot from the GUI at the receiving station, visually indicating the contents of the associated pill box. The box reports pill removal automatically via wireless communication, eliminating any additional action by the user to properly operate the device. The user simply removes the pills as they would with a traditional blister pack medication package, and the device records the action, providing a simple and effective medication adherence tracking solution.

2.6 Avoiding Pulse Inhibition in Pacemakers and Implanted Cardiac Defibrillators

Radio Frequency Identification (RFID) is a rapidly growing technology finding applications in a multitude of fields including in healthcare settings [30], [31], [32], [33], [34]. It has been suggested that RFID technology holds the promise to contribute very significant improvements to the future of the healthcare industry [35], [36]. Personnel and patient tracking systems, drug counterfeiting protections, and asset tracking systems have all been proposed in order to improve quality of care and patient safety as well as to provide significant time and cost savings. As RFID technologies

are becoming more commonplace in the healthcare environment, however, it becomes necessary to address possible complications these systems may cause. Most significantly, the radio frequency (RF) signals emitted by these systems have the possibility to cause electromagnetic interference (EMI) in critical care equipment. For instance, it has been reported that RFID systems have the capacity to interfere with the normal operation of pacemakers

A Pittsburgh based medical device company was recently interested in the incorporation of passive RFID technology into surgical equipment such as surgical sponges in order to solve the problem of accidentally leaving this equipment in a surgical patient post-operatively. As a consequence, the company sponsored a study conducted at the RFID Center of Excellence that was aimed at assessing the extent and causes of interference between RFID systems and cardiac rhythm management devices (CRMDs) including pacemakers and cardioverter defibrillators in order to ensure patient safety [37]. A relatively large team of graduate student and post-doctoral researchers were involved in this study that targeted three of the most commonly utilized RFID frequency bands, 143.75 kHz (LF), 13.56 MHz (HF) and 915 MHz (UHF). Additionally, multiple tissue simulation systems, shown in Figure 6, were fabricated and tested in order to model the effects of the human body on implantable CRMDs when exposed to RF energy.

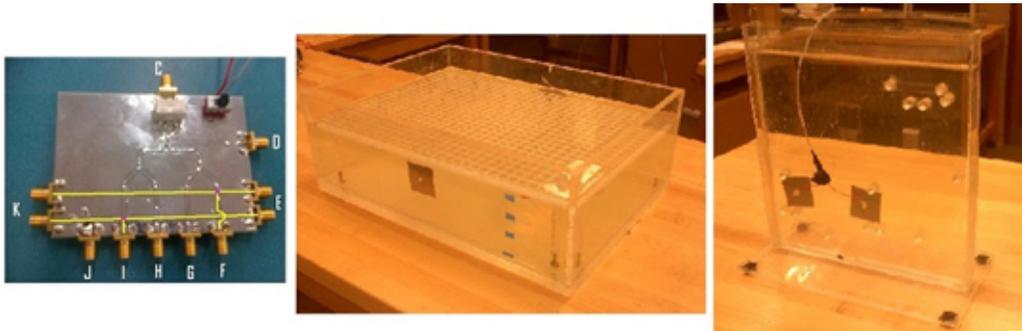


Figure 6: Tissue simulation devices: from left to right - tissue interface circuit, horizontal saline tank phantom, vertical saline tank phantom.

This large scale study [38], based on over 7400 laboratory tests, confirmed the capacity of RFID systems to cause clinically significant interference on implantable CRMD systems mainly in the lower frequency bands (LF, and HF) while UHF bands were shown to be relatively harmless to these critical care devices. More importantly, however, this study identified the mechanism of the most common form of CRMD interference, pacing inhibition, and proposes a possible solution. Pacing inhibition is a scenario in which the CRMD system should pace the heart but fails to do

so due to the presence of EMI that is mistaken for a normal sinus rhythm. In previous studies it was assumed that pacing inhibition due to EMI is a function of RF power output only. While RF power level is undoubtedly a significant factor, this study concluded that the rate of change of this power was also significant. Many experimental observations were recorded where the cause of pacing inhibition was the rapid on/off transition of the RF carrier wave (CW) as shown in Figure 7. Through the utilization of the comprehensive testing framework developed at the RFID Center

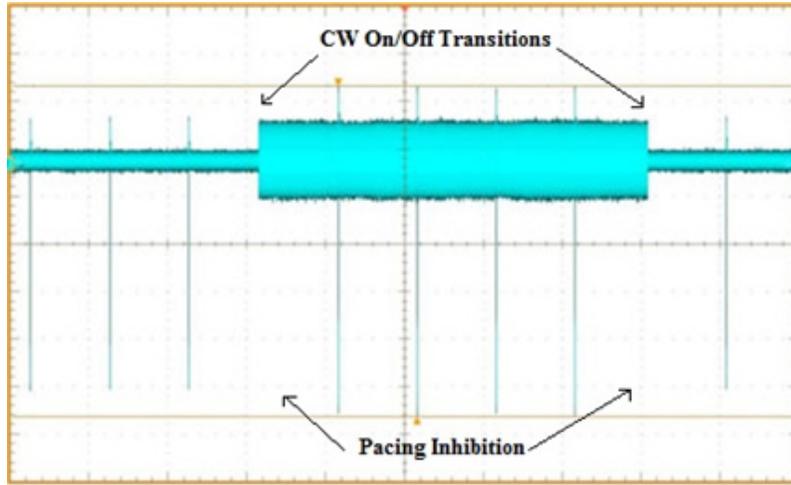


Figure 7: Pacing Inhibition Due to Rapid On/Off CW Transitions.

in conjunction with state-of-the-art RF design equipment, a simple mitigation method has been proposed, mathematically analyzed and verified experimentally. In this mitigation technique rather than the abrupt on/off transition shown above, the CW power is more slowly ramped up and down at the on/off transitions as shown in Figure 8. In initial testing this method has been shown to reduce the incidence of clinically significant interference by 79.24%.

Through the dedicated efforts of the research team at the University of Pittsburgh RFID Center, utilizing cutting edge facilities and equipment, a comprehensive testing framework has been developed that may be utilized in future electromagnetic compatibility testing between arbitrary wireless devices and CRMDs. This will become invaluable in order to ensure patient safety as RF energy is utilized in an ever increasing number of everyday scenarios. Additionally, the University of Pittsburgh holds an issued patent on the mitigation method discussed previously, on which a number of graduate students and post-doctoral fellows have been named inventors. The university is currently engaged in efforts to license this technology to relevant device manufacturers.

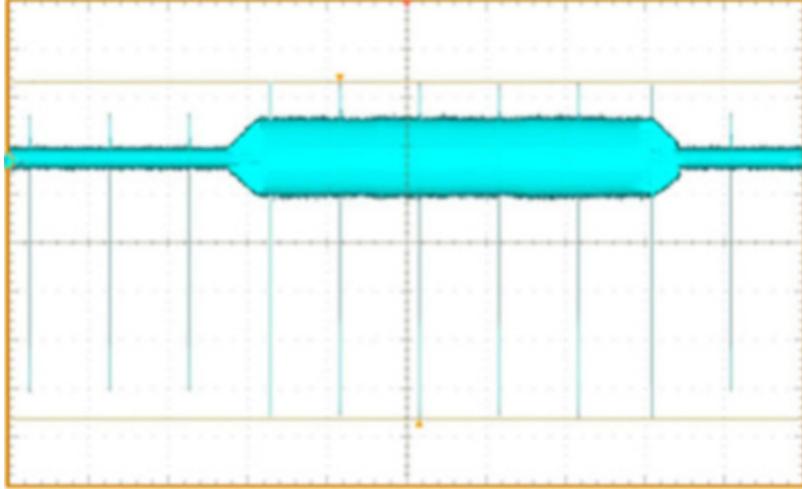


Figure 8: Ramped Amplitude Modulation Technique Shown to Reduce Pacing Inhibition.

2.7 Wearable Pulse Oximeters

Pulse oximetry provides a non-invasive method of quickly and efficiently measuring the saturation of peripheral oxygen (SpO₂) levels in the blood and heart rate of a patient. With this continuous monitoring, physicians are able to provide more efficient care to their patients [39], [40]. Pulse oximeters are widely used in households and hospitals where continuous monitoring of a patient is required [41]. The wide spread use of pulse oximetry is attributed to the low cost of the device and the ability to accurately and continuously monitor required vital signs from the patient [42].

Miniature low power electronics provide an opportunity for a wide spectrum of implantable medical devices resulting in new functionality to allow existing wired sensors and devices to be wireless and conveniently implantable. Many wired and battery powered devices can now be powered and communicate wirelessly providing improved healing and monitoring at internal sites. The pulse oximeter is an example of a wired or interconnected device that can be made implantable by powering the device by a battery and by reducing the size of the electronics to the absolute minimum. The implantable pulse oximeter demonstrates the RFID Center of Excellence's early-stage exploration into battery-powered implantable devices, where device austerity is paramount to prolong battery life and minimize patient discomfort due to implant size.

The RFID Center of Excellence has developed a wireless pulse oximetry system using commercial-off-the-shelf parts (COTS) that was designed for use in a body area network (BAN). A BAN consists of multiple sensors on the body that are wireless connected and continuously communicating with each other while periodically sending data to the physician. The system uses a pulse oximeter to

measure the SpO₂ and pulse rate of the patient while simultaneously providing a wireless up-link to the physician's office. The IR sensor electronics were evaluated and a decision was made to wirelessly transmit the complete LCD display, mainly to reduce the amount of re-engineering required, as the pulse oximeter was invented over 35 years ago [43].

The proof of concept, shown in Figure 9, consists of two pulse oximeters; the transmitting pulse oximeter is attached to the patient and actively monitors their SpO₂ levels with the receiving pulse oximeter mirroring the display. In this example, the pulse oximeters are interfaced to a Texas Instruments CC2510 RF system-on-chip (SOC) that is designed for low power wireless applications with an on-board 2.45 GHz RF transceiver. The transmitting CC2510 reads in serial display data and packets it into frames for transmission. The receiving CC2510 decodes the data and transmits the screen information to the receiving pulse oximeter. The proof of concept was developed as a body area network for use in telemedicine applications.

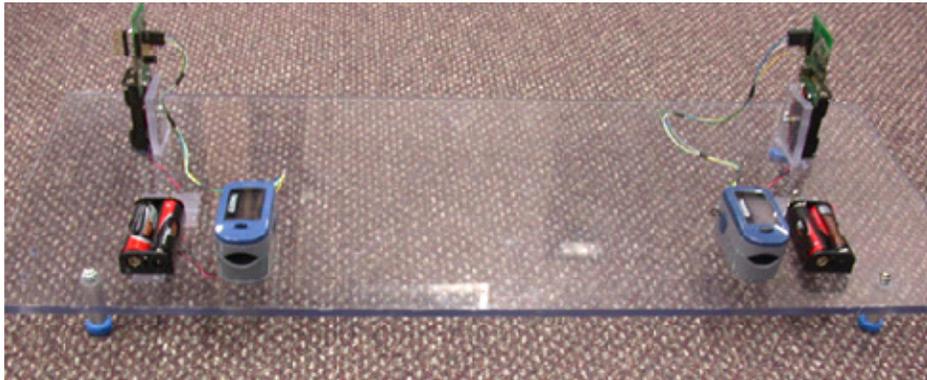


Figure 9: Body area network proof of concept demo.

Multiple telemedicine proof of concepts were developed to provide a wide range of access to user including 802.11b/g/n Wi-Fi networks, Cellular 3G networks and Bluetooth, as shown in Figure 10. This provides a means of linking the body area network to the physician. The receiving pulse oximeter and CC2510 were also replaced with a smartphone application that was capable of recreating the display of the pulse oximeter. The wide range of connectivity options provides a plug-and-play connectivity to the user, where no knowledge of the technology is required. The idea being that a patient would have the ability to walk into a coffee shop with Wi-Fi and have the body area network automatically update the physician on the current and past status of the patient.

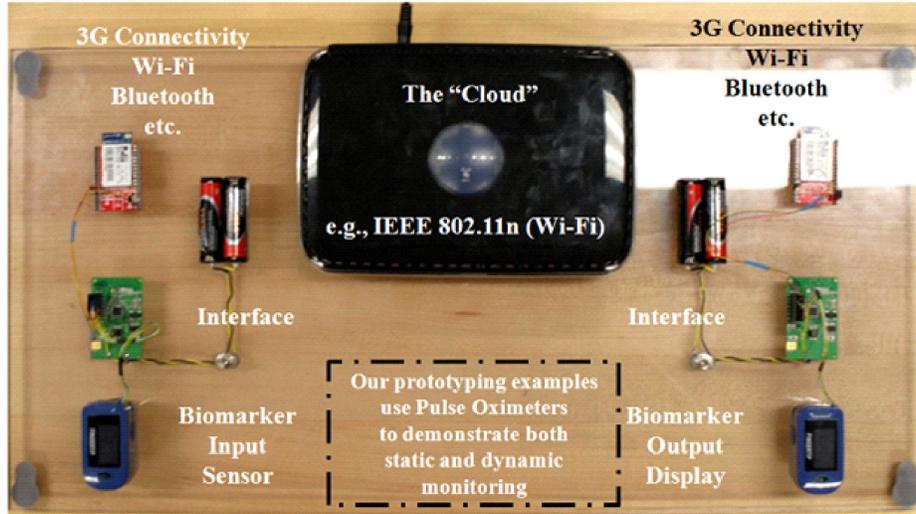


Figure 10: Telemedicine proof of concept demo.

2.8 “Talking” Knees and Hips

An increasing number of patients are undergoing total hip and knee replacement surgeries [44], [45], [46]. When joint replacement surgeries are performed, associated information must be kept on file, including the implant model, manufacturer, and the surgery location and personnel [47]. Retrieving this information for follow-up visits can be inconvenient and costly, and the information is important in the event that post-operative complications necessitate revision surgery [47], [48]. The initial motivation for this project was to allow identification of orthopedic implants and to simplify access to necessary information by wirelessly reading information directly from the implant itself.

The technology for a prototype device, deemed the Ortho-tag system, was developed in the RFID Center, and formed the basis for a spin-off company, Ortho-tag Inc., in 2010. The prototype Ortho-tag system consists of an RFID chip mounted on an implantable tag, and a patented touch probe as shown in Figure 11. The tag is designed to be attached directly to an orthopedic implant and implanted during joint replacement surgery. The touch probe reads information from the chip wirelessly through the skin. The information is then sent to a computer, where it can be linked to a patient database.

The Ortho-tag system is batteryless, utilizing transcutaneous near field communication (TNFC) to passively power and communicate with the tag via the touch probe. This eliminates the need to replace or recharge batteries, and allows the tag to remain implanted indefinitely (or for the lifetime of the orthopedic implant). TNFC is a proprietary communication method that utilizes



Figure 11: Implementable RFID chip on an artificial knee.

the electrical properties of the skin to transfer energy, developed through research efforts in the Center.

The first generation design consists of a unique serial number stored on the tag that can then be read and associated with patient information in a database. Research is currently underway to store additional information directly on the tag, including the implant model and manufacturer, or surgery location and personnel. The tag can only be read by using the patented touch probe, and the system functions only when the probe is in direct contact with the skin, adding a layer of security to any patient information stored on the tag.

Current research in the RFID Center of Excellence is focused on incorporating biosensing capabilities onto the Ortho-tag. In collaboration with the Department of Chemistry, we are exploring the detection of local tissue pH and temperature as early indicators of infection at an implant site. The RFID chip mounted on the tag reads changes in an attached biosensor and communicates these values along with the patient information stored on the chip. In this way, information about the implant site can be read from the tag wirelessly with the touch probe and logged in a patient database, assisting in comprehensive monitoring by a physician and potentially providing early warning of infection. Collaborative efforts, such as combining wireless implant identification and biosensing, are facilitated by the diverse research environment at the University, where developments like the Ortho-tag system benefit from multidisciplinary research contributions.

2.9 Doppler Flow Monitor

During free flap surgery, veins and arteries at the transfer site and of the free flap are connected to facilitate perfusion of blood through the transferred tissue [49]. If the vascular connections fail, the transferred tissue often dies and additional surgery will be required, with failure most likely to occur in the first 48 hours after surgery [49], [50]. There are approximately 19,000 free flap surgeries in United States each year [51]. Flap complication rates requiring reoperation can range from 3-14% [51], [52].

Current *in situ* blood flow monitoring systems in free flap surgery require a transcutaneous tether (i.e., wire) affixed to the vein or artery of a patient. The patient is tethered to a bulky bedside monitor. These protruding wires limit patient mobility, and they increase the risk of vessel trauma, false readings, and probe/tether dislodgement. A totally implantable blood flow monitor can completely solve or significantly ameliorate all of the problems associated with the gold standard for free flap monitoring.

A proof-of-concept wireless implantable blood flow monitor was developed at the University of Pittsburgh as shown in Figure 12. The devices successfully detected occlusion in the femoral arteries of swine, and the devices remained implanted for 3 days. The implanted devices' clinical metric is to detect the presence of blood flow; therefore, the accuracy demands are considerably relaxed compared to commercial units. Even though the total implanted volume is larger in the case of the wireless implant device than the tethered option (e.g., bedside monitor), clinicians deemed this larger wireless implant volume an acceptable tradeoff for the proof-of-concept device.

The implantable flow monitor exploits the Doppler shift experienced by a traveling wave as it passes from a transmitter transducer to a receiver transducer through a flowing blood stream within a vessel. The implant's design is a continuous-wave configuration, and the piezoelectric transducers operate at 5MHz with a single element for the transmitter and a single element for the receiver. Frequency translation to analog baseband is performed in a homodyne receiver configuration, which precludes the need for precise frequency calibration when the transmitter and receiver are clocked from the same time reference. The diameter of the electronics is currently about the size of a U.S. 50 Cent piece.

The blood velocity information is carried in analog baseband, which is wirelessly transmitted by a radio transmitter onboard the implant. The transmitter operates in the 915MHz ISM band, and the analog baseband directly modulates the carrier frequency. In this embodiment, the implantable device is contained entirely within the test animal's body; no wires protrude through the test

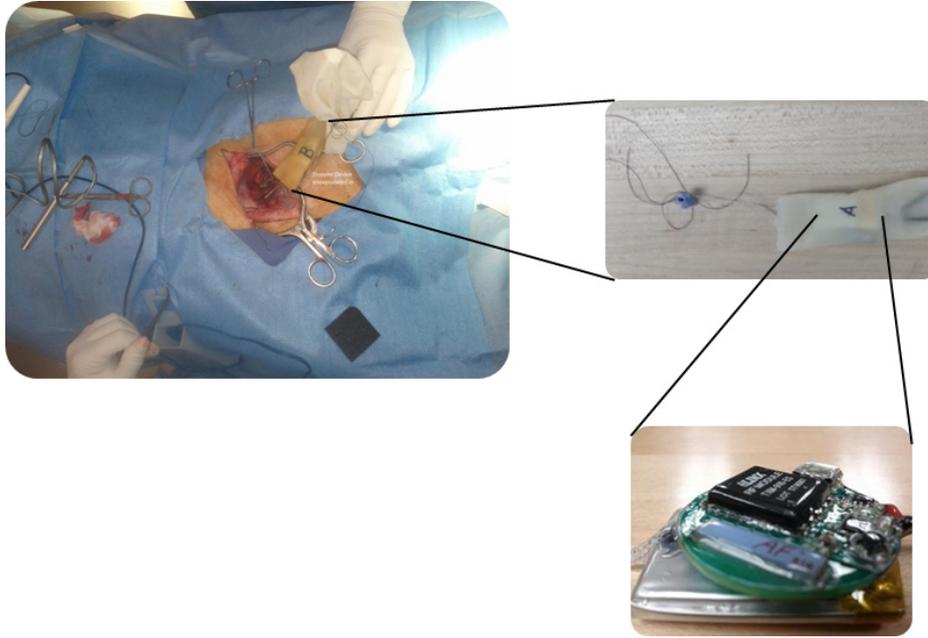


Figure 12: A prototype of a wireless Doppler device.

animal's skin. Transmitted blood velocity information is wirelessly received by a remote receiver located external to the test animal. The receiver converts the wireless information back to analog baseband. Afterwards, the receiver amplifies the baseband information sufficiently to drive a speaker for clinical blood flow assessment. Audible blood velocity information is a clinically familiar format.

The implantable wireless Doppler device represents another innovation that was possible only through The University of Pittsburgh's unique partnership with the University of Pittsburgh Medical Center (UPMC). Along the same line as the RFID Center's exploration into miniature pulse oximeters, the wireless Doppler device represents another example of enabling existing sensors to be conveniently implantable.

3 Our Translational Efforts

The origins of our translational efforts began with the desire to better acquaint students with real engineering problems while also giving them the opportunity to see their solutions be used by industry and, as a bonus, take part in the surrounding media coverage. The starting point was an Engineering course in the Swanson School of Engineering at the University of Pittsburgh where corporate sponsored projects became the student projects to be developed in terms of both technology and business. A center was created initially by Professor Michael Lovell with funding

Table 1: A summary of intellectual property covered in previous sections.

Technology	Patent Application Number or Patent Number
Robo-Rat	USPTO Application # 20070191908
Wireless Deep Brain Stimulation	USPTO Applications # 20070142872 and # 20060136007
Vagus Nerve Stimulation	USPTO Application # 20090105782
Mass Immunization Device	USPTO Application # 20100191174
“Smart” Pill Dispenser	US Patent # 8,091,790
Pulse Inhibition in Pacemakers	USPTO Application # 20120071115
“Talking” Knees and Hips	US Patents #6,847,844; # 7,228,183 and # 7,825,807
Doppler Flow Monitor	USPTO Application # 13,668,656

from John Swanson, National Collegiate Inventors and Innovators Alliance, the Heinz Endowments, and the Kresge and Keck Foundations. The new center was named the Swanson Center for Product Innovation (SCPI). SCPI was an initial success with numerous projects many of which involved radio frequency (RF) aspects. Professor Lovell became Associate Dean for Research and Professor Marlin H. Mickle became the Director of SCPI. From that point, an Institute was created and in 2005, and the RF projects were moved to a newly created center within the Institute named the RFID Center of Excellence with Professor Mickle as Executive Director. Both Professors Lovell and Mickle had interests in translating research into products while creating value. In addition, it was their desire to involve students in all levels of the translational process including press coverage, intellectual property and understanding how value is created through both innovation and research. In the case of the RFID Center, seven companies have been spun off where the major focus has been on integrating RF transmission with medical devices where the transmission medium is the human body as opposed to the traditional air medium.

Of the seven companies, five have products and technologies directly related to the research reported in this paper, one is related through the tracking of patients and the other is related by being able to directly print RF devices on nonstandard media such as poly inserts in orthopedic joints.

The translational research efforts have produced 37 patents and numerous options and licenses. Table 1 provides a summary of the intellectual property considered here. The intellectual property disclosures have more than 25 named student inventors. In addition to being inventors on the intellectual property disclosures, students’ contributions have been featured at various museums

such as the Smithsonian Institution, the Boston Museum of Science and the Reuben H. Fleet Science Center in San Diego. For example, the exhibition in San Diego was a part of the March Madness for the Mind sponsored by the National Collegiate Inventors and Innovators Alliance and the project presented was one of fourteen selected in the country for presentation. Furthermore, over the years, there have been dozens of projects which have supported the core technologies of these developments. These groups were typically composed of 2 to 4 students. In addition to the citations, at least four students supported the University at functions in Chicago, Harrisburg (PA), and Pittsburgh. These functions were for both alumni and legislators. Also, two students now serve as Chief Technology Officer and Chief Scientific Officer for spin off companies licensing technologies developed through the translational efforts. Last, but not least, there have been 103 joint publications with our trainees since the RFID Center of Excellence started with 107 students named on the papers. The students also attended about a dozen of conferences.

4 Epilogue

In this paper, we overviewed innovation and translation efforts at the RFID Center of Excellence at the University of Pittsburgh. In our experiences, the key ingredient for successful innovation and translation is to set up an environment where translational efforts such as patents and start-ups are encouraged as long as they are accompanied by traditional academic achievement such as research manuscripts and training of highly qualified personnel. The RFID Center of Excellence continues to be at the heart of innovation at Pitt, and an integral bridge between academics and our always-expanding base of industrial and medical collaborators.

The next big challenge that our Center is already considering deals with the idea of Internet of Things (IoT) and its effects on the health care system and patient care. We anticipate that IoT will dramatically enhance the patient care as patients will be continuously monitored. This ability to continuously monitor patients in real-life settings will enable physicians and researchers to understand how the patient surroundings affect his/her health. This is essentially critical in cases when a patient performs well during a clinical exam, but has a severe medical event in a real-life scenario outside a hospital (e.g., patients perform well during a clinical gait assessment, but fall around the corner of the hospital). Furthermore, IoT enables us to warn a patient that she/he has missed medication, or that her/his blood glucose levels are dangerously high. From the health care system point of view, IoT can significantly diminish the cost of the patient care, as continuous monitoring of patients will enable clinicians to preemptively react to deteriorating

patient's condition. Needless to say, to achieve this state of the art technology, there are a number of engineering challenges ahead of us involving device miniaturization, signal processing, database management, just to name a few.

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