NEST 4 – Design Selection

Revised 22 June 2023

This document describes the design choices for the microfabricated cuff electrode. The lead (developed by Med-Ally) and insertion tool are not included in this document.

The document begins with design requirements and decisions made based on those requirements, follows with detailed mechanical design options and the selection process, and ends with an outline of planned testing (which will be further developed in Y2).

1 Design Requirements

The following design requirements were set for the microfabricated cuff design:

1. All materials must be biocompatible and have a history of chronic *in vivo* use
2. Cuff must fit a target nerve of 0.5-1.0 mm diameter
3. Cuff must wrap at least 1.5x around nerve diameter
4. Cuff must be self-sizing (within ranges below)
    a. Small size: 0.5-0.8 mm diameter
    b. Large size: 0.7-1.0 mm diameter
5. Electrodes must be spaced to allow for efficient stimulation
6. Electrodes and traces must be sized to allow for typical stimulation parameters (based on vagus nerve stimulation values)

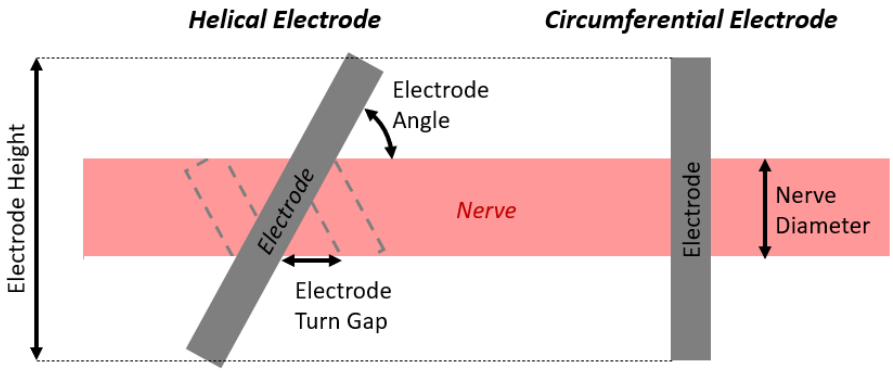
To achieve each of these requirements, the following design decisions were made:

1.1 Material Selection

The microfabricated cuff is made of Parylene C as the backbone and insulation material and platinum as the conductive material. Both materials are compatible with existing, well-established microfabrication techniques, are biocompatible, and have been used extensively in chronic implants. The Med-Ally leads (as used in all NESTs and described in NEST 3) are made entirely of biocompatible materials and are attached to the microfabricated cuff either using a welding/bonding process (which does not add any additional material) or using biocompatible silver epoxy (Epo-TEK MED H20E). The connection point is insulated with medical grade silicone or epoxy.

1.2 Cuff Dimensions

Helical electrodes and circumferential electrodes were considered. The electrode height (see figure below) for each cuff size was selected to allow the electrode to wrap 1.5 times around the largest nerve diameter in the size range. For helical electrode designs, the angle of the electrode was selected to ensure the cuff did not overlap itself (electrode turn gap > 0 in the figure below) when wrapped around any nerve diameter in the size range. The electrode width was defined by stimulation requirements (described later in this section).



1.3 Self-Sizing Property

The backbone material, Parylene C, is a thermoplastic polymer, allowing it to be thermoformed and permanently hold a 3D shape. Parylene C is also flexible, allowing it to be manually and temporarily flexed out of its formed shape. The microfabricated cuff electrode is thermoformed into a cuff shape matching the smallest diameter in the corresponding size range (i.e. 0.5 mm for small, 0.7 mm for large). After thermoforming, the cuff can be manually expanded to a larger size, then closes back to its original size when released. When expanded and placed on the nerve (with diameter greater than or equal to the cuff), the cuff closes until it contacts the nerve.

1.4 Electrode Spacing

The distance between electrodes was set based on recommendations from experts in the field, literature on ideal electrode spacing, and geometry of existing larger cuff electrodes. In general, the ideal distance between electrodes is proportional to nerve diameter, so the electrode spacing found in the existing Liva Nova cuff (9 mm spacing for 2 mm diameter nerve) was scaled down to fit the target nerve diameters for the microfabricated cuff (3 mm spacing for 0.5-0.8 mm diameter nerve; 4 mm spacing for 0.7-1.0 mm diameter nerve).

1.5 Electrode Size

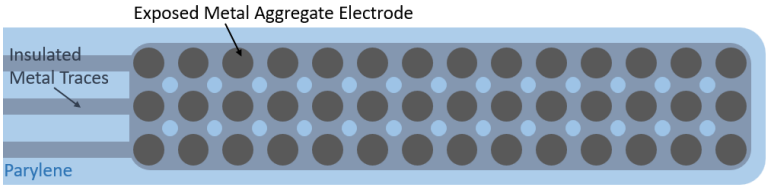
The surface area of the electrodes was dictated by charge injection limits and desired stimulation parameters. Based on research summarized below, a charge storage capacity of 100 µC/cm^2 was used to calculate required electrode surface area. If this is not achieved with bare thin film Pt, electrode size can be later increased or charge storage capacity can be increased with surface treatments such as roughening, electroplating, or deposition of conductive polymers.

- Typical stimulation parameters for VNS
    - 0.5-4.2 mA at 100 µs [1]
    - 1.25-2.25 mA at 250 µs [2]
    - 0.3-2.4 mA at 300 µs [1]
    - 0.2-2.0 mA at 500 µs [1]
    - Maximum allowable stimulation for LivaNova VNS: 3.5 mA, 1000 µs [3], [4]
- Charge injection capacity for platinum
    - Foil

        - 35-200 µC/cm^2 [5]
        - 50-100 µC/cm^2 at 0.2 ms (charge balanced biphasic) [6]
    - Thin film
        - 170 µC/cm^2 at 0.2 ms [7]
        - 260 µC/cm^2 at 0.75-1.0 ms [7]
- Charge injection limits for tissue
    - 50-100 µC/cm^2 [internal recommendation]
    - Shannon limit - dependent on electrode area [8]
        - 200 µm circular electrode: 317 µC/cm^2
        - 600 µm x 2000 µm rectangular electrode: 51 µC/cm^2

1.6 Electrode Shape

Rather than using one large rectangular electrode, an array of closely packed, shorted microelectrodes was used. This prevents the high likelihood of cracking in the large electrode area during handling or stimulation by reducing the size of the large metal area and adding open areas in the electrode where the top and bottom Parylene layers can adhere to each other.



Based on the typical VNS parameters listed in the previous paragraph and a charge storage capacity of 100 µC/cm^2, the required electrode area and number of subelectrodes was calculated:

VNS Stimulation Parameters		**Charge Per Phase**	**Required Electrode Area**	**Number of Microelectrodes**	
Amplitude	**Pulse Width**			**200 µm Diameter**	**300 µm Diameter**
4.2 mA	100 µs	0.42 µC	0.42 mm^2	14	6
2.25 mA	250 µs	0.56 µC	0.56 mm^2	18	8
2.4 mA	200 µs	0.72 µC	0.72 mm^2	23	11
2.0 mA	*500 µs*	*1.00 µC*	*1.00 mm^2*	*32*	*15*

The maximum values (italicized) were used to select the number of microelectrodes, and a safety factor of at least 1.5 was used.

For helical electrodes, a width of 3 and 4 microelectrodes (small and large sizes) was selected as it allows for a moderate helix angle (55°) without any electrode overlap at the smallest nerve size and produces sufficient electrode area when wrapped ~1.5x around the nerve.

- Small cuff (0.5-0.8 mm dia): 3x18 200 µm microelectrodes (1.70 mm^2 total area)
- Large cuff (0.7-1.0 mm dia): 4x22 200 µm microelectrodes (2.77 mm^2 total area)

For circumferential electrodes, the minimum nerve circumference dictated the electrode layout (electrodes were wider due to the overlapping arms of the electrodes blocking part of the stimulation area).

- Small cuff (0.5-0.8 mm dia): 9x14 200 µm microelectrodes (1.70 mm^2 total area, 1.56 mm^2 contact area with smallest nerve)
- Large cuff (0.7-1.0 mm dia): 6x18 200 µm microelectrodes (3.39 mm^2 total area, ~1.60 mm^2 area in contact with smallest nerve)

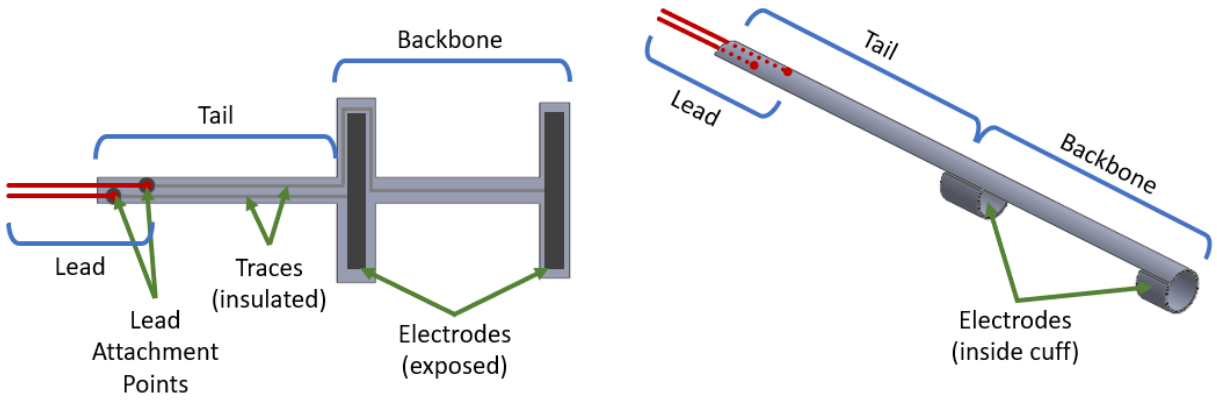
1.7 Trace Width

The minimum allowable trace width (to prevent overheating) was dictated by maximum current requirements and calculated using a PCB trace width calculator (with formulas sourced from IPC-2221). A total minimum trace width of 72 µm was calculated (from parameters: 4.2 mA, 200 nm trace thickness, 10 °C rise at 37 °C ambient temperature). Four connected, parallel 36 µm traces with intermittent bridges between them are used to maintain device flexibility and add in a safety factor of 2, still with sufficient width if two traces are broken.

2 Mechanical Design Options

There are numerous mechanical designs which would meet the device requirements. Several experts in the field stated no preference on backbone and electrode shape for surgical, anatomical, or electrochemical considerations. To select a mechanical design, several designs were fabricated and tested to determine the best option for fabrication, surgical handling, and potential failure modes. The design options are described in this section; details on the fabricated designs and testing protocol is described later in this document.

The microfabricated cuff has three regions: the backbone, the tail, and the lead. As shown in the image below, the backbone is the main body of the device which holds the electrodes and forms the cuff architecture, the tail extends from the backbone and connects the electrodes to the lead with insulated traces, and the lead attaches to the traces at the end of the tail at the lead attachment point.



Note: In all images in the remainder of this section, the shape of the flat electrode array (as it is fabricated) is shown on the left, and the electrode array after thermoforming into shape is shown on the right. Only the Parylene is shown in these images, the electrodes are not drawn in.

2.1 Parylene Backbone Designs

The Parylene backbone is the main part of the device which supports the electrodes. It is microfabricated in a flat configuration on a carrier wafer and then thermoformed into the cuff shape. The considered designs are shown here with basic notes pointing out their main features.

Note: the images in this section only show the backbone portion of the device, not the tail portion.

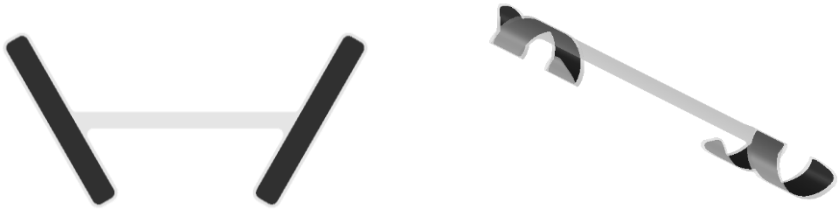
2.1.1 Design A: U-Shaped

Design A not considered for final design

- Dual helical cuff (opposite directions)
    - Similar to design B, but with center Parylene bridge at the bottom of the electrodes

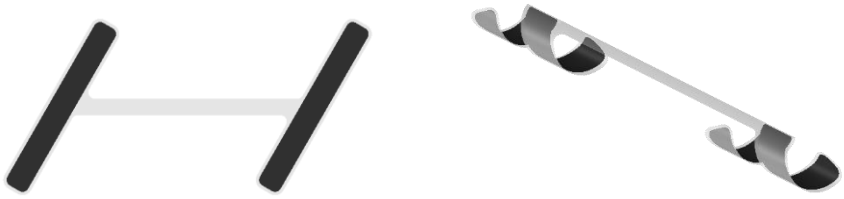
2.1.2 Design B: I-Shaped (tilted, opposite)

- Dual helical cuff (opposite directions)
- 360°+ electrode coverage over a ~1.5-3 mm span (single helical cuff width)



2.1.3 Design C: I-Shaped (tilted, same)

- Dual helical cuff (same direction)
- 360°+ electrode coverage over a ~1.5-3 mm span (single helical cuff width)

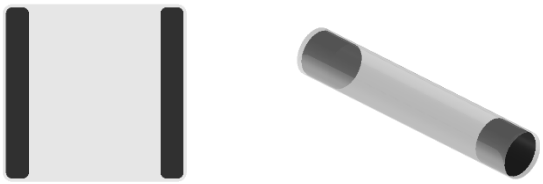


2.1.4 Design D: I-shaped (straight)

- Dual circumferential cuff
- ~335° electrode coverage over a ~0.5-1 mm span (electrode width)

2.1.5 Design E: Full cuff

- Single circumferential cuff with 2 isolated electrodes
- ~355° electrode coverage over a ~0.5-1 mm span (electrode width)



2.2 Cable Routing Designs

To connect the electrodes to the lead, a tail must be attached to the backbone to connect metal traces from each electrode to a bondpad which connects to the lead. The tail must have some length (~2 cm) and slack to allow for motion during the implantation procedure and any motion of the nerve relative to the point where the lead is anchored. The considered tail options are listed here with some potential issues and advantages.

Note: All cable options are shown on backbone design B, but can be applied to any design

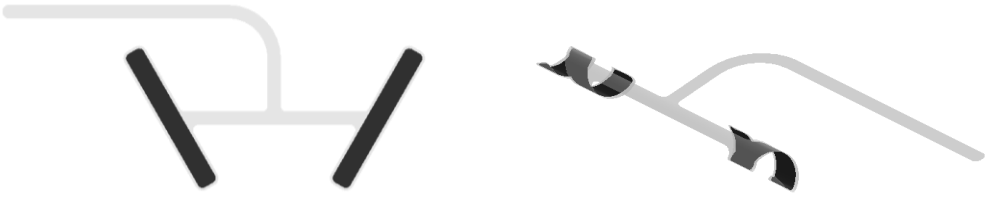
2.2.1 Tail 1: End

Tail 1 not considered for final design

- Tail extending straight from one end
- No strain relief or slack

2.2.2 Tail 2: Centered

- Any torque on tail will be centered on cuff
- Difficult to implement with fins or full cuff designs

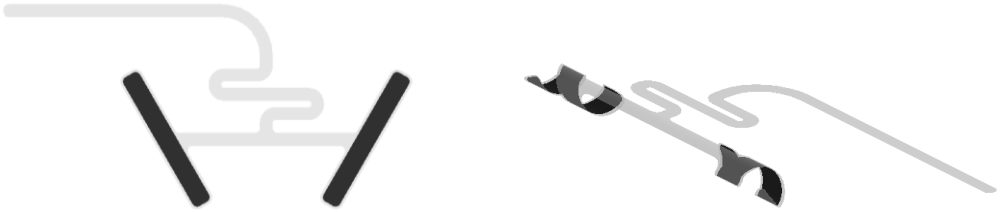


2.2.3 Tail 3: U-turn

- Prevents torque by adding more slack (service loop)

2.2.4 Optional Serpentine Strain Relief

- Auxetic structure to allow stretching
- Could be added at any point in the tail

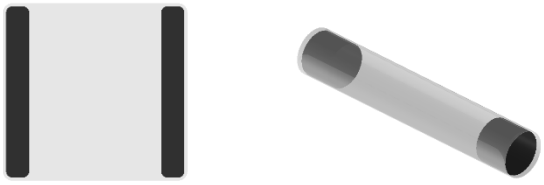


2.3 Nerve Insulation

Insulation of the nerve between the electrodes is critical to constrain the electric field during stimulation. Insulation can be done either with Parylene (fabricated with the rest of the cuff) or PDMS (either a separate cuff added at the end or molded onto the Parylene backbone). Several options (listed here) were considered for nerve insulation.

2.3.1 Solid Parylene

- Design E: Full cuff



2.3.2 Parylene Fins

- Designs A-D: Parylene fins added between electrodes
- More mechanically flexible than solid Parylene cuff
- E-field leakage between the fins

2.3.3 PDMS Insulation

- Separate molded PDMS cuff (can be attached to Parylene or added separately after implantation)
- PDMS can be solid (with any Parylene design) or with fins (with designs A-D)
- E-field leakage if fins are used

3 MECHANICAL DESIGN SELECTION

3.1 DESIGNS TO TEST

The large number of design combinations could not be exhaustively tested, so a subset of 8 designs which spanned all backbone shapes, tails, and other features were selected. Designs are numbered using the following component labels (crossed out designs were not considered):

Backbone	**Tail**	**Other Feature**
~~**(A)** U-shaped~~	~~**(1)** End~~	**(s)** serpentine strain relief
(B) I-shaped (tilted/opposite)	**(2)** Centered	**(f)** fins
(C) I-shaped (tilted/same)	**(3)** U-turn	**(-)** none
(D) I-shaped (straight)		
(E) Full cuff		

The following designs were tested:

- **B2-:** I-shaped/tilted/opposite, centered tail
- **B2s:** I-shaped/tilted/opposite, centered tail with serpentine
- **C2-:** I-shaped/tilted/same, centered tail
- **C3-:** I-shaped/tilted/same, u-turn tail
- **D2-:** I-shaped/straight, centered tail
- **D2f:** I-shaped/straight with fins, centered tail
- **D3f:** I-shaped/straight with fins, u-turn tail
- **E3-:** Full cuff, u-turn tail

To evaluate backbone shape, compare: B2- vs. C2- vs. D2- vs. E3-

To evaluate tails, compare: C2- vs C3- and D2f vs D3f

To evaluate serpentine strain relief, compare: B2- vs B2s

To evaluate fins, compare: D2- vs D2f

3.2 DESIGN SELECTION PROTOCOL

The following testing protocol was used to rank each design and each component. 6 parts for each design were tested (n=6). Steps that may improve with repetition (fixturing for thermoforming, implanting) were tested in varying order for each iteration. Tests which were recorded and scored are labeled and bolded within the protocol.

3.2.1 Thin Film Fabrication

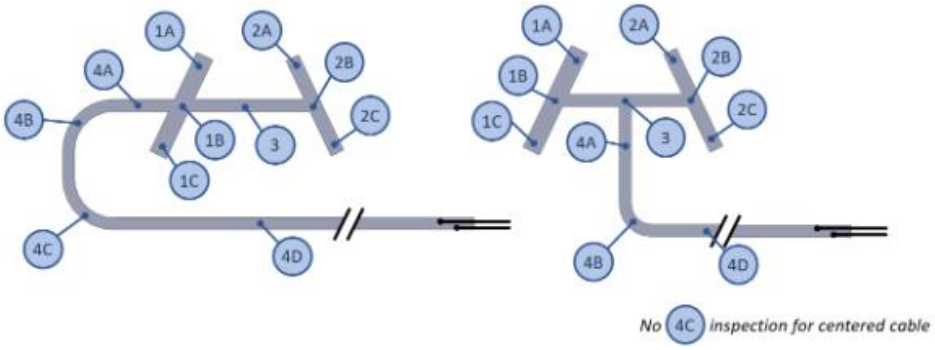
1. Fabricate dummy parts (no metal) using standard thin film processing
2. Using varying base layer annealing conditions (impacts the curvature of the device prior to thermoforming)
    a. 60, 100, and 150 °C
    b. Two parts for each annealing condition (total n=6) were processed in all remaining steps

3.2.2 Thermoforming

1. Release the parts from the carrier wafer
2. Fixture into a 0.5 mm cuff and thermoform at 200 °C for 12 hours
    a. **Test 1 (Fabrication Difficulty):** Record the amount of time required to release the device from the wafer and fixture for thermoforming
        i. A single trained operator thermoformed all parts within each annealing group to prevent data errors from variability between operators
        ii. Captures if any device geometries are difficult to work with
3. Remove parts from fixture

3.2.3 Visual Inspection

1. Inspect parts using a stereoscope (best magnification to visualize the full device - same scope and magnification was used for all devices)
2. **Test 2a (Post-Thermoform Inspection - Shape):** Calculate the fabrication yield for all devices of a given design, where devices that do not hold the fixtured shape are failures
    a. Determines if any geometries are prone to thermoforming shape failures
3. Inspect parts using a 10x microscope at each of the inspection points shown below



4. **Test 2b (Post-Thermoform Inspection - Cracking):** Count the total length of cracks in the Parylene in a 0.25x0.25 mm square area at each inspection point
    a. Determines if any geometries are more prone to cracking during fabrication and at what location cracks are more common
    b. Balances any errors in test 1 (i.e. if a part is fixtured quickly but badly, the good score in test 1 will be balanced by a bad score in test 2)

3.2.4 Evaluate Opening Force

1. Fixture parts with one end of cuff secured to load cell and one end secured to a micrometer stage
2. Use wires to fixture parts such that the cuff is able to open and close as it will in the implantation tools
3. Adjust the micrometer such that the cuff is opened to a 0.5 mm width (the thermoformed size) where the opening force is zero
4. Expand the cuff using the micrometer to 0.8, 1.2, 1.6, and 2.4 mm
5. **Test 3a (Opening Force - Preliminary):** Measure the force required to open the cuff to each of the listed micrometer readings
    a. Proxy for cuff pressure measurements (pressure measurement setup not available at the time of testing)

6. Return the cuff to its closed form (0.5 mm), open to 2.4 mm, then close to 0.5 mm; repeat 18x (including the first measurement, this will be 19 cycles)
7. Expand the cuff using the micrometer (20th cycle) to 0.8, 1.2, 1.6, and 2.4 mm
8. **Test 3b (Opening Force - Cycled):** Measure the change in force required to open the cuff to each of the listed micrometer readings as compared to the first cycle
    a. Proxy for cuff pressure measurements (pressure measurement setup not available at the time of testing)

3.2.5 Implant Cuff

1. Mount cuff onto an interim implantation tool (tweezers modified with wires)
    a. Place cuff on flat surface
    b. Close tweezers and thread tweezer tips into the center of the cuff
    c. Open tweezers and align over nerve
    d. Lower tweezers and close below the nerve, placing cuff
    e. Retract tweezers out of cuff, open, and pull away from nerve
    f. Adjust cuff (if needed) to close snugly around nerve
2. "Implant" (place) cuff onto a dummy nerve
    a. For the dummy nerve, use a wet/overcooked rice noodle ~0.7-0.9 mm in diameter
    b. Hold dummy nerve between two supports suspended 1 mm above a flat surface to simulate allowable space during surgery
3. **Test 4 (Implantation Difficulty):** Rank the devices from least to most difficult to implant
   ** Note: The initial plan was to record the time required to implant the device, however timing was not consistent with the interim implantation tool, so a ranked qualitative comparison was used instead – see Appendix for details on testing*
   ** Note: This test was only performed on one set of devices – it did not accurately represent implantation difficulty because the surgical tool has not yet been developed and the interim tool was not consistent in use*
    a. Will capture if any device geometries are relatively more difficult to implant
    b. A single trained operator performed the simulated implant on all parts within each annealing group to prevent data errors from variability between operators

3.2.6 Simulate Body Movement

1. Simulate stress on device during surgery by pulling tail perpendicular and parallel to the nerve
2. Simulate stress on device during body movement by stretching the nerve along and perpendicular to its length
3. **Test 5 (Cuff Movement):** Measure the distance the cuff moves during the simulated stress
   ** Note: Due to difficulties in performing test 4, cuff movement was observed qualitatively instead of quantitatively; quantitative measurements will be taken with future device generations once a more reliable surgical tool has been developed*
   ** Note: This test was only performed on one set of devices due to the constraint with the implantation tool described under test 4*
    a. Determines if any device geometries are prone to shifting out of place during or after implantation

3.2.7 Repeat Visual Inspection

1. **Test 6a (Post-Implantation Inspection - Shape):** Calculate the shape yield for all devices of a given design, where devices that do not hold the fixtured shape are failures
    a. Determines if any geometries are prone to shape failures during surgical handling
2. **Test 6b (Post-Implantation Inspection - Cracking):** Count the total length of cracks in the Parylene in a 0.25x0.25 mm square area at each inspection point, and subtract the initial inspection length from test 2b
    a. Determines if any geometries are more prone to cracking during surgical handling

3.2.8 Failure Testing

1. Mount cuff on nerve underneath the load cell, then pull the tail end perpendicular to the nerve until failure (n=2 per design)
2. **Test 7a (Pull Failure - Perpendicular):** Measure the force at failure and record the failure point
3. Mount cuff on nerve underneath the load cell, then pull the tail end parallel to the nerve in the direction of the tail until failure (n=2 per design)
4. **Test 7b (Pull Failure - Parallel):** Measure the force at failure and record the failure point

3.3 Score Calculations

Results of each test were scaled to produce a score from 0 to 1 for each tested device and each design component, with 0 being the worst score and 1 being the best score. Tests were also weighted, with higher weights given to more important or more significant tests. Details of how scores were calculated and weights were selected are below:

Test 1: Fabrication Difficulty

$$Design\ Score = 1 - \frac{avg\ fixturing\ time\ (single\ design) - min\ fixturing\ time\ (all\ parts)}{max\ fixturing\ time\ (all\ parts) - min\ fixturing\ time\ (all\ parts)}$$

Note: parts with fixturing times more than 2 standard deviations above the mean were considered outliers and not used for score calculations

Test 2a: Post-Thermoform Inspection – Shape

$$Design\ Score = yield\ (single\ design)$$

Test 2b: Post-Thermoform Inspection – Cracking

$$Design\ Score\ (max\ cracks) = 1 - \frac{max\ cracks\ per\ area\ (single\ design)}{max\ cracks\ per\ area\ (all\ parts)}$$

$$Design\ Score\ (avg\ cracks) = 1 - \frac{avg\ cracks\ per\ area\ (single\ design)}{max\ cracks\ per\ area\ (all\ parts)}$$

$$Design\ Score = \frac{Design\ Score\ (max\ cracks) + Design\ Score\ (avg\ cracks)}{2}$$

Test 3a: Opening Force – Preliminary

$$Design\ Score\ (X\ mm\ opening) = 1 - \frac{avg\ force\ @\ X\ mm\ (single\ design) - min\ force\ @\ X\ mm\ (all\ parts)}{max\ force\ @\ X\ mm\ (all\ parts) - min\ force\ @\ X\ mm\ (all\ parts)}$$

$$Design\ Score = \frac{Design\ Score\ (0.8\ mm) + Design\ Score\ (1.2\ mm) + Design\ Score\ (1.6\ mm) + Design\ Score\ (2.4\ mm)}{4}$$

Test 3b: Opening Force – Cycled

$$Design\ Score\ (X\ mm\ opening) = 1 - \frac{avg\ force\ decrease\ @\ X\ mm\ (single\ design) - min\ force\ decrease\ @\ X\ mm\ (all\ parts)}{max\ force\ decrease\ @\ X\ mm\ (all\ parts) - min\ force\ decrease\ @\ X\ mm\ (all\ parts)}$$

$$Design\ Score = \frac{Design\ Score\ (0.8\ mm) + Design\ Score\ (1.2\ mm) + Design\ Score\ (1.6\ mm) + Design\ Score\ (2.4\ mm)}{4}$$

Test 4: Implantation Difficulty

$$Design\ Score = 1 - \frac{ranking\ (single\ design) - highest\ rank\ (all\ parts)}{highest\ rank\ (all\ parts)}$$

Test 5: Cuff Movement

$$Design\ Score = 1 - \frac{avg\ movement\ distance\ (single\ design)}{\max movement\ distance\ (all\ parts)}$$

Test 6a: Post-Implant Inspection – Shape

$$Design\ Score = yield\ (single\ design)$$

Test 6b: Post-Implant Inspection – Cracking

$$Design\ Score\ (max\ cracks) = 1 - \frac{max\ cracks\ per\ area\ (single\ design)}{max\ cracks\ per\ area\ (all\ parts)}$$

$$Design\ Score\ (avg\ cracks) = 1 - \frac{avg\ cracks\ per\ area\ (single\ design)}{max\ cracks\ per\ area\ (all\ parts)}$$

$$Design\ Score = \frac{Design\ Score\ (max\ cracks) + Design\ Score\ (avg\ cracks)}{2}$$

Test 7a: Pull Failure – Perpendicular

$$Design\ Score = \frac{avg\ failure\ force\ (single\ design) - min\ failure\ force\ (all\ parts)}{max\ failure\ force\ (all\ parts) - min\ failure\ force\ (all\ parts)}$$

Test 7b: Pull Failure – Parallel

$$Design\ Score = \frac{avg\ failure\ force\ (single\ design) - min\ failure\ force\ (all\ parts)}{max\ failure\ force\ (all\ parts) - min\ failure\ force\ (all\ parts)}$$

3.3.1 Test Weights

	Test	Weight
1	Fabrication Difficulty	1
2a	Post-Thermoform Inspection – Shape	1
2b	Post-Thermoform Inspection – Cracking	3
3a	Opening Force – Preliminary	2
3b	Opening Force – Cycled	1
4	Implantation Difficulty	1
5	Cuff Movement	0*
6a	Post-Implant Inspection – Shape	1
6b	Post-Implant Inspection – Cracking	3
7a	Pull Failure – Perpendicular	2
7b	Pull Failure – Parallel	2

** no movement was observed qualitatively, so test 5 was not considered for design selection*

3.4 Design Selection Results

The design selection protocol was performed on n=6 parts for each design and yielded the following results. Full dataset is included as a separate attachment.

Test	Tested Designs							
	B2-	**B2s**	**C2-**	**C3-**	**D2-**	**D2f**	**D3f**	**E3-**
1 (Fab Difficulty)	0.58	0.74	0.59	0.74	0.85	0.81	0.65	0.85
2a (Post TF Shape)	1.00	1.00	1.00	1.00	1.00	0.86	1.00	1.00
2b (Post TF Cracking)	0.86	0.49	0.53	0.74	0.57	1.00	0.75	0.71
3a (Prelim Force)								
3b (Cycled Force)								
4 (Implant Difficulty)	0.43	0.29	0.43	0.57	0.71	0.00	0.14	0.86
5 (Movement)	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
6a (Post Implant Shape)								
6b (Post Implant Cracking)								
7a (Perpendicular Failure)								
7b (Parallel Failure)								
Weighted Aggregate	0.76	0.58	0.60	0.76	0.71	0.78	0.68	0.81

Although these scores indicate that E3- and D2f performed best, this list of designs is not exhaustive, and the component scores should be considered to select the best design.

Scores were compared and separated for each design component (backbone shape, tail shape, other features, and annealing temperature) to produce component scores:

Test	Backbone Shapes			
	B	**C**	**D**	**E**
1 (Fab Difficulty)	0.58	0.67	0.85	0.85
2a (Post TF Shape)	1.00	1.00	1.00	1.00
2b (Post TF Cracking)	0.85	0.65	0.57	0.71
3a (Prelim Force)				

3b (Cycled Force)				
4 (Implant Difficulty)	0.43	0.50	0.71	0.86
5 (Movement)	1.00	1.00	1.00	1.00
6a (Post Implant Shape)				
6b (Post Implant Cracking)				
7a (Perpendicular Failure)				
7b (Parallel Failure)				
Weighted Aggregate	0.76	0.69	0.71	0.80

Test	**Cable Routing**	
	2	**3**
1 (Fab Difficulty)	0.69	0.69
2a (Post TF Shape)	0.92	1.00
2b (Post TF Cracking)	0.54	0.94
3a (Prelim Force)		
3b (Cycled Force)		
4 (Implant Difficulty)	0.21	0.36
5 (Movement)	1.00	1.00
6a (Post Implant Shape)		
6b (Post Implant Cracking)		
7a (Perpendicular Failure)		
7b (Parallel Failure)		
Weighted Aggregate	0.57	0.81

Test	**Other Features**			
	-(s)	**s**	**-(f)**	**f**
1 (Fab Difficulty)	0.58	0.74	0.85	0.81
2a (Post TF Shape)	1.00	1.00	1.00	0.86
2b (Post TF Cracking)	0.86	0.49	0.57	1.00
3a (Prelim Force)				
3b (Cycled Force)				
4 (Implant Difficulty)	0.43	0.29	0.71	0.00
5 (Movement)	1.00	1.00	1.00	1.00
6a (Post Implant Shape)				
6b (Post Implant Cracking)				
7a (Perpendicular Failure)				
7b (Parallel Failure)				
Weighted Aggregate	0.76	0.58	0.71	0.78

Test	**Base Anneal**		
	60°C	**100°C**	**150°C**
1 (Fab Difficulty)	0.84	0.87	0.49
2a (Post TF Shape)	1.00	0.94	1.00
2b (Post TF Cracking)	0.49	0.75	0.65

3a (Prelim Force)			
3b (Cycled Force)			
4 (Implant Difficulty)	n/a	n/a	n/a
5 (Movement)			
6a (Post Implant Shape)			
6b (Post Implant Cracking)			
7a (Perpendicular Failure)			
7b (Parallel Failure)			
Weighted Aggregate	0.66	0.81	0.69

These preliminary scores show that all backbones performed similarly, with B and E slightly outperforming the others. Tail 3 significantly outperformed tail 2, with the serpentine strain relief decreasing scores. Fins improved scores for fabrication steps (tests 1 and 2) but was the most difficult to implant (test 4). Parts with a 100 °C base anneal (moderate curl) performed better than those with high temperature anneal (high curl) or no anneal (flat).

Based on these results, two backbone shapes have been tentatively selected:

1. B3-: I-shaped (tilted, opposite) with u-turned tail
2. E3-: Full cuff with u-turned tail

When testing is completed, the final selections will be re-evaluated.

The curvature due to the base anneal used in these test parts (towards the base layer) was calculated using the model described in Thielen and Meng 2023 [9]. In the functional parts, we are aiming for curvature in the opposite direction (curling towards the top layer) so that the exposed metal will be in contact with the nerve. This curvature is accomplished by adjusting the ratio of the base to top layer thickness. The following parameters were used for this calculation:

Parameter	**Value (Test Parts)**	**Value (Real Parts)**
Base Parylene Width	1200 µm	880 µm
Top Parylene Width	1200 µm	580 µm ** average of 280 µm width across microelectrode openings and 880 µm width between microelectrode openings*
Total Parylene Thickness	8.6 µm	10 µm ** Thickest that will not crack when thermoformed to 0.5 mm diameter*
Base to Top Parylene Thickness Ratio (variable)	3.33:5.27	3:7 to 7:3 ** Minimum Parylene thickness of 3 µm to ensure good insulation*
Parylene Stress	7.8 MPa (at 90 °C) 9.4 MPa (at 100 °C) 17.5 MPa (at 150 °C	7.8 MPa

	** From fit data 90 °C (highest fabrication processing temperature), 100 °C, and 150 °C in Thielen and Meng 2023*	** From fit data at 90 °C (highest fabrication processing temperature) in Thielen and Meng 2023*
Metal Width	0	568 µm ** average of 760 µm width across microelectrode openings and 376 µm width between microelectrode openings*
Metal Thickness	0	220 nm ** 20 nm Ti + 25 nm Pt + 150 nm Au + 25 nm Pt*
Metal Stress	0	-100 MPa ** From fit data in Thielen and Meng 2023*

This yields the following results:

Base Anneal (Test Parts)	**Curvature Diameter (Test Parts)**		**Curvature Diameter (Real Parts)**	**Parylene Thicknesses (Real Parts)**
60 °C	Flat	→	Flat	4.5 µm base 5.5 µm top
100 °C	-21 mm	→	21 mm	4 µm base 6 µm top
150 °C	-3.5 mm	→	7.5 mm ** minimum diameter within constraints*	3 µm base 7 µm top

4 Final Design Summary

Electrode Size:

- Small/helical cuff: 3x18 200 µm microelectrodes (1.70 mm^2 total area)
- Large/helical cuff: 4x22 200 µm microelectrodes (2.77 mm^2 total area)
- Small/circumferential cuff: 9x14 200 µm microelectrodes (1.70 mm^2 total area, 1.56 mm^2 contact area with smallest nerve)
- Large/circumferential cuff: 6x18 200 µm microelectrodes (3.39 mm^2 total area, ~1.60 mm^2 area in contact with smallest nerve)

Backbone Shape (two options):

- I-shaped, tilted, opposite directions with u-turned tail
- Full cuff with u-turned tail

Parylene Thickness:

- 4 µm base + 6 µm top (promotes mild curvature towards top layer)

Mask Design:

- 4x36 µm traces to each electrode, connected at periodic intervals
- 36 µm gap between traces
- 20 µm or greater gap between all metal edges and Parylene edges (i.e. metal edge is insulated by at least 20 µm wide Parylene)

CAD files (3D model and 2D mask layout) are available as a separate document.

5 Attachment from Lead to Parylene

Med-Ally is working to develop a process to attach the Parylene cuff to their leads. This will be completed in Y2. In the interim, the leads (or other wires for benchtop testing) can be attached to the traces of the Parylene cuff using conductive silver epoxy (Epo-TEK MED H20E)

6 Testing

A battery of tests will be used to ensure the parts are working as designed on the benchtop and in vivo. Detailed testing plans will be developed in Y2, but the section below outlines the tests that will be included.

6.1 Visual Inspection

- Optical microscopy
- Electron microscopy

6.2 Mechanical Testing

- T-peel testing (adhesion strength)
- Motion of nerves
    - Nerve phantom in matrix on shaker table
- Nerve compression
    - Requirements: <20 mm Hg pressure (chronic), <80 mm Hg pressure (acute)

6.3 Electrical Testing

- Identify defects (shorts/cracks)
- Leakage (insulation integrity)

6.4 Electrochemical Testing

- Cyclic voltammetry (CV): determine charge storage capacity, electrode surface area
- Electrochemical impedance spectroscopy (EIS): determine electrode impedance, device integrity
- Cross talk: determine insulation integrity, defects

6.5 Accelerated Lifetime Testing

- Saline with reactive oxygen species
- Repeat visual and electrochemical testing

7 Timeline

Y1	Q4	Aug 2023	Complete first design of microfabricated cuff (documentation and prototype)
Y2	Q2	Feb 2023	Complete first design of surgical placement tool (documentation and prototype)
			Develop test procedures and performance metrics
	Q4	Aug 2024	Demonstrate benchtop reliability of cuff and placement tool
Y3	Q1	Nov 2024	Release feature-complete documentation and open-source libraries
			Establish collaborations with other HORNET teams
	Q4	Aug 2025	Complete evaluation of cuff and placement tool

8 Appendix: Test 4 / Implantation Difficulty

After the successful microfabrication of the Parylene device, a preliminary implantation test on a nerve-like model was performed. Overcooked wet noodles were used owing to their physical properties being close to nerves and being in the sub-mm range.

A noodle is elevated by two glass slides at its extremities. The Parylene device is opened by a tweezer extended by one straight metal wire at each handling tip. Then it is put on the noodle before cuffing it when retracting the two wires from the device.

The goal of this preliminary approach is to assess all the main parameters to properly place the device and to sort all the different designs according to the placement difficulty.

Several parameters were retained to appraise the placement difficulty.

1. Wire placement: The two wires must be perfectly joined without crossing each other. In this case, the two wires couldn't enter the cuff.
2. Device orientation: A particular heed should be paid to ensure that the cuff is open in the correct position, facing down.
3. Opening range trade-off: Large cuff opening enable an easier placement but increases the chance that the cuff goes out of the wires.
4. Incomplete cuffing: When placed on the noodle, part of the backbone can be partially folded, preventing the cuff from perfectly cuffing the nerve.

Each of the 8 fabricated designs were evaluated.

Evaluation by their backbones:

- B and C are quite equivalent during the placement procedure. Their main issue is that they easily create partial folding, and the end of the cuff does not fully cuff the noodle.
- D is equivalent to B and C but tends to not create partial folding.
- Df is difficult to operate when trying to open it as some fins easily go out from the wire.
- E is the least difficult one to place.

Evaluation by their tail:

As we must hold the device by its extremities when placing the wires, a 3 U-turn tail is much more practical than a 2-centered tail generally. But this observation is only linked to this placement procedure which is not optimal yet.

Sorting from the easiest to place to the most difficult:

1. **E3-:** Full cuff, u-turn tail
2. **D2-:** I-shaped/straight, centered tail
3. **C3-:** I-shaped/tilted/same, u-turn tail
4. **C2-:** I-shaped/tilted/same, centered tail, **B2**-: I-shaped/tilted/opposite, centered tail
5. **B2s:** I-shaped/tilted/opposite, centered tail with serpentine
6. **D3f:** I-shaped/straight with fins, u-turn tail
7. **D2f:** I-shaped/straight with fins, centered tail

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