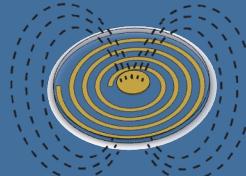


impact neuromod

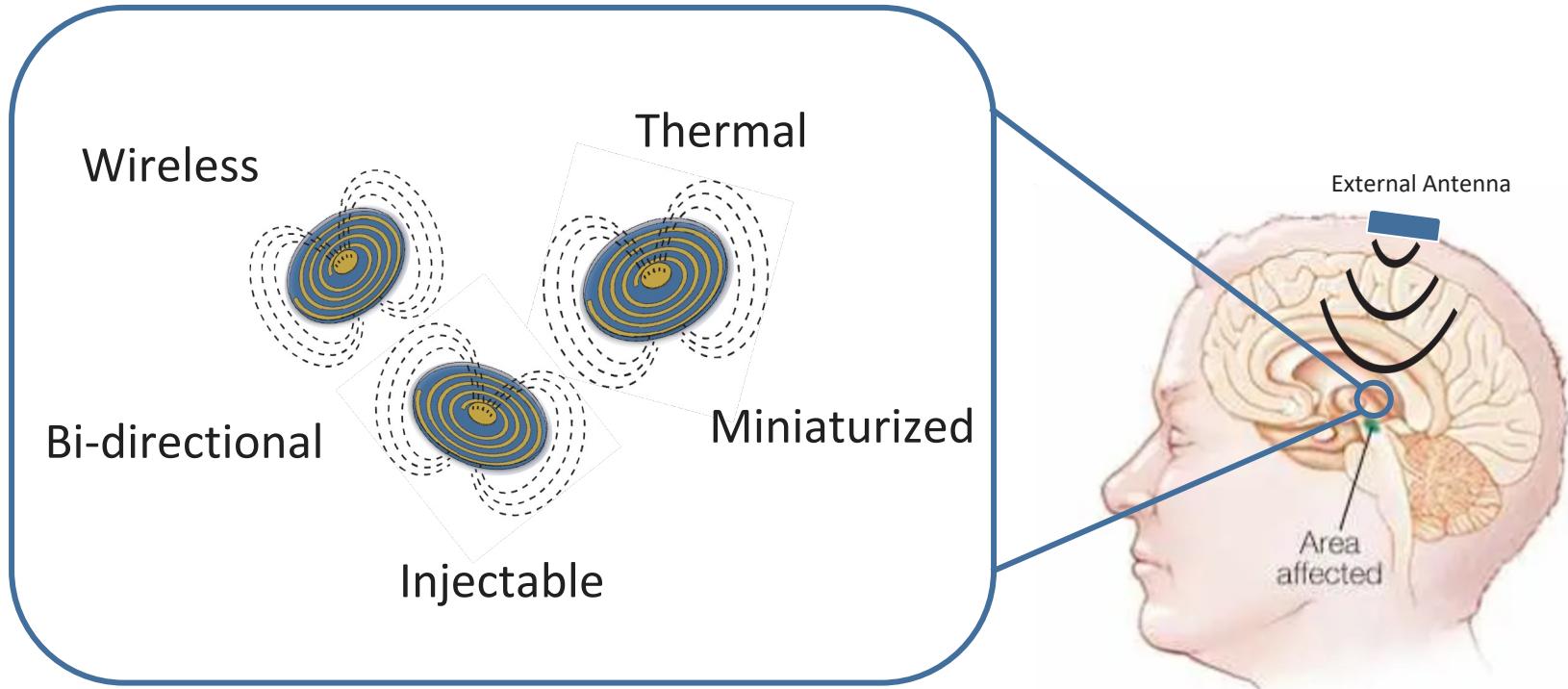


Hazard Analysis

Emily Masterson, TShawn Zhu, Lance Johnson, Aaron Gholston, Adam Vareberg, Lily Xistris, Ido Haber

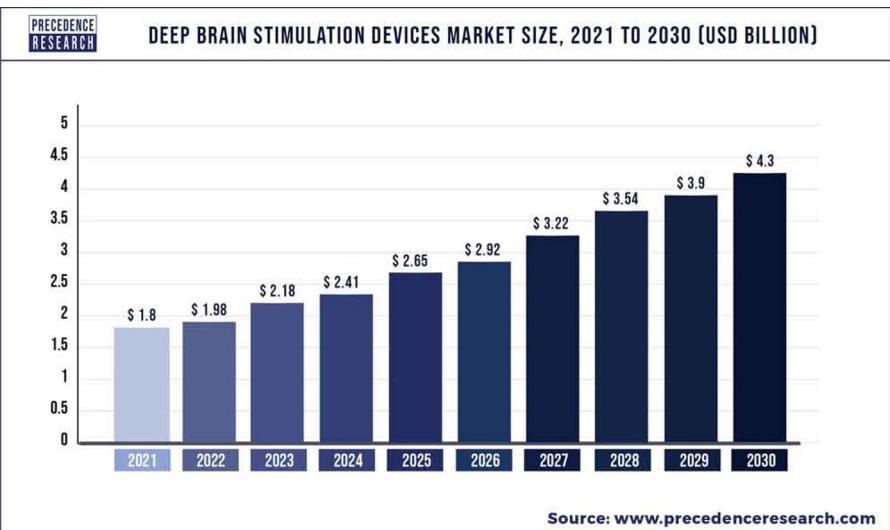
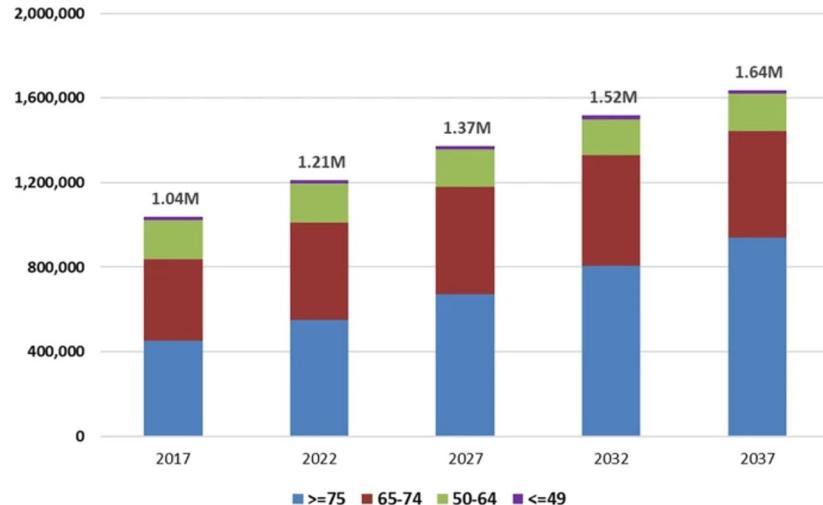
University of Wisconsin-Madison, Departments of Biomedical Engineering and Mechanical Engineering

Impact Neuromod Overview



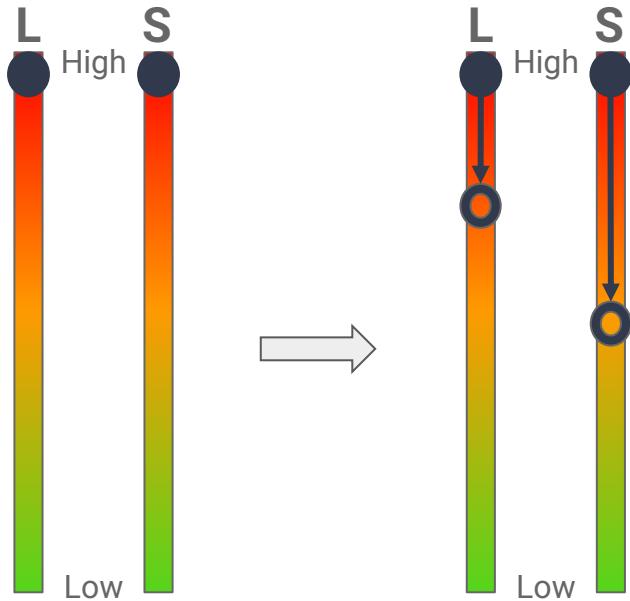
Background: Parkinson's Disease

- Second most common neurodegenerative disease diagnosed in U.S.
- ~15% growth in patient number every 5 years
- DBS market valued at ~\$1.8B in 2021



Projected number of patients by 2037 grouped by age[2]

Visualization Key



Priority score is calculate based on the difference between the product pre and post mitigation

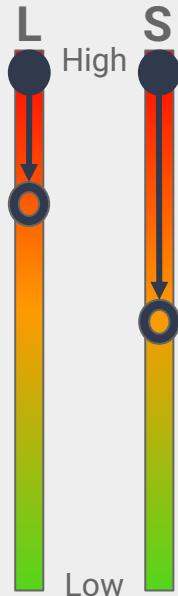
Business Case Hazards - Competition

1. Large Competitors Possess Marketshare

4/22 

Description

Large biotechnology companies like Abbott, Boston Scientific, and Medtronic have the resources to replicate our idea and commercialize it much faster



Mitigation

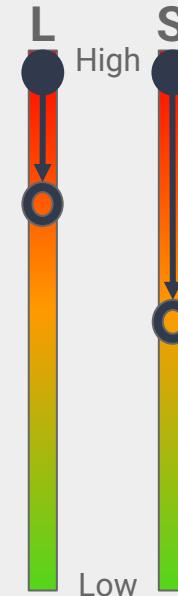
Going dark about internal R&D efforts and milestones. Perhaps waiting until IP portfolio is more elaborate before founding the company.

2. Limited Exclusive IP

5/22 

Description

Only one awarded patent that does not cover desired thermal stimulation paradigm, device design or minimally invasive surgical procedure



Mitigation

Create IP that provides coverage of device fabrication, Resonator design and minimally invasive surgical procedure.

Business Case Hazards - Market

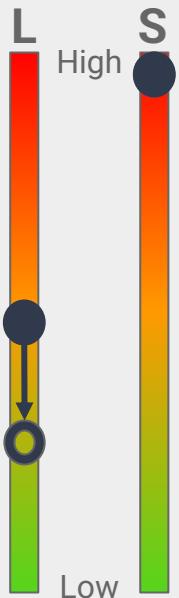
3. Hesitancy towards adoption

15/22



Description

Low adoption rate by physicians and healthcare systems due to large companies having existing relationships with our target market.



Mitigation

Develop a marketing strategy to deploy in partnership with healthcare systems; train physicians to feel comfortable with surgical technique

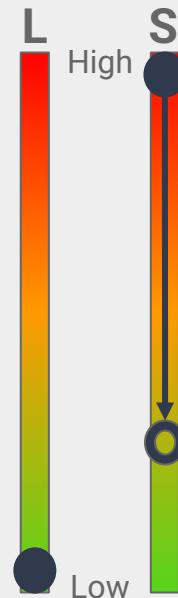
4. PD cure developed

18/22



Description

A novel cure is developed for PD, eliminating the market.



Mitigation

Small-scale studies for applications in other target diseases. Prepare to study other diseases

Business Case Hazards - Regulatory

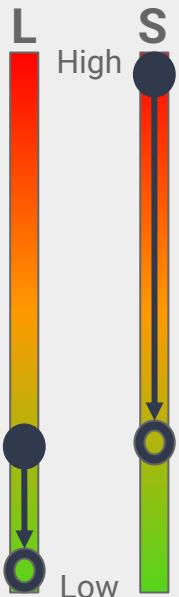
5. Violations of SAR limits

10/22



Description

FCC limits the specific absorption rate (W/kg) so heat to cells must be within the limits.



Mitigation

Obtain good short and longterm data of absorption rates to ensure that exposure levels are within a safe range.

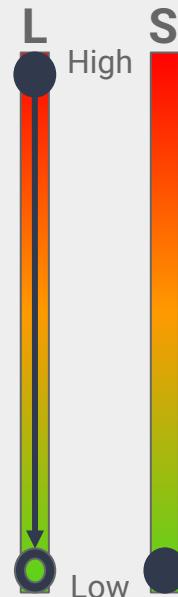
6. FDA Pre-Market Approval

17/22



Description

PMA route required due to the lack of preexisting devices that utilize thermal stimulation.



Mitigation

Have sufficient scientific evidence to ensure device is safe and effective for intended use to obtain PMA approval from the FDA

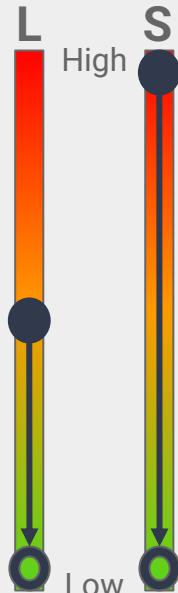
Business Case Hazards - Team

7. No PD Expert

2/22 

Description

Lack of Parkinson's expert on executive team and/or advisory board.



Mitigation

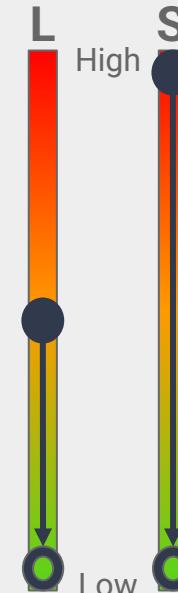
Hire a Parkinson's expert

8. Lack of Commercialization Experience

3/22 

Description

Team currently lacks commercialization experience and relationships with customers to open up distribution channels to break into market.



Mitigation

Identify candidates who have heavy commercialization experience, especially in the implantables space.

Scientific Case Hazards - Safety

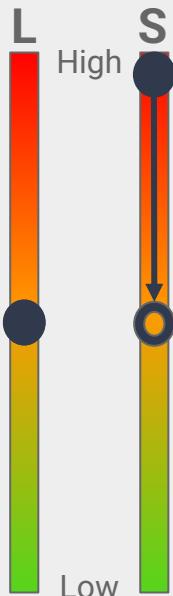
9. Tissue Damage

13/22



Description

Neuronal damage in proximal tissue



Mitigation

Preclinical studies looking at heat dissipation in vivo and chronic tolerance of surrounding tissue

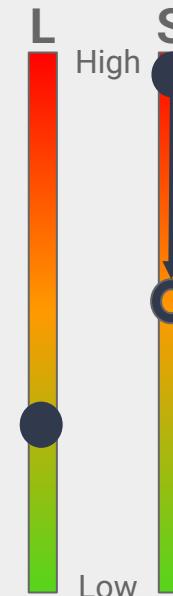
10. Infection

21/22



Description

Infection during injection procedure



Mitigation

Reference existing DBS procedures protocols. Ensure surgeons have extensive DBS implantation training

Scientific Case Hazards - Stimulation

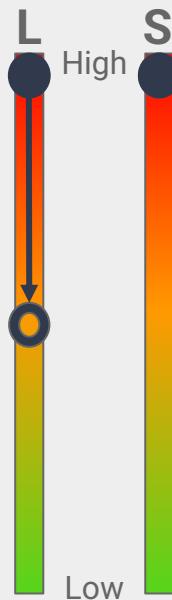
11. Off-Target Effects

7/22



Description

Stimulating unwanted nuclei due to improper injection/migration/heat radiation



Mitigation

Preclinical studies working on ideal device injection and chronic migration mitigation, Minimize heat emission so the temperature is controlled within range

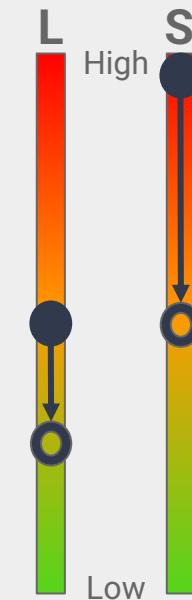
12. Non-intended Neuronal Response

9/22



Description

Thermal stimulation does not produce intended neuronal response in brain targets



Mitigation

More animal studies on heat stimulation in targeted neuron; Couple thermal stim with electrical and magnetic stimulation

Scientific Case Hazards - Stimulation

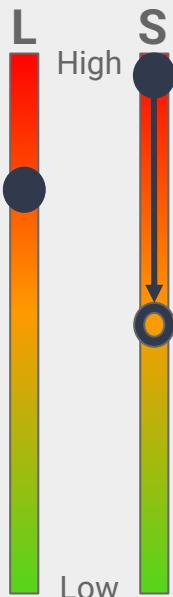
13. Poor Translation

11/22



Description

Stimulation paradigm does not translate well to humans



Mitigation

Reconfigure stimulation and device to replicate the electrical paradigm in traditional DBS

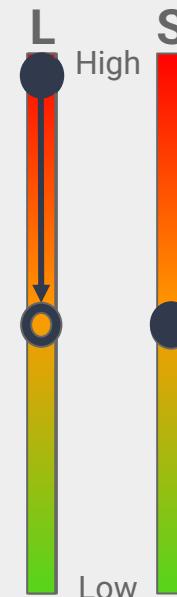
14. Slow Response Time

22/22



Description

Hysteresis effects with thermal stimulation could limit the effectiveness of the treatment.



Mitigation

Preclinical studies to analyze and model the heat dissipation effects over time.

Scientific Case Hazards - Surgery

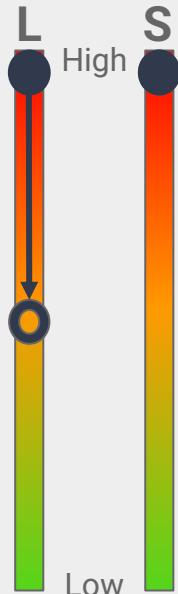
15. Device Removal

8/22



Description

Hard to locate and remove all implanted capsules. Also could damage tissue while removing device



Mitigation

Further develop surgery procedure/tools to locate devices

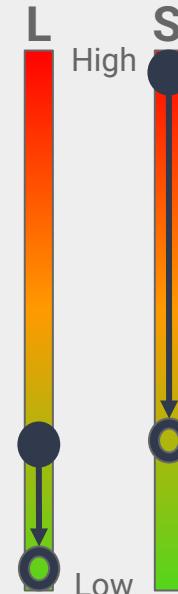
16. Device Injection

12/22



Description

Missed the surgical target during initial injection



Mitigation

Develop a protocol for intraoperative relocation of device in all 3 dimensions;
Develop a protocol for MRI-assisted surgery

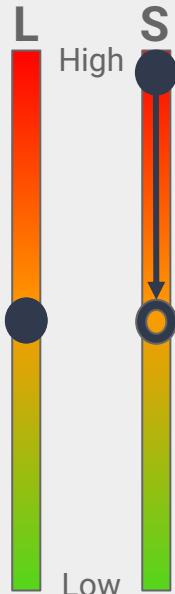
Technical Case Hazards - Capsule Hardware

17. Internal Encapsulation Degradation

14/22 

Description

Encapsulation degraded leading to direct contact of device to CSF or current leakage to local tissue



Mitigation

Chronic benchtop and in vivo characterization of device degradation with iterative modifications of material and stimulation parameters as needed

18. System Heats Up

20/22 

Description

Encapsulated electronics fail and dissipate more heat than expected



Mitigation

Develop system well within clinical safety values and develop components with physical constraints on heat dissipation

Technical Case Hazards - External Hardware

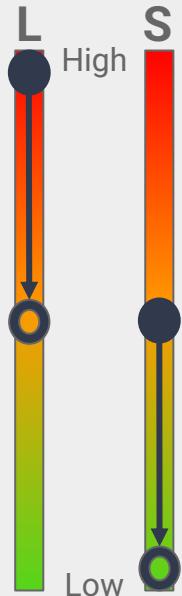
19. Can't Stop Stimulation

6/22



Description

Can't stop stimulation immediately due to time for cool down



Mitigation

Optimize pulse signal to control the heat emission to include more downtime

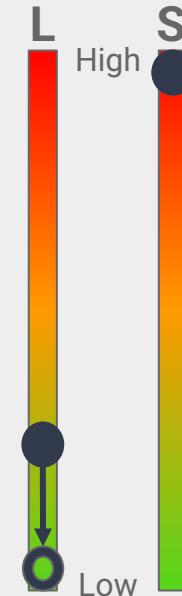
20. Incorrect Pulse Sequence

16/22



Description

Incorrect pulse generation sequence for stimulation



Mitigation

Rigorous version control and debugging prior to deployment in humans

Technical Case Hazards - Supply Chain

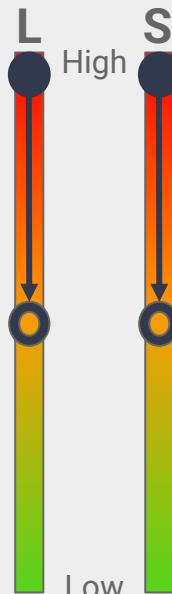
21. Contaminant Material

1/22



Description

Material in contact with tissue from supplier has contaminant



Mitigation

Become ISO 13485 Certified for Quality Systems

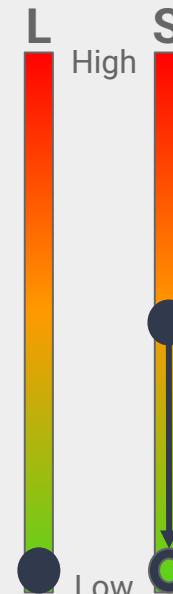
22. Limited Partnerships

19/22



Description

Low production quantities limit partnerships for manufacturing



Mitigation

Form partnerships with companies for the external components