impact neuromod

Strategic Review and Regulatory Assessment

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Executive Summary

Impact Neuromod is a start-up that has developed an innovative medical device for deep brain stimulation (DBS) to treat Parkinson's disease and other movement disorders. The device is wireless and miniaturized which is advantageous over existing invasive DBS treatments. The novel device utilizes heat to modulate neural activity. The DBS market for Parkinson's disease is expected to double by 2040, creating a significant opportunity for Impact Neuromod. The company is well connected with lab partnerships at the University of Wisconsin-Madison and is working to expand the leadership team to include industry experts.

The Impact Neuromod device utilizes radio frequency signals to wirelessly stimulate without an implanted battery. This minimizes the size of the implanted device which is advantageous over major competitors like Abbott, Boston Scientific, and Medtronic. The implanted devices are also receptive to changes in the brain, which can provide useful information to physicians. The devices are fabricated with biocompatible materials and on the submillimeter scale which decreases likelihood of infection. The small size also provides increased localization of stimulation. The intellectual property (IP) related to Impact Neuromod is in development, with one patent awarded related to the inductive coupling between the coils and the transducer. Further IP covering the device itself as well as the stimulation parameters is needed.

Existing funding is in the form of NIH and DOD grants totalling $2.55 million. This funding has gone towards creating the prototype and preclinical testing in animals. Impact is seeking $1.5 million in seed funding to acquire a leadership team and continue testing. Ultimately the reimbursement route will be analogous to that of existing DBS systems of Abbot and Metronic. Intracranial procedures done by medtronic average $31,146 for reimbursement.

A comprehensive hazard analysis was performed to identify and mitigate risk. Scientific, business case, and technical risks were evaluated and ranked in priority based on severity and likelihood. The largest business risk identified was the size of the competing companies and their market power. The mitigation strategy focuses on going dark and establishing more IP coverage, including the fabrication and surgical procedures. Scientific risks were identified in regards to safety, stimulation, and the surgical procedure to implant the device. Mitigation strategies include proper training and further testing to decrease the likelihood of adverse events. The technical risks cover supply chain concerns and hardware failure. To avoid hardware failure while implanted, such as encapsulation degradation, chronic benchtop and in vivo testing can be implemented. Working to create strong partnerships with suppliers and ensuring they are ISO 13485 certified could preempt supply chain issues.

The hazard analysis was evaluated by key opinion leaders (KOLs) who provided feedback on the risks and their likelihood and severity ratings. KOLs shared concerns relating to the company’s IP position and path to FDA approval. They suggested hiring a PMA expert and team of lawyers to address IP concerns. The KOLs also had scientific concerns relating to the removal of the device and its ability to remain in place. Further testing both bench top and in vivo testing is crucial for Impact Neuromod’s growth.

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Company Overview

Background

Impact Neuromod is a start-up based in Madison, Wisconsin that is dedicated to developing innovative medical devices for deep brain stimulation (DBS). DBS is a procedure that involves the implantation of the device that delivers stimulation to specific brain regions to treat conditions such as Parkinson's disease, essential tremor, and dystonia. Parkinson's disease is an incurable neurodegenerative disorder that causes severe movement disorders, and it is one of the primary areas of focus for Impact Neuromod. The company has developed a wireless, miniaturized radiofrequency (RF) device that utilizes heat to modulate neural activity. The device is designed to have a smaller footprint and less invasiveness than existing DBS devices. By offering this new treatment, Impact Neuromod's technology could improve the life quality of patients and expand the DBS market for Parkinson's disease.

Management team

Although Impact Neuromod is an early stage biotechnology company, it is apparent that an Executive Board and Scientific Advisory board will need to be established. The key positions on the executive board that are Impact Neuromod's highest priority to fill are Chief Executive Officer (CEO), Chief Medical Officer (CMO), Chief Operations Officer (COO) and Chief Technology Officer (CTO).

After careful consideration, Impact Neuromod has decided to recruit; Davilynn Erickson to serve as CEO, Ashwini Sharan to serve as CMO, Jeff Erb to serve as COO and Rafael Carbunaru to serve as CTO. These candidates were selected based on their extensive track records within the medical device industry. Davilynn is the current CFO of Neuromodulation at Medtronic with over 20 years of finance experience. Ashwini Sharan is the current CMO of Neuromodulation at Medtronic and is a world-renowned neurosurgeon. Jeff Erb served as the Sr. Director of Business Development and Strategy of Medtronic's Neuromodulation group for nearly 19 years. Finally, Rafael Carbunaru is the current CTO at Boston Scientific and has over 20 years of experience related to the R&D of neuromodulation devices. Rafael has also worked on RF powered implantable microstimulators in the past.

The next recruitment priority for Impact Neuromod is the Scientific Advisory Board of which the company has selected Dr. Aviad Hai, Dr. Aaron Suminski, Dr. Kip Ludwig and Dr. Justin Williams. Dr. Aviad Hai is the inventor of the wireless RF neural actuators and will serve as the company's in-house product science expert. Dr. Aaron Suminski has extensive expertise in modern DBS surgical interventions which will aid in the development of a minimally invasive surgical procedure. Dr. Kip Ludwig and Dr. Justin Williams are current neuromodulation experts with experience in the translation of neuromodulation devices. Their expertise will help the company translate this technology from preclinical in-vivo studies to humans.

Partnerships

Impact's institutional partnerships, both in government and academia, further extend their pool of intellectual resources and stakeholdership. Dr. Aviad Hai's spearhead lab at the University of Wisconsin - Madison maintains particular skill and dedicated efforts toward Impact's mission, with collaboration from various labs at the university and beyond. A focused

research initiative, the Wisconsin Institute of Translational Neuroengineering (WITNE), provides the intellectual and physical capital as a shared resource to those within the group, including Impact and the Hai Lab. Government investment from the National Institutes of Health and the Department of Defense lend the support of federally-backed programs and professionals, both in the specific clinical space that Impact intends to operate and in a broader range of tangential fields. Altogether, these institutional partnerships can support the foundation of Impact's efforts and subsequent progress.

Market

Parkinson's Disease (PD)

Parkinson's Disease is a neurodegenerative disease that is caused by the loss of dopaminergic cells in the substantia nigra. The cell loss leads to a hypokinetic behavior, inducing disorders such as tremors, slowness of movement, and speech impairment. PD is the second most common neurodegenerative disease diagnosed in the US. There are about 0.5M people in the US and about 1M people in North America diagnosed with PD, but given that there could be undiagnosed or misdiagnosed cases the actual number is likely higher [1]. Current treatments for PD include medications, surgical interventions, and complementary therapies. The cost of treating PD in the US alone is estimated to be $14 billion annually, and the market is expected to rise rapidly as the number of patients diagnosed with PD is expected to double by 2040 [2]. Among the treatments, the global DBS devices market for Parkinson's disease was valued at $1.8 billion in 2021 and is expected to grow 11.5% annually [3], which means the total addressable market for the company would be around $4.3 billion in 2030.

General analysis

In the United States, the market for neuromodulation devices has been growing rapidly in recent years. This growth is driven mainly by the aging population and the increasing prevalence of neurological disorders[4]. According to a report by MarketsandMarkets, the global neuromodulation market is expected to grow at a CAGR of 11.2% until 2025, with the United States accounting for the largest share of it[5].

DBS analysis

More specifically, in the United States the market for DBS devices has been growing steadily as well. With the increasing adoption of biotechnology by neurosurgeons and the general population, the DBS market is expected to grow at a CAGR of 8.9% up until 2030[6]. According to Grand View Research, it is estimated that by 2030, the DBS market will reach a value of 2.5 billion. However, with major players like Abbott, Medtronic, Boston Scientific and others, the serviceable market will be significantly reduced. In conclusion, from a market perspective, entering the neuromodulation landscape seems like a safe bet, given that the lifespan keeps increasing and with that the prevalence of neurological disorder. However, it is important to consider the other players in the field.

Competitive landscape

Impact Neuromod's major competitors in the PD DBS treatment market are Boston Scientific, Abott, and Medtronic. Boston Scientific has developed a DBS system called Vercise, which applies the stimulation to bilateral subthalamic nucleus (STN). The implantable pulse generator (IPG) of the system has 16 channels and can support up to 8-contact leads. The key feature Boston Scientific proposed is the system could deliver a different level of stimulation to each contact lead. The stimulation parameter of the Vercise is determined by a clinician programmer and could be turned on/off via a remote control. The Abbott Infinity DBS system could stimulate STN or ventral intermediate nucleus (VIM) and is proposed to suppress upper tremor more effectively. The Infinity system also has a 16 channel IPG with 8-contact leads support. They provide a bluetooth controlled system that allows patients to manage stimulation parameters based on a recommended range from physicians. The Medtronic Percept system could provide GPi and STN stimulation. It's the only system on the market that has a sensing and feedback system monitoring the LFPs during the stimulation.These are major companies that provide DBS systems to about 4,000 patients in the US per year [7], with over $40,000 per patient reimbursement [8].However, these systems all require daily battery recharge or replacement every 5-7 years. The device from Impact Neuromod is wireless and battery free, which could avoid the possible infection and immune reactions caused by replacement surgery. Additionally, patients with these implantations are not able to receive MRI scans as there could be electrodes heating and IPG dysfunction. Impact Neuromod's device is proved to be MRI compatible in animal models[9].Thus, the company's device could potentially take the market share of the patient that is susceptible to multiple surgical operations or needs regular MRI diagnosis.

Product Overview

Technical basis

Impact's devices rely on five fundamental technical principles, which as a whole provide distinct advantages over competitors' options (Supp. Fig. 1). By utilizing radio frequency (RF) technology and closed resonating circuits to transfer power, the devices can operate (1) wirelessly without on-board batteries or complex circuit topology (Fig. 1a). This wireless paradigm eliminates the long leads required to reach the deep brain regions targeted in DBS, minimizing its invasiveness and reducing the potential for severe immune response. Further, RF communication is (2) bi-directional and the devices can communicate to the external transceiver various changes in the local cellular environment that are indicative of neural activity and disease progression (Fig. 1b). This gives patients and physicians a tool for not only treating PD, but monitoring its physiology. To modulate activity, Impact tunes and subsequently employs (3) thermal dissipation inherent in resistive electronics, which further minimizes the device size and circuit complexity (Fig. 1c). Modern fabrication techniques enable production of these devices on the sub-millimeter scale necessary for improved localization and (4) injectability, which limits the surgical failures that exist with traditional implants. Finally, careful and deliberate material, packaging and form-factor selection ensure (5) biocompatibility for chronic use in a neural environment (Fig. 1d).

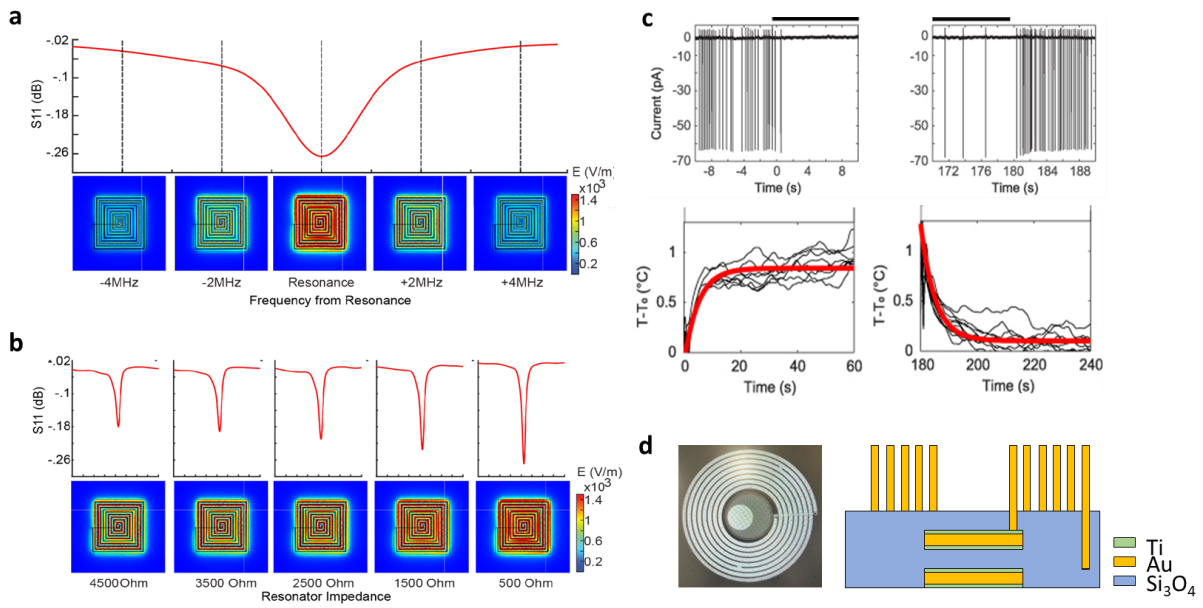

Figure1: Competitive advantages of Impact devices include (a) wireless power transfer (adapted from Bhatt & Masterson *et al.[10])* (b) bi-directional communication for monitoring neural environment (adapted from Bhatt & Masterson *et al[10[.)*, (c) thermal modulation (adapted from Kim, Kadji, Whalen *et al.[11])*, and (d) improved biocompatibility and injectability.

Intellectual property

Current IP that Impact has is limited to one patent. The idea of using inductively coupled coil-based transducers and their ability to be tuned using MRI. This is done by changing the resonance frequency of the RLC or LC circuit. Using an FET the change in resonance can be driven. Although this is a good first step, there are still lots of holes in the existing IP structure. Critical areas where IP will look to be developed include the device design, the stimulation paradigm, and the insertion and removal procedure. Impact Neuromod's current portfolio in no way gives the company exclusivity in the space so by going dark with R&D efforts the IP portfolio can be broadened. From an IP perspective, Impact has lots of room for growth because of the novelty of the product. Areas that have heavier IP such as the signal type can be navigated by making small tweaks to the signal types in order to bypass existing IP. By altering things such as wave type, amplitude, and frequency, common signals used by large competitors such as Medtronic and Boston Scientific can be somewhat replicated. The next funding round will be used to hire an IP lawyer that will help the company navigate existing IP in a space occupied by large players in industry.

Developmental timeline

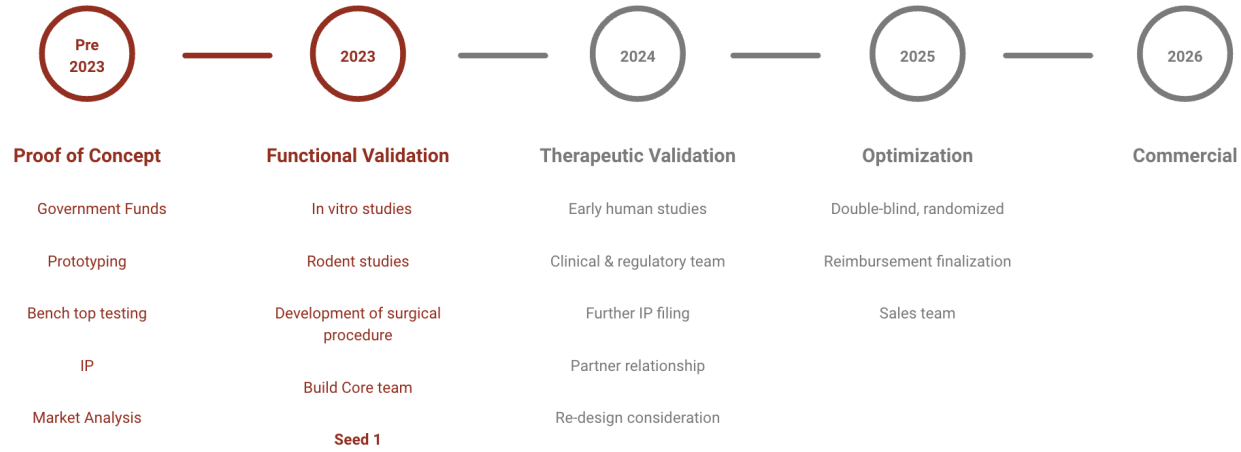

Figure2: Timeline outlines past stages and future developmental process of impact neuromod. Pre-2023 represents the early stages which focused on basic science and preclinical studies. The next few years through 2026 are expected to represent the validation and clinical stages. While the specific stages may vary in length, the progression follows the general structure and steps biomedical companies are expected to go through.

Financial Analysis

Existing funding

Currently the funding supporting the project came from the NIH and DoD which supported the company's biological proof of concept testing. With 2.55 million Impact Neuromodmanaged to prototype, perform preclinical studies, receive two IPs, and perform market analysis.

Reimbursement

Impact will look to pursue a similar reimbursement pathway used by competitors such as Abbott and Medtornic who have existing reimbursement codes. The procedure draws similarities to existing products because of the similar placement in the brain. The only difference being a lack of a lead because the device is wireless. A mechanism may be implemented to keep the device in place. Existing Medtronic codes for a craniotomy or endovascular intracranial procedure list a Medicare average of $31,146. Using other existing reimbursement standards for things like the placement of a cranial neurostimulator will be important for achieving a strong reimbursement strategy for Impact.

Investment outlook

Impact is currently seeking initial seed funding with a goal of $1.5M for the round. By leveraging non-dilutive funds, Impact aims to spend $1M toward recruiting to fill the aforementioned leadership positions, $100k to strengthen their patent portfolio, and $400k to begin developing the required supplemental surgical techniques and hardware systems. At this

early stage, Impact is targeting high-risk investors who understand the antiquity and challenges of current DBS and trust that the technical advantages of a wireless approach are feasible and efficacious.

Hazard Analysis

Analysis Design

Identified hazards were categorized into business case, scientific, and technical risks which were then further split up into subcategories as shown in table 1. The priority score was calculated based on the difference between the product before and after mitigation strategies were implemented. This score is shown on the rightmost column of the table, with 1 being of highest priority and 22 being of lowest priority. Different hazards may have the same priority if the differences before and after mitigation are the same. Since Impact Neuromod is an early-stage company, many of the hazards proposed below focus on building this venture into a well-established company and further developing the proof-of-concept.

Business Case Risks

Business hazards include the competition, market, regulatory, and team categories. Both competition hazards after mitigation can be reduced in likelihood from high to medium-high and in severity from high to medium. The first hazard of large competitors having more resources to dominate the market can be mitigated by going dark until a more well established IP portfolio is established by the team. Expanding that IP exclusivity could be achieved by receiving awarded IP that specifically targets fabrication and surgical procedures.

Hesitancy towards adopting a novel system is a market hazard for the team that could be reduced in likelihood from medium to medium-low if a strong marketing strategy and partnerships is developed. In the rare instance that a cure for PD has emerged, the team would focus on smaller-scale studies of other diseases in preparation to move to these studies full time with more ease if necessary, diminishing the hazard's severity from high to medium-low.

In the regulatory realm, two hazards have been identified for the team. The first being the violation of specific absorption rate (SAR) limits. Reducing the likelihood from medium-low to low and the severity from high to medium low could be achieved by developing chronic studies at safe levels. The second hazard applies to the novel application of thermal stimulation for DBS, in which a PMA route is required. With obtaining PMA approval through effective data, the likelihood of this risk drops significantly from high to low. As for the team, there was previously no expertise in PD nor commercialization. Through the hiring of both a PD expert and a commercialization expert, these hazards, deemed very important in priority, could reduce both the likelihood from medium to low and the severity from high to low.

Scientific Risks

Scientific case hazards consist of risks regarding safety, stimulation, and surgery. Starting with safety, damage to tissue could be mitigated by testing heat dissipation chronically, effectively reducing the severity from high to medium. The severity of infection could be reduced from high to low if referencing other DBS protocols and ensuring proper training. Two

stimulation risks, causing unwanted nuclei and hysteresis effects could both be reduced from high to medium likelihood if chronic migration and heat dissipation effect studies were conducted, respectively. If stimulation does not produce its intended effects, thermal stimulation coupled with electrical stimulation could lower the severity from high to medium and the likelihood from medium to medium-low. In the case of poor translation from animal models to human models, reconstructing the stimulation could decrease the severity from high to medium.

Technical Risks

Several technical risks highlighted include hazards related to capsule hardware, external hardware, and supply chain. For capsule hardware, internal encapsulation degradation may occur such that the device is in direct contact with the CSF or surrounding tissue. Although the likelihood would not change, preparing chronic benchtop and in vivo characterization of degradation may decrease the severity from high to medium. The system could heat up, dissipating more heat than expected. Ensuring the device falls within clinical safety values and creating a physical constraint on the temperature would lower the severity from high to medium.

External hardware poses the risk of the inability to immediately stop the stimulation to cool down. If the team can control the heat emission to optimize the pulse signal, the likelihood of occurrence would drop from high to medium, and the severity from medium to low. If an incorrect pulse sequence were to occur, the likelihood of stimulation would drop from medium-low to low if version control and debugging were performed.

Supply chain risks, such as contaminant material and limited partnerships, pose risks to the team. First, if the supplier's material has contaminants, becoming ISO 13485 certified would both change the likelihood and severity of this risk from high to medium. If the team were to face limited partnerships leading to low production, forming relationships with companies for external components would decrease the severity from medium to low.

Hazard	Hazard Description	Likelihood	Severity	Mitigation Strategy	Revised Likelihood	Revised Severity	Priority Score
Business Case Risks							
Category 1: Competition							
Large Competitors Possess Market Share	Large companies (Abbott, Boston Scientific, and Medtronic) have the resources to replicate idea and more quickly commercialize it	High	High	Going dark about internal R&D efforts and milestones. Waiting until the IP portfolio is more elaborate before founding the company	Med-High	Medium	13
Limited Exclusive IP	Only one awarded patent that does not cover desired thermal stimulation paradigm, device design or	High	High	Create IP that provides coverage of device fabrication, Resonator design and minimally invasive surgical procedure	Med-High	Medium	13

	minimally invasive surgical procedure						
Category 2: Market							
Hesitancy towards adoption	Low adoption rate by physicians and healthcare systems due to large companies having existing relationships with target market	Medium	High	Develop a marketing strategy to deploy in partnership with healthcare systems; train physicians to feel comfortable with surgical technique	Med-low	High	5
PD cure developed	A novel cure is developed for PD, eliminating the market	Low	High	Small-scale studies for applications in other target diseases. Prepare to study other diseases	Low	Med-low	3
Category 3: Regulatory							
Violations of SAR limits	FCC limits the specific absorption rate (W/kg) so heat to cells must be within the limits	Med-low	High	Obtain short and long term data of absorption rates to ensure exposure levels are within a safe range.	Low	Med-low	8
FDA Pre Market Approval	PMA route required due to the lack of preexisting devices that utilize thermal stimulation	High	Low	Have sufficient scientific evidence to ensure device is safe and effective for intended use to obtain PMA approval fromFDA	Low	Low	4
Category 4: Team							
No PD Expert	Lack of Parkinson's expert on the executive team and/or advisory board.	Medium	High	Hire a Parkinson's expert	Low	Low	14
Lack of Commercialization Experience	Currently lacks commercialization experience and relationships with customers to open up distribution channels	Medium	High	Identify candidates who have heavy commercialization experience, especially in the implantables space.	Low	Low	14
Scientific Risks							
Category 1: Stimulation							
Off-Target Effects	Stimulating unwanted nuclei due to improper injection/migration/heat radiation	High	High	Preclinical studies on ideal device injection and chronic migration mitigation. Minimize heat emission so temperature is controlled within range	Medium	High	10

Non-intended Neuronal Response	Thermal stimulation does not produce intended neuronal response in brain targets	Medium	High	More animal studies on heat stimulation in targeted neuron; Couple thermal stimulation with electrical and magnetic stimulation	Med-low	Medium	9
Slow Response Time	Hysteresis effects with thermal stimulation could limit the effectiveness of the treatment	High	High	Preclinical studies to analyze and model the heat dissipation effects over time	High	High	0
Poor Translation	Stimulation paradigm does not translate well to humans	Med-high	High	Reconfigure stimulation and device to replicate the electrical paradigm in traditional DBS	Med-high	Medium	8
Category 2: Surgery							
Device Removal	Hard to locate and remove all implanted capsules. Damage tissue during device removal	High	High	Further develop surgery procedure/tools to locate devices	Medium	High	10
Device Injection	Missed the surgical target during initial injection	Med-low	High	Develop a protocol for intraoperative relocation of device in all 3 dimensions and for MRI-assisted surgery	Low	Med-low	8
Category 3: Safety							
Tissue Damage	Neuronal damage in proximal tissue	Medium	High	Preclinical studies for heat dissipation in vivo and chronic tolerance of surrounding tissue	Medium	Medium	6
Infection	Infection during injection procedure	Low	High	Reference existing DBS procedures protocols. Ensure surgeons have extensive DBS implantation training	Low	Med-High	1
Technical Risks							
Category 1: Supply Chain							
Contaminant Material	Material in contact with tissue from supplier has contaminant	High	High	Become ISO 13485 Certified for Quality Systems	Medium	Medium	16
Low Production	Low production quantities limit partnerships for manufacturing	Low	Medium	Utilize existing off-the-shelf devices for external components	Low	Low	2
Category 2: Capsule (Internal) Hardware							
System Heats Up	Encapsulated electronics fail and dissipate more heat	Low	High	Develop system well within clinical safety values and develop	Low	Medium	2

	than expected			components with physical constraints on heat dissipation			
Internal Encapsulation Degradation	Encapsulation degraded leading to direct contact of device to CSF or current leakage to local tissue	Medium	High	Chronic benchtop and in vivo characterization of device degradation with iterative modifications of material and stimulation parameters	Medium	Medium	6
Category 3: External Hardware							
Can't Stop Stimulation	Can't stop stimulation immediately due to time for cool down	High	Medium	Optimize pulse signal to control the heat emission	Medium	Low	12
Incorrect Pulse Sequence	Incorrect pulse generation sequence for stimulation	Med-low	High	Rigorous version control and debugging prior to deployment in humans	Low	High	5

Table 1: Proposed hazards characterized by type of risk, with likelihood and severity described before and after mitigation strategy is implemented along with a priority score.

Summarized KOL Feedback

After compiling these hazards, Impact Neuromod presented them to a panel of key opinion leaders (KOLs). In this session, several concerns were raised regarding the hesitancy toward product adoption given the already established, large competitors. Many KOLs also mentioned that hesitancy to adoption could potentially be a large deterrent for the implementation of this technology. A suggestion was posed to prioritize hiring a PMA approval expert to navigate the FDA approval process and ensure that adequate evidence is obtained to prove this product is better than the current state of the art. Another suggestion was to ensure that a company representative is present at every procedure to aid the physicians.

Several KOLs also shared concerns about the priority of the hazards related to the device producing unintended neuronal response, one stated that the entire business case is moot if the product does not produce the intended response. Another KOL emphasized that the choice of animal model will be crucial to facilitate the translation of Impact Neuromod's technology to humans.

Given the microscopic geometry and minimally invasive delivery method, there is currently no proven way to explant the device after implantation. This poses several risks in the event of device failure, and several KOLs did not believe that the mitigation strategy proposed by Impact Neuromod was sufficient. A suggestion that the team received to further mitigate this issue was to create IP around a failsafe mechanism that eluted neuroprotective agents in the event of a device failure.

Another area of concern from KOLs is the lack of IP in the space. The company shares the same concern as there are many large competitors in the space. The company believes that

there is still a possibility to operate in the space because of the novelty of Impact Neuromod's product. While there is no IP covering the device procedure and other things like device design and stimulation paradigm. It is important to use the company's next round of funding to develop a strategy with IP lawyers to navigate the IP landscape for DBS.

Positive feedback was given on the company's strategy to pivot away from Parkinsons because of the saturation of the market. The company believes that Impact Neuromod's technology is applicable to other diseases and by gaining IP on the technology itself it may be possible to select a disease to focus on by developing new studies that prove efficacy. This is beneficial for the company's fundraising rounds and product development because there's lots of overlap on the R&D side with Parkinsons and other diseases because the fundamental technology and process can stay relatively the same.

KOLs also mentioned the trouble of keeping the implant in place within the brain. With the implementation of a wireless device there is concern for movement within the brain. While Impact is very early in the design phase this will be a key point of interest in the design process. Device migration can result in stimulating unintended areas of the brain so understanding how external forces could cause the implant to be moved will be critical to understanding device safety. Addressing ways to anchor the device is important from a technological hazard viewpoint and will be extremely high on the company's priority list. In terms of addressing proximal tissue being stimulated this is where clinical studies will look to understand this effect. This includes staying within the guidelines of SAR limits set by the FCC.

Recommendations

The team has compiled hazard analysis results and KOL feedback to determine the best course of action. Given the limited current IP, Impact Neuromod should go dark while developing more comprehensive IP especially in regards to the surgical procedure and fabrication methods. Focusing on patents related to the device and not Parkinsons is important given the current saturation of DBS in the Parkinson's market. Partnerships will be important for clinical adoption and supply chain management and should be made a priority. The leadership team also needs to be built out to include relevant experts especially with fundraising and PMA approval experience. Overall more preclinical studies are needed to mitigate scientific and technical risks. Further testing both benchtop and in vivo should be prioritized to optimize efficacy of the device.

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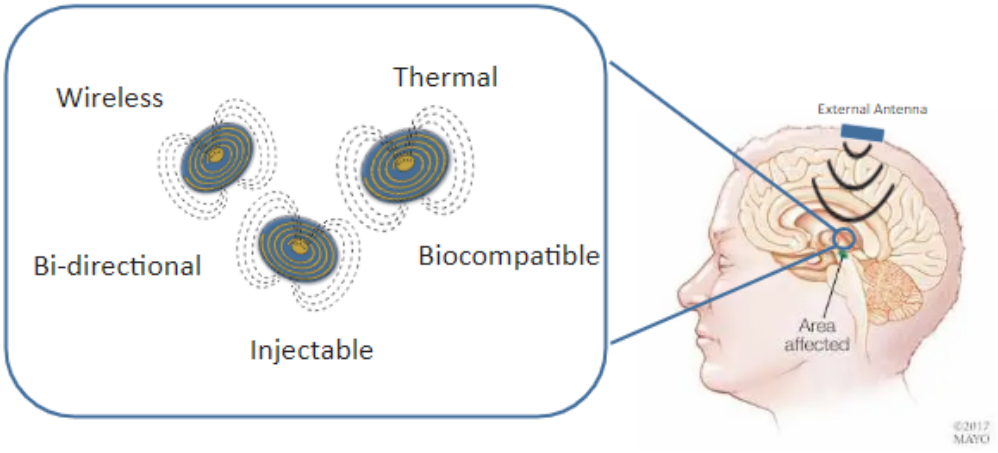
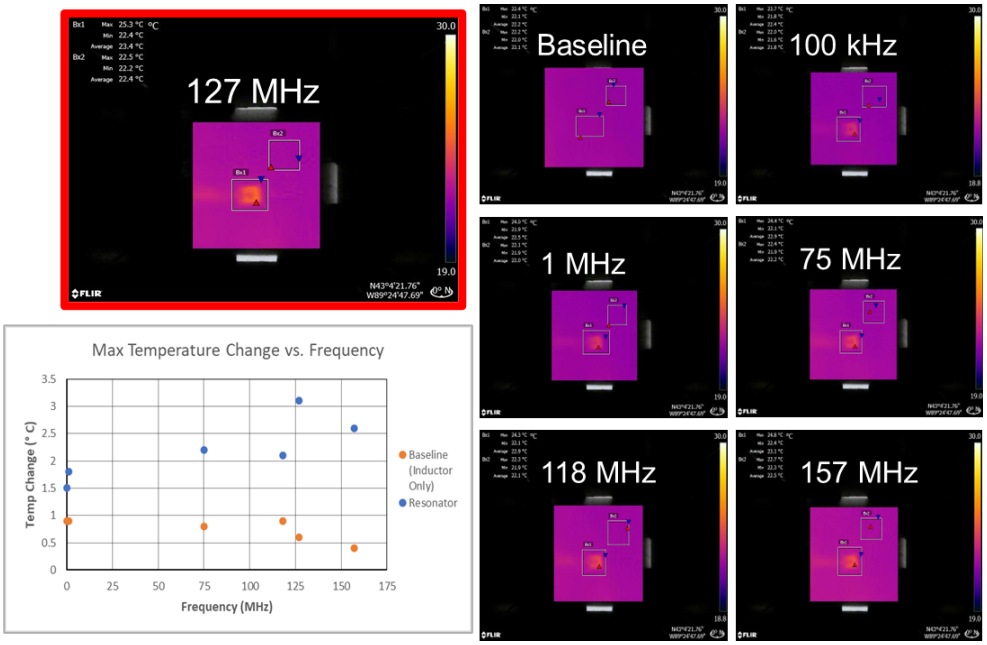
Appendix

Supplemental figures



Supplemental Figure 1: RF communication and micro-scale fabrication enable wireless and miniaturized DBS while reducing peri- and post-operative complications



Supplemental Figure 2: Demonstration of micro-scale wireless devices dissipating clinically relevant levels of heat at targeted resonant frequencies.