Team Results Document

A-Levo



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SensUs 2026
Parkinson's Disease

SensUs

1. Abstract

Parkinson's disease affects millions worldwide, and managing it well depends on getting the right dose of levodopa at the right time. But today, dosing is largely guesswork: patients and doctors rely on symptom diaries and trial-and-error, leaving over half of patients reporting debilitating symptoms from improper dosage. There is currently no clinical tool that tracks these changes objectively and in real time.

A-Levo is developing a wearable biosensor that continuously monitors levodopa levels just beneath the skin, giving patients and clinicians a real-time window into how their body is responding to medication. Our design enhances enzymatic recognition technology with metal-organic frameworks to produce a clear, reliable signal even with continuous use. In lab testing, our sensor accurately and linearly tracked levodopa concentrations from 2 to 50 μM, covering the full clinically relevant range, stayed reliable after a week of storage, and showed minimal interference from other substances naturally found in the body.

Recognizing that drug levels alone don't tell the whole story, we are pairing our sensor with a wrist-worn motion tracker that detects Parkinson's-related movement symptoms. Together, these two data streams can help build a personalized picture of each patient's therapeutic window, supporting smarter, individualized dosing decisions.

Guided by conversations with patients, caregivers, and clinicians, A-Levo aims to end 50 years of blind Parkinson’s dosing.

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2. AP award: Biosensor Developed for the Eindhoven Testing Event

2.1. Molecular recognition

A-Levo employs tyrosinase enzyme encapsulated into a zeolitic imidazolate framework-8 (Tyr@ZIF-8) as the biorecognition element. ZIF-8 is a porous metal-organic framework (MOF) formed from zinc ions and 2-methylimidazolate ligands, offering high surface area, tunable porosity, and mild aqueous synthesis conditions suitable for enzyme immobilization (Wei et al., 2022). Here, tyrosinase is encapsulated within ZIF-8 during MOF formation rather than only adsorbed onto the surface. This reduces leaching and provides a protective microenvironment against denaturation (Liang et al., 2015). ZIF-8 therefore functions as a protective host for tyrosinase while regulating L-DOPA transport and limiting access to larger interferents (Xiao et al., 2022).

L-DOPA reaches tyrosinase through flexible pores in the ZIF-8 structure, where it is catalytically oxidized to dopaquinone. Dopaquinone is then electrochemically reduced at the underlying electrode, producing a current that increases linearly with L-DOPA concentration (**Fig. 1A**) (Tesoro et al., 2023). A thin Nafion layer is applied as the outermost component of the sensing architecture, helping anchor Tyr@ZIF-8 to the electrode while acting as a protective barrier to anionic interferents, such as ascorbic acid and uric acid. The membrane also reduces contact with larger proteins or biological components, helping limit surface fouling and preserving the accessibility of the sensing layer during repeated measurements (Brunetti et al., 2014).

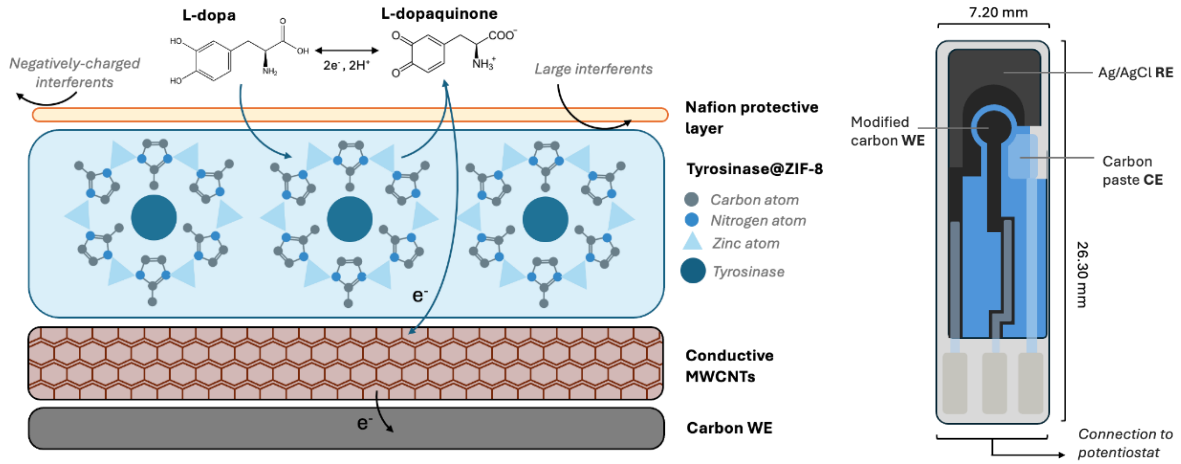


Figure 1. (A) Working electrode (WE) architecture comprising a charge-selective Nafion barrier, a Tyr@ZIF-8 biorecognition layer, and a conductive MWCNT band on a carbon surface, which allows reversible electrochemical conversion of L-DOPA to L-dopaquinone. **(B)** Screen-printed setup comprising an Ag/AgCl reference, carbon paste counter and functionalized working electrode.

2.2. Physical Transduction

An innermost multiwalled carbon nanotube (MWCNT) layer forms the conductive foundation between the recognition layer and the carbon electrode. MWCNTs form an interconnected conductive network across the electrode surface, creating a nanostructured layer that increases the electrochemically active surface area and shortens the electron transfer pathway between dopaquinone and the electrode, improving kinetics and amplifying current (Mollamohammadi et al., 2023; Tsai & Chiu, 2007). Alongside the working electrode, an Ag/AgCl reference electrode and carbon paste counter electrode—all formatted on a screen-printed platform—complete the circuit (**Fig. 1B**).

2.3. Cartridge Technology

We use a Zimmer Peacock microfluidic flow cell, with the electrode seated in a bottom slot beneath a top layer containing an oval sample chamber. The chamber connects to the outside via two 1 mm channels, linked to 1/64" ID tubing through 1/4-28 adapters, and is sealed with a rubber O-ring; the two layers are secured by two screws. A syringe attached to the outlet enables periodic sample draw (**Fig. 2**).

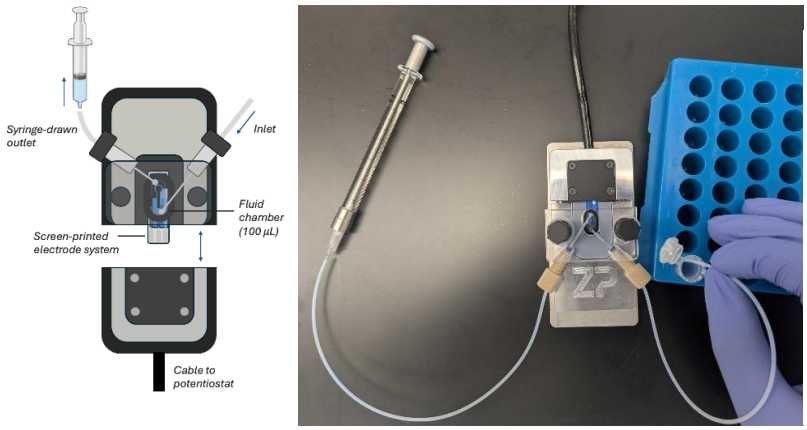


Figure 2. Flow cell setup comprising our screen-printed electrode fixed in a microfluidic chamber. Liquid moves from the inlet to the outlet via a syringe-drawn flow. The cartridge system connects via a cable adapter to the potentiostat.

2.4. Reader Instrument and User Interaction

The Zimmer Peacock Anapot potentiostat is used as a stand-in for our future system. After a sample is drawn in through the flow cell, chronoamperometry is performed using the PSTrace software. First, the working electrode is cleaned at -0.3V for 60s, after which current is read at 0.2V for 120s. The final current value is then input into a separate Python script containing our previously-characterized calibration curve to obtain an accurate LD concentration.

3. IN award: Biosensor Innovation

Parkinson's disease (PD) management requires continuous monitoring of levodopa (LD) because of its narrow and fluctuating therapeutic range. These fluctuations drive complications like dyskinesia, which affects over 50% of patients and can emerge just 10–15 minutes after dosing, meaning effective monitoring needs to function on that same timescale. No current clinical tool offers this resolution; dosing instead relies on trial-and-error, leading to poor symptom control. **A-Levo addresses this gap:** we present a continuous, nano-functionalized electrochemical sensor built on a wearable, microneedle-based platform. Its carbon working electrode uses a three-layer design: multi-walled carbon nanotubes (MWCNTs) for conductivity, tyrosinase enzyme encapsulated in ZIF-8 (Tyr@ZIF-8) for stable enzymatic detection, and a Nafion layer for specificity, enabling sensitive, specific LD detection. Paired with a complementary wrist-worn module that tracks motor symptoms, this dual-mode platform aims to enable personalized PD care.

3.1. Wearable Sensor

3.1.1. Technological Novelty of Wearable Sensor

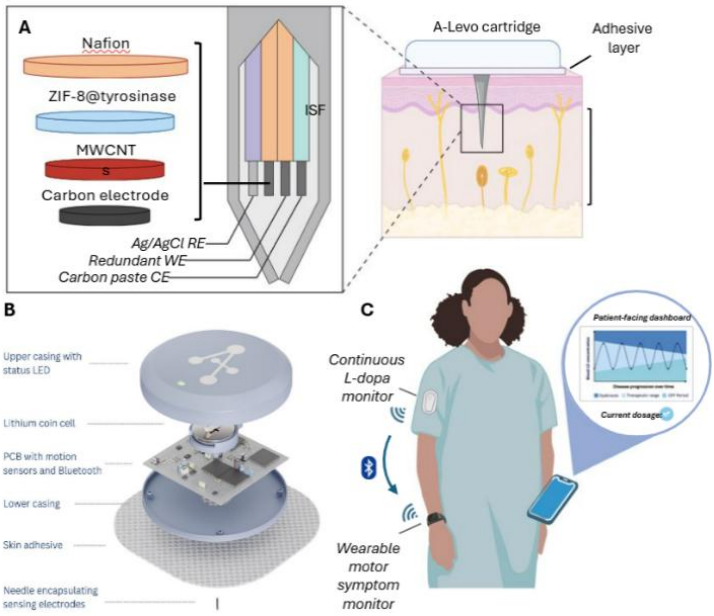


Figure 3. (A) Overview of functionalized, single-needle architecture for continuous ISF sampling and electrochemical readout. **(B)** Exploded view of sensor with custom cartridge, PCB electronics and adhesive patch. **(C)** Bluetooth-paired, dual-mode sensing platform encompassing L-DOPA levels and

The central novelty of our sensor design lies in the complementary relationship between each layer of the working electrode (**Fig. 3A**). Tyrosinase enzyme provides molecular recognition, but may be unstable or leach when immobilized without protection (Bounegru & Apetrei, 2023). ZIF-8 metal-organic framework (MOF) encapsulation stabilizes and spatially confines the enzyme while regulating transport to the catalytic sites, but the MOF itself may not provide sufficient electrical conductivity (Paul et al., 2022). Thus, the MWCNT network compensates for this limitation by providing a conductive pathway beneath the MOF–enzyme layer (Mollamohammadi et al., 2023). Finally, the Nafion membrane mechanically stabilizes the complete architecture and reduces interference and fouling, while the

underlying porous and conductive layers maintain analyte transport and signal generation. In this hierarchical arrangement, each component compensates for a limitation of the others, producing an integrated sensing interface designed to provide the sensitivity, selectivity, and stability required for wearable L-DOPA monitoring.

Our sensor is a single microneedle platform containing four insulated platinum wires, each exposed only at the tip to form the active electrode surface (**Fig. 3A**). The first three wires include the Ag/AgCl reference, carbon paste counter, and functionalized working electrodes, the latter sequentially dip-coated with MWCNT, Tyr@ZIF-8, and Nafion. The fourth wire is a redundant working electrode that lacks active tyrosinase, serving as a calibration control. The microneedle itself is 1000 µm long, balancing interstitial fluid (ISF) access with patient comfort, with a 30 µm radius, 80° wall angle, and 58 µm wall thickness for mechanical robustness, according to the literature (Davis et al., 2004) (**Appendix 8.1.1.**). We selected medical-grade stainless steel for its strength, versatility, and durability. Additionally, since enzymatic activity is temperature-sensitive, a skin-interface thermistor is included for real-time adjustments.

3.1.2. Technical Feasibility of Wearable Sensor

Electrochemical characterization: We characterized each modification layer by cyclic voltammetry in potassium ferricyanide to confirm its intended effect. Adding MWCNTs reliably raised the peak current compared to the bare carbon electrode: drop casting 1 µL of 1.5 mg/mL MWCNTs produced a 3.4-fold increase in oxidation/reduction peak currents (**Fig. 4A**), while peak-to-peak separation dropped from 0.3 V to 0.16 V, indicating faster electron transfer kinetics (Kaliyaraj Selva Kumar et al., 2022). Peak currents rose further with higher loadings, up to a 5.6-fold increase at the maximum tested. Despite the associated increase in background capacitive current and peak separation, we selected the highest MWCNT loading to maximize sensitivity (Afraz et al., 2014). In LD, the electrode reliably distinguished peak currents across varying concentrations (**Fig. 4B**). CV in LD also confirmed the effect of the Nafion: peak current generally increased with lower Nafion concentration down to 0.1%, before the effect plateaued (**Fig. 4C**).

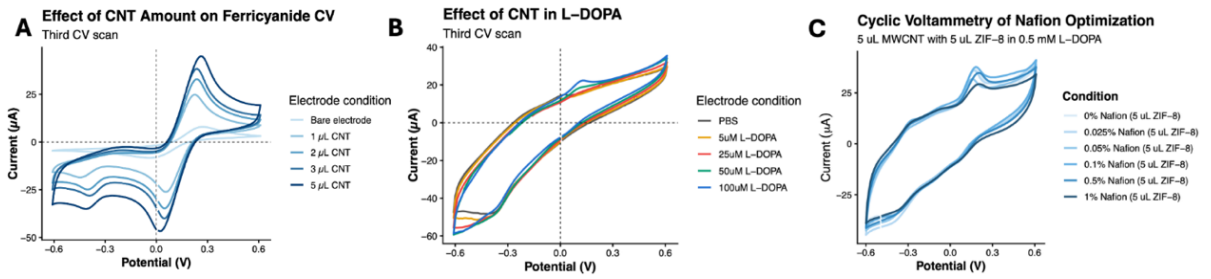


Figure 4. (A) Effect of MWCNT amount on peak CV current in ferricyanide standard **(B)** Effect of MWCNT (5 µL) on LD peak resolution in CV. **(C)** Effect of Nafion membrane concentration on LD peak in CV.

Analytical performance: We then evaluated the assembled biosensor and verified that its calibration curve and sensitivity meet the requirements for continuous LD monitoring under physiological and Parkinson's disease-relevant conditions. The sensor showed a reliable increase in both CV peak current and chronoamperometric current with increasing LD concentration (**Fig. A-B**), leading to a calibration curve with an R^2 value of 0.98 (**Fig. 5C**). Critically, the sensor was able to adequately predict LD concentrations in the range of 2 to 50 µM, encompassing both physiologically and therapeutically relevant LD levels (Nutt & Woodward, 1986; Probst et al., 2024).

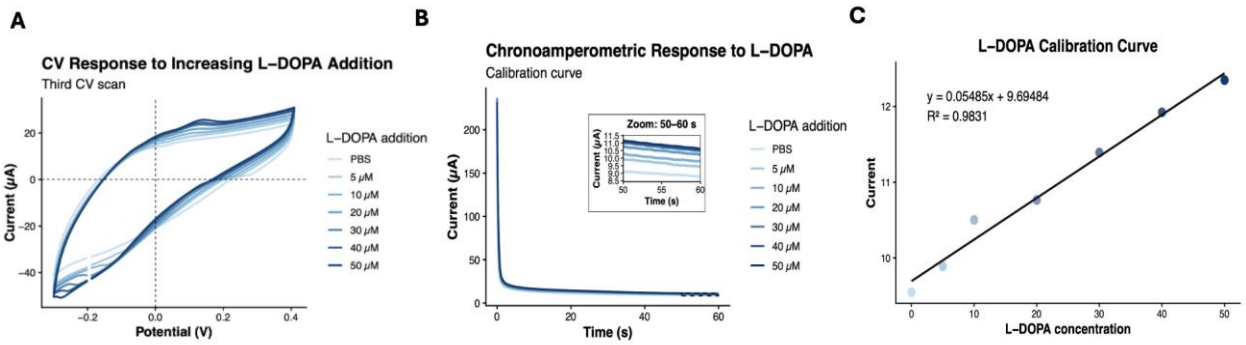


Figure 5. (A-B) Effect of increasing LD on CV and chronoamperometry **(C)** LD calibration curve, taken from final currents from chronoamperometry measurements.

3.2. Reliability of Sensor Output

3.2.1. Technological Novelty of Reliability Concept

Tyr@ZIF-8 layer: This layer provides the stability needed for reliable signal output. We encapsulate tyrosinase within ZIF-8 via biomimetic mineralization, a one-pot reaction in which microporous ZIF-8—made of Zn^{2+} ions and 2-methylimidazole (2-MI) linkers—crystallizes around the enzyme. Briefly, tyrosinase's net negative surface charge drives interaction with Zn^{2+} ions, nucleating local ZIF-8 growth (Wei et al., 2022). Unlike conventional surface adsorption, this 3D encapsulation reduces enzyme leaching and protects against degradation, substantially improving operational and storage stability (Wei et al., 2022). Encapsulated Tyr@ZIF-8 has shown excellent catalytic performance toward LD with greater resistance to temperature and pH changes than bare tyrosinase (Chen et al., 2026). Further, ZIF-8's aperture (<0.34 nm) is smaller than most proteins and can physically exclude interfering macromolecules while still allowing L-Dopa transport. Previous studies have confirmed selectivity against uric acid, glucose, lactate, and ascorbic acid (Wei et al., 2022; Xiao et al., 2022). However, encapsulation poses trade-offs between protection and enzyme accessibility: the Zn^{2+}/2-MI ratio determines whether the framework forms a porous sodalite or dense diamondoid structure, which can restrict substrate access, reduce activity, and raise the process's Michaelis constant (Talosig et al.,

2024; Wei et al., 2022; Xiao et al., 2022). A-Levo optimizes this trade-off using a 35:1 2-MI/Zn^{2+} molar ratio with tuned ZIF-8 loading to balance enzyme stability with the catalytic activity needed for reliable signal detection.

Nafion layer: Nafion supports the sensor by mechanically stabilizing the structure and preventing leaching. Its negative charge repels anionic interferents that could disrupt the signal or degrade the enzyme/ZIF-8 layer, and as the outermost layer it also acts as a biocompatible barrier against biofouling (Kelarakis, 2025).

Calibration strategy: A-Levo uses a three-pronged calibration approach. **(1) Sensor-to-sensor**: manufacturing variation between devices is corrected using a linear model with sensor-specific slope/offset parameters (**Appendix 8.1.2.**) (Forlenza et al., 2019). **(2) Person-to-person**: since no established population-level conversion exists between ISF and blood LD, we pair HPLC-measured blood levels with their corresponding ISF signal using a linear model with a time-lag term to be characterized in future PK studies (**Appendix 8.1.2.**) (Saha et al., 2026; Zhou et al., 2025). **(3) Drift and biofouling**: rather than requiring daily blood draws, we use a redundant working electrode — identical to the active electrode but lacking active tyrosinase — measured in parallel to subtract background drift and biofouling (Brister et al., 2008; Zhang et al., 2022). To further address tyrosinase-associated dopaquinone accumulation on the active electrode, we periodically apply a negative voltage to electrochemically regenerate L-dopa and clear the surface. Finally, though we expect ZIF-8 stabilization to help prevent enzymatic decay, we plan to apply an average decay correction onto the background-subtraction model (Hu et al., 2025).

3.2.2. Technical feasibility of reliability concept

ZIF-8 synthesis: To validate the proper synthesis of encapsulated Tyr@ZIF-8, we performed several structural characterization techniques, including powder X-ray diffraction (PXRD) and electron microscopy (SEM and TEM). **PXRD** diffraction angles for both Tyr@ZIF-8 and a blank ZIF-8 control matched those of simulated PXRD scans, confirming proper MOF geometry (**Fig. 6**). Critically, the decrease in peak intensity at 7 degrees—representing one of ZIF-8's characteristic crystal planes—indicates loss of crystalline order, reflecting both enzyme incorporation and potential structural defects to be further studied. **SEM** images show polyhedron-shaped ZIF-8 particles with single-micrometre diameters (**Fig. 7A-B**), consistent with literature-reported ranges of 50 nm–10 µm (Gao et al., 2018; Jongert et al., 2024; Lyu et al., 2014; Wei et

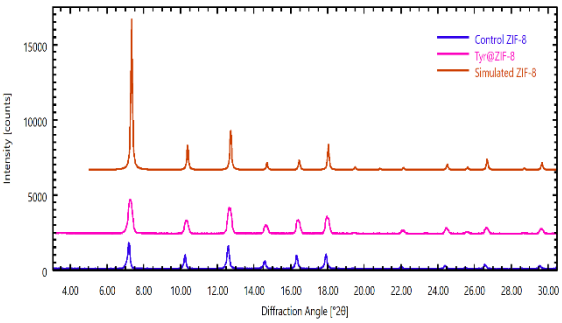


Figure 6. PXRD result for ZIF-8 control and Tyr@ZIF-8 compared to a simulated ZIF-8 structure (Bruker database).

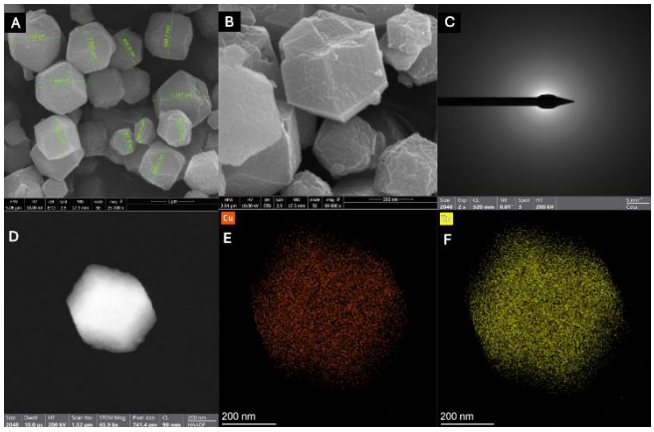


Figure 7. Structural characterization of Tyr@ZIF-8, synthesized with a 35:1 ratio of 2-methylimidazole: zinc acetate. **(A-B)** SEM characterization of Tyr@ZIF-8. **(C-F)** TEM characterization of Tyr@ZIF-8 with selected area diffraction pattern, high-angle annular dark field imaging (HAADF), and EDAX scans of copper in red (Tyr) and zinc in yellow (ZIF-8).

al., 2022). Critically, free tyrosinase (120 kDa) typically appears on SEM as irregular ~0.5 µm particles (Zdarta et al., 2020), yet these are absent from most ZIF-8 particle surfaces, potentially indicating enzyme encapsulation. TEM supports this result: the observed diffuse concentric-ring halos (**Fig. 7C**) are characteristic of a partially amorphous material, consistent with enzymes contributing to the internal structure (Roslova et al., 2023). Equally, energy dispersive X-ray analysis (EDAX) mapping shows copper atoms distributed within the area spanned by zinc and at lower density than zinc (**Fig. 7E-F**) — evidence that copper-containing tyrosinase is present within the zinc-containing ZIF-8 particles, not merely coating their exterior. This conclusion was informed by Dr. Hatem Titi of McGill University.

Interferent testing: Interferents including dopamine, uric acid and glucose caused only minimal differences (1% bias) in current response, demonstrating our sensor's ability to reject signals from structurally similar and electroactive interferents in ISF (**Fig. 8**). See **Appendix 8.1.3.** for a more in-depth discussion of interferent prevention.

Long-term signal stability: Additionally, the sensor remained stable after being stored at room temperature for a week, indicating sufficient shelf stability (**Fig. 8**). Future in vivo stability testing will confirm long-term feasibility in ISF.

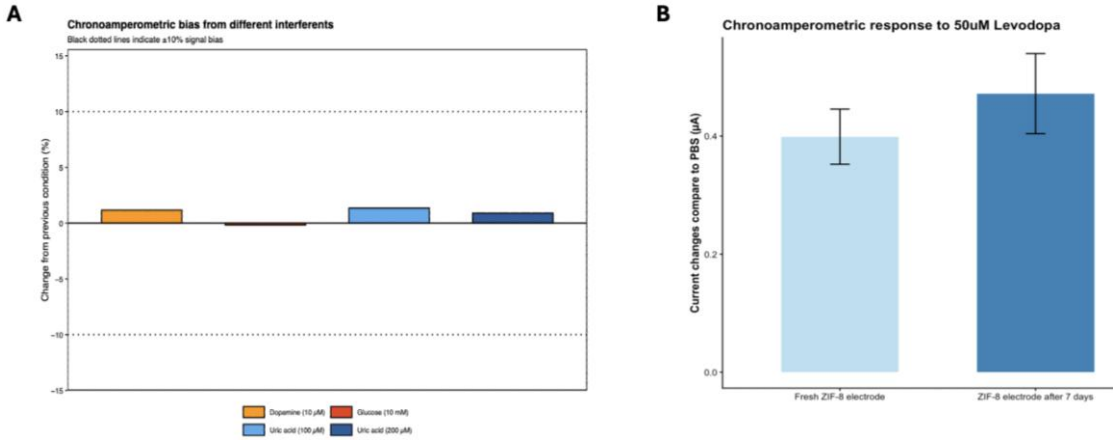


Figure 8. (A) Chronoamperometric response to subsequent addition of interferents: dopamine (orange), glucose (red), low concentration uric acid (light blue), and high concentration uric acid (dark blue). **(B)** Chronoamperometric response to 50uM Levodopa after 7 days storage at room temperature.

3.3. Original Contributions

Student's Section

Our team developed a novel continuous biosensor for Parkinson's management. Guided by an engineering design approach, we started by defining the problem using in-depth literature review and consultations with stakeholders and experts, and identified interference and stability as major issues towards continuous levodopa sensing. In this vein, we considered many approaches before settling on our main novelty, enzyme encapsulation inside of a metal-organic framework. This method allowed us to tackle the main issues that we had identified and deliver a credible and novel device. Through iterative design, guided by further research, advice from experts, and our own experiments, we improved our sensor piece by piece to come to the current design.

As an additional novelty, our team assessed early on that the biosensor could not solve the issue of Parkinson's dosing on its own. To obtain a full pharmacokinetic picture of levodopa dosing, symptom detection was necessary. As such, we explored multiple methods of symptom detection before settling on an IMU for motor symptom detection.

Our device was conceived, designed, tested, and iterated upon by the team. A summary of alternatives explored during our design process is included in **Appendix 8.2.7.** Outside help was limited to references to the literature and existing technology, stakeholder and specialist consultations, and feedback from experts and advisors.

Supervisor's Section

I supervised this team throughout the year and I can attest that the biosensor's design and development were driven by the students themselves. My involvement was limited to providing resources, ensuring lab access and safety, connecting them with relevant experts, and providing feedback on the data they collected.

Through their own research, the students evaluated multiple sensing approaches before selecting MOF-based methods, and later settled on enzyme encapsulation within a metal-organic framework. They also recognized on their own that tremor detection would be necessary, and independently pursued IMU-based symptom detection.

The team independently built, optimized, and tested their device. Where outside input occurred, it took the form of literature, stakeholder conversations, and occasional expert consultation.

3.4. Bonus Criteria Innovation

Our team identified a core problem: managing levodopa today is largely guesswork. Because each patient has a different therapeutic window, dosage must be individually tuned, but this is currently done through trial and error using self-reported symptom diaries. Our goal is to provide objective data to determine each patient's therapeutic window and ideal dosage schedule. Unfortunately, a continuous drug sensor isn't enough: it shows us pharmacokinetics (how drug levels change), in **Fig. 9A**, but not pharmacodynamics (how the patient responds). Thus, we plan on combining our levodopa continuous sensor with a wrist-worn IMU that tracks motor symptoms in real time. Symptoms can be detected via spectral power in specific frequency bands, with tremors concentrated in the 4-7 Hz band, while dyskinesia is found in the 0.25-3 Hz range (Dai et al., 2015).

To link drug levels and symptoms, we propose a two-compartment PK/PD model (Harder & Baas, 1998; Suksai et al., 2026). The body is modeled as two compartments: a central compartment and an effect compartment representing levodopa in the brain. Levodopa absorption, clearance, and movement between compartments follows standard first-order kinetics. From there, a sigmoidal curve converts effect compartment concentration to predicted symptom severity. Full equations and justifications are provided in **Appendix 8.1.4.**

Fig. 9B demonstrates the use of the model to obtain patient tremor response from a given dosage schedule, including time delay between levodopa concentration and response. In practice, the dual-sensor data would be fit to the model to obtain a patient's specific model parameters and could then be used to simulate the effect of any dosage schedule. In addition, this tool could be used to track Parkinson's disease progression and drug resistance.

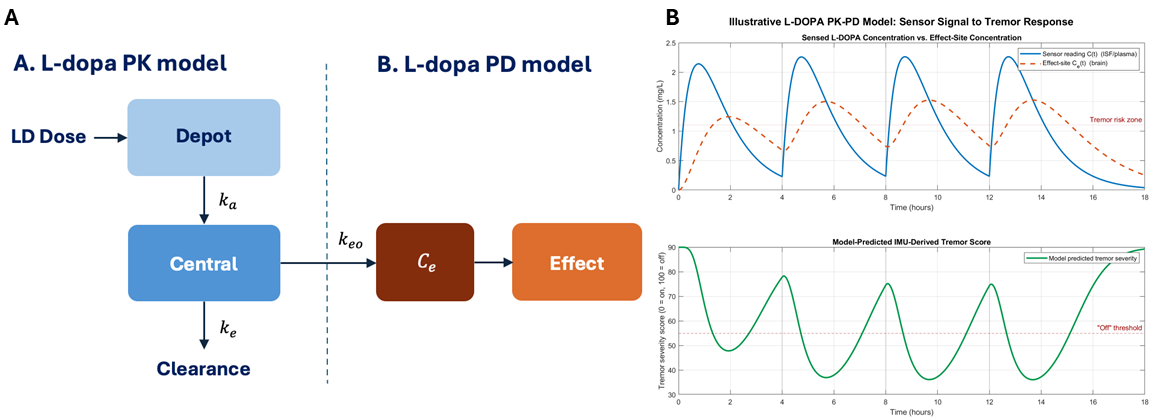


Figure 9. (A) PKPD Model Schema **(B)** Representative simulation of a patient's response to levodopa dosing every 4 hours. Top: Systemic and effect-side levodopa concentrations. Middle: predicted tremor severity.

4. TP award: Translation potential

4.1. Customer interviews

4.1.1. Identification of Potential Stakeholders

Through patient consultations, A-Levo identified potential stakeholders by tracing each patient's lived care journey and mapping the complete Canadian PD management ecosystem. Stakeholders were contacted through personal referrals, patient advocacy communities, and McGill clinical and academic networks across multiple provinces. As patients discussed their individual PD care journeys, all relevant stakeholders involved in daily disease management and medication adjustment were identified. We identified stakeholders across direct care (patients, caregivers), clinical management (neurologists, MDS, pharmacists, GPs, physiotherapists), and systemic infrastructure (payers, insurance, procurement), ensuring that no critical perspective was overlooked. To account for regional variations in healthcare regulation, we consulted stakeholders across different provinces, ensuring we built a solution fit for nationwide PD support. A network map visualizing the relevance and roles of each stakeholder in the Canadian PD care ecosystem is provided in **Appendix 8.2.1.**

4.1.2. Interview Approach and Execution

We conducted structured interviews, consisting of a prepared questionnaire tailored to each stakeholder's experience or expertise, followed by an open-ended discussion. The questionnaire and discussion topics evolved as we recurrently delved deeper with previously consulted stakeholders and as we developed our use case. Our semi-structured interview system reproducibly uncovered stakeholders' experiences, challenges, unmet needs, and desired improvements, while enabling consistent discovery of fresh insights. We documented discussions manually and with meeting audio transcription software to ensure no nuances were overlooked. After each interview, we summarized key points, comparing them against our previous assumptions, and formulated corresponding implications for our use case and design. All consultations were conducted with informed verbal consent, with participants made aware that their insights may appear in academic and competition deliverables. Stakeholders are identified by name only where explicit permission was granted. Our consultation process continued until themes converged consistently across stakeholder types, with later interviews confirming established insights rather than surfacing new ones. Full interview guides can be found in **Appendix 8.2.2.**

4.1.3. Interview Results and Conclusions

Across consultations, we heard problems from one stakeholder and learned the cause from another, elucidating that the greatest challenges in PD care are cyclical, each reinforcing the next. We recognized that disrupting the root of this cycle, the absence of objective data, would cascade improvements across every node. A visual graph illustrating how A-Levo breaks the cycle of issues is provided in **Fig. 10** and **Appendix 8.2.3**

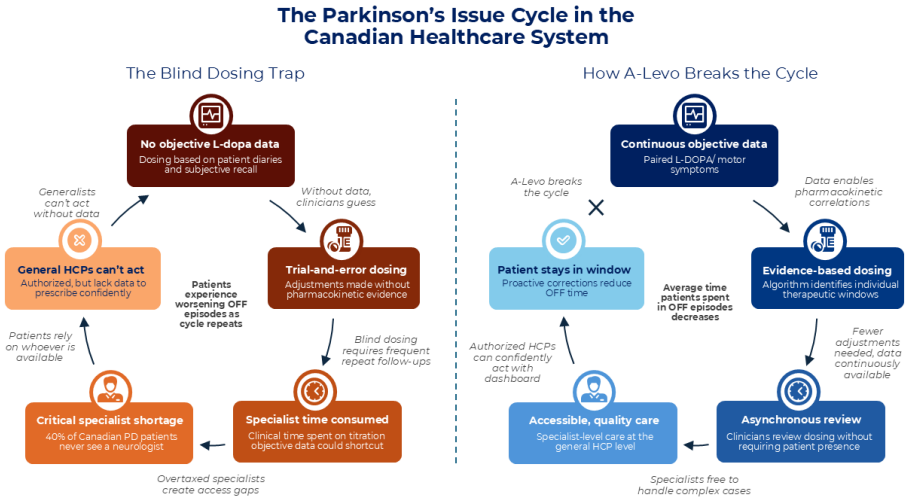


Figure 10. Schema of Parkinson's issue cycle from stakeholder consultations.

In our initial consultations with patients and caregivers, we consistently encountered the following pain points:

1. Patients expressed that meaningful dosing adjustments require a neurologist or an MDS. Yet as Adrian Ziemczonek's clinic observed firsthand, patients routinely wait 6–12 months for that appointment.
2. While awaiting medication adjustments by their neurologist, patients described struggling to perform tasks most take for granted (walking down stairs, drinking hot coffee, buttoning a shirt) without assistance.
3. Out of necessity, long specialist wait times force patients to shift their primary PD care to more accessible, non-specialized HCPs (GPs and pharmacists).

Following the patient's care pathway, we consulted the GPs, pharmacists, and physiotherapists who fill the gap left by specialist inaccessibility. Pharmacists and GPs alike noted patients struggle to communicate their experience for two reasons:

1. The elderly majority found it difficult to reliably recall the timing of frequent daily events, including medication doses, meals, and symptom onset, which makes even their best efforts at reporting incomplete.
2. Many patients, unfamiliar with the full spectrum of PD symptoms, fail to report relevant experiences to their HCPs due to not recognizing them as disease-related.

To inform treatment, some patients are asked to keep timestamped diaries of their symptoms and medication use. Even the most diligent diary-keepers leave significant gaps, despite the moments between entries being when the most clinically relevant fluctuations occur, making it difficult to inform treatment decisions. We discovered that in two Canadian provinces, Quebec and Alberta, pharmacists have legal prescribing authority for levodopa. However, without objective pharmacokinetic data to guide them, few exercise it confidently. Similarly, GPs hold full levodopa prescribing authority nationwide but, without PD-specific expertise, rarely initiate or adjust complex regimens. An example patient diary is provided in **Appendix 8.2.4**, and a table detailing the levodopa prescribing authority and patients' accessibility to different HCPs in Canada is provided in **Appendix 8.2.5.**

MDSs reaffirmed that Parkinson's treatment is especially difficult due to interpatient variability and nonlinear changes of therapeutic levodopa windows throughout disease progression. In addition to the pain points voiced by the other HCPs we consulted, MDSs see approximately 12 patients per session (Only 20 minutes per appointment to assess, adjust, and document), leaving insufficient time to comprehensively evaluate the nuanced fluctuations that inform levodopa management. Specialists are then left to rely on trial-and-error methodologies to find optimal medication dosing, which entails repeat appointments to reassess the tested dosing plan and readjust as necessary. As reassessments add strain to the already extensive patient list for which specialists are responsible, it becomes a self-reinforcing burden that compounds the very access problem patients described.

HCPs across the ecosystem converged on a single primary unmet need: objective, continuous visibility into whether a patient's dosing plan is working and why, so they can develop more effective treatment plans without trial-and-error. Specialists consistently identified automated, continuous data collection as the most viable method of meeting that need. See **Appendix 8.2.6.** for other needs, pain points, and concerns addressed by A-Levo's design.

As clinical pharmacist Adrian Ziemczonek explained, isolated absolute levodopa concentration measurements provide no standalone clinical benefit because the therapeutic window differs from patient to patient and shifts continuously as the disease progresses. The pairing of continuous levodopa sensing with individualized motor symptom monitoring was validated by specialists as the approach most likely to yield clinically actionable identification of the therapeutic window.

We initially considered autonomic biomarkers (sweat, heart rate variability) for symptom state detection, but clinicians noted that these signals are too easily confounded

by exercise, stress, and temperature to reliably isolate PD-specific patterns. See **Appendix 8.2.7.** for other design choices we considered but rejected after expert evaluation.

This finding informed our choice of kinematic sensing (accelerometer and gyroscope data, which have well-established correlations with symptom states such as bradykinesia, dyskinesia, and tremor) as the most effective motor-detection modality, rather than autonomic or biochemical proxies. Specialists emphasized that motor symptom profiles vary by PD stage and subtype, underscoring the need for individualized motor-levodopa correlations rather than population-level assumptions.

Our consultations elucidated that Parkinson's care in Canada does not lack treatment options, but it lacks the data needed to use them effectively. That is the gap A-Levo is built to close.

4.2. Design of validation study

4.2.1. Selection of the problem

Current monitoring of Parkinson's disease relies on intermittent neurologist visits and subjective recall of symptoms. Across interviews with patients and professionals in the Parkinson's management ecosystem, the same core frustration emerged: medication adjustments are made based on singular brief appointments, reconstructed from a patient's fluctuating clinical picture, rather than on evidence gathered during those fluctuations. Clinicians described relying on trial-and-error dosing because they lack the data to inform when and why a patient's response to levodopa breaks down between visits. This lack of objective data perpetuates the Parkinson's issue cycle described in **Appendix 8.2.3.**, thereby directing A-Levo's value proposition: a way to objectively monitor patient experiences between appointments.

4.2.2. Conceptual design and use case

Our interviews confirmed that levodopa concentration measurements alone cannot inform clinical decision-making because it does not indicate whether symptoms were adequately controlled at the time. Both the pharmacokinetic and motor-state information are therefore required. There is no existing wearable that currently combines pharmacokinetic and motor symptom monitoring. To address this gap, we propose A-Levo, a wearable biosensor that continuously measures interstitial levodopa concentrations via an adhesive skin patch and pairs this with continuous motor state tracking from a companion wrist-worn sensor, providing clinicians with objective, time-stamped drug-response and tremor data between visits. The proposed clinical workflow of A-Levo is demonstrated in the following diagram.

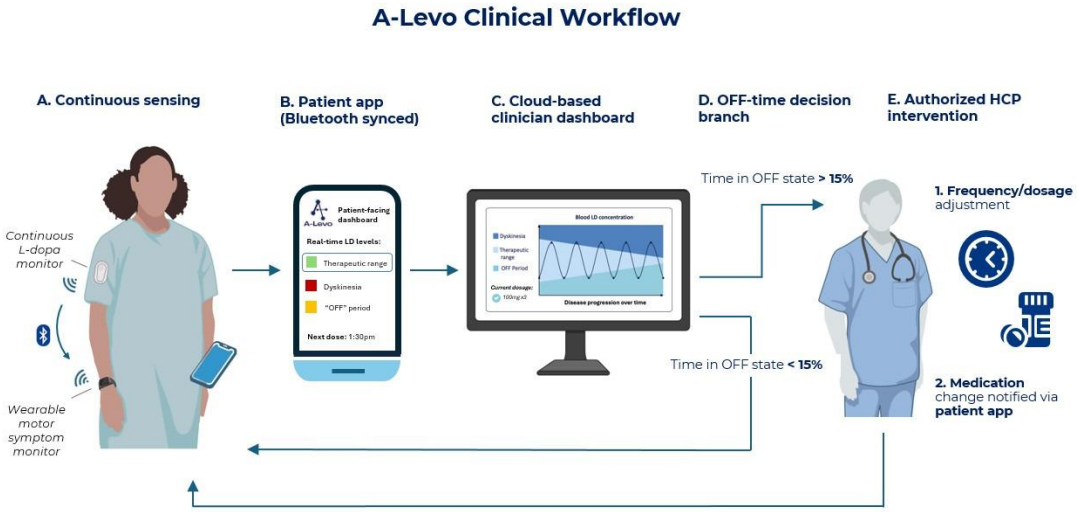


Figure 11. The patient wears the biosensor patch, replacing it once every 10 days. Instead of relying on patient memory, A-Levo collects objective levodopa and motor data. This data is synced to a companion smartphone app and then uploaded to the clinical dashboard. Neurologist-built algorithms identifies the patient's personal therapeutic window and evaluates dosing plan quality, supporting both PD-specialized and authorized generalist HCPs in medication adjustment. The system escalates to the patient's HCP only when intervention is needed, enabling proactive, data-driven dosing adjustments without requiring a clinic visit. The clinician retains full prescribing authority at every step.

As illustrated in **Appendix 8.2.3**, A-Levo disrupts the entire Parkinson's issue cycle by enabling objectively informed dosing decisions and proactive medication management. This cascades into reducing specialist burden, increasing quality of generalized HCP care, and improving overall patient quality of life. The following study aims to validate that paired continuous levodopa and motor-state monitoring enables clinician's to more accurately identify patient-specific therapeutic windows and make more confident dosing decisions, relative to concentration data alone.

4.2.3. Validation Study Design

We hypothesize that pairing continuous levodopa measurements with continuous motor-state data will improve clinician's ability to identify patient-specific therapeutic windows and make confident dosing decisions, when compared to concentration data alone. To test this hypothesis, we will conduct a pilot feasibility study with movement-disorder neurologists, using the mock-data instrument described in **Appendix 8.3.1**.

A minimum of 8–10 movement disorder specialists, neurologists, and general HCPs will each review two randomly assigned simulated patient cases. For each case, they will evaluate three graph versions containing progressively more information. Each case displays a single day of waking-hour data alongside patient context (disease stage and subtype), reflecting what clinicians would see on the A-Levo dashboard. Three graph

versions are presented: (1) levodopa concentration only, (2) levodopa concentration with sporadic patient-reported symptom logs, and (3) levodopa concentration with continuous motor state data and predicted therapeutic window, representing A-Levo's dual-detection output. See **Appendix 8.3.2** for the Target Patient Profile for adopting patients of A-Levo.

For each graph version, clinicians indicate — in Yes/No/Unsure format with open comment space — whether they would confidently adjust the patient's dosing regimen, whether they can distinguish wearing-off from dyskinesia onset, and what additional information they would need, then rate their overall confidence on a 1–5 scale. For the dual-detection version only, clinicians also identify the concentration threshold or percentage change from baseline at which they would flag the patient for review. Full questionnaire in Appendix 8.3.1.

Our primary outcome is clinician confidence in dosing decisions, measured using the (Yes/No/Unsure) response and 5-point confidence rating, comparing the levodopa-only and dual-detection conditions. The secondary outcomes are the comparison between the sporadic and continuous data presentation (Graph 2 vs Graph 3), the clinician's ability to distinguish wearing-off episodes from dyskinesia, and the dosing adjustment threshold values as seen in **Appendix 8.3.1**. We will first test for an overall difference across the three paired conditions and will group data separately for each type of clinician.

The hypothesis is supported if a majority of clinicians report higher confidence and clearer dosing decisions in the dual-detection condition than in either comparator. The study will be conducted under institutional ethics approval. Future work will expand inclusion criteria to assess benefit across a broader range of disease stages.

Secondary Validation: Use Experience

To evaluate long-term wear comfort, 10 patients will wear non-functional mock versions of the A-Levo patch and wristband (matching the device in size, shape, and weight) for three weeks. Patients will rate comfort, ease of application, and usability on a 1–5 scale, compared against current monitoring practices and validated quality of life measures including the PDQ-39., a 39-item surgery covering quality of life to mobility.

In parallel, 8–10 clinicians will evaluate a prototype dashboard, rating ease of navigation, data clarity, clinical usefulness, and likelihood of adoption. This interface will also be reviewed by patients to assess whether different levels of provided information affect interpretation and anxiety. Patients will also review three dashboard interface versions — a simple colour-coded display, a fully detailed numerical graph, and a hybrid with optional expanded detail — rating each on interpretability, emotional response, and UI preference.

4.3. Bonus Criteria: Translation Potential

From the outset, A-Levo was built with the explicit intention of becoming a viable commercial venture, which shaped every decision from stakeholder consultations to intellectual property, regulatory planning, and market entry strategy. We are a multidisciplinary team at the intersection of bioengineering, clinical science, and commercialization, built to reflect the full translation journey.

We entered multiple pitch and innovation competitions to pressure-test our concept and receive Canada-centric commercialization guidance. Notably, winning the Vitruvius Launchpad Prize at the McGill Clinical Innovation Competition provided A-Levo with funding and a six-month in-kind residency at the Vitruvius Medtech Venture Studio, along with hands-on mentorship in product development, regulatory strategy, clinical translation, and venture formation. The full traction milestone timeline is provided in **Appendix 8.4.1.**

Our consultation process was designed not only to inform device design, but to validate our commercial assumptions directly with the people who will prescribe, purchase, reimburse, and use A-Levo. Consultations spanned across multiple Canadian provinces, ensuring our strategy reflects the realities of nationwide implementation. Our clinical proposition is detailed in the Customer Interviews section (4.1).

On the industry side, we consulted partners in consumer wearable hardware, wearable electrochemical sensing, and pharmaceutical development to shape both our technical decisions and commercial model. Two tables detailing explored design choices implemented and rejected are provided in **Appendix 8.2.6** and **8.2.7**, respectively.

Our commercial model generates revenue through two recurring streams: disposable sensor patches and a clinical analytics platform subscription, with the patient interface being delivered via a smartphone app. At approximately C$2,000 per patient per year, A-Levo pays for itself by preventing fewer than one hospitalization annually, and our cost-effectiveness proxy of approximately C$25,000 per quality-adjusted life year compares favourably against existing advanced therapies. Full commercial model, market sizing, health economics, and competitive positioning are provided in the **Appendices 8.4.2**, **8.4.3**, **8.4.4**, **8.4.5**, respectively.

Regulatory strategy has been a design constraint from the beginning. A-Levo is pursuing a Canada-first pathway, prioritizing the Canadian public health system and maintaining Canadian intellectual property sovereignty. Our regulatory strategy is detailed in **Appendix 8.4.6.**

Our payer strategy is designed around getting A-Levo to the patients who need it most, through the systems that already serve them. Provincial government adoption is the primary coverage pathway, supported by federal research funding to build the clinical evidence base. Direct procurement at our beachhead movement disorder and neurology centres bridges the gap in the interim. Full payer landscape analysis is detailed in **Appendix 8.4.7.**

A-Levo is a company in formation. Our near- and long-term commercialization milestones are outlined in **Appendix 8.4.1** and **8.4.6**. The Parkinson's issue cycle caused by a lack of objective data has plagued patients and HCPs in Canada for over 50 years, and we believe the solution is finally within reach. A-Levo is ready to break the cycle.

5. Team and Support

5.1. Contributions of the team members

Dr. Sebastian Wachsmann-Hogiu (Project Supervisor) ensured that this project could occur, providing valuable feedback and guiding lab efforts and sensor design.

Julianna Farias (Team Mentor) was an invaluable addition to the team, helping guide both research and TP efforts and providing key insights into how to bring A-Levo to market.

Syphax Ramdani and **Siqi Mi** (Team Leads) were responsible for the global organization of the project, running weekly meetings and spearheading lab efforts including MOF synthesis, electrochemical validation and sensor design.

Lucy Wiggers and **Gabriel Linaje-Ferrel** (Research Leads) organized research efforts and and assisted heavily in MOF synthesis, electrochemical validation and sensor design.

Jung Hao Cau and **William Prato-Deriet** (TP Leads) oversaw consultations with key stakeholders and spearheaded A-Levo's business and go-to-market strategy.

Juan Manuel Rocha Angel, Ruolin Hu, Naia Kim, Lanyun Wu, and **Yuzuha Isetani** (Research Team) were all invaluable to sensor and creation, contributing weekly research ideas and participating in lab efforts.

Daniel Tang, Yazan Abu-Al-Failat, Olivia Del Degan, Ellie Griffiths-Barnhart, and **Tesnim Obey** (Translation Potential Team) were the workforce behind A-Levo's TP efforts, connecting with key stakeholders and outlining design considerations.

5.2. People Who Have Given Support

On the research side, **Dr. Hatem Titi** provided mentorship and access to PXRD equipment; **Hudson Bicalho** and **Adam Giles** helped guide MOF synthesis and microneedle design, respectively; **Dr. David Liu** (McGill Facility for Electron Microscopy) assisted with SEM and TEM operation; **Marinieve Montero** and **Felipe Perez** provided lab access and supervision. Several key healthcare professionals guided our TP efforts, including **Dr. Ron Postuma, Adrian Ziemczonek, Sally-Anne Stelling,** and **Sawsan Ibrahim.** The personal experiences and stories of **countless patients** across Canada (kept anonymous) were invaluable.

5.3. Sponsors and Partners

Several organizations provided financial and institutional support that ensured that this project could occur, including **McGill BioDesign,** the **McGill Department of Bioengineering** and **McGill Faculty Medicine and Health Sciences**, the **McGill Clinical Innovations Platform**, the **McGill Dobson Centre for Entrepreneurship**, the **McGill Junior Hong Kong Canada Business Association** and **Vitruvius Venture Studios.**

6. Final Remarks

Building A-Levo has been a transformative experience; what began as a curiosity-driven exploration of continuous monitoring technology grew, through months of conversations with patients, clinicians and PD experts, into a project we now see as much as a human problem as an engineering one. We are proud of what we built this year, but we see A-Levo as a starting point rather than a finished product. Looking ahead, our priorities are validating sensor performance *in vivo*, integrating our biosensor with motion-tracking data, and continuing to foster stakeholder relationships as we move toward clinical translation.

We are deeply grateful to Julianna Farias and Dr. Hatem Titi for their mentorship; to Dr. Sebastian Wachsmann-Hogiu, Marinieve Montero, and Felipe Perez for lab access and resources; to Dr. David Liu at the McGill Facility for Electron Microscopy for microscope operation; to McGill BioDesign, the McGill Clinical Innovations Platform, the McGill Dobson Centre for Entrepreneurship, the McGill Junior Hong Kong Canada Business Association and Vitruvius Venture Studios for financial support; to the patients, caregivers, and clinicians who generously shared their time and experiences with us; and to the SensUs organizing team for creating a competition that enables students to build real solutions to real problems.

Finally, thank you to every member of our team for a year of long lab days, endless troubleshooting, and genuine collaboration. This project would not exist without each of you. We are excited for the next chapter of A-Levo will bring!

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8. Appendix

8.1.1. Justification of Microneedle Design Choices

An in-depth exploration of microneedle dimensions is presented in the following table:

Design Parameter	Chosen Value	Justification
Needle length	1000 µm	Balances ISF access with patient comfort. Full skin penetration (stratum corneum + epidermis + dermis) would require up to ~2150 µm, and deeper layers hold more ISF (Kim et al., 2024). However, length has the largest effect on pain; studies showed that a 3-fold length increase causes a 7-fold increase in perceived pain (Gill et al., 2008). 1000 µm was thus chosen as the best compromise, informed by consultation with Adam Giles (McGill University).
Needle radius	30 µm	Smaller tip radius improves mechanical strength and reduces the force needed to pierce skin, per literature on microneedle mechanical optimization (Davis et al., 2004). Radius has no significant effect on patient pain.
Wall angle	80 °	Larger wall angle improves resistance to insertion forces (0.1–3 N) and everyday mechanical stress without deforming or fracturing (Davis et al., 2004). No significant effect on pain perception.
Wall thickness	58 µm	Larger wall thickness increases mechanical strength and safety margin against fracture during insertion and daily use (Davis et al., 2004). No significant effect on pain perception.
Material	Medical-grade stainless steel	Metals offer strong biocompatibility, ductility, and mechanical strength; stainless steel specifically balances manufacturing cost with high versatility and reliability compared to other commonly used materials (Kim et al., 2024).

8.1.2. Calibration Model Equations

A more in-depth discussion of sensor calibration, including linear calibration models, biofouling prevention and future directions through device scale-up, is presented in this section.

Sensor-to-sensor calibration: to prevent variability between sensor readouts due to manufacturing differences, factory-level calibration will be employed. In practice, this will involve testing each sensor against simulated ISF solutions of known L-dopa concentration, and fitting the response to the following function:

$$LD_{ISF}(t) = m_{sensor}(I(t) - I_0) + b_{sensor}$$

Here, $LD_{ISF}(t)$ are the ISF L-dopa levels over time, $I(t)$ is the measured current at a given time, and I_0 is the baseline current. We hardcode the resulting sensor-specific parameters, m_{sensor} (slope) and b_{sensor} (baseline offset), into that sensor's calibration function, eliminating sensor-to-sensor error.

Person-to-person calibration: to account for physiological and pharmacokinetic differences between patients, the calibration step between ISF L-dopa (LD_{ISF}) and blood L-dopa levels (BLD) will be performed individually for each patient, using HPLC data and following:

$$BLD(t) = m_{patient} \cdot LD_{ISF}(t - \tau) + BLD_0$$

Here, $m_{patient}$ and BLD_0 are patient-specific parameters, and τ is the blood-ISF time lag, which will be validated during in vivo PK studies (reported in the literature as approximately 12–15 minutes in rats (Zhou et al., 2025)). This model builds directly on the factory calibration above and deliberately avoids conflating sensor-level and patient-level sources of error—a distinction that will be critical for future sensor optimization.

Future calibration directions: Beyond the current calibration approach, several optimizations are planned as we bring A-Levo through clinical trials and scale-up: ***(a)*** *Eliminating sensor-to-sensor calibration:* Sufficient batch-level reproducibility— which can be achieved through manufacturing process optimization (e.g. ensuring precise layering of electrode functional components) — would allow us to apply a fixed set of parameters across an entire sensor batch, rather than calibrating each device individually (Forlenza et al., 2019). ***(b)*** *Moving to a two-compartment PK model:* L-dopa pharmacokinetics typically show more complex, nonlinear behaviour, which a two-point linear calibration cannot fully encompass. Adopting a more sophisticated model, such as a two-compartment model between ISF and blood, would prove beneficial once sufficient clinical trial data is available (Zhou et al., 2025). ***(c)*** *Eliminating external blood L-dopa measurements:* As large-scale datasets of blood L-dopa concentrations become available, we can use this data to derive average best-fit calibration parameters, or to train an ML model that continuously adjusts calibration based on L-dopa levels and even other continuously measured physiological signals (PD symptoms, blood pressure, etc.) (Saha et al., 2026).

8.1.3. Overview of Key Interferents

While our sensor picked up negligible interference from key molecules such as dopamine, uric acid and glucose, a complete list of potential interfering molecules is presented below, alongside our proposed selectivity mechanisms to be further validated.

Interferent Type	Interferent name (s)	Mechanism of interference	Proposed mechanism of selectivity
Endogenous L-dopa metabolite	Dopamine, 3-O-Methydopa, epinephrine, norepinephrine, 3,4-dihydroxyphenyl ethanol, 3,,4-dihydroxyphenylacetic acid, homovanillic acid	Structurally similar to L-dopa (catechol or monophenol) and may interact non-specifically with tyrosinase, producing a false positive signal	Our sensor's preliminary reliability against physiologically relevant dopamine concentrations suggests resistance to other structurally similar metabolites; if they prove non-negligible upon further testing, their signal contributions could be filtered out using differential pulse or square-wave voltammetry
Exogenous interferents commonly found in ISF	Glucose and other sugars, ascorbic acid, uric acid, acetaminophen	Ascorbic acid, uric acid and acetaminophen will not interact with tyrosinase, but may oxidize at the carbon electrode. Sugars are not electrochemically active, but present biofouling concerns	ZIF-8 size selectivity (larger sugars), Nafion (ascorbic acid, uric acid), background subtraction using the redundant working electrode (all)
Adjunct medication	Carbidopa, amantadine, chlorthalidone	May be introduced into the body alongside L-dopa at relevant concentrations (uM range)	Background subtraction using redundant electrode (amantadine, chlorthalidone); carbidopa may need to be directly accounted for due to its active catechol group.

8.1.4. Pharmacokinetic/Pharmacodynamic Modelling

Our PK/PD model simplifies the human body into two compartments: a central compartment representing most of the body, and an effect compartment representing the drug amount that is in the brain contributing to the measured symptom. Calibration between ISF and plasma allows us to use this simplification and avoid using a separate "peripheral" compartment.

Pharmacokinetics: Transport to and between compartments is modelled using first-order kinetics. As such, when levodopa is ingested, absorption of drug amount from the gut to the central compartment is modelled as:

$$\frac{dA_{gut}}{dt} = -k_a A_{gut}$$

Where A_{gut} is the gut levodopa amount and k_a is the absorption constant.

Levodopa in the central compartment is either absorbed from the gut or cleared using simple first-order kinetics:

$$\frac{dC}{dt} = -\frac{k_a}{V}A_{gut} - k_e C$$

Where C is the central compartment levodopa concentration, k_a is the absorption constant, k_e is the elimination constant, and V is an apparent volume,

Pharmacodynamics: An equilibration equation is used to link central and effect compartments. This matches with observations of a time delay between peak levodopa levels and occurrence of symptoms (Harder & Baas, 1998):

$$\frac{dC_e}{dt} = -k_{e0}(C - C_e)$$

Where C is the central compartment levodopa concentration, C_e is the effect compartment levodopa concentration, and k_{e0} is the equilibration constant.

Since it is expected that symptoms would plateau in the case of too little or too much levodopa, a sigmoidal relationship is used to tie the "effect" (in our case tremor or dyskinesia intensity) to effect compartment concentration:

$$E = E_0 - \frac{E_{max} C_e^{\gamma}}{C_{50}^{\gamma} + C_e^{\gamma}}$$

Where E is the "effect" amplitude, E_0 is the "effect" amplitude in the absence of levodopa, E_{max} is the maximum "effect" achievable with levodopa, C_e is the effect compartment levodopa concentration, C_{50} is the effect compartment concentration at half-maximal response, and γ is the Hill coefficient.

Using biosensor data (giving C) and IMU data (giving E), it is possible to determine patient specific parameters ($\frac{k_a}{V}$, k_e, k_{e0}, E_0, E_{max}, C_{50}, γ) using nonlinear least-sum-of-squares regression.

8.2.1. Stakeholder Groups in Parkinson's Care Pathway

Stakeholders were identified early in the design process to understand the different roles involved in Parkinson's care and guide customer interviews. This ensured key perspectives were considered when defining the problem and developing A-Levo.

Group	Role in PD Management	Examples
Patients	Track symptoms and manage complex daily medication schedules with limited objective feedback.	Levodopa-treated PD patients, particularly those with motor fluctuations.
Caregivers	Observe day-to-day changes, assist with medication timing, and liaise with the clinical team.	Spouses, adult children, home care aides.
General Practitioners / Family Physicians	First-line prescribers managing PD where specialist access is unavailable. Most accessible HCP, especially in rural areas.	Family physicians, general internists.
Pharmacists	Dispense levodopa, advise on dosing and interactions. Hold expanded prescribing authority in Quebec and Alberta.	Community and hospital pharmacists.
Neurologists	Specialist prescribers who initiate and adjust levodopa. Rely on patient recall and symptom diaries due to short appointment windows.	General neurologists in academic and community settings.
Movement Disorder Specialists (MDS)	Subspecialists for complex PD cases including advanced motor fluctuations and dyskinesia.	MDS neurologists at academic centres and designated PD clinics.
Nurses / PDNS	Monitor symptoms and educate patients between appointments. Administer levodopa in inpatient settings where timing errors are a known safety risk.	Neurology ward nurses, Parkinson's Disease Nurse Specialists.
Physiotherapists	Deliver exercise interventions proven to slow PD progression. Session effectiveness depends directly on whether patients are in an ON or OFF state.	PD-specialized physiotherapists in clinics and wellness programs.

8.2.2. Semi-Structured Stakeholder Interview Guides

Stakeholder consultations were conducted using semi-structured interview guides which combine a predetermined interview setup with the flexibility to ask open-ended, spontaneous follow-up questions. This approach provided consistency across interviews while allowing participants to share relevant experiences and enabling emerging insights to be explored through follow-up questions.

Patients and Caregivers

Purpose

The lived experience of Parkinson's disease is nuanced and individualized. It is important to identify challenges associated with levodopa therapy. These include personal symptom fluctuations, difficulties with communication among healthcare providers, and rejection of continuous monitoring technologies.

Representative Discussion Topics and Questions

- Can you describe what a typical day living with Parkinson's disease looks like?
- Can you describe what "wearing off" feels like, and how you recognize it?
- Which symptoms have the greatest impact on your daily activities?
- How do you currently determine when your medication is working well or beginning to lose effectiveness?
- What challenges do you experience when timing your medication throughout the day?
- Are there days when the same medication dose works differently? What factors do you think contribute to this?
- How do you currently communicate symptom fluctuations to your healthcare providers?
- How reliable do you find your own memory when describing symptoms that occurred several days or weeks earlier?
- Have you used symptom diaries or other tracking tools? What aspects work well, and what are their limitations?
- What information do you wish your healthcare team knew before your appointments?
- If a wearable device could monitor your condition continuously, what concerns or expectations would you have regarding comfort, wearability, privacy, and ease of use?

Guide Evolution

Early interviews focused on understanding current/modern daily disease management and medication experiences without introducing a proposed solution. These early interviews found that participants independently described difficulty recalling

symptom timing and medication response. A few patients discussed, in later interviews, the reliability of symptom diaries and the associated challenges, such as: identifying non-motor symptoms or factors influencing medication variability. Following development of the preliminary A-Levo concept, additional questions examined willingness to adopt passive monitoring technologies, preferred device placement, and expectations regarding patient access to biosensor data.

Neurologists, Movement Disorder Specialists, General Practitioners, and Pharmacists

Purpose

To understand current approaches to levodopa optimization, identify limitations in existing clinical decision-making and characterize information gaps affect treatment management within current clinical workflows.

Representative Discussion Topics and Questions

- Walk us through a typical Parkinson's disease follow-up appointment.
- How do you currently assess whether a patient is within their therapeutic window?
- What information guides decisions to modify levodopa dose or timing?
- Which patients are most difficult to optimize, and why?
- What are the greatest challenges associated with levodopa therapy in clinical practice?
- How reliable are patient diaries and self-reported symptom histories?
- What information do you wish you had available between clinic visits?
- Which current monitoring tools are most useful, and where do they fall short?
- If continuous levodopa monitoring existed, how would it influence your treatment decisions?
- Would levodopa concentration alone be clinically useful, or would correlated motor-state information also be necessary?
- What characteristics would make biosensor data clinically actionable?
- How could continuous monitoring best integrate into your current workflow?
- What concerns would influence adoption of this technology within routine clinical practice?

Guide Evolution

Initial discussions explored current medication optimization practices, therapeutic windows, and unmet clinical needs. Clinicians identified the absence of longitudinal data as a challenge. So subsequent interviews. So subsequent interviews investigated clinically useful monitoring metrics, acceptable performance requirements, workflow integration, and dashboard design. After the proposed A-Levo workflow had been developed, later

consultations focused on validating clinical utility, identifying implementation barriers, and understanding how objective monitoring could support collaborative care amongst HCPs.

Physiotherapists and Occupational Therapists

Purpose

To understand the role of rehabilitation professionals within Parkinson's disease care. This includes identifying barriers to multidisciplinary communication and determining how objective monitoring could support rehabilitation planning and coordinate patient management.

Representative Discussion Topics and Questions

- Can you describe a typical rehabilitation session with a Parkinson's disease patient?
- How does your role change as disease progression advances?
- At what stage are patients typically referred to your service?
- How do you currently communicate with neurologists, family physicians, or pharmacists?
- How frequently do medication fluctuations affect patient performance during rehabilitation?
- What information do you wish you had before beginning a treatment session?
- How do patients typically describe their symptoms, and how reliable do you find these descriptions?
- Are there important observations made during therapy that are difficult to communicate back to prescribing clinicians?
- What would improve coordination between rehabilitation professionals and the broader Parkinson's care team?
- How might continuous information regarding medication response and motor function influence your treatment planning?
- What concerns would you have regarding implementation of a continuous monitoring system?

Guide Evolution

The initial consultations discussed rehabilitation and its barriers. As physiotherapists consistently described observing medication-related motor fluctuations that were not routinely communicated to prescribing clinicians, later interviews explored interdisciplinary communication, functional indicators of medication effectiveness, and opportunities for improving care coordination. After introducing A-Levo to physiotherapists, consultations explored longitudinal motor-state utility in rehabilitation planning and communication with other healthcare providers.

Biosensor Researchers, Academic Experts, and Technical Advisors

Purpose

To inform biosensor architecture, sensing strategy, engineering feasibility, translation pathways, and commercialization considerations relevant to continuous levodopa monitoring.

Representative Discussion Topics and Questions

- What motivated the selection of your target analyte and sensing approach?
- How did you determine the most appropriate recognition element and transduction mechanism?
- Which performance characteristics most strongly influenced your design?
- What technical challenges arose during sensor development?
- How were issues such as signal drift, biofouling, calibration, and long-term stability addressed?
- What trade-offs existed between sensitivity, selectivity, wearability, and manufacturability?
- What lessons did you learn when translating laboratory prototypes toward clinical use?
- Which regulatory challenges proved most significant?
- How did clinician or end-user feedback influence your technology?
- What advice would you provide to a team developing a continuous levodopa biosensor?

Guide Evolution

Early discussions focused primarily on biosensor chemistry, transduction mechanisms, and analytical performance. As stakeholder consultations clarified the intended clinical application, later interviews increasingly emphasized the importance of wearable integration, engineering trade-offs, and regulatory and commercial challenges. Following refinement to the strategy, experts were asked to evaluate the feasibility of the selected biosensor architecture, identify remaining technical risks, and provide recommendations for future development.

Parkinson's Disease Advocacy Organizations

Purpose

Understanding community perspectives on Parkinson's disease management allows for a better device. The identification of barriers beyond individual clinical

encounters or in implementation allows for equitable access to new monitoring technologies.

Representative Discussion Topics and Questions

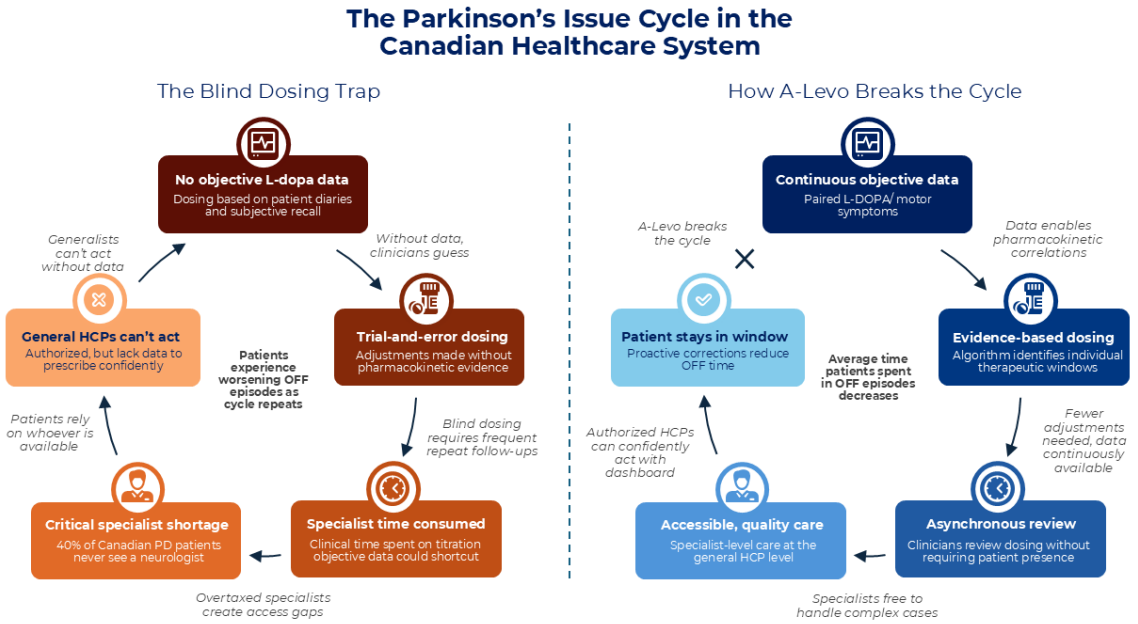
- What challenges are most frequently raised by individuals living with Parkinson's disease and their caregivers?
- What barriers exist when accessing specialist care?
- Which aspects of current Parkinson's disease management are most inadequately addressed?
- What educational resources do patients and caregivers most frequently request?
- What concerns do patients typically express regarding wearable medical technologies?
- What factors influence long-term adoption of new health technologies?
- Are there patient populations that may face greater barriers to accessing continuous monitoring technologies?
- How could patient organizations support implementation of new monitoring approaches?

Guide Evolution

The first discussions aimed to broaden overlooked needs of afflicted Parkinson's groups, instead of individual patients only. Recurring themes regarding delayed specialist access, caregiver burden, and health system variability emerged. Therefore, it was necessary that later interviews explored regional differences in care delivery, accessibility considerations, digital literacy, and strategies for equitable implementation through patient advocacy networks.

8.2.3. The Parkinson's Issue Cycle in the Canadian Healthcare System

Interview findings were mapped to identify relationships between stakeholder challenges across the Parkinson's care pathway. This helped distinguish root causes from downstream effects and informed the problem definition addressed by A-Levo.



8.2.4. Example Patient Diary

The provided example diary is based directly off a real anonymous patient diary provided from a clinical pharmacist consult.

Time	ON	Dyskinesia	OFF	Asleep	Meal	Medication
6–7 AM				X		
7–8 AM	X					X
8–9 AM	X				X	
9–10 AM		X				
10–11 AM	X					
11 AM–12 PM			X			X
12–1 PM			X			
1–2 PM	X				X	
2–3 PM	X					
3–4 PM	X					

8.2.5. HCP Prescribing Authority and Accessibility

Prescribing authority refers to the legal ability of healthcare professionals to initiate, modify, or discontinue medications. This overview clarifies the role each medical stakeholder can play in Parkinson's treatment decisions and how A-Levo's solution can support these professionals.

Levodopa Prescribing Authority & Accessibility of Healthcare Professionals in Canada

HCP Type	Prescribing Authority	PD Expertise	Patient Accessibility	A-Levo Role
Movement Disorder Specialist (MDS)	**FULL**	**HIGHEST** Only 660 MDS nationally (~1 per 1,800 PD patients).	**VERY LOW** 12-18 months wait. 40% of Canadian PD patients have NEVER seen an MDS.	**PRIMARY USER** Dashboard co-designed with MDS input. Algorithm parameters set and adjusted by MDS. A-Levo enhances each MDS's effective patient capacity through asynchronous review.
Neurologist (General)	**FULL**	**HIGH** Most PD patients under specialist care see a general neurologist, not an MDS.	**LOW** 4-12 months wait.	**PRIMARY USER** A-Levo's algorithm-generated dosing suggestions enable general neurologists to optimize levodopa with MDS-level data, reducing inappropriate dosage escalations and extending specialist capacity.
General Practitioner	**FULL**	**LOW** GPs have very limited PD expertise, serving more as an emergency stop-gap due to limited specialists.	**HIGHEST** *Same/next-day appointments for established patients in most cases. However, 1 in 5 Canadian adults (6.5M) have no regular GP.	**KEY SECONDARY USER** Algorithm-generated dosing suggestions fill the expertise gap that currently makes GPs reluctant to act on PD management. Enables GPs to proactively adjust levodopa rather than waiting for specialist review.
Clinical Pharmacist	**CONDITIONAL** Province-Specific	**MODERATE** Strong medication management expertise, but interpreting motor symptom data is less within their scope.	**HIGH** *No referral required, walk-in availability in most regions. Interact with patients at every prescription refill..	**KEY SECONDARY USER** Under Bill 67, QC pharmacists with consultation authority from a neurologist can review A-Levo dashboard data and make protocol-guided dosing adjustments.
Registered Nurse (RN)	**NONE**	**LOW** *PD-Specialized Nurses have specialized training beyond that of standard RNs.	**HIGH** *Most frequently encountered HCP for hospitalized PD patients. *PDNS (where available) see patients between neurologist appointments.	**MONITORING & ALERT USER** Cannot adjust levodopa independently but can monitor A-Levo dashboard, identify patients approaching OFF episodes, and notify prescribing HCP.

8.2.6. Stakeholder Needs and Corresponding Design Choices

Purpose & Method

This section maps concerns surfaced across all engagement types. This includes primary customer interviews (patients, neurologists, allied HCPs), academic and industry technical consultations, literature, and market scans. Per the SensUs Translational Potential rubric, "customer interviews" is a specifically scored category (patients + healthcare professionals). A meaningful share of A-Levo's concrete design decisions, such as: needle geometry, electrode material selectivity, regulatory pathway, sensing/delivery decoupling, trace back to the academic and industry technical consultations rather than the primary customer interviews. This appendix makes that traceability explicit.

Source Type key (used in each table):

Tag	Meaning
CI–Patient	Primary customer interview, patient
CI–HCP	Primary customer interview, clinician/allied HCP
Tech Consult	Academic or technical expert consultation (not a customer interview)
Industry Partner	Industry / clinical-trials partnership consultation
Team Synthesis	Internal working notes, generally informed by multiple interviews but not individually attributed

1. Compliance & Adherence

Patient Considerations

Concern	Source	Design Feature
Some patients don't want a 24/7 continuous monitor or fixed dosage plan. Some prefer to dose by feel, taking pills only until symptoms ease	Team Synthesis (Patient Experience notes)	Passive, always-on ISF sensing requires zero patient action to "log" anything; the DCI reflects actual physiological state rather than asking patients to follow a prescribed regimen - the device measures reality instead of enforcing a schedule
Daily need to remove/reapply a device discourages long-term wear	Team Synthesis	24/7 wearable patch form factor, no daily off/on cycle, multi-day wear window before replacement
Some symptoms often aren't attributed to Parkinson's by the patient, so they never reach the doctor and dosing never gets adjusted	CI–HCP	DCI trend + rate-of-change flagging is designed to surface "silent" under/over-treatment windows to the care team even when the patient has yet to self-reported
Patients with reduced mobility don't want to fiddle with settings; keep	Patient Experience notes	Same as above; patient app scope kept to viewing status, not adjusting parameters

patient-facing controls as simple/straightforward as possible	Team Synthesis	

Generalized HCP Considerations

Concern	Source	Design Feature
No reliable way to confirm adherence remotely, especially in rehab/CLSC settings where a doctor isn't present	CI–HCP	Objective ISF-derived adherence data made visible to any authorized care-team member (pharmacist, PT, neurologist) via the platform, not only the prescribing physician
Patients go years without follow-up and dosing errors go uncorrected	CI–HCP	Continuous remote monitoring positioned explicitly to close the inter-visit follow-up gap

2. Comfort & Wearability

Patient Considerations

Concern	Source	Design Feature
Nothing big or bulk. Shouldn't restrict movement or interfere with sleep (many PD patients already have sleep/mobility issues)	Team Synthesis	Patch-format wearable, not a device class that adds bulk.
Patients don't want an "extra" device to carry, two smartphones was already too much, a belt is a no-go, a watch is borderline; non-pocket items are best	Industry Partner	Skin-adhered patch form factor (non-pocket, non-carry item), computing offloaded to the patient's existing phone via Bluetooth rather than adding a second device
Placement should target skin, not muscle, mainly the arm (under a sleeve) or thigh, not the face	Tech Consult	Patch placement sited on forearm/thigh, chosen for discretion (coverable by clothing) and consistency of tissue depth

3. Alerting & Notification Design

Patient Considerations

Concern	Source	Design Feature Implemented
Interest in a fall-risk warning tied to changes in motor/neuron activity	Team Synthesis	Fall-risk early-warning sits on the roadmap, reusing the same fused ISF + wrist IMU dataset already collected for the DCI model rather than requiring new hardware

4. Clinical Workflow & HCP Configurability

Generalized HCP / Neurologist Considerations

Concern	Source	Design Feature Implemented

Algorithm sets a therapeutic window, but a neurologist may need to widen/tighten the upper (dyskinesia) or lower (OFF) bound based on clinical judgment	Team Synthesis (CI–HCP informed)	Therapeutic window bounds are manually adjustable per patient on the clinician dashboard
Algorithm-recommended dosing timing may not fit a patient's existing schedule (e.g., "max 4x/day")	Team Synthesis (CI–HCP informed)	Dosing interval constraints are configurable by the HCP
Different clinicians want different amounts of advance warning before a predicted OFF episode (e.g., 30 vs. 60 min)	Team Synthesis (CI–HCP informed)	Alert lead-time is an adjustable parameter
When motor signal (IMU) and biochemical signal (ISF levodopa) disagree, the HCP should be able to say which one to trust more	Team Synthesis (CI–HCP informed)	Signal-weighting between motor and biochemical inputs is HCP-adjustable

5. Patient Autonomy & Control (Sensing–Delivery Coupling)

Patient / Generalized HCP Considerations

Concern	Source	Design Feature Implemented
Non-autonomous / reduced-mobility population shouldn't be burdened with fiddly controls	Team Synthesis	Reinforces the minimal-control design above; patient-facing interface has no dosing decisions to make

6. Regulatory Pathway & Ethics Strategy

Industry / Clinical Partner Considerations

Concern	Source	Design Feature Implemented
A stent-based sensor would need a full risk-benefit case as minor surgery and gets harder still if it adds a therapeutic (drug-release) component. Comparable to how a skin biopsy already requires significant patient discussion	Industry Partner	A-Levo deliberately avoids the implant/stent route in favor of a microneedle patch, lowering the regulatory and ethics burden from the outset
Macroneedles are the easiest ethics-approval path if positioned like a continuous glucose monitor (CGM), since CGM precedent/data can be leveraged directly	Industry Partner	A-Levo's regulatory and commercial strategy explicitly follows the CGM analogy, targeting an SaMD Class II classification and a CGM-to-insulin-pump-style three-phase roadmap
Suggested finding a supervising MD for the clinical side.	Industry Partner	Dr. Postuma engaged as a clinician consultant on the project
A provisional patent should be filed to protect design IP before public disclosure	Team Synthesis / competition timeline	Provisional patent filing targeted before Innovation Days

8.2.7. Rejected Design Choices

Design alternatives were evaluated to compare different approaches for addressing the identified problem and determine the most suitable solution pathway. This provides context on the trade-offs considered and the rationale behind A-Levo's final design decisions.

Design Alternative	Proposed Benefit	Basis for Rejection
Predictive ML for Therapeutic Window On-device model trained on each patient's own data (levodopa trend, meals, exercise) to warn before they leave their therapeutic window.	Enables proactive alerts. On-device training avoids cross-patient data-sharing concerns.	**Expert Consulted: Tech Consult; AI Researcher (University of Waterloo).** Requires a large per-patient dataset we don't have yet. Deferred to Phase 2, after clinical trials generate data. Not abandoned / A future roadmap item.
AI-Based Motor Symptom Classification Trained model to separate PD tremor from everyday movement, and to filter motion-artifact noise using context like temperature and position.	Adapts to individual movement variation. Context-aware filtering could improve real-world accuracy.	**Expert Consulted: Tech Consult; AI Researcher (University of Waterloo).** PD tremor sits in a known clinical frequency range, so rule-based classification is enough. Noise-filtering AI was ruled out. Insufficient training data at this stage.
Microneedle Array for ISF Sensing A short, patch-based microneedle array (CGM-inspired) as the ISF-levodopa sensing interface.	Painless and minimally invasive. Follows CGM regulatory precedent. Low-profile and comfortable.	**Expert Consulted: Industry Partner; Clinical Trials Partner (Neuro MNI). Tech Consult; Graduate Researchers (McGill / The Neuro).** True microneedles can't reach deep enough to sense reliably. Sensing needs a longer (~5–7mm) single probe, losing the microneedle advantage. A single longer sensing filament (CGM-style) was adopted instead. Microneedles remain an option for future drug delivery only.
Implantable / Stent-Based Sensor A more invasive, direct tissue- or vessel-contact sensor instead of a skin-surface patch.	More stable, direct signal. Avoids skin-interface variability (motion, sweat, adhesion).	**Expert Consulted: Industry Partner; Clinical Trials Partner (Neuro MNI).** Requires minor surgery, raising the regulatory bar significantly. Harder still with an added drug-release component. Skin-surface route chosen to stay aligned with the CGM pathway (SaMD Class II).

Aptamer-Based Sensing Chemistry DNA aptamer biorecognition elements as the core levodopa-sensing mechanism.	High specificity once validated. Well-precedented in biosensing literature.	**Expert Consulted: Tech Consult; Chemistry Professor (McGill).** Literature aptamer sequences don't always bind in practice; validation would be needed. Synthesis equipment access was limited and budget constrained. MOF electrode transduction adopted instead.
Non-Motor Biomarkers (Sweat / HRV) Detecting PD symptom state via sweat biomarkers, HRV, or other autonomic signals instead of motor signals.	Fully non-invasive. Leverages validated consumer HRV algorithms. Could capture autonomic involvement.	**Expert Consulted: Team Synthesis; Market Scan (Garmin HRV Status reference).** Too easily confounded by exercise, stress, and temperature. Motor detection via accelerometer/gyroscope gives a cleaner, literature-grounded signal.
Closed-Loop Automated Drug Delivery One integrated patch that senses ISF levodopa and automatically delivers a corrective dose (CGM-to-insulin-pump style).	Matches the strongest commercial narrative. Maximizes clinical value. Removes dosing decisions from patients.	**Expert Consulted: Industry Partner; Clinical Trials Partner (Neuro MNI). Tech Consult; Graduate Researchers (McGill / The Neuro).** Combining sensing and drug release raises the regulatory bar substantially. Automated dosing control also wasn't favored at this stage. Launching first with sensing-only monitoring. However, it is still a valuable consideration for future design direction after clinical and commercial validation of the monitoring device.

8.3.1. Clinician Questionnaire (with mock data)

Context

The following questionnaire will help A-Levo decide if our product creates a genuine improvement for healthcare outcomes in Parkinson's disease afflicted groups. You will be shown multiple graphs which indicate L-Dopa concentration and motor symptoms from two hypothetical patients. Completing these questions should take approximately 15-20 minutes.

Through prior stakeholder consultations, A-Levo has found that an absolute levodopa concentration measurement without symptom context provides clinicians with data they cannot act on.

We have paired levodopa readings with motor symptoms, allowing us to provide more context for caregivers and patients to understand their current trajectory with PD's progression.

By reducing reliance on unreliable patient 'feelings' or slow journals, our device can help speed up treatment and lessen the burden on healthcare systems and improve quality of life. The following breakdown is provided:

1. The patient is prescribed, wears, and uses the A-Levo system.
2. The patient's device learns the therapeutic window of the afflicted.
3. Advice is given to the patient on drug timings and expected motor symptoms.
4. During the new doctor's visit, the device gives the caregiver a report and feedback on drug administration.

The following are one-day reports and excerpts that you, as a doctor, will be provided if an A-Levo device was used.

Patients are 75-year-old, cognitively intact individuals with idiopathic PD at Hoehn and Yahr Stage 3, with no significant comorbidities. Clinical status is stable throughout the monitoring period. Patients adhere to a fixed dosing schedule of X mg levodopa every 4 hours from 7 AM to 11 PM (5 doses daily). They exhibit typical dyskinesia (involuntary movements) at supratherapeutic concentrations and typical bradykinesia (difficulty initiating movement) at subtherapeutic concentrations."

A-Levo Validation Questionnaire: Case 1

To be administered after the clinician has viewed Graph 1, Graph 2, and Graph 3, with patient background provided.

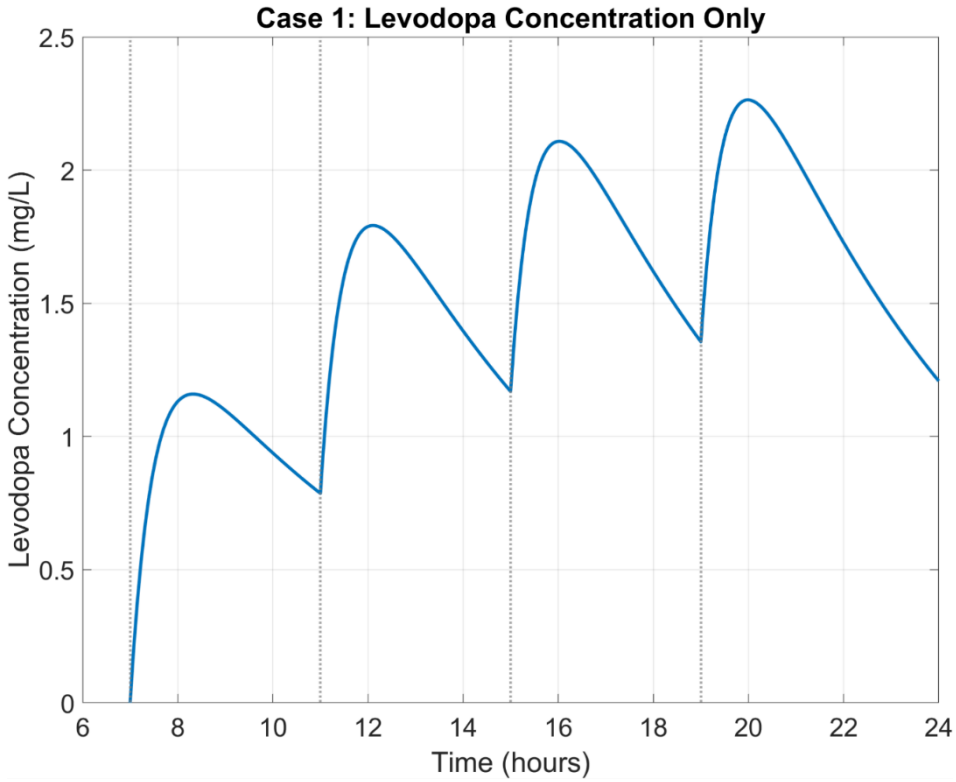
Section 1: Realism Check

This section establishes that the simulated data is credible.

1.1 Does the levodopa concentration curve in Graph 1 look realistic for a patient on levodopa 4–5 times per day? *(Yes / Mostly / No - Please comment)*

1.2 Does the pattern of ON/OFF states in **Graph 3** reflect what you typically observe in a patient with motor fluctuations at this stage of PD? *(Yes / Mostly / No - Please comment)*

Section 2: Clinical Utility of Graph 1 (Levodopa Only)



2.1 Would you feel confident adjusting this patient's dosing regimen based on Graph 1 alone? *(Yes / No / Unsure)*

- If yes: what specific change would you make, and why?
- If no/unsure: what additional information would you need before acting?

2.2 How confident are you in the dosing decision above? *(1 = not at all confident, 5 = fully confident)*

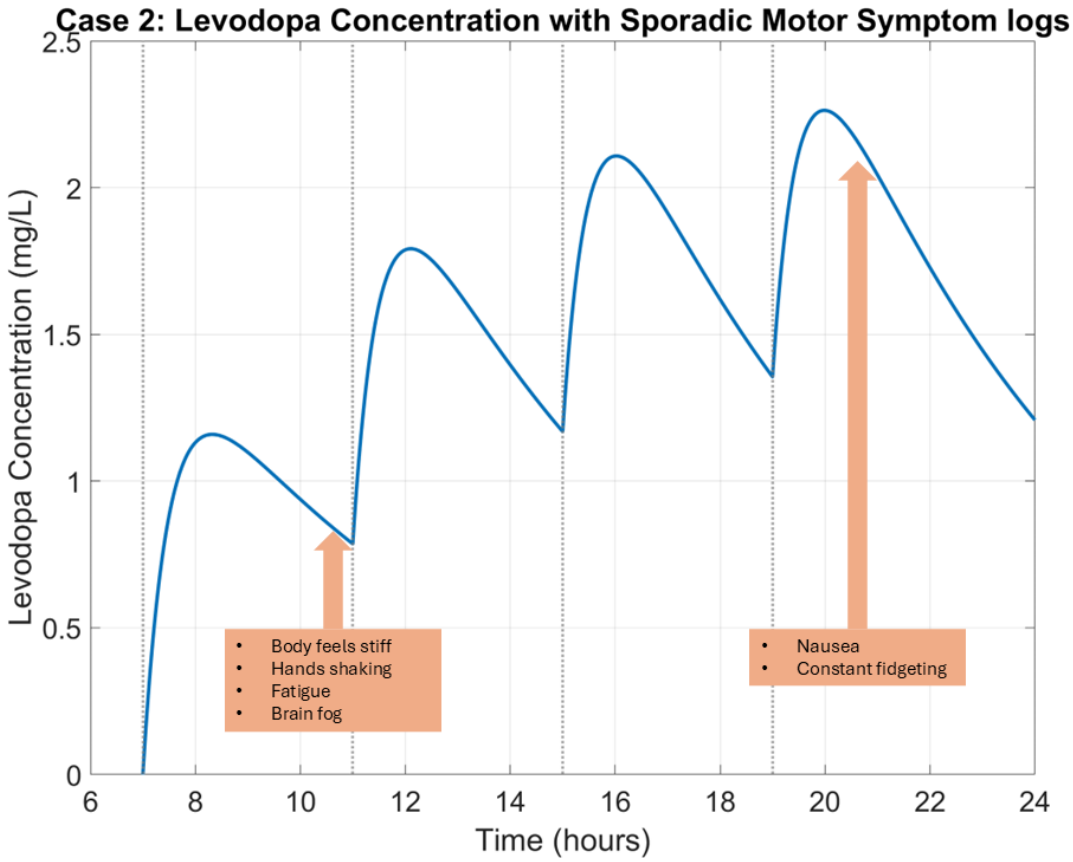
2.3 How useful is this graph for informing a dosing decision overall? (*1 = not useful at all, 5 = fully sufficient)*

2.4 Based on this graph, could you distinguish a wearing-off episode from a dyskinesia episode? *(Yes / Mostly / No - Please comment)*

2.5 This graph gives no information about the patient's motor state at the time of each reading. How risky do you consider it to make a dosing decision without that context? *(1 = not risky at all, 5 = very risky)*

Section 3: Clinical Utility of Graph 2 and Graph 3

3A. Graph 2: Sporadic Motor State Logging



3A.1 Would you feel confident adjusting this patient's dosing regimen based on this graph? *(Yes / No / Unsure)*

- If yes: what specific change would you make, and why?

3A.2 How confident are you in the dosing decision above? *(1 = not at all confident, 5 = fully confident)*

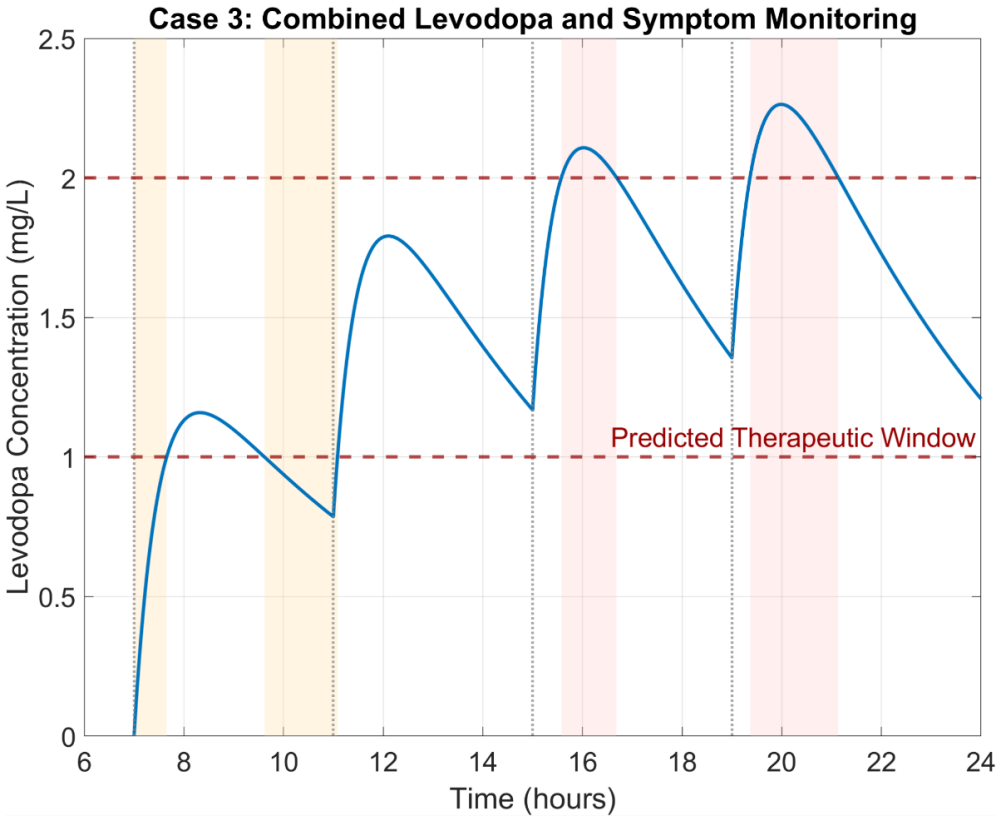
3A.3 How useful is this graph for informing a dosing decision overall? (*1 = not useful at all, 5 = fully sufficient)*

3A.4 Based on this graph, could you distinguish a wearing-off episode from a dyskinesia episode? *(Yes / Mostly / No - Please comment)*

3A.5 This graph only captures motor state at two isolate moments in the day. How risky is it to rely on this kind of sporadic sampling, given that clinically meaningful transitions could occur between those timestamps and go undetected? *(1 = not risky at all, 5 = very risky)*

3A.6 Based on this graph alone, would you feel confident that no clinically significant ON/OFF transition or dyskinesia episode is being missed elsewhere in the day? *(Yes / No / Unsure)*

3B. Graph 3: Continuous Motor State + Therapeutic Window



Context: Using motor sensing and a neurologist-built algorithm, The yellow sections represent sensed bradyskinesia symptom state, whereas the pink sections correspond to sensed dyskinesia symptom state.

3B.1 Would you feel confident adjusting this patient's dosing regimen based on this graph? *(Yes / No / Unsure)*

- If yes: what specific change would you make, and why?

3B.2 How confident are you in the dosing decision above? *(1 = not at all confident, 5 = fully confident)*

3B.3 How useful is this graph for informing a dosing decision overall? (*1 = not useful at all, 5 = fully sufficient)*

3B.4 Based on this graph, could you distinguish a wearing-off episode from a dyskinesia episode? *(Yes / Mostly / No - Please comment)*

3B.5 The graph marks an estimated therapeutic window (upper/lower threshold) for this patient. Do these thresholds look clinically reasonable? If you were setting them yourself, what values would you choose?

3B.6 What personal alert threshold would you set for this patient (a levodopa concentration, or a percentage change from baseline) at which you would want to be flagged for review?

3B.7 At what point in the day would you have intervened based on this graph and what would that intervention have been (ex: dose adjustment, timing shift, adjunct therapy)?

3B. 8 Patients often show expected, medication-related fluctuation in ON/OFF timing. Based on Graph 3, how well can you distinguish that expected pattern from something that would concern you as a sign of worsening disease control? *(1 = not at all, 5 = very well)*

3C. Cross-Graph Comparison

3C.1 Comparing the levodopa-only graph and sporadic-logging graph: does adding sporadic motor state timestamps meaningfully change your ability to make a dosing decision? *(Yes / No / Unsure. Please comment)*

3C.2 Comparing the sporadic-logging graph and the continuous graph and Graph 3: how much does moving from two isolated timestamps to continuous motor state monitoring change your confidence in the dosing decision you'd make? *(1 = no difference, 5 = major difference)*

3C.3 What specific information across the graphs was most useful to you? Was anything shown that felt redundant or unnecessary?

Section 4: Workflow Integration

This section helps us understand how this would fit into real clinical practice.

4.1 How long did it take you to interpret Graph 3 and arrive at a dosing decision? *(Under 2 min / 2–5 min / More than 5 min)*

4.2 Would data in this format be practical to review between patient appointments, without the patient present? *(Yes / No / Unsure)*

4.3 Would you be comfortable delegating review of this dashboard to a clinical pharmacist or GP with your oversight? *(Yes / No / Unsure. Please comment)*

4.4 If this dashboard were reviewed periodically (e.g., once every 1–2 weeks) rather than continuously, how many days of unaddressed OFF-state time or dyskinesia episodes would you consider acceptable before wanting an earlier review or an alert?

4.5 What changes to the format or presentation would make this easier to act on?

Section 5: Broader Validation

The following are open-ended clinical insights the structured questions may miss.

5.1 Is there anything about this data presentation that concerns you from a patient safety perspective?

5.2 What additional data points, alongside levodopa concentration and motor state, would most improve your ability to manage this patient's therapy?

5.3 Was there a specific moment in Graph 3 (e.g. a state transition) where deciding the right treatment response felt genuinely difficult or ambiguous, even with continuous data? Please describe.

5.4 Would you use a tool like this in your clinical practice if it were available? *(Yes / No / Maybe. Please comment)*

A-Levo Validation Questionnaire: Case 2

To be administered after the clinician has viewed Graph 1, Graph 2, and Graph 3, with patient background provided.

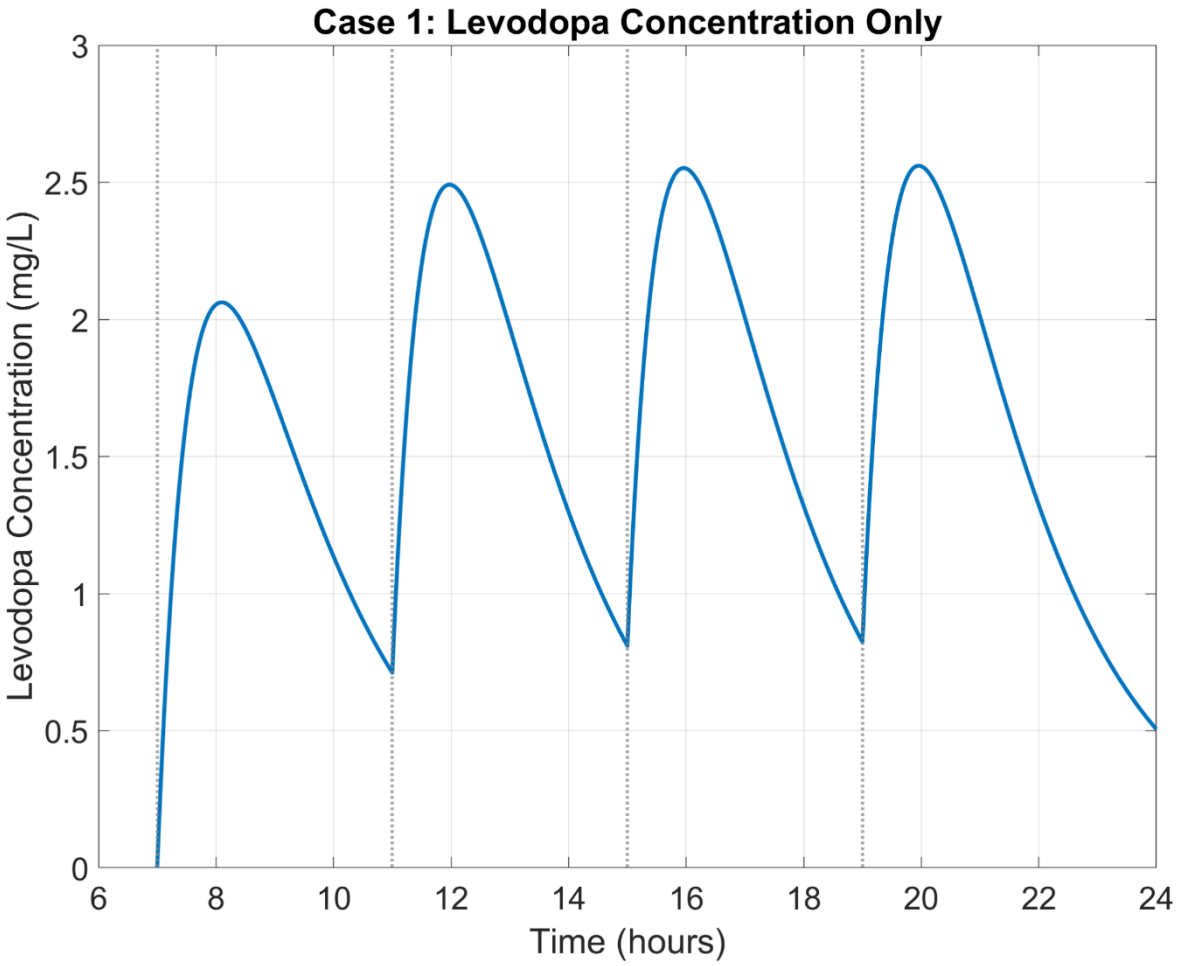
Section 1: Realism Check

This section establishes that the simulated data is credible.

1.1 Does the levodopa concentration curve in Graph 1 look realistic for a patient on levodopa 4–5 times per day? *(Yes / Mostly / No - Please comment)*

1.2 Does the pattern of ON/OFF states in **Graph 3** reflect what you typically observe in a patient with motor fluctuations at this stage of PD? *(Yes / Mostly / No - Please comment)*

Section 2: Clinical Utility of Graph 1 (Levodopa Only)



2.1 Would you feel confident adjusting this patient's dosing regimen based on Graph 1 alone? *(Yes / No / Unsure)*

- If yes: what specific change would you make, and why?
- If no/unsure: what additional information would you need before acting?

2.2 How confident are you in the dosing decision above? *(1 = not at all confident, 5 = fully confident)*

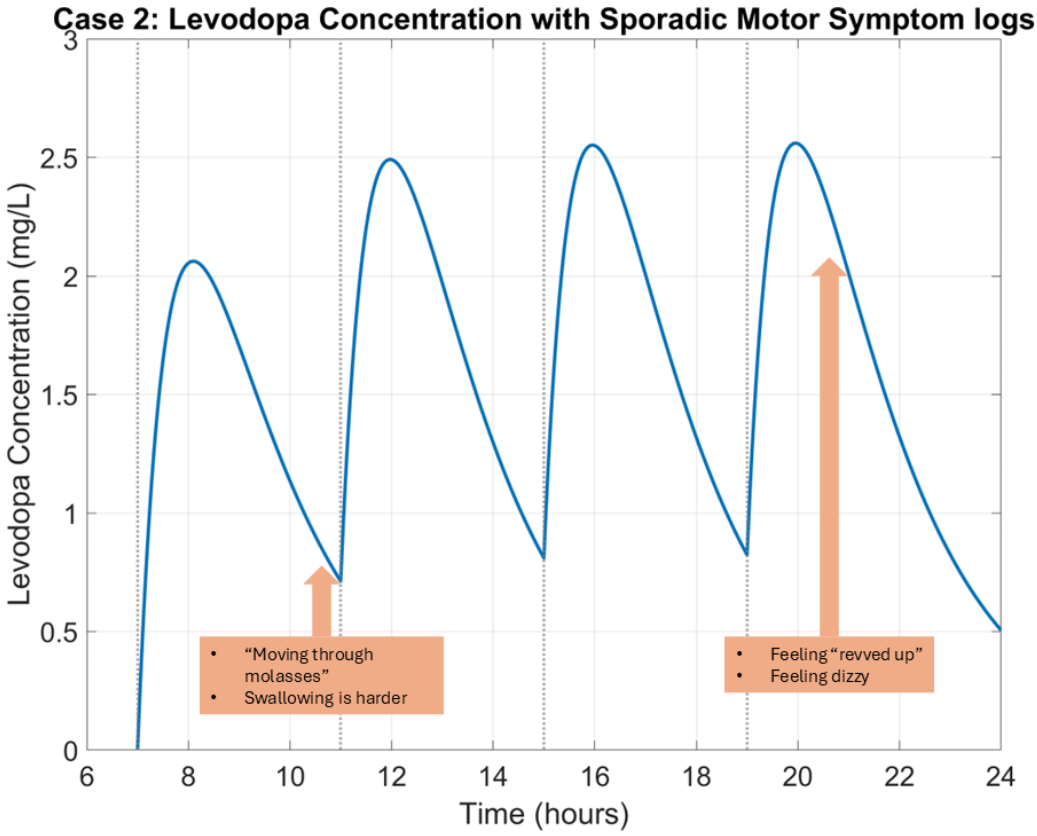
2.3 How useful is this graph for informing a dosing decision overall? (*1 = not useful at all, 5 = fully sufficient)*

2.4 Based on this graph, could you distinguish a wearing-off episode from a dyskinesia episode? *(Yes / Mostly / No - Please comment)*

2.5 This graph gives no information about the patient's motor state at the time of each reading. How risky do you consider it to make a dosing decision without that context? *(1 = not risky at all, 5 = very risky)*

Section 3: Clinical Utility of Graph 2 and Graph 3

3A. Graph 2: Sporadic Motor State Logging



3A.1 Would you feel confident adjusting this patient's dosing regimen based on this graph? *(Yes / No / Unsure)*

- If yes: what specific change would you make, and why?

3A.2 How confident are you in the dosing decision above? *(1 = not at all confident, 5 = fully confident)*

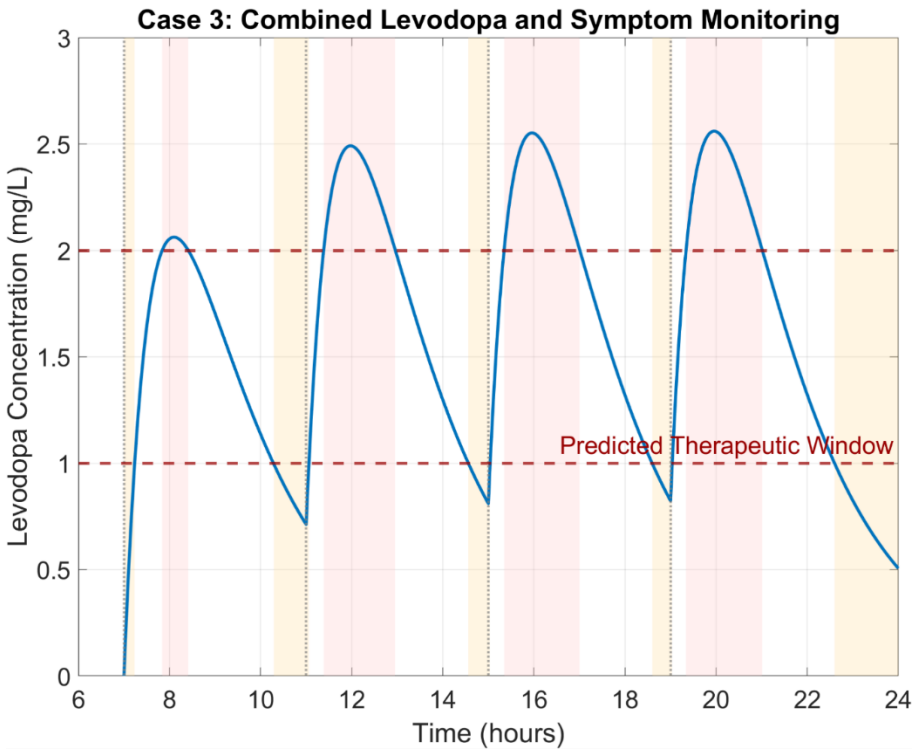
3A.3 How useful is this graph for informing a dosing decision overall? (*1 = not useful at all, 5 = fully sufficient)*

3A.4 Based on this graph, could you distinguish a wearing-off episode from a dyskinesia episode? *(Yes / Mostly / No - Please comment)*

3A.5 This graph only captures motor state at two isolate moments in the day. How risky is it to rely on this kind of sporadic sampling, given that clinically meaningful transitions could occur between those timestamps and go undetected? *(1 = not risky at all, 5 = very risky)*

3A.6 Based on this graph alone, would you feel confident that no clinically significant ON/OFF transition or dyskinesia episode is being missed elsewhere in the day? *(Yes / No / Unsure)*

3B. Graph 3: Continuous Motor State + Therapeutic Window



Context: Using motor sensing and a neurologist-built algorithm, The yellow sections represent sensed bradyskinesia symptom state, whereas the pink sections correspond to sensed dyskinesia symptom state.

3B.1 Would you feel confident adjusting this patient's dosing regimen based on this graph? *(Yes / No / Unsure)*

- If yes: what specific change would you make, and why?

3B.2 How confident are you in the dosing decision above? *(1 = not at all confident, 5 = fully confident)*

3B.3 How useful is this graph for informing a dosing decision overall? (*1 = not useful at all, 5 = fully sufficient)*

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3B.5 The graph marks an estimated therapeutic window (upper/lower threshold) for this patient. Do these thresholds look clinically reasonable? If you were setting them yourself, what values would you choose?

3B.6 What personal alert threshold would you set for this patient (a levodopa concentration, or a percentage change from baseline) at which you would want to be flagged for review?

3B.7 At what point in the day would you have intervened based on this graph and what would that intervention have been (ex: dose adjustment, timing shift, adjunct therapy)?

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5.4 Would you use a tool like this in your clinical practice if it were available? *(Yes / No / Maybe. Please comment)*

8.3.2: Target Patient Profile for Initial Adopting Users of A-Levo

Condition(s)	Justification
Hoehn & Yahr Stage 3, assessed while in ON state	This is the inflection point where motor fluctuations begin meaningfully impairing daily life but the patient is still outpatient, cognitively intact, and able to engage with the device. Stage 3 in ON state confirms the patient still has functional capacity, but the same patient may appear Stage 4 during an OFF episode. Earlier stages (1–2) don't yet have a problematic enough therapeutic window to justify monitoring. Later stages (4–5) are too complex and often institutionalized, making device management impractical for a first pilot.
On levodopa for at least 3 years	Motor fluctuations typically emerge 1–5 years after levodopa initiation. A patient recently started on levodopa is unlikely to have a narrowing or problematic therapeutic window yet. Three years is the minimum threshold where wearing-off becomes clinically meaningful for most patients.
Taking levodopa at least 3 times per day	This signals active dose-titration territory as the neurologist is already trying to manage the window by increasing frequency. Multiple daily doses also means enough pharmacokinetic events per day for the algorithm to build a reliable concentration-motor state map within the 10-day wear cycle.
Documented wearing-off with at least 1–2 hours of daily OFF time	The patient must be experiencing and recognizing predictable end-of-dose wearing-off. This is the standard inclusion criterion across almost every levodopa monitoring clinical trial. Patients who still haven't noticed their own wearing-off symptoms can't understand the merit of using A-Levo yet, so patients that had negative experiences with PD are more ready to adopt A-Levo.
Psychographic profile: Adherers and adopters	Beyond clinical criteria, the ideal early adopter has these characteristics, drawn from our patient consultations and the digital health adoption literature: • **Diagnosed under 70**: Younger patients are more digitally literate and more motivated to extend their functional years. • **Actively involved in their own care**: Patients who already track symptoms and communicate proactively with their neurologist, like Adrian Ziemczonek's self-referring patient population, have the highest motivation to use a device that validates what they're already noticing. • **Has experienced a consequential OFF episode**: A patient who has fallen, frozen in public, or been in a dangerous situation during an OFF state has a visceral, concrete incentive that "it might help your treatment" cannot match. • **Some prior comfort with smartphones or wearables**: Not a strict criterion but a practical one for the pilot. Garmin's Jesse Blackstock confirmed compliance is higher with devices that look like consumer products rather than medical equipment.
Exclusions	• Patients with atypical parkinsonism (MSA, PSP, CBD) because of its different disease course and levodopa response. • Patients post-DBS. • Patients with severe nausea-dominant levodopa intolerance • Patients with MMSE below 25. • Patients not under any specialist care.

8.4.1. Entrepreneurial Traction and Near-Term Plans

Entrepreneurial Traction and Near-Term Commercialization Plans			
Date	**Milestone**	**Category**	**Significance**
Oct 2025	**JHKCBA Innovation Competition** 3rd Place	Pitch Competition	First external validation of A-Levo's concept and business model.
Nov 2025 - Feb 2026	**Stakeholder Consultation** Across Canadian PD care ecosystem	Customer Discovery	Insights from patients, MDS specialists, neurologists, clinical pharmacists, physiotherapists, industry partners, and payers. Directly shaped device design and commercial strategy.
Apr 2026	**Dobson Innovation for Impact 2026** 2nd Place	Pitch Competition	McGill Dobson Centre for Entrepreneurship. Recognized for social impact potential and diligent business modelling.
May 2026	**McGill Clinical Innovation Competition** Vitruvius Launchpad Prize	Pitch Competition	Prize includes: - direct and matching funds - 6-month in-kind residency at Vitruvius Medtech Venture Studio
Aug 2026	**SensUs 2026 International Biosensor Competition** (Eindhoven, Netherlands)	Pitch Competition	Representing McGill University against biosensor teams from global universities.
Sep 2026 - Dec 2026	**Incubator enrollment** (pending)	Venture Development	Health technology incubator program providing mentorship, industry network access, and structured startup resources.
Sep 2026 - Feb 2027	**Vitruvius Venture Studio** Residency	Venture Development	Access to workspace, mentorship, and support across product development, regulatory strategy, clinical translation, and fundraising.
2026-2027	**Patent filing**	IP Protection	Protects core A-Levo innovations in continuous wearable levodopa biosensing and individualized therapeutic window identification.
2026-2027	**Federal non-dilutive funding applications**	Funding	Federal funding generates clinical evidence required for CADTH HTA submission -> provincial formulary listing pathway.
Oct 2027	**Formal incorporation**	Company Formation	Legal entity established to enable investment, IP ownership, and commercial partnerships.

8.4.2. HCP Prescribing Authority and Accessibility

Prices are commercial assumptions, not yet validated through reimbursement decisions. All figures in CAD.

Commercial Model Overview				
Model Element	**Position**	**Commercial Interpretation**		
Clinical proposition	Continuous levodopa monitoring paired with patient symptom state identification	Objective drug-level and symptom data inform personalized, evidence-based treatment decisions		
Revenue architecture	Consumable sensor patches + clinical analytics platform subscription	Patch creates recurring hardware revenue; analytics creates recurring SaaS revenue. No reader hardware — patient interface is smartphone app.		
Price	Approximately C$2,000 per patient per year (recurring)	Annual figure is a rounded customer-revenue assumption		
Initial customer channel	Movement disorder and neurology specialist clinics	Specialist-led adoption before expansion toward standard generalist care		
Payment hypothesis	Provincial public coverage using CGM adoption as analogy	Coverage pathway not yet established; RAMQ listing and CADTH HTA are primary targets		
Price Schedule — Per Patient (Annual Recurring)				
Component	**Unit Price (CAD)**	**Frequency**	**Annual Revenue (CAD)**	**Notes**
Disposable sensor patch	C$46	Every 10 days	$1,679	36.5 patches per year
Clinical analytics platform	C$350	Annual subscription	$350	Per-patient SaaS fee billed to clinic
Total recurring annual revenue			**$2,029**	**Patches + analytics**
Note: Patient-facing interface (medication reminders, status indicator, adherence tracking) delivered via smartphone app on iOS and Android.				

8.4.3. Market Sizing

Addressable Market Sizing					
Figures are market ceilings, not revenue forecasts.					
Market Level	**Definition**	**Patient Calculation**	**Patients**	**Annual Revenue (CAD)**	**Notes**
TAM	All North American levodopa-treated PD patients	1,200,000 x 90% x C$2,000	1,080,000	**$2,160,000,000**	Total addressable market ceiling
SAM	Levodopa-treated patients experiencing motor fluctuations (70%)	1,080,000 x 70% x C$2,000	756,000	**$1,512,000,000**	Primary clinical target population
SOM Yr 1-3	Montreal beachhead: eligible advanced PD patients at 1-2 MDS centres (~150 eligible per centre)	~300 eligible patients (2 centres x ~150)	~300	**$600,000**	Proof-of-concept cohort
SOM Yr 3-5	Quebec + Ontario expansion + 8-10 neurology centres	5,000-8,000 eligible patients	5,000-8,000	**$16,000,000**	Formulary listing target for provincial coverage

Market Funnel — Progressive Patient Qualification				
Funnel Stage	**Patient Calculation**	**Patients**	**% of Prior Stage**	**Notes**
North American PD population	1,200,000 total PD patients in North America	$1,200,000	Base population	Source: Parkinson's Foundation; Statistics Canada 2024
Levodopa-treated patients	1,200,000 x 90%	$1,080,000	90% of PD population	Primary target population for A-Levo
Patients with motor fluctuations / OFF symptoms	1,080,000 x 70%	$756,000	70% of levodopa-treated patients	Advanced PD with documented wearing-off; highest unmet need and clearest payer ROI

8.4.4. Healthcare Economics & QALY Analysis

Canadian Health System Savings Scenario				
All figures in CAD unless noted.				
Input / Step	**Assumption**	**Formula**	**Calculated Result**	**Interpretation**
North American PD population	1,200,000 total PD patients	Base figure	$1,200,000	Source: Parkinson's Foundation; Statistics Canada 2024
Levodopa-treated patients	90% of total PD population	1,200,000 x 90%	$1,080,000	Primary A-Levo target population
Patients with motor fluctuations	70% of levodopa-treated patients	1,080,000 x 70%	$756,000	Population used in savings scenario — highest unmet need
Annual healthcare cost per patient	C$10,000 average (range C$8,000-14,000)	C$10,000 x 756,000 patients	$7,560,000,000	Total system cost baseline for this population
Assumed cost reduction from monitoring	20% reduction with optimized dosing	20% x C$10,000 = C$2,000/patient	$1,512,000,000	Equal to A-Levo annual price — cost-neutral at 20% reduction
Potential annual system savings	**20% cost reduction across fluctuating population**	**756,000 x C$2,000**	**$1,512,000,000**	**Sensitivity scenario; does not claim realized savings**
Hospitalization comparison	C$10,000-20,000 per PD admission in Canada	C$10,000 / C$2,000/yr	5 patient-years	One avoided admission offsets 5 years of A-Levo subscription

QALY Analysis & Cost-Effectiveness			
Metric	**Calculation**	**Result**	**Interpretation**
QALY gain estimate	0.04 EQ-5D gain/hr OFF reduced x 2 hrs x 10 remaining years	0.8 QALY	See competitor matrix in Appendix 8.4.# for comparison with competitors.
Estimated A-Levo $/QALY	**C$20,290 / 0.8 QALY**	**~C$25,363/QALY**	**Early-stage value hypothesis; well within cost-effective range**

8.4.5. Healthcare Economics & QALY Analysis

Competitive Positioning Matrix

Updated as of August 2026

Criterion	A-Levo	Rune Labs (StrivePD)	PKG Health (KinetiGraph)	AbbVie VYALEV	AbbVie DUOPA
Continuous levodopa monitoring	X				
Motor / symptom state detection	X	X	X		
Biochemical + motor data paired	X				
Patient-specific therapeutic window ID	X				
Wearable / non-invasive	X	X	X		
Continuous (not episodic)	X	X	X	X	X
FDA / Health Canada approved	In development	FDA cleared	FDA cleared, CE marked	Approved	Approved
Estimated annual cost (CAD)	~C$2,000	~C$2,000-5,000	~C$1,500	~C$62,000-119,000	~C$40,000-60,000
ICER ($/QALY estimate)	~C$25,675/QALY	Not published	Not published	~C$44,000/QALY	~C$48,000/QALY
Clinical decision support	Yes — algorithm + dashboard	Report-based	Report-based		
Stage of care	Early to advanced PD (H&Y Stage 3+)	Mid to advanced PD	Mid to advanced PD	Advanced PD only	Advanced PD only
Why A-Levo wins	First system to make levodopa visible, quantifiable, and actionable in real time — paired with motor state	Cannot measure levodopa. Cannot explain why fluctuations occur.	No biochemical data. Trial-and-error titration continues.	Does not measure levodopa levels. Invasive. High-cost late-stage only.	Highly invasive. No real-time feedback on whether dosing is optimal.

8.4.6. Regulatory & Commercialization Roadmap

Regulatory & Commercialization Roadmap					
Canada-first strategy: Secure Canadian regulatory approval before pursuing US approval. Prioritizes the Canadian healthcare system, keeping intellectual property in Canada, and building a local supply chain. US entry will follow, using data gathered in Canada.					
Period	**Stage**	**Key Activities**	**Regulatory Milestone**	**Revenue / Funding**	**Canada-First Rationale**
2026-2029	**Foundation & Prototype Development**	- Sensor research and lab testing - Patient mobile app development - HCP dashboard software development - Filing for patents - Meet with Canadian regulators - Government research grants	Initial meeting with Canadian regulators. Initial patent filed. Software tracking systems set up.	Government grants (up to C$10M) Startup studio program (Sep 2026-Feb 2027) Academic research awards	Multinational IP and Government funding applications submitted. University partnerships established. Patient and doctor software built for Canadian healthcare.
2029-2031	**Initial Patient Study**	- Small initial patient study (20 patients) conducted at MDS/neurology centres matches patient symptoms - Improve dashboard based on doctor feedback - Patient compliance study	Ethics board approval. Completion of initial study. Finalizing device design for the main clinical trial.	Data partnerships with pharmaceutical companies Early-stage investment funding	Real-world patient data collected in Canada. Build the case for provincial healthcare coverage.
2031-2035	**Major Clinical Trial**	- Large-scale clinical trial (150 patients across 3 provinces) - Submission for Canadian health technology assessment - International manufacturing quality certification - Creating financial models for provincial healthcare coverage	Canadian medical device approval. Submission to national health technology assessors. International manufacturing quality certification.	Major investment funding round Revenue from pharmaceutical partnerships based on achieving goals	Canadian regulatory approval secured. National recommendation helps start coverage talks with all provinces. Canadian clinical data prepared for US regulatory submission.
2035-2037	**Canada Commercial Launch**	- Provincial healthcare coverage in Quebec and Ontario - Roll out to 8-10 major neurology clinics nationally - Training programs for HCPs - Meet with key US healthcare players	Coverage by provincial healthcare plans. Initial meeting with US regulators.	Revenue from provincial healthcare coverage Growth-stage investment funding Licensing data to pharmaceutical companies	Public healthcare coverage achieved across Canada. US discussions begin (recognizing the US system is different from Canada's).
2037+	**US Entry & International Scale**	- Submit for US regulatory approval and insurance billing codes - Discussions with US specialists and insurers - Apply for regulatory approval in Europe and Australia	US regulatory approval. US insurance billing codes established for remote monitoring.	Revenue from US Medicare Licensing the technology internationally	US entry planned with local experts as Canadian strategies differ from US healthcare and insurance systems.

8.4.7. Payer Landscape & Coverage Pathways

Payer Landscape & Coverage Pathways				
Our discussions with healthcare groups were only done in Canada. Information about US payers comes from public data; we plan to talk to US groups in the future.				
Coverage Pathway	**Who Pays**	**Applicability to A-Levo**	**Evidence Required**	**Timeline**
Provincial Government	Provincial health ministry	Main pathway. Older Parkinson's patients (65+) are covered by provincial plans. Reaches the most people if adopted.	Health Canada approval -> National review -> Provincial listing. Needs proof it works well and is cost-effective.	Yr 4–6 post-approval
Federal Government Grants	Federal granting agencies	Funding to help gather clinical proof for national review. Doesn't pay for the product directly, but helps get it covered later.	Apply for federal grants. Being connected to a university helps a lot.	Yr 1–3 (apply now)
Direct Hospital Purchase	Academic hospital department budgets	Starting point. Major hospitals buy the product directly before it's officially listed. Helps gather real-world data.	Results from early studies at major research centers. Doesn't need official insurance coverage yet.	Yr 1–3
Private Insurance through Employers	Employer on behalf of employee	Limited use. Only covers working people. Most Parkinson's patients are 65+ and retired, so they aren't on these plans.	Proof that it improves quality of life. Must show it works clinically.	Yr 5+ (secondary)
Direct Out-of-Pocket (Patient pays)	Patient	Good for highly motivated patients, especially younger ones (under 65) who don't have senior coverage yet.	Checking if patients are willing to pay for it themselves. Similar to how continuous glucose monitors started.	Ongoing (parallel)
US Medicare / Supplemental Insurance (Future)	US federal (Medicare) + supplemental insurers	Future pathway. Billing codes for remote monitoring already exist. Needs US FDA approval first.	US FDA approval using Canadian data. Still need to talk to US groups.	Yr 6+ (post-Canada)

8.5. Glossary

CADTH – Canadian Agency for Drugs and Technologies in Health

CBD – Corticobasal Degeneration

CE – Counter electrode

CGM – Continuous Glucose Monitor

CV – Cyclic voltammetry

DBS – Deep Brain Stimulation

EDAX – Energy dispersive X-ray analysis

GP – General Practitioner

HAADF – High-angle annular dark field (imaging)

HCP – Healthcare Practitioner

HPLC – High-performance liquid chromatography

HTA – Health Technology Assessment

ICER – Incremental Cost-Effectiveness Ratio

IMU – Inertial measurement unit

IP – Intellectual Property

ISF – Interstitial fluid

LD – Levodopa or L-DOPA

MDS – Movement Disorder Specialist

MMSE – Mini-Mental State Examination

MoCA – Montreal Cognitive Assessment

MOF – Metal-organic framework

MSA – Multiple System Atrophy

MWCNT – Multiwalled carbon nanotubes

NP – Nurse Practitioner

PCB – Printed circuit board

PD – Parkinson's disease

PDNS – Parkinson's Disease Nurse Specialist

PDQ-39 – Parkinson's Disease Questionnaire (39-item)

PK – Pharmacokinetic(s)

PSP – Progressive Supranuclear Palsy

PXRD – Powder X-ray diffraction

QALY – Quality-Adjusted Life Year

RAMQ – Régie de l'assurance maladie du Québec

RE – Reference electrode

RN – Registered Nurse

SAM – Serviceable Addressable Market

SaMD – Software as a Medical Device

SEM – Scanning electron microscopy

SOM – Serviceable Obtainable Market

TAM – Total Addressable Market

TEM – Transmission electron microscopy

Tyr@ZIF-8 – Tyrosinase encapsulated in ZIF-8

WE – Working electrode

ZIF-8 – Zeolitic imidazolate framework-8


A-Levo