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Neuro-Kinesis EP Laboratory Technology

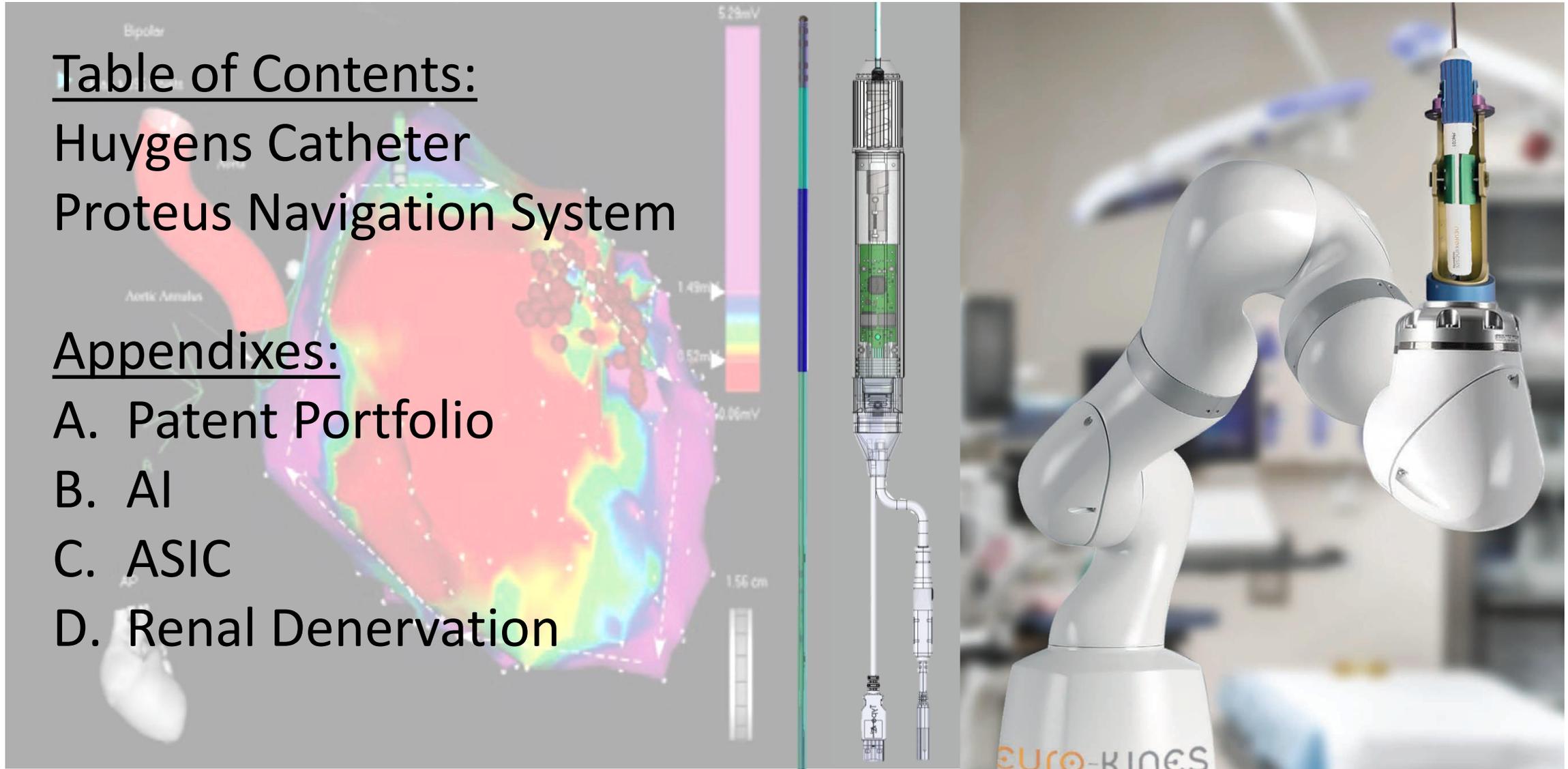
“What you can’t see, you can’t treat”



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Clinical Indication

Patient Condition

- Recurrent episodes of Ventricular Tachycardia (VT) and Ventricular Fibrillation (VF) result in 300,000 deaths per year in the US. (1)
- A small subset of these patients (< 8,000 per year) have scar-related VT, a potentially fatal cardiac rhythm disorder. (2)

Current Electrical Mapping Techniques:

- An electroanatomical map of the heart is generated to identify low voltage scar tissue (<0.5 mV)
- Entrainment and Pace-mapping are used to locate critical sites where the VT re-enters the healthy myocardium and disrupts the heart rhythm.

Treatment Approach:

- Perform RF or Pulsed Field Ablation at critical sites identified in the electroanatomical map.
- Ablation at targeted sites "dechannels" the scar and connects areas of electrically unexcitable scars to remove the arrhythmia.

Patient Outcome:

- With current technology, recurrence of VT is reported in 35% of cases.

1. Foth C, et al. *Ventricular Tachycardia*. StatPearls Publishing; 2025 Jan

2. Yousuf OK, et al. *Trends and Outcomes of Catheter Ablation for Ventricular Tachycardia in a Community Cohort*. *JACC Clin Electrophysiol*. 2018 Sep;4(9):1189-1199. Figure 1.

Comparison

Catheter	Measurement methods available			Cardiac Signal Transmission		Detectable Signal
	Biopotential mapping	Impedance mapping	Pacing	Analog	Digital	< 50 μ V
Current Mapping Catheters	✓	X	✓	✓	X	X
Huygens Catheter	✓	✓	✓	✓	✓	✓

- Current diagnostic and mapping technologies provide incomplete mapping data, complicating the accurate identification and treatment of arrhythmias
- As a result, ablation success rates for chronic heart rhythm disorders remain low - **only 50% to 70%**
- Patients with nonstandard or complex arrhythmias often require **multiple procedures**. Increasing patient burden which contributes to rising healthcare costs.

Huygens Catheter Features

A Better Microscope:

- Local amplification and digitization improves SNR to enable detection below 100 microvolts
- New split-electrode array design to remove background noise.
- Enables measurement of low voltage biopotential signals for detailed characterization of scar tissue.

Local Impedance Spectroscopy:

- An effective method of mapping the impedance of the endocardium to characterize subsurface scar tissue.
- Combined with biopotential mapping data to generate a map to guide the ablation procedure.

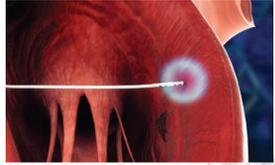
AI implementation:

- AI-based data processing to optimize signal quality for a better patient outcome.

Huygens™ Catheter Concept of Operation

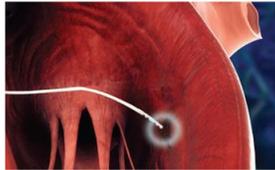
1. Electrode array

- Intracardiac Signal Detection
- Potential and Impedance



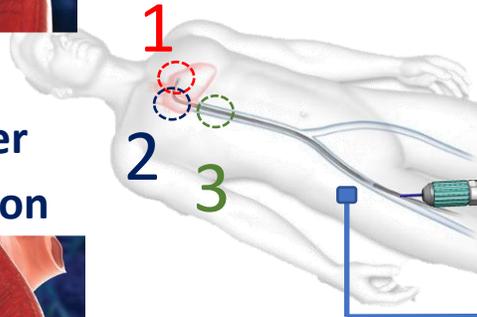
2. Catheter

- Deflection

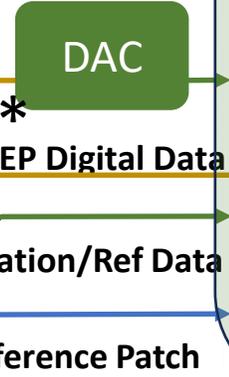


3. Signal Processing

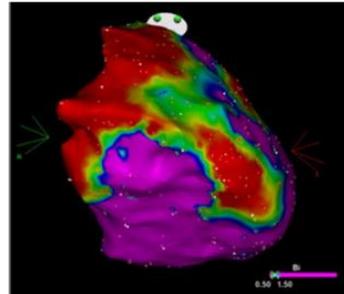
- Filtering
- Analog to Digital Conv.



Interconnect Cable



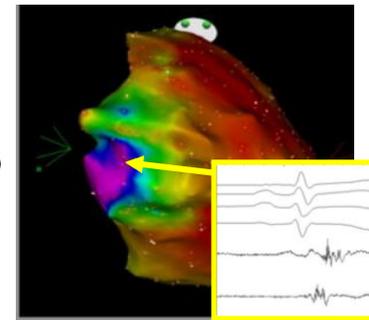
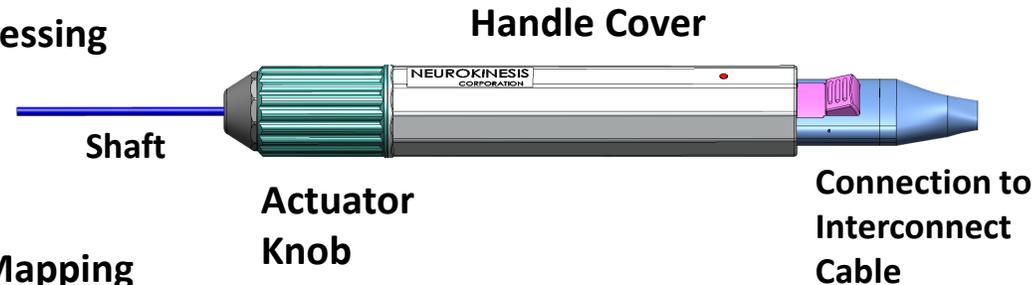
Commercial Mapping System



Electro-anatomical Mapping

4. Handle

- Catheter Tip Deflection
- AI-based data processing
- System Control
- Conductivity
- Data Management
- Interface with EP Mapping Station



Substrate Impedance Mapping

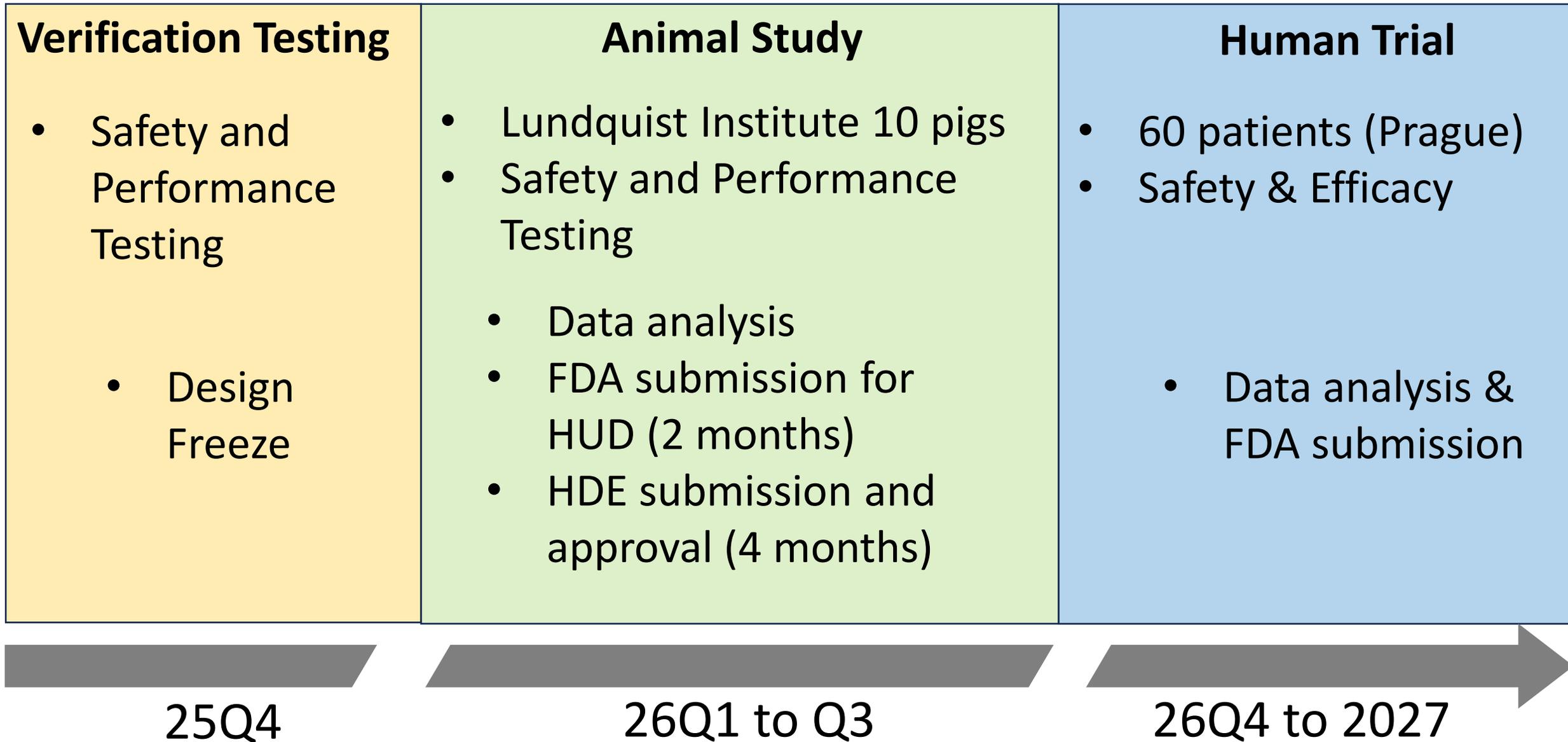
* DAC for commercial systems that do not accept direct digital data

HDE Fastrack Pathway

- NKC aims to utilize the Humanitarian Use Device (HUD)/Humanitarian Device Exemption (HDE) pathway to fast-track approval for in human testing of the Huygens Catheter (3)
- Provides an expedited pathway for human trials in 24 months
- Conventional 510k PMA pathway averages 5 years
- The HUD/HDE Pathway
 - A medical device intended to benefit patients in the treatment or diagnosis of a disease or condition that affects or is manifested in not more than 8,000 individuals in the United States per year (Section 3052 of the 21st Century Cures Act (Pub. L. No. 114-255))
 - Humanitarian Device Exemption (HDE): a marketing application for an HUD (Section 520(m) of the Federal Food, Drug, and Cosmetic Act (FD&C Act)). An HDE is exempt from the effectiveness requirements of Sections 514 and 515 of the FD&C Act and is subject to certain profit and use restrictions.

[3. Humanitarian Device Exemption | FDA](#)

HDE Fastrack Regulatory and Clinical Plan

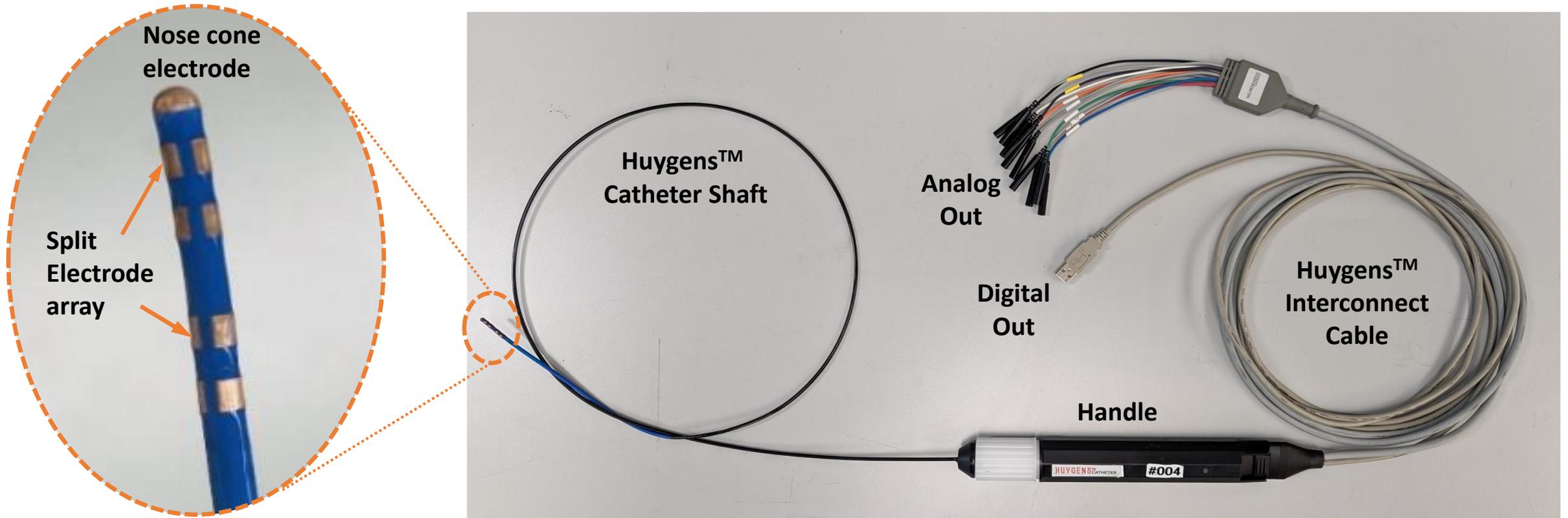


Huygens Catheter Technology



Huygens™ Catheter Design

Design based on the mechanical form factor utilized in commercial EP catheter designs.
Adaptable to Quadripolar, decapolar, or basket catheter designs.

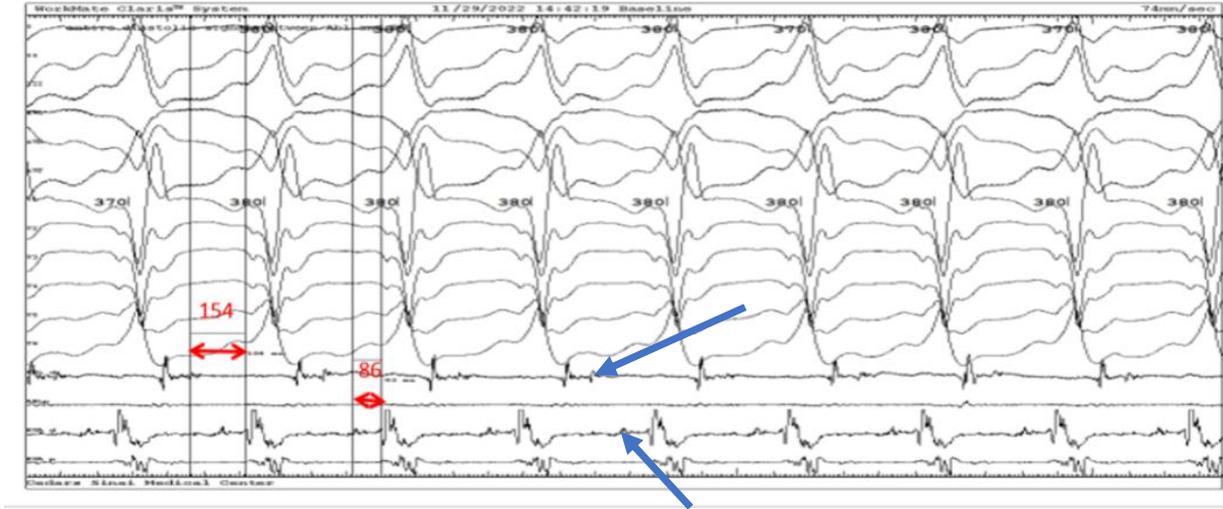


Method and Apparatus for Creating a High-Resolution Map of the Electrical and Mechanical Properties of the Heart, Patent # US 2012/031066A1

Limitations of Current EP Mapping Technology

Mapping/ablation procedures for treating arrhythmias have a success rate of 60% to 70%.

1. Conventional arrhythmias.
 - Well characterized and treated with great success
 - **Established rule book for diagnosis and treatment**
2. Persistent complex arrhythmias
 - Difficult to identify the origin/cause of the arrhythmia
 - Patients do not respond to conventional ablation protocols
 - Multiple ablation procedures are common with low success
3. Complex arrhythmias are caused by the development of recurring or reentrant electrical circuits within patches of dense scar tissue.
 - The signature signals of reentrant electrical circuits are Complex Fractionated Atrial Electrograms (CFAEs).
 - CFAEs can be found at areas of slow conduction, the pivot point of turning wavelets, wave collision, fibrillatory conduction, and rotor meandering. [1]
 - Current mapping systems that rely on post collection data processing are unable to detect many of these signals reliably due to their **short time course and magnitude**.



Examples of CFAEs, sub-50 microvolt signals (blue arrows) and time shifts (red arrows) that are used to make diagnostic conclusions that direct administration of ablative therapy.

*Personal Communication
Dr. Eli Gang, MD*

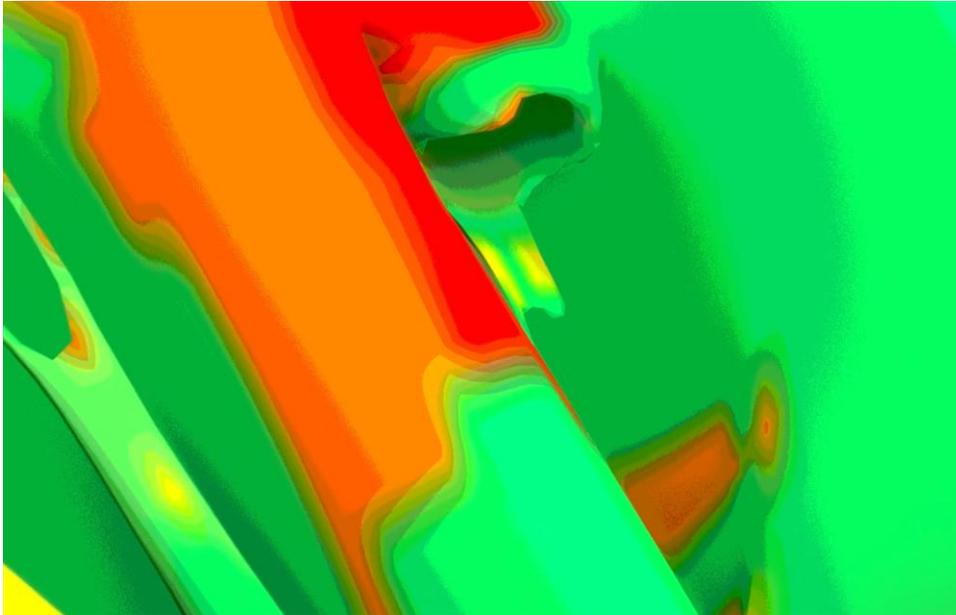
➤ **The rules learned through performing mapping and pacing procedures to treat conventional arrhythmias have had limited success when treating complex arrhythmias.**

[1] Zaman JA, Peters NS, Narayan SM. Rotor mapping and ablation to treat atrial fibrillation. *Curr Opin Cardiol.* 2015 Jan;30(1):24-32. doi: 10.1097/HCO.000000000000123.

Need	Huygens™ Solution
<p>A Better Microscope: Detection of Low Voltage EP signals at or near Scar Tissue</p>	<ul style="list-style-type: none"> • <u>Local</u> EP signal processing at the point of sample collection to improve signal fidelity. <ul style="list-style-type: none"> ➤ Each electrode detects the EP signal at its unique position on the tissue. ➤ “Smart electrodes” multiplex, amplify, filter, and digitize the EP signal <u>locally at the distal tip</u>. ➤ Eliminates any noise characteristics and immunizes the sample from noise contamination during transit through the catheter shaft. ➤ Improves SNR to enable detection below 100 microvolts. • Implementation of split electrode array design enables removal of far-field signals to give a more accurate measurement of the cardiac potential during mapping.
<p>Characterization of Scar Tissue by Local Impedance Spectroscopy</p>	<ul style="list-style-type: none"> • Local impedance spectroscopy is utilized as a method of mapping the endocardium. • Proven to be a more effective way to characterize scar tissue than existing EP methods. • Provides additional information on possible mechanism and location of myocardial scar tissue, which improves targeting for ablation for treatment of persistent complex arrhythmia. • Combines impedance and EP map data to generate a map to locate rotors
<p>AI to improve safety, efficiency and patient outcome.</p>	<ul style="list-style-type: none"> • AI-based data processing • AI-assisted diagnosis • AI-based cooperative robot arm technology (COBOT) that works with the EP physician to improve precision and efficiency of the ablation procedure.

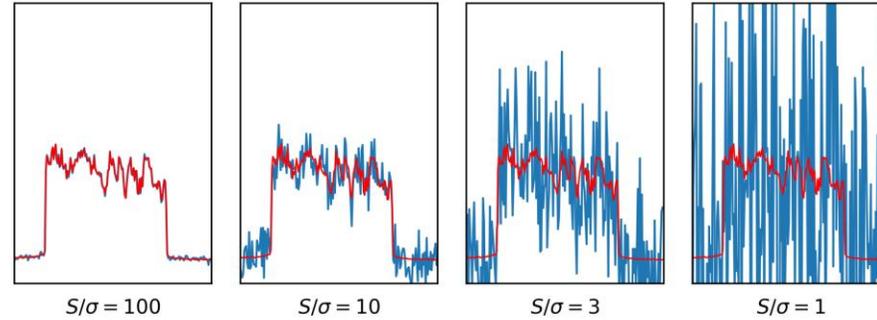
A Better Microscope

High Resolution EP Mapping



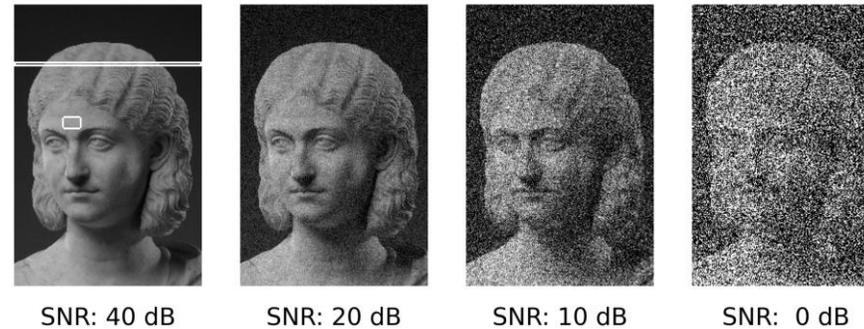
The Signal to Noise Ratio

Current EP mapping technologies are unable to detect CFAEs and other low magnitude signals because the signal is often lost in the background noise.



$$SNR = \frac{\text{Signal}}{\text{Noise}}$$

In imaging, improving the signal to noise ratio (SNR) reveals fine features that were previously invisible.



Common SNR level criteria:
 <10 Insufficient
 10 to 15 minimum
 15 to 24 acceptable
 25 to 40 deemed good.
 >41 excellent

Source Wikipedia: A gray-scale photography with different signal-to-noise ratios (SNRs). The SNR values are given for the rectangular region on the forehead. The plots at the bottom show the signal intensity in the indicated row of the image (red: original signal, blue: with noise).

In electro-anatomical mapping this is significant, because what we can't see, we can't treat.

The Signal to Noise Ratio

SNR example

(N°) Referenc...	(N°) Test Image	SNR [dB]	PSNR [dB]	RMSE	MAE
(1) lena.jpg	(1) Additive Gaussian Noise	14.64264767	19.22412607	25.03970330	20.02188399
(1) lena.jpg	(1) median	24.06156606	28.64304447	8.46609737	4.05889893
(1) lena.jpg	(1) Salt and pepper	11.89652663	16.47800504	34.35067143	19.50747681

Original signal →

Current analog catheter
SNR 15dB →

← NKC digital catheter
SNR 25dB

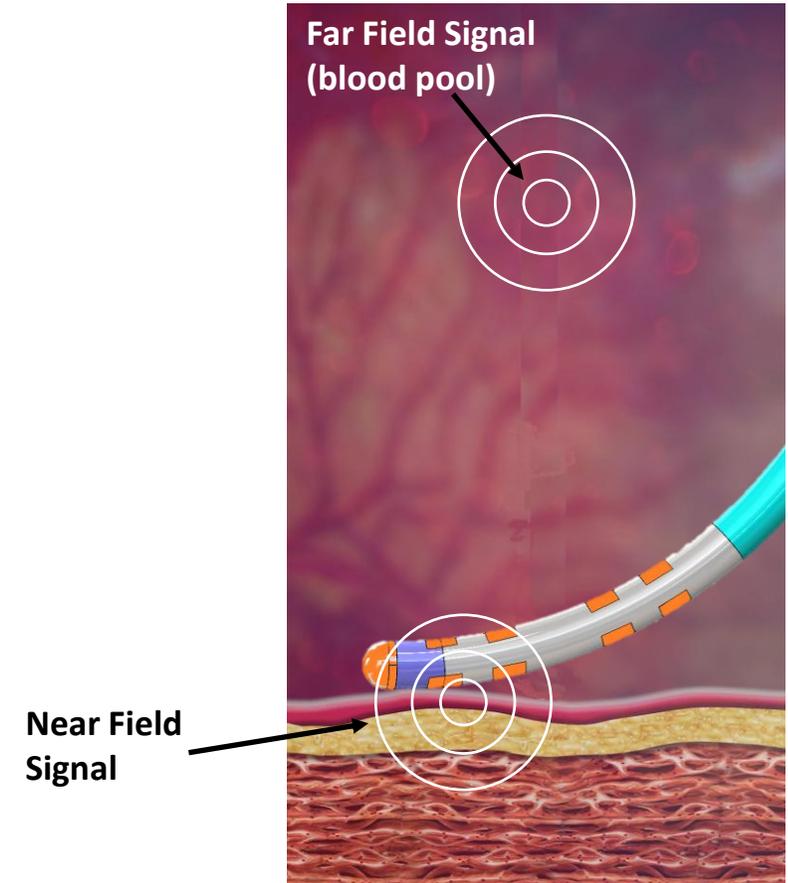
- Better quality image
- Better resolution

Source: Image by Daniel Sage at the Biomedical Image Group, EPFL, Switzerland

Huygens™ Catheter Approaches to Improving SNR

Far-field noise reduction

- In a full ring electrode configuration, the measurement represents an imprecise average of blood pool and tissue and additional far field signals including pulmonary vein ostia and sources in the OR.
- The Huygens™ Catheter features a split electrode design.
- Enables separate measurement of tissue and blood pool
- Far-field signal contributions can be removed from the measurement, giving a more accurate measurement of the cardiac potential during mapping.



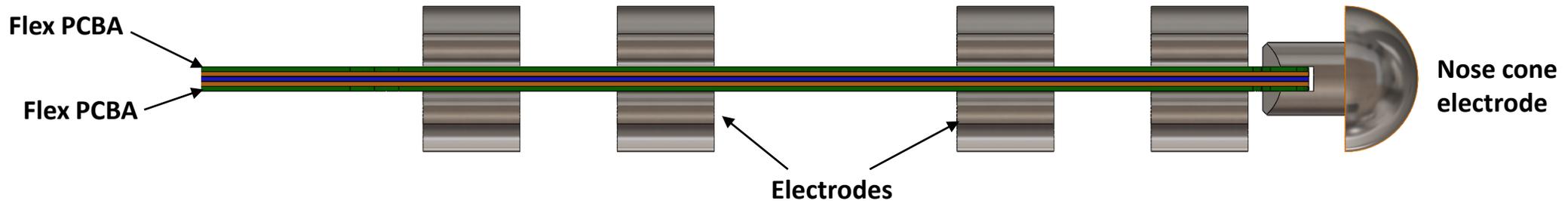
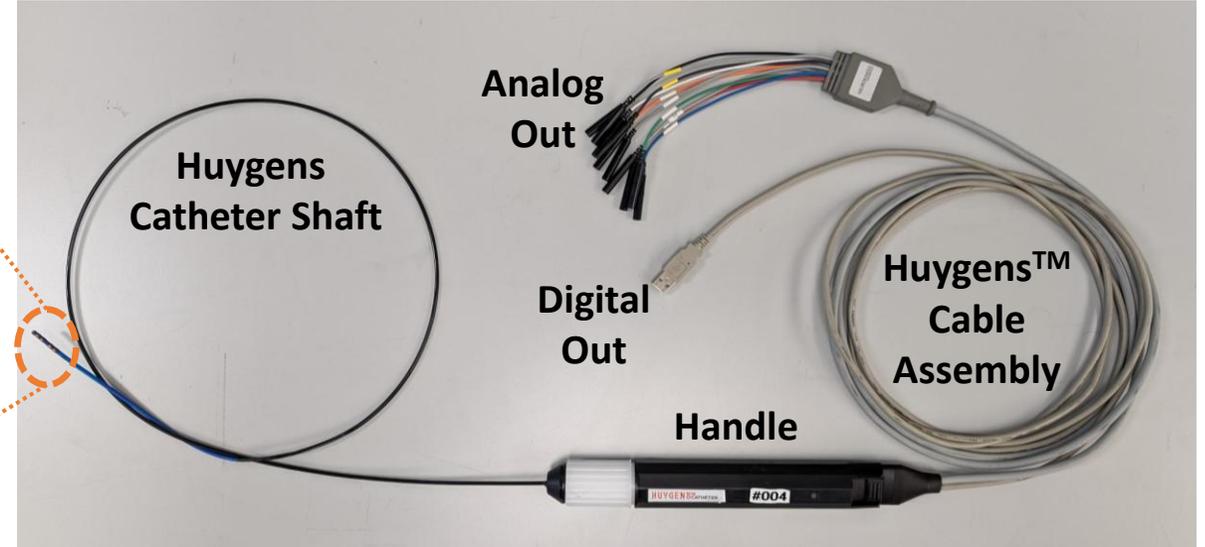
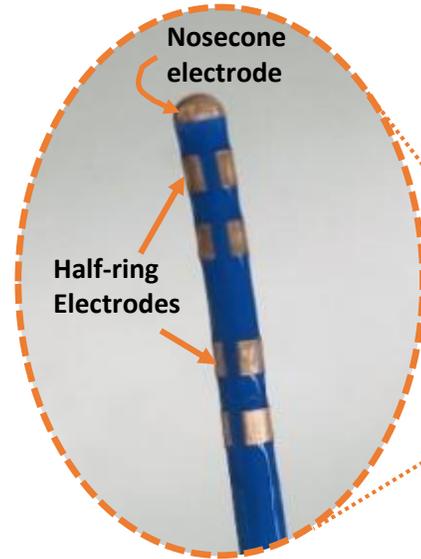
Method And Apparatus For Measuring Biopotential And Mapping Ephaptic Coupling Employing A Catheter With Mosfet Sensor Array, Patent # US2014/00181114 A1

Huygens™ Catheter Approaches to Improving SNR

Half ring electrode design to reduce far-field signal contribution

Detection:

- 8 Half-ring electrodes
- 1 Nose cone reference electrode.
- 2 mm spaced electrode pairs separated by 5 mm for localized bipolar measurements.



Method and Apparatus for Creating a High Resolution Map of the Electrical and Mechanical Properties of the Heart, Patent # US 2012/031066A1

Huygens™ Catheter Electronics Design

Digital to Analog Signal Conversion protects signal from noise pickup



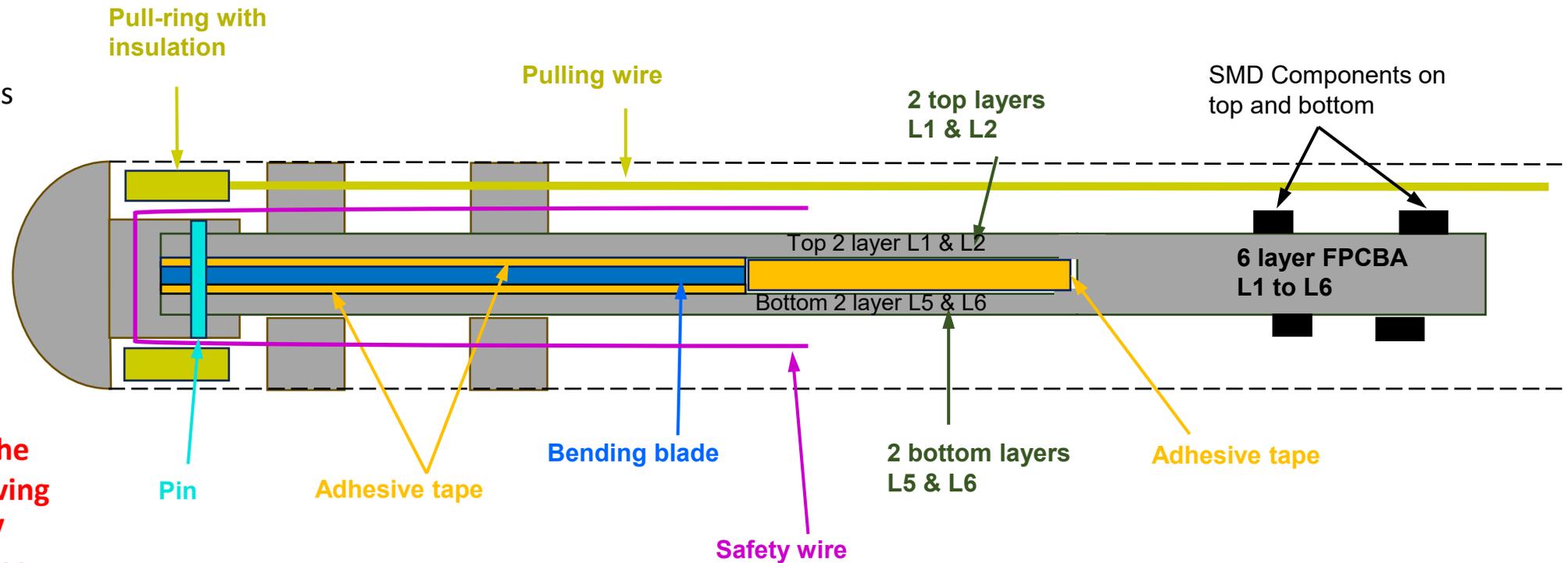
Signal capture:

- 8 channels
- 1 reference
- 4 on two flexible PCBs

Local Signal Processing:

- Filtering
- Digital to Analog conversion
- Sent to handle

- **Reduces noise contributions from the environment, improving resolution to < 50 μ V**
- **Improved SNR enables detection of CFAEs**



Method and Apparatus for Creating a High Resolution Map of the Electrical and Mechanical Properties of the Heart, Patent # US 2012/031066A1

Huygens™ Catheter High-Res Mapping

Improvement in signal to noise ratio leads to high resolution EP mapping

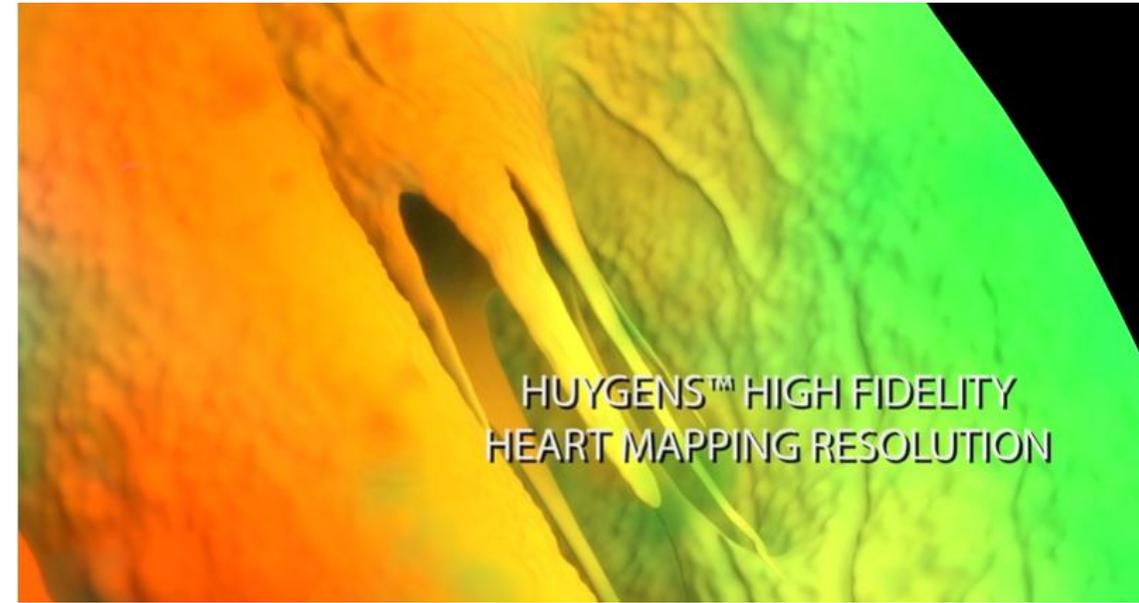
Current analog catheter



VS

NKC digital catheter

- Better quality image
- Better resolution



Local Impedance Mapping

Mapping Scar Tissue
with Impedance
Spectroscopy

Link: [Impedance](#)

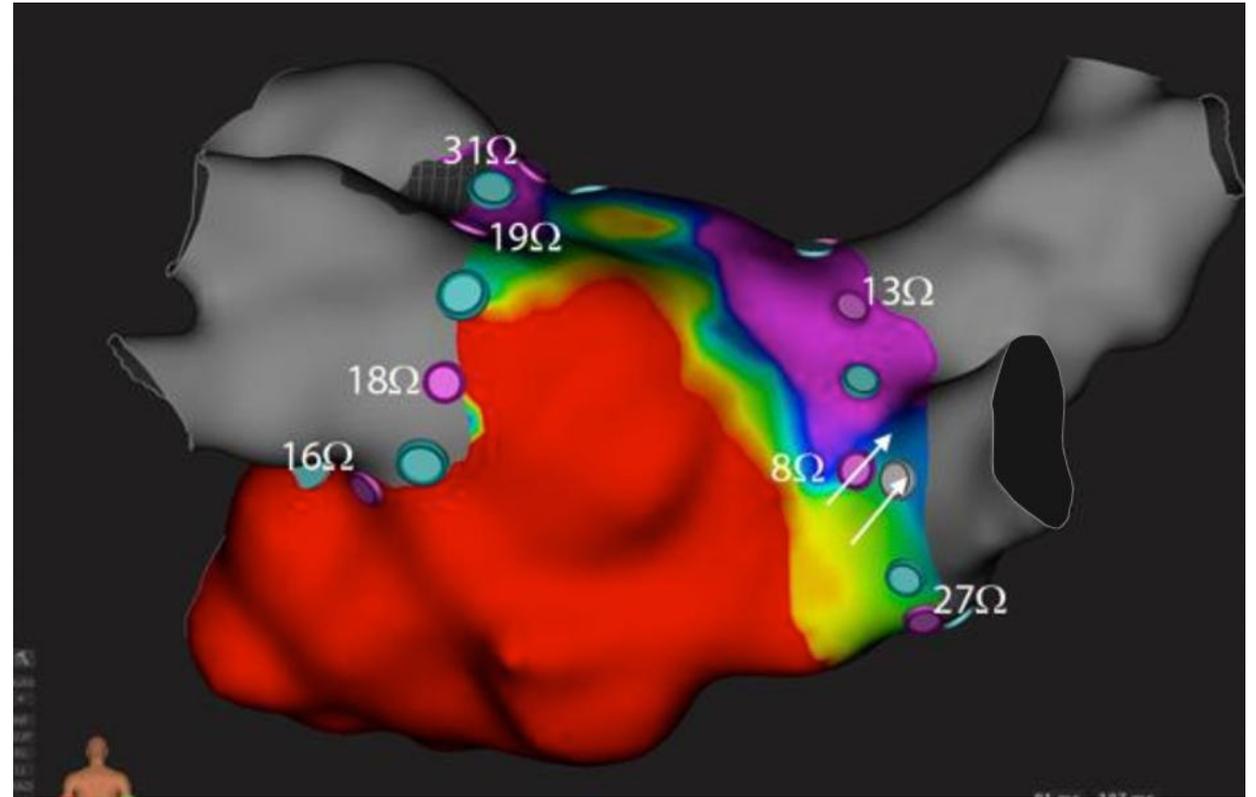


Image reference: Ignacio Garcia-Bolao, MD, et al, Local Impedance Drop During Pulmonary Vein Isolation Predicts Late Reconnection in Patients with Paroxysmal Atrial Fibrillation, Heart Rhythm. 2020; 17(5, Supplement):S341

Impedance Mapping as a tool for electroanatomical mapping

Impedance can be used to map scar tissue

Study by Unger et al.

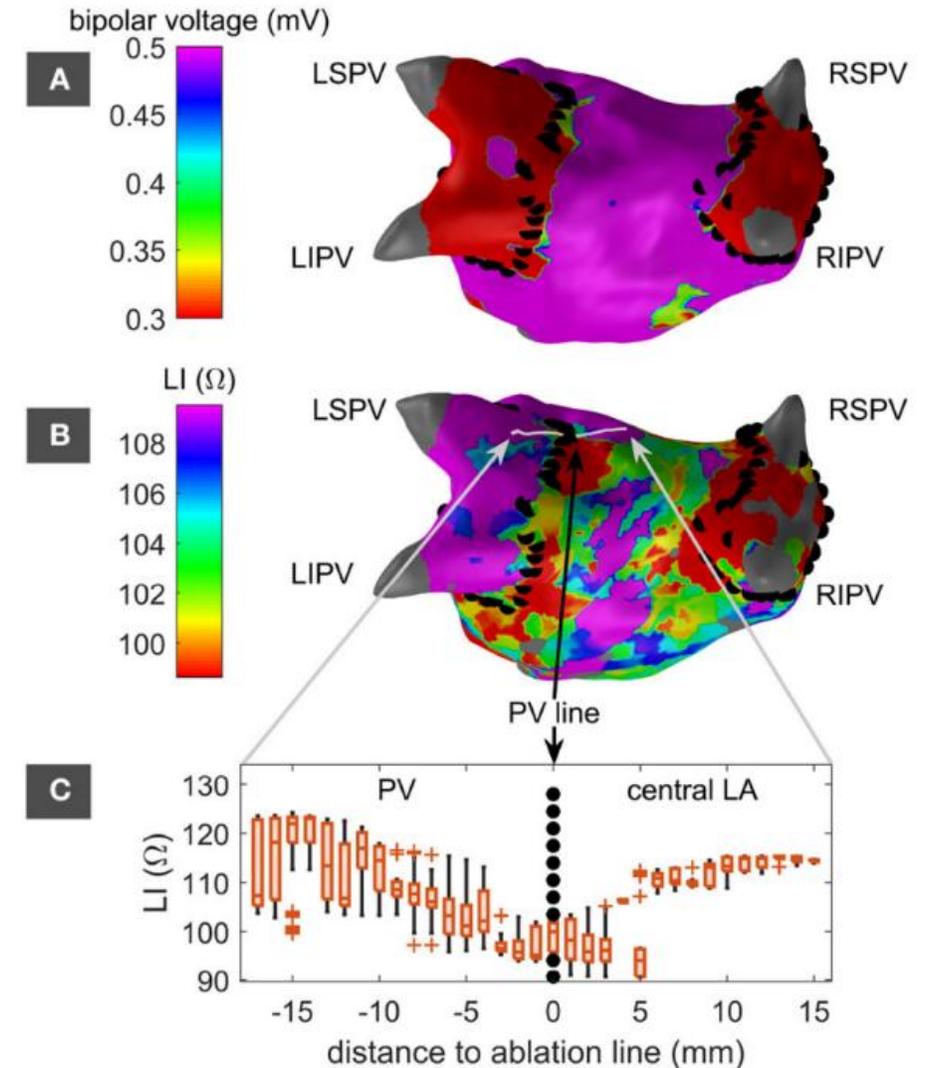
- Myocardial tissue from a Pulmonary Vein Isolation procedure was measured using EP mapping and Local Impedance (LI) measurements by the DirectSense™ Impedance Analyzer (Boston Scientific).

Result:

- EP mapping measured a block of tissue between the ablation zones at 0.3-0.5 mV, near the threshold limitation of existing EP catheters
- **Impedance Spectroscopy was capable of characterizing tissue behind closed ablation lines that did not show any voltage by EP mapping.**

Conclusion:

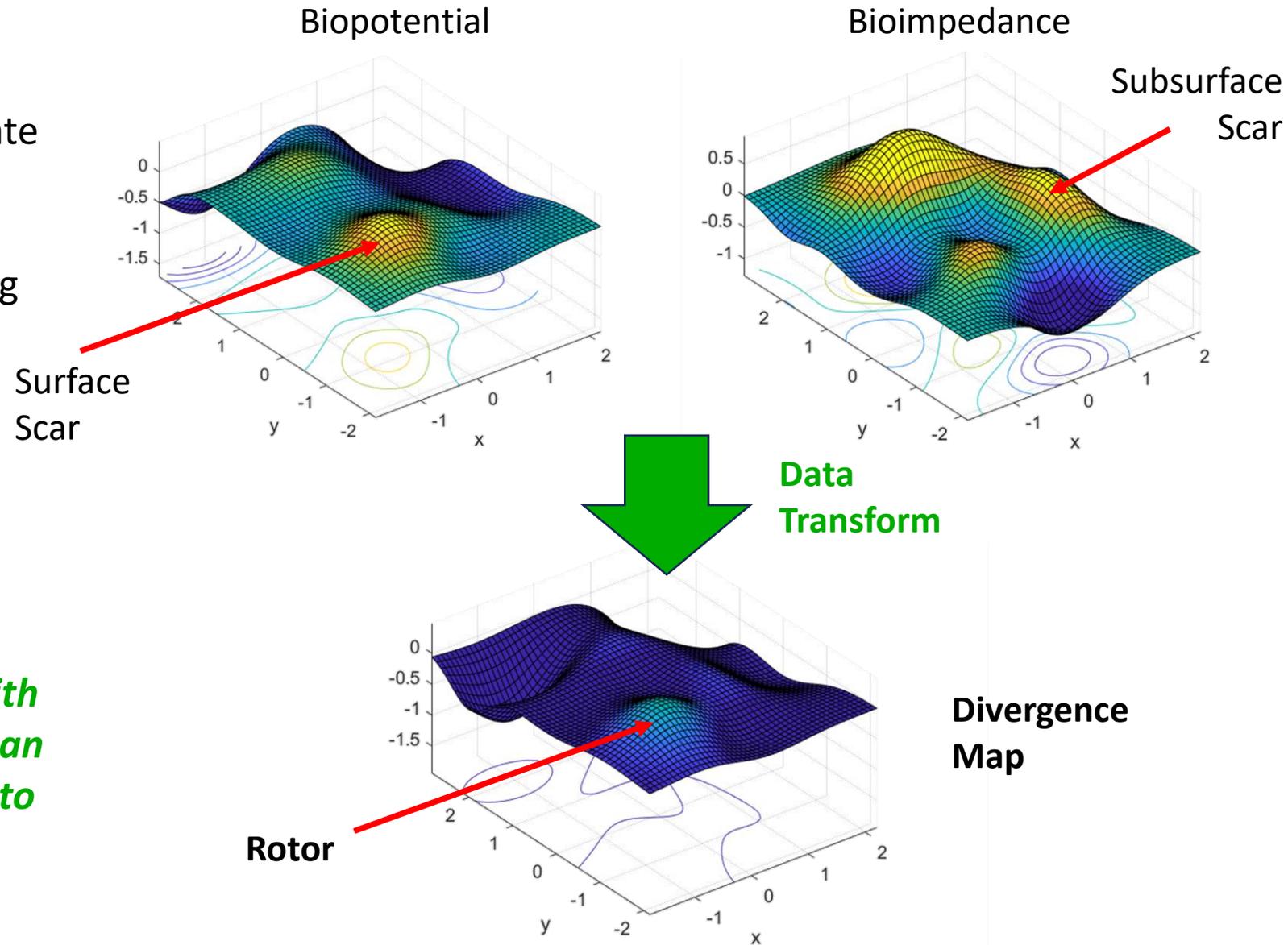
- **Local impedance mapping can complement electrogram based substrate mapping to build up an extensive picture of the myocardial tissue to improve patient outcomes.**



Unger LA, et al (2022) Local Electrical Impedance Mapping of the Atria: Conclusions on Substrate Properties and Confounding Factors. *Front. Physiol.* 12:788885. doi: 10.3389/fphys.2021.788885

Huygens Catheter Approach

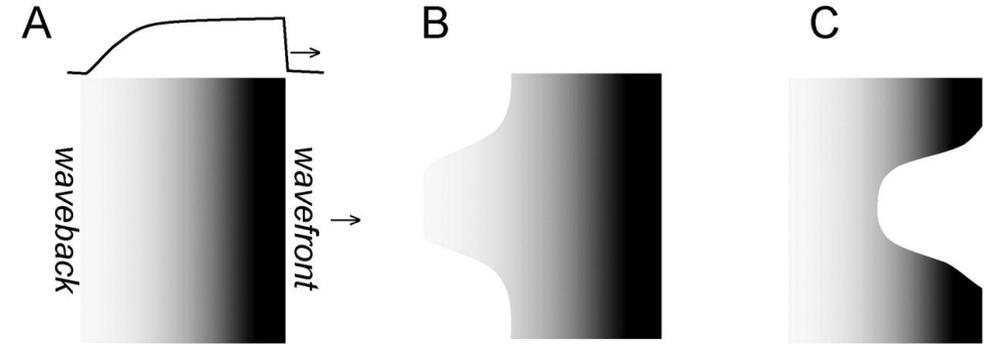
1. Improve EP Mapping Resolution by
 - Using split electrodes to eliminate far field signals from the EP measurement
 - Converting EP signal from analog to digital to minimize environmental noise
2. Use substrate impedance spectroscopy to generate a cardiac impedance map.
3. **Combine high-resolution EP data with cardiac impedance data to develop an energy flux map of the heart tissue to define the origin of CFAEs (e.g., rotors) as locations for ablation therapy.**



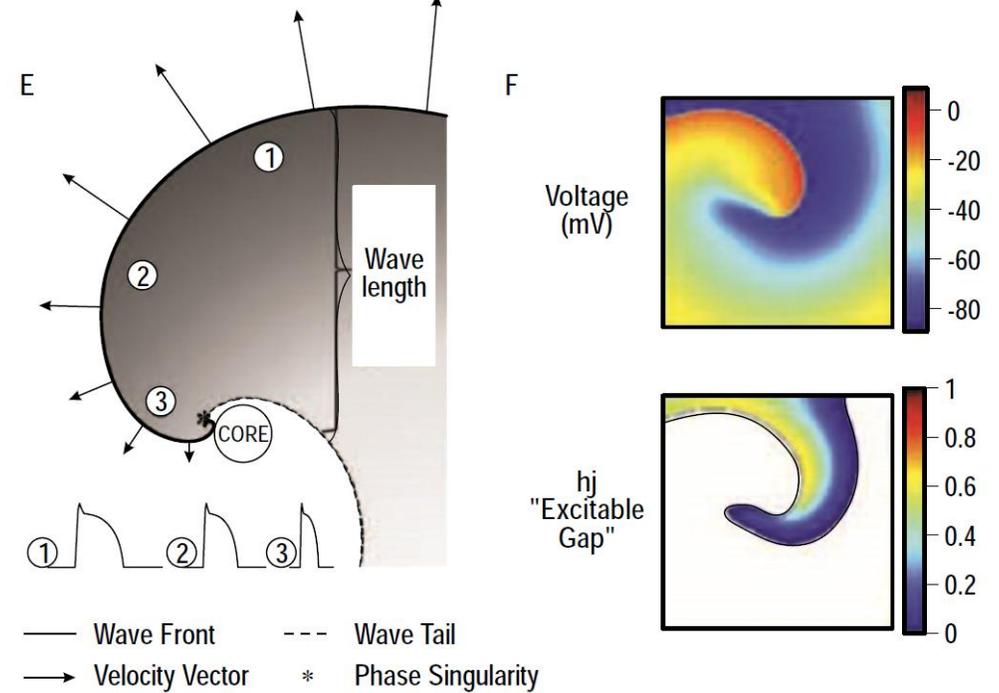
THE USE OF LOCAL AMPLIFIERS AND A HUYGENS SENSOR ARRAY IN MEASURING BIOELECTRIC SIGNALS AND CLINICAL APPLICATIONS THEREOF, Patent PCT/US2022/030399

Rotors – A Crucial Driver of Fibrillation in Persistent Afib

- Rotor: A wave that processes around a central core.
- Formation:
 - Cardiac excitation produces an electrical *wave*, with a *wavefront* and a *waveback*.
 - In a healthy heart, the wavefront and waveback rarely touch.
 - In patients with Afib, the wavefront and waveback can intersect, causing a rotation and strong curvature in the wave.
 - If the wavebreak rotates around an anatomically defined circuit (such as a scar), it is called an anatomic reentry.
 - If the wavebreak rotates without an anatomic circuit, it is called a **rotor**.
- ***Rotors are difficult to detect with existing EP technology***
 - ***Signal below 0.5 mV***
 - ***Can shift position in the myocardial tissue.***



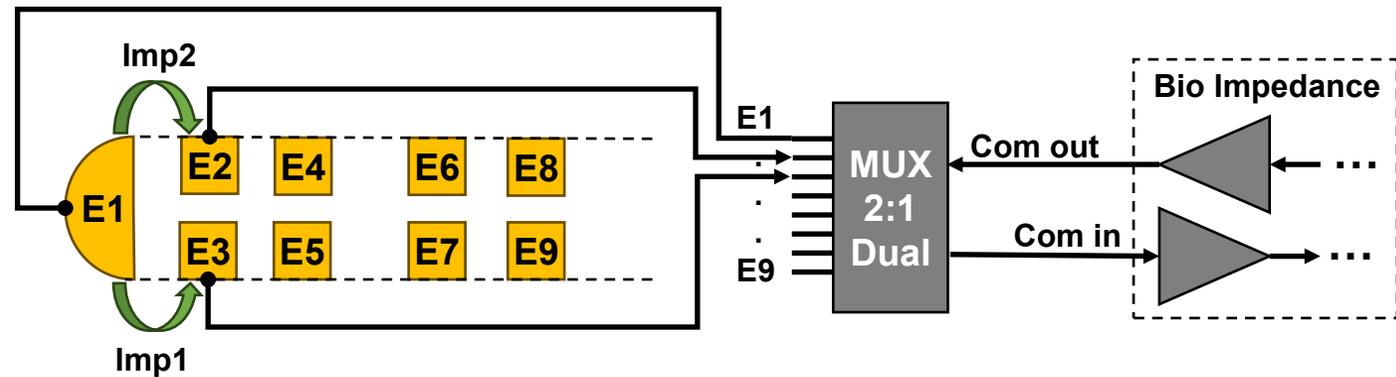
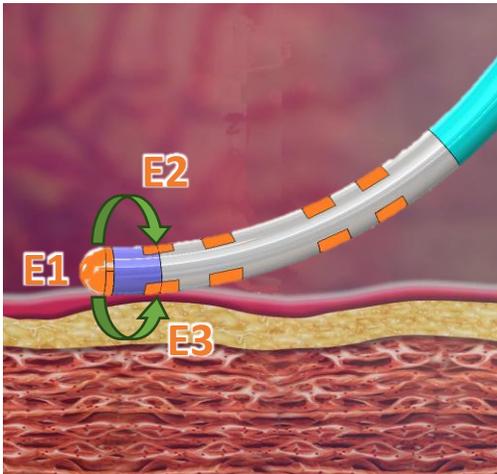
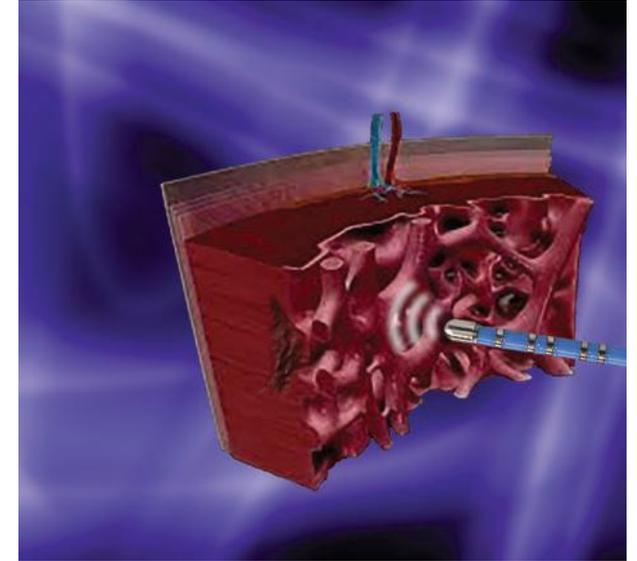
Weiss, et al, Dynamics of Atrial Fibrillation <https://doi.org/10.1161/CIRCULATIONAHA.104.529545>



THE USE OF LOCAL AMPLIFIERS AND A HUYGENS SENSOR ARRAY IN MEASURING BIOELECTRIC SIGNALS AND CLINICAL APPLICATIONS THEREOF, Patent PCT/US2022/030399

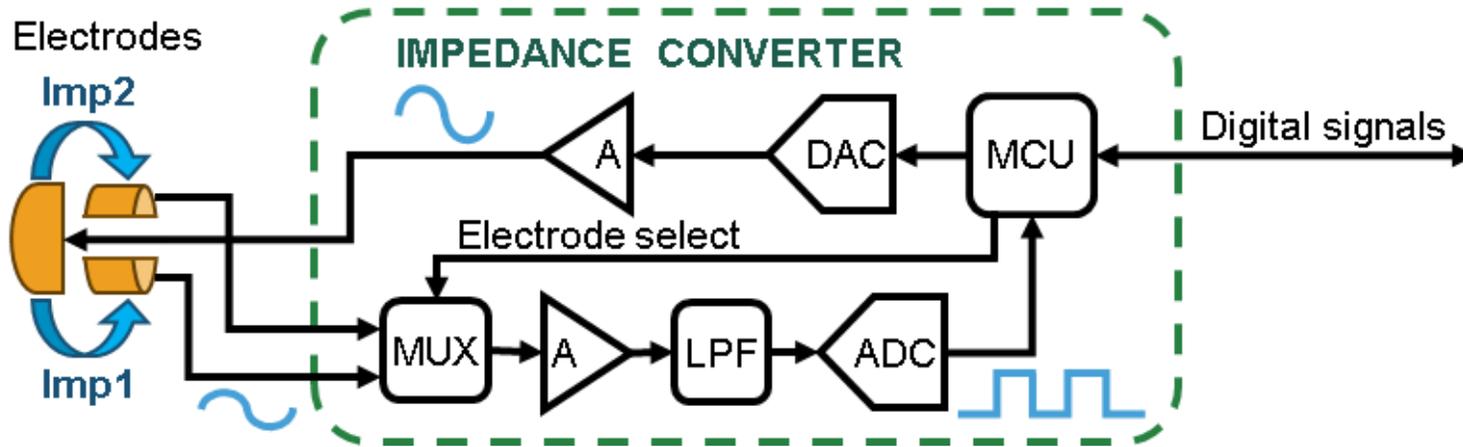
Huygens™ Catheter Electrical Function – Impedance Spectroscopy

- The Huygens Catheter impedance spectroscopy feature is designed to detect scar tissue features that are invisible to conventional EP catheters.
 - Small superficial scars with deep subsurface features
 - Large superficial scars with shallow depth
- Localized tissue conductance measurements are taken between at tissue spanned by E2, E3, and E1.



System and Method for a Catheter Impedance Seeking Device, Patent #US 2010/0130854 A1

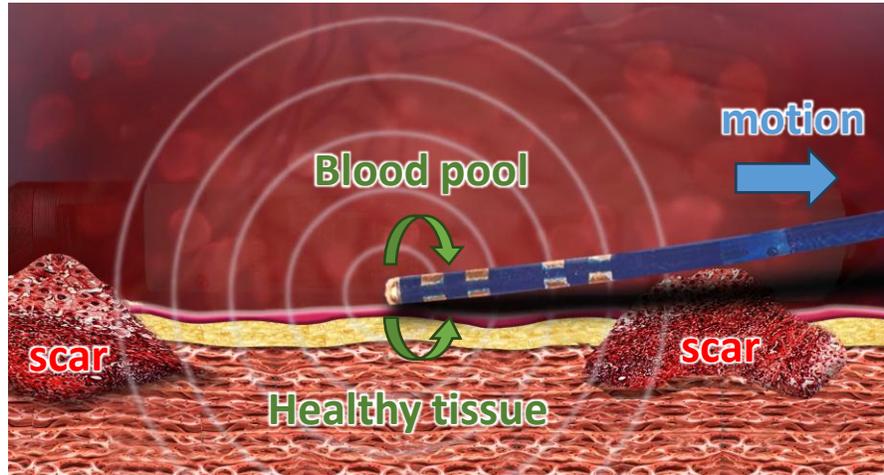
Huygens™ Catheter Electrical Function – Impedance Spectroscopy



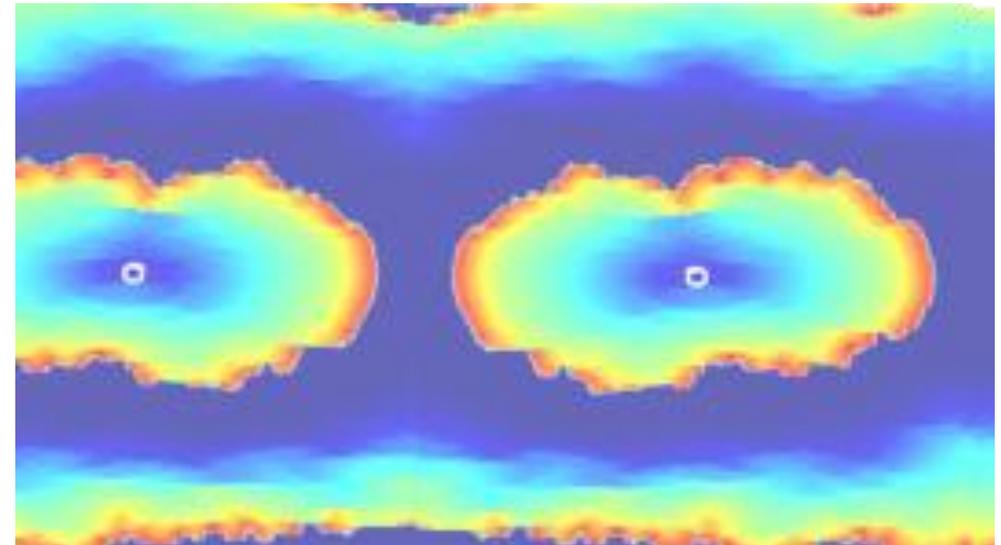
- The impedance converter contains a high-speed DAC that generates an AC signal sweeping from 1 to 100KHz (default for measurement is 3KHz).
- This AC signal is conditioned and isolated and then sent to the nosecone electrode.
- The AC signals travels through the tissue or blood pool and is captured by the half-split electrode.
- The input signal is then amplified, filtered and read with an ADC converter.
- Inside the MCU a Direct Fourier Transform DFT is processed and returns the complex impedance value Imp1 and Imp2.

Huygens™ Catheter Electrical Function – Local Impedance Spectroscopy

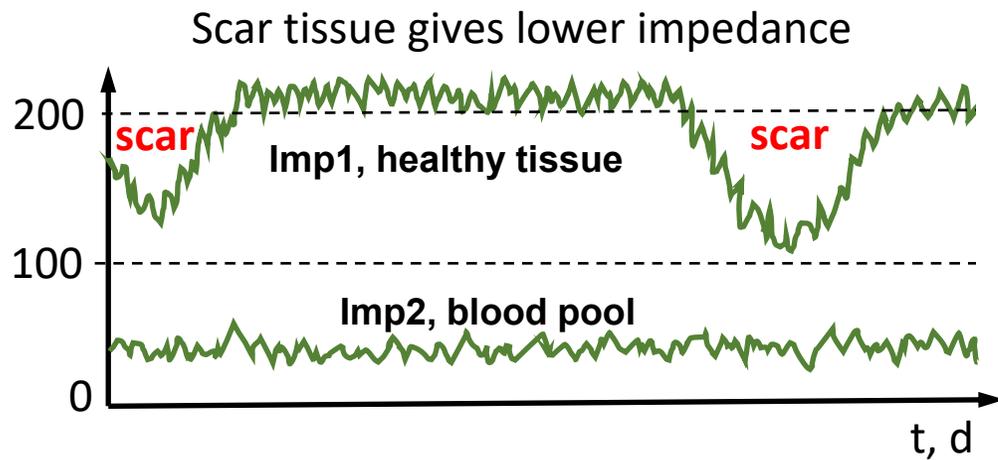
- Impedance Mapping of scar tissue with the Huygens Catheter



Impedance map



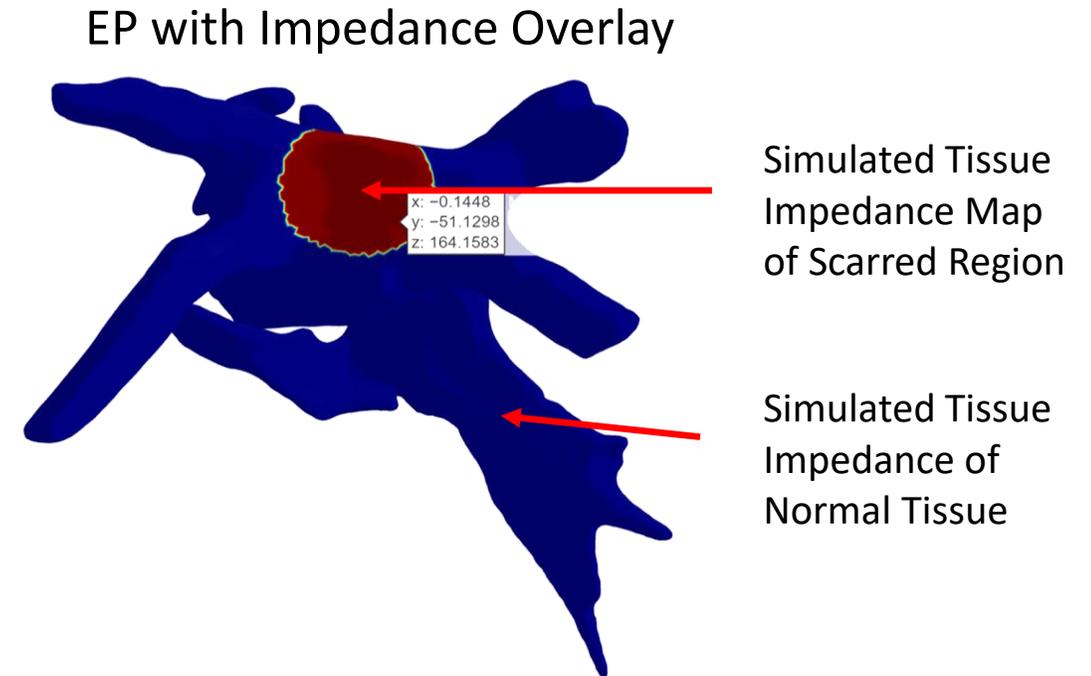
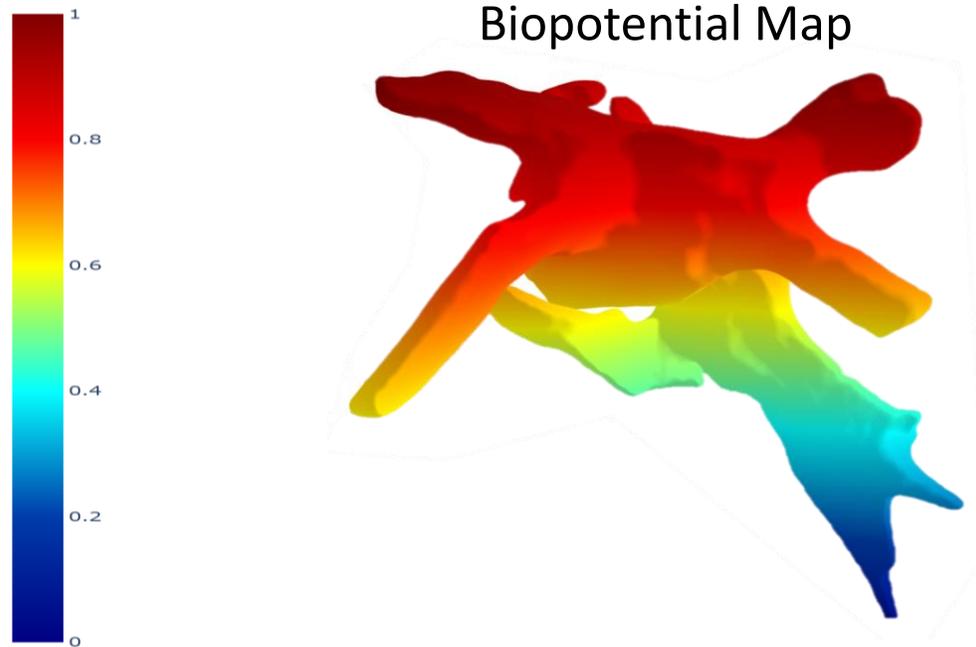
Ganesan et al., Locating Atrial Fibrillation Rotor and Focal Sources Using Iterative Navigation of Multipole Diagnostic Catheters, Biomedical Engineering Society, 2019



System and Method for a Catheter Impedance Seeking Device, Patent #US 2010/0130854 A1

LIS and Biopotential Modeling with a commercial mapping system

- The Huygens Catheter transmits biopotential and impedance data to a commercial mapping station for display and can be viewed separately or overlaid.
- The maps below were generated using software developed at NKC. EP data was derived from a clinical study and impedance assigned a single value over a specific region of the map to simulate a scar.



→ The data in these maps will be used to calculate an energy flux map of the heart tissue to define the origin of CFAEs (e.g., rotors) as locations for ablation therapy.

Detection of Rotors with the Huygens™ Catheter

The propagation of electrical waves through the heart generates an electrical (E) and magnetic field B_{MHV} .

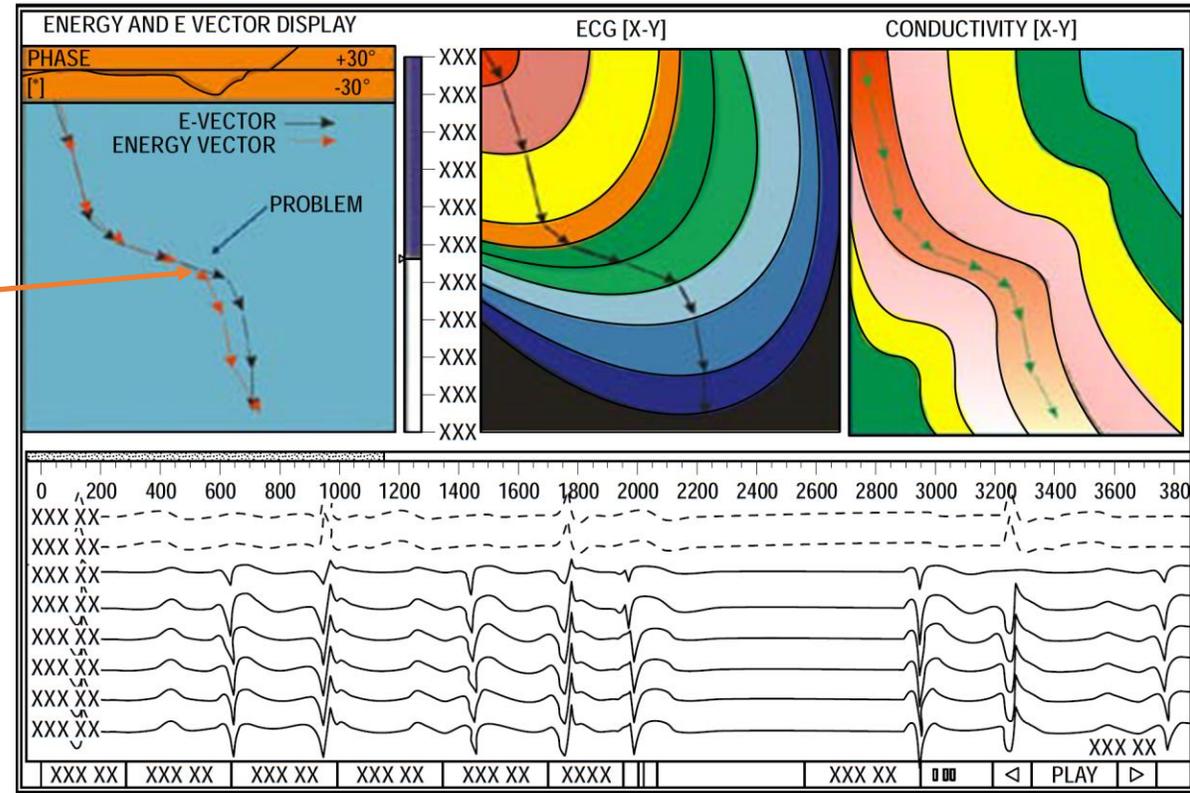
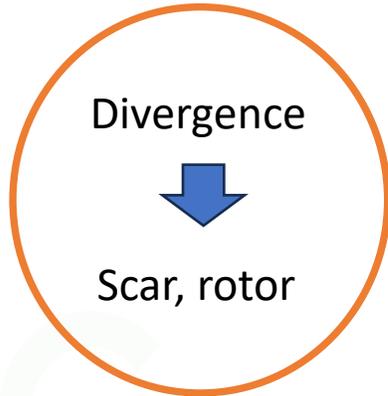
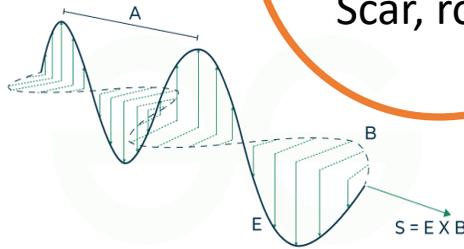
$E = Z J$ Ohm's law

$\nabla \times B_{MHV} = \mu_0 J$ Ampere's law

From Ohms and Ampere's Law, we get:

$\nabla \times B_{MHV} = \mu_0 \frac{E}{Z}$ (1)

$PEV = \frac{1}{\mu_0} E \times B$ (2)



THE USE OF LOCAL AMPLIFIERS AND A HUYGENS SENSOR ARRAY IN MEASURING BIOELECTRIC SIGNALS AND CLINICAL APPLICATIONS THEREOF, Patent PCT/US2022/030399

- From equations 1 and 2, the direction of energy flow or Poynting Energy Vector (PEV) can be computed in terms of the measured values E and Z , where μ_0 is the permittivity.
- In healthy tissue, the direction of the PEV follows the electrical wavefront (E), which minimizes energy loss.
- In unhealthy tissue, anisotropies (**changes in μ_0**) will cause these vectors to diverge, increasing energy loss.
- **The location of this divergence defines an abnormality (scar, rotor) where ablation therapy should be performed.**

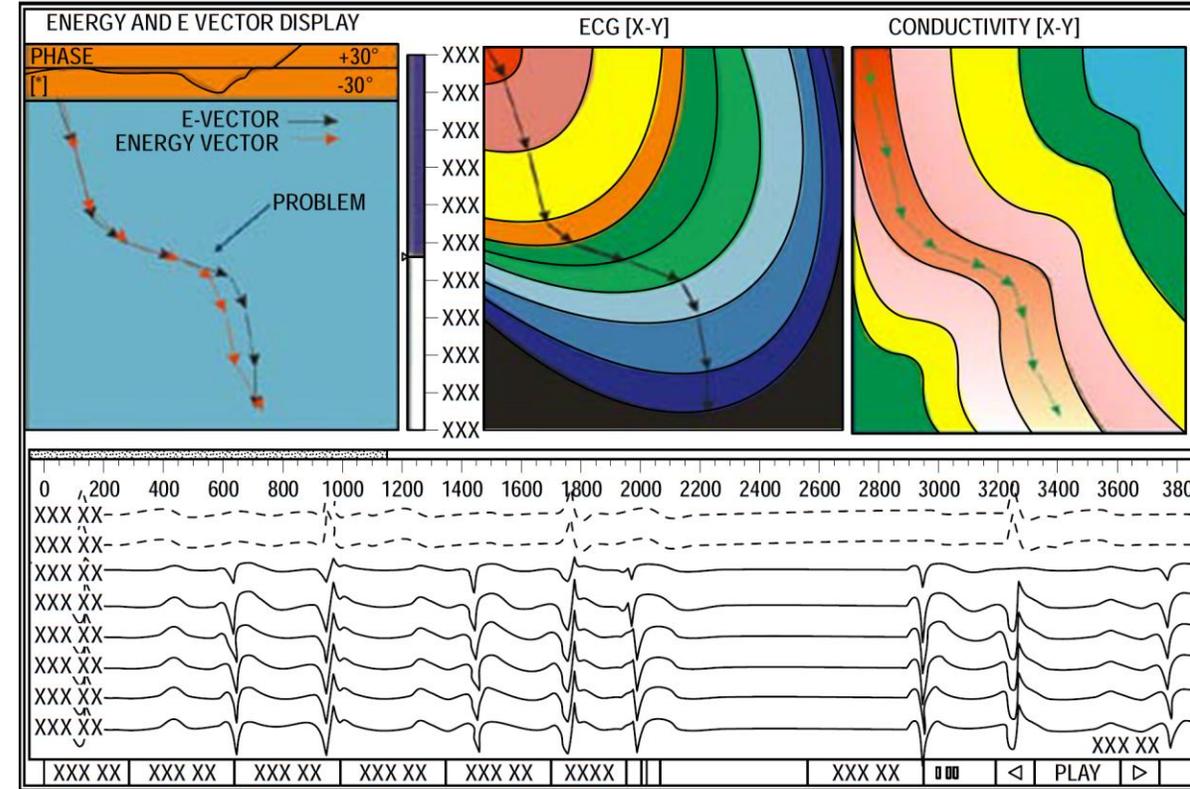
Locating Rotors with the Huygens™ Catheter

NKC's catheter measures this divergence through simultaneous measurement of impedance value (**Z**) and DC potential (electro-anatomical map) at the same endocardial tissue site.

The measured value of the impedance (**Z**) is used to recover the true Magnetic Heart Vector, \mathbf{B}_{MHV}

$$\nabla \times \mathbf{B}_{MHV} = \mu_0 \frac{\mathbf{E}}{\mathbf{Z}} \quad (1) \quad \mathbf{PEV} = \frac{1}{\mu_0} \mathbf{E} \times \mathbf{B}_{MHV} \quad (2)$$

- From the Poynting equation, the Poynting Energy Vector (**PEV**) can be computed and compared to \mathbf{B}_{MHV} .
- The phase angle ($90-\beta$) between **PEV** and \mathbf{B}_{MHV} measures the divergence between electrical wavefront (**E**) and **PEV**.
- This divergence is used to detect anisotropy in the myocardium.
- The Huygens Catheter computes this measurement locally in real time, using a set algorithm embedded within the catheter electronics.
- This is a unique solution to the problem in complex arrhythmia provided by the Huygens™ catheter.

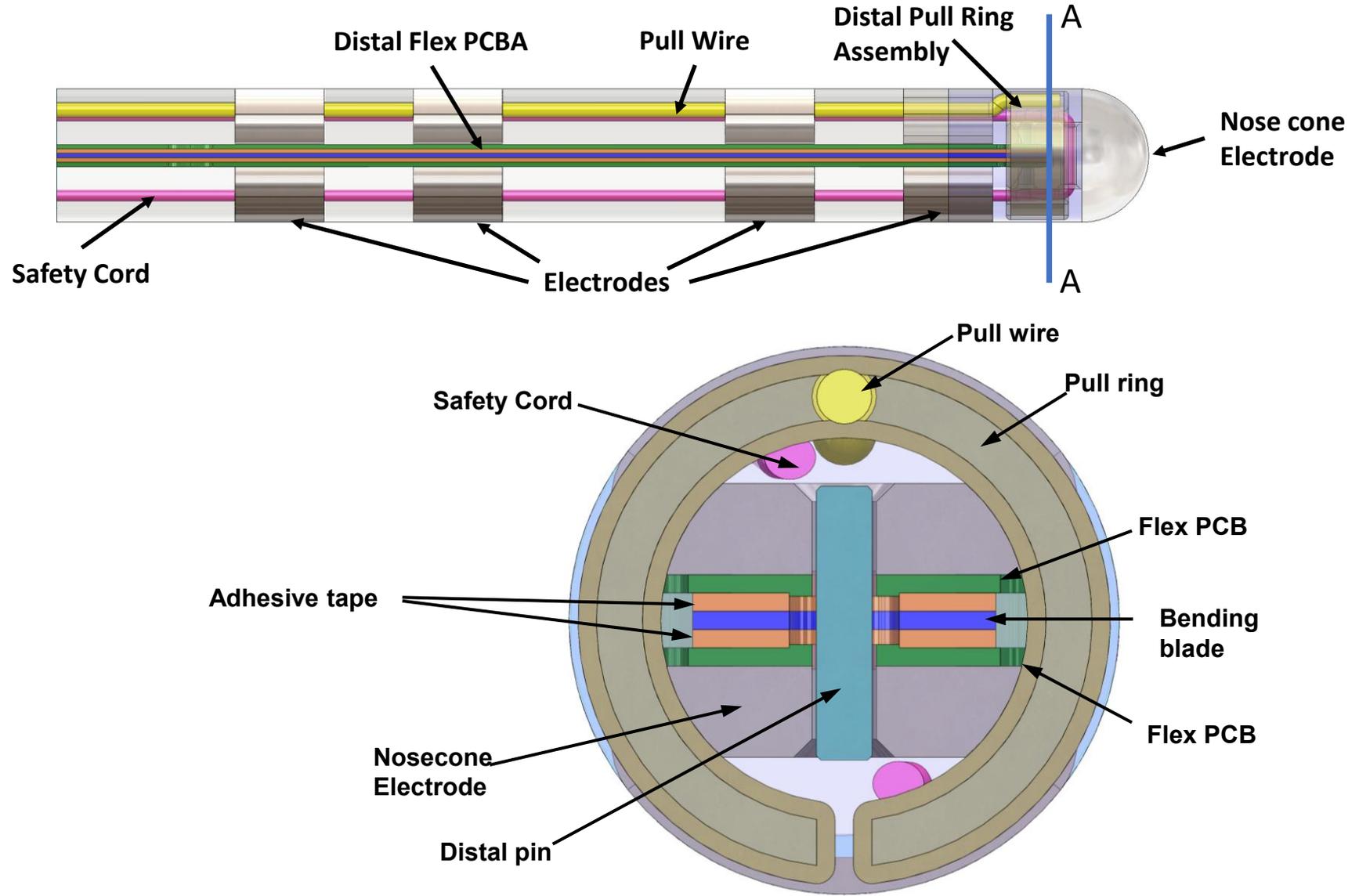


THE USE OF LOCAL AMPLIFIERS AND A HUYGENS SENSOR ARRAY IN MEASURING BIOELECTRIC SIGNALS AND CLINICAL APPLICATIONS THEREOF, Patent PCT/US2022/030399

Huygens™ Catheter Shaft Design

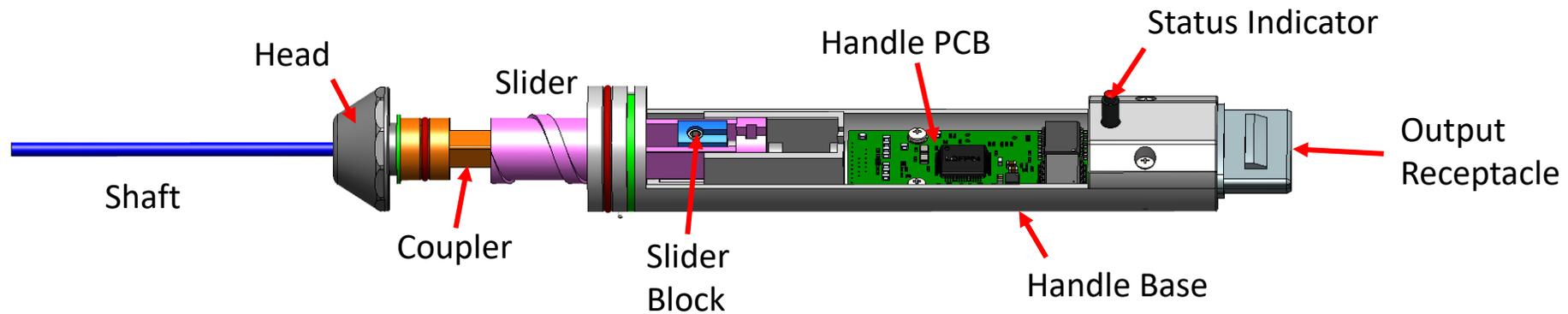
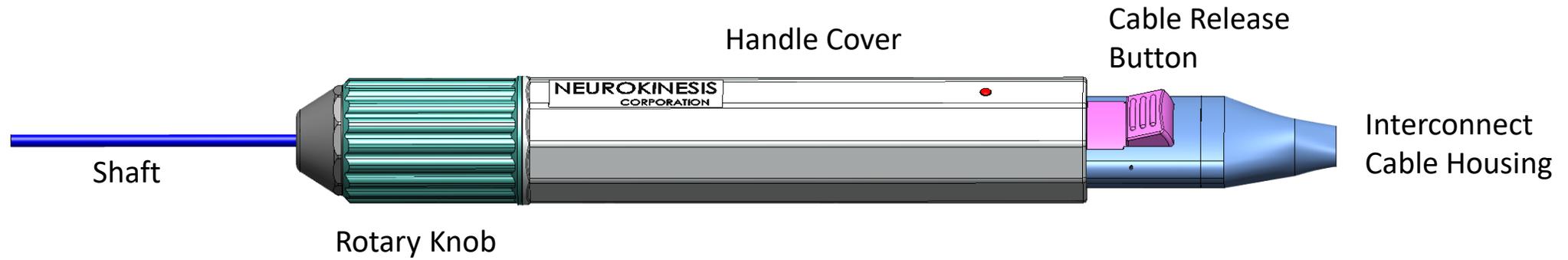
Overview

- Stainless steel bending strip
- Embedded in catheter tip between electrode FPCBs
- Anchored to the distal pull ring assembly and nose cone electrode.
- Provides stiffness to return to 0 deflection
- Insulated to prevent electrical shorting
- All metal components are electrically insulated from Flex PCB



System and Method for a Catheter Impedance Seeking Device, Patent #US 2010/0130854 A1

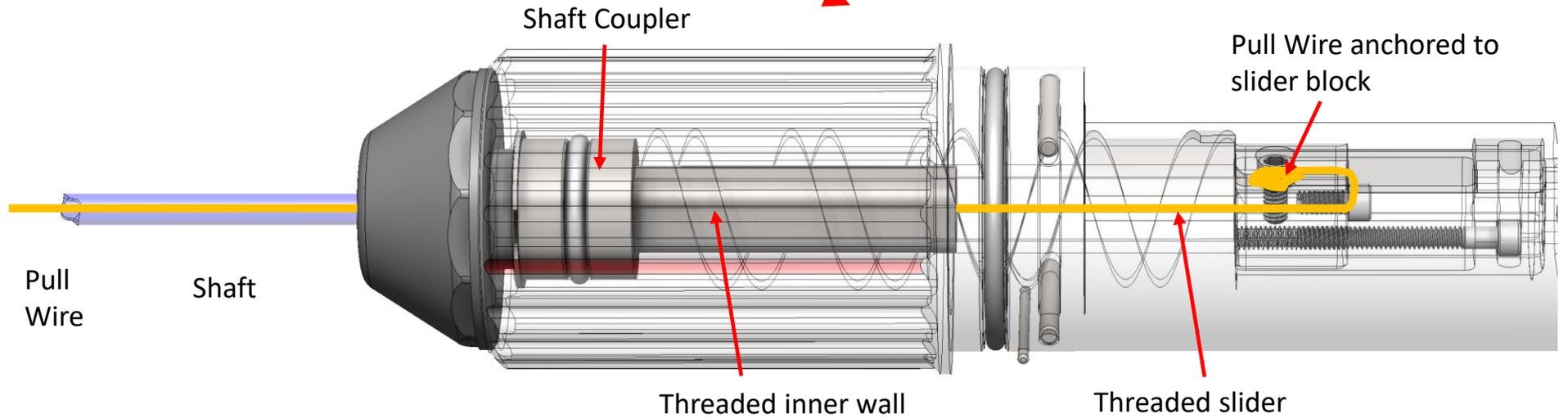
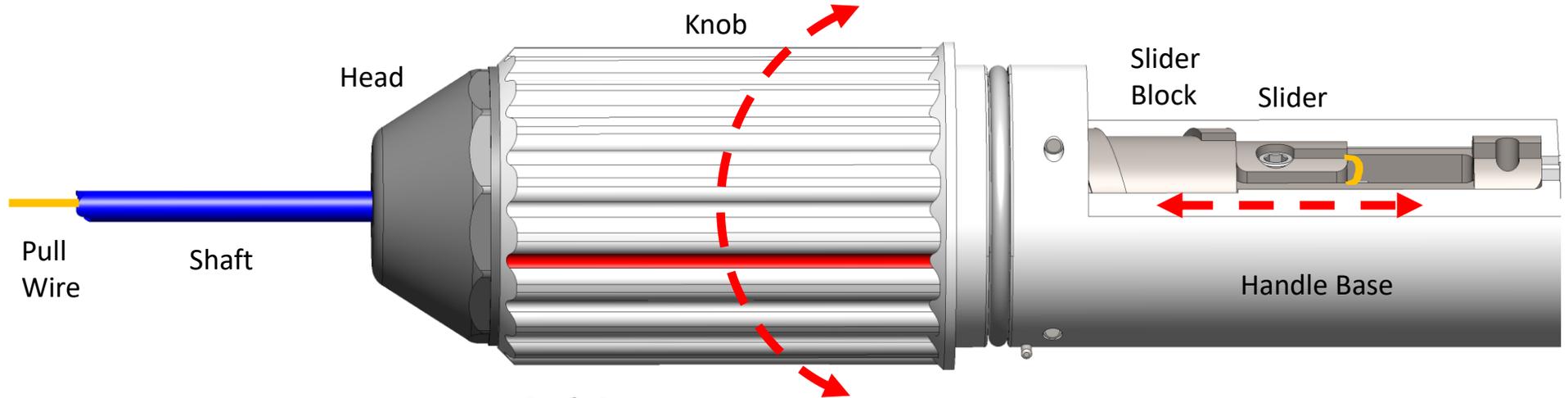
Huygens™ Catheter Handle Design



System and Method for a Catheter Impedance Seeking Device, Patent #US 2010/0130854 A1

Huygens™ Catheter Deflection

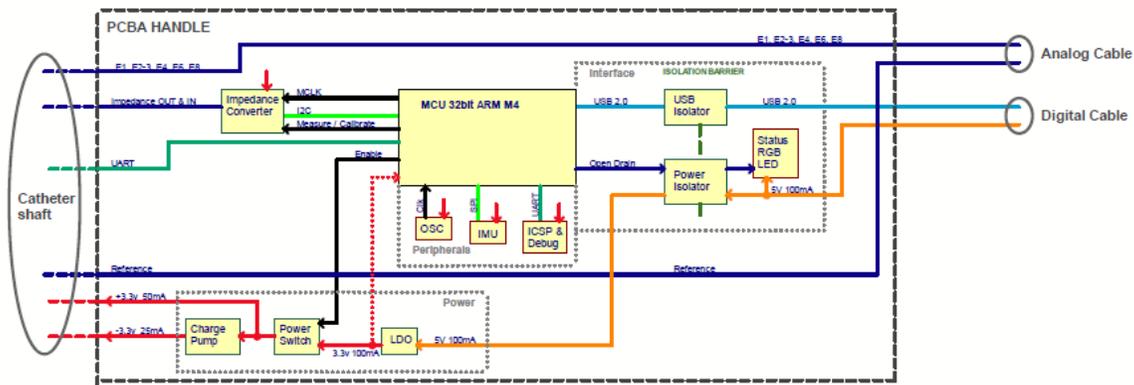
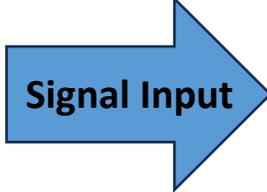
Rotation of the knob translates the slider and pulls on the pull wire, causing deflection at the tip



Method and Apparatus for Creating a High Resolution Map of the Electrical and Mechanical Properties of the Heart, Patent # US 2012/031066A1

Huygens™ Catheter Electrical Design - Handle Electronics

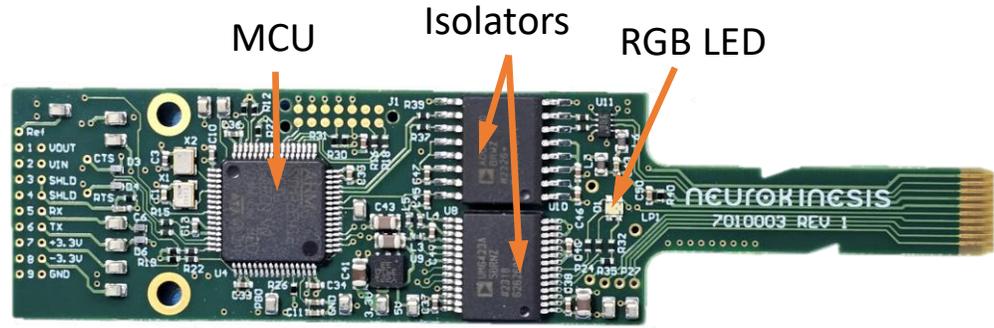
Electronics Integrated into the Handle



Handle PCB

Top

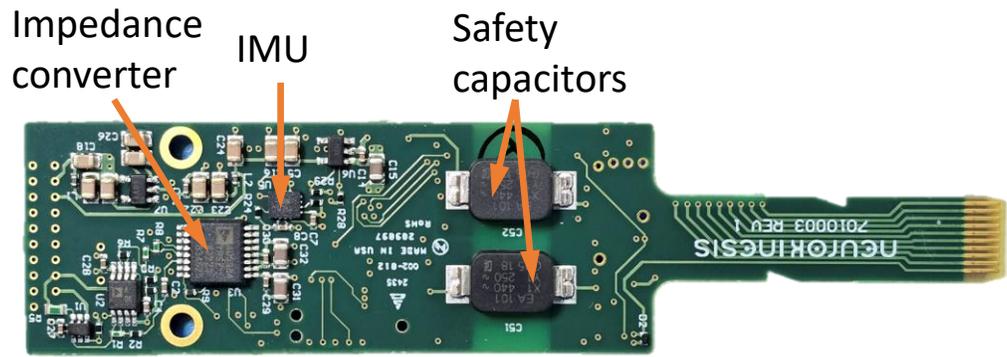
From proximal



To Cable

Bottom

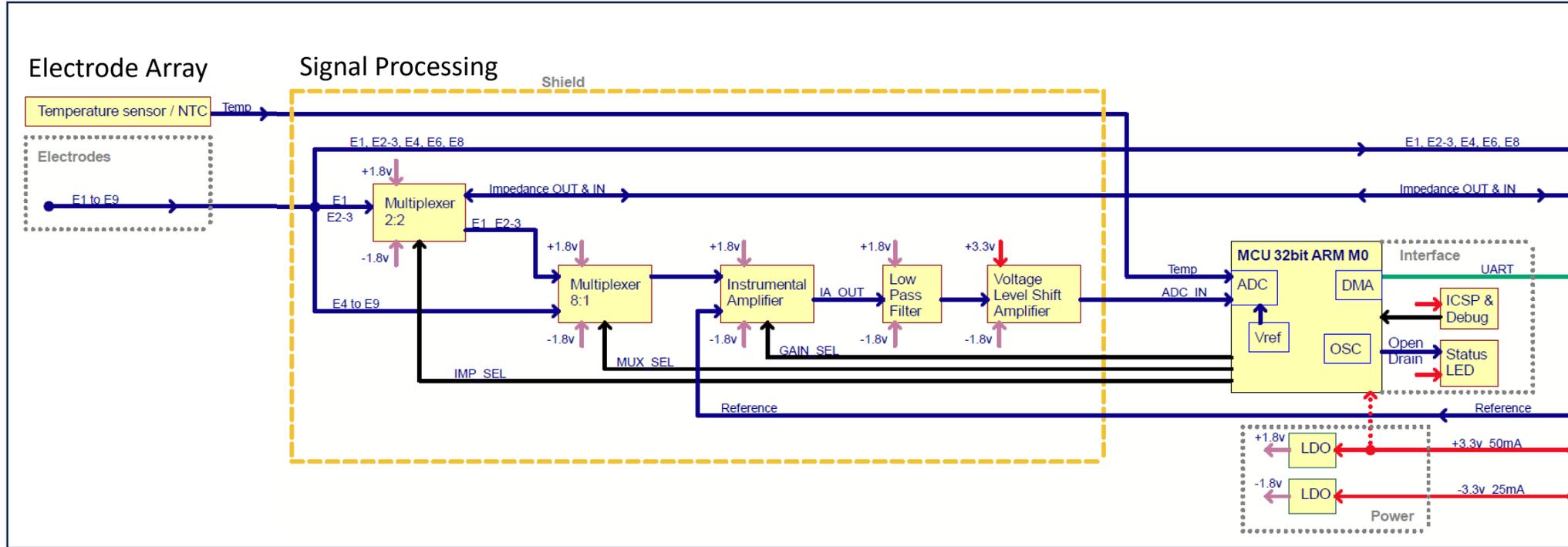
From proximal



To Cable

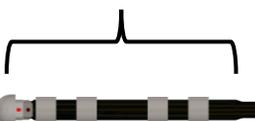
System and Method for a Catheter Impedance Seeking Device, Patent #US 2010/0130854 A1

Huygens™ Catheter Electrical Design - Flex PCBA Design



To Handle PCBA

Electrode Array



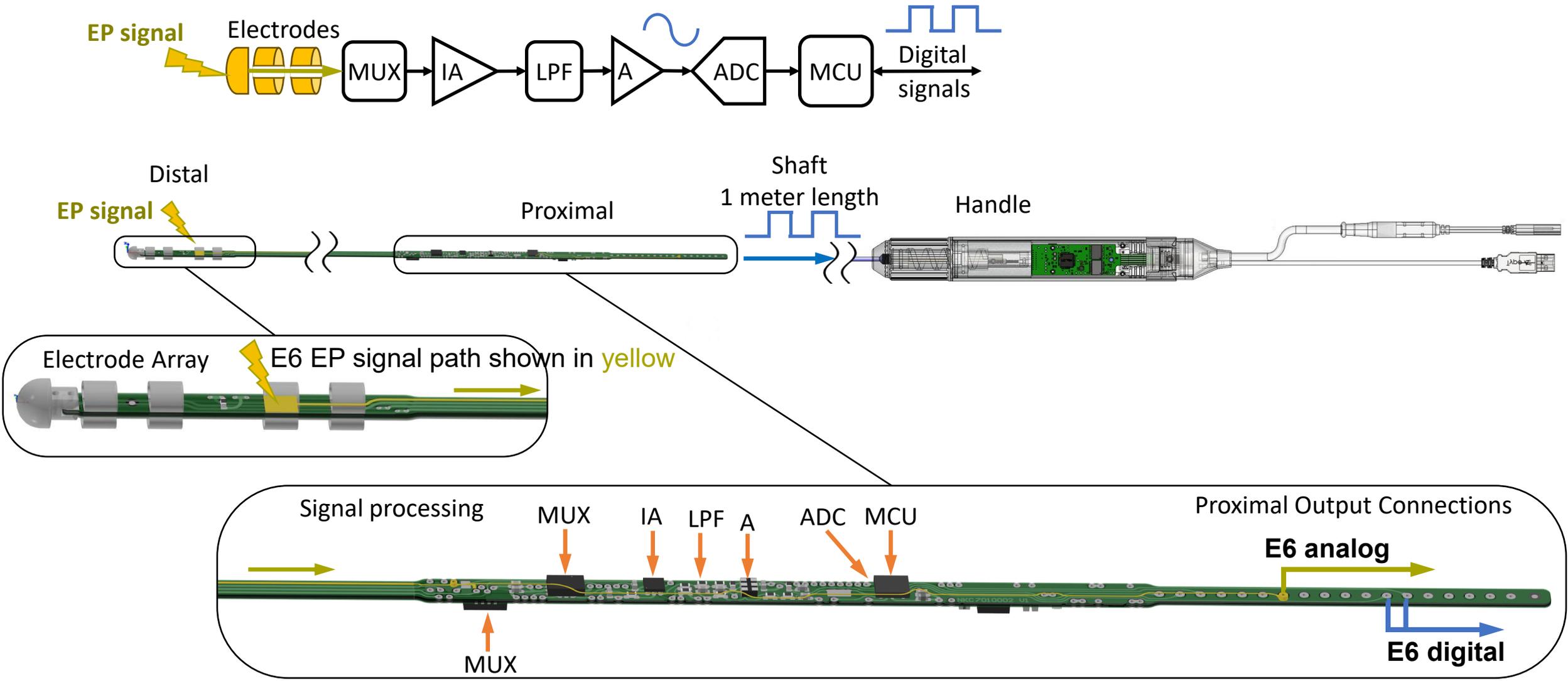
Proximal Output Connections



Signal Processing
Multiplexing, Amplification, and Filtering

System and Method for a Catheter Impedance Seeking Device, Patent #US 2010/0130854 A1

Huygens™ Catheter Electrical Local Amplification

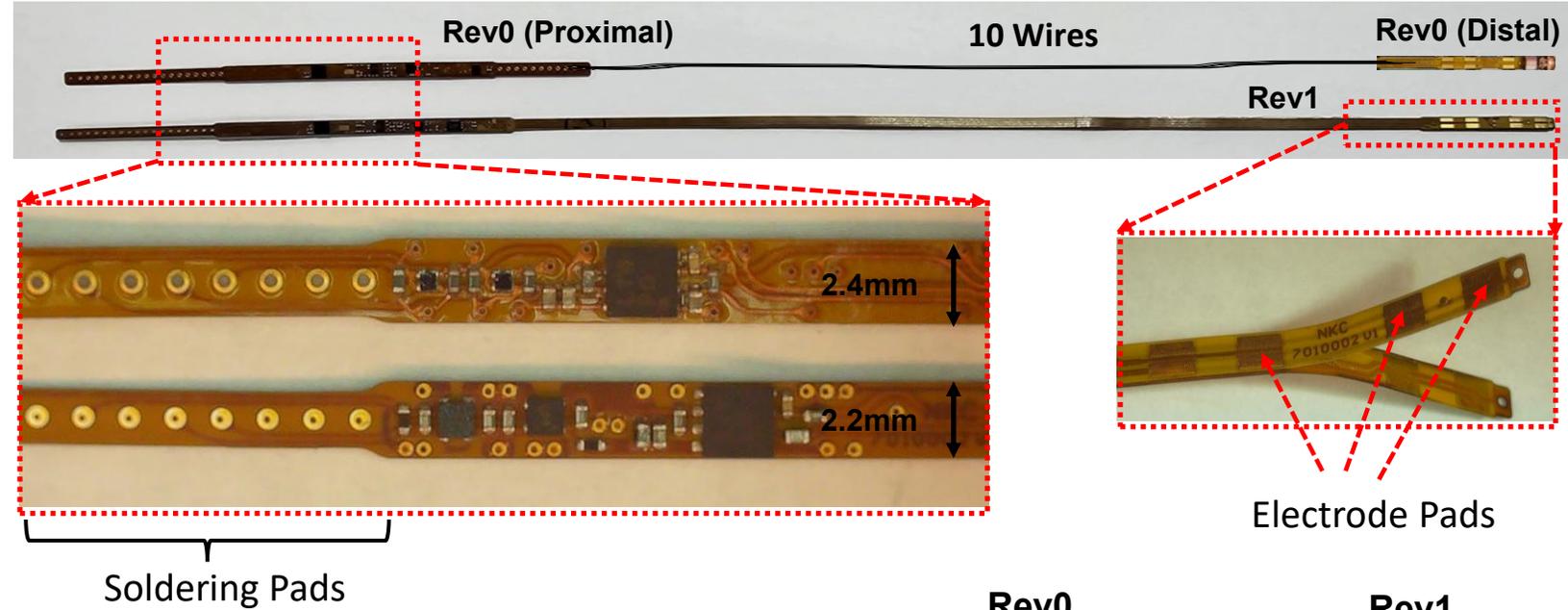


System and Method for a Catheter Impedance Seeking Device, Patent #US 2010/0130854 A1

Design for Manufacturing

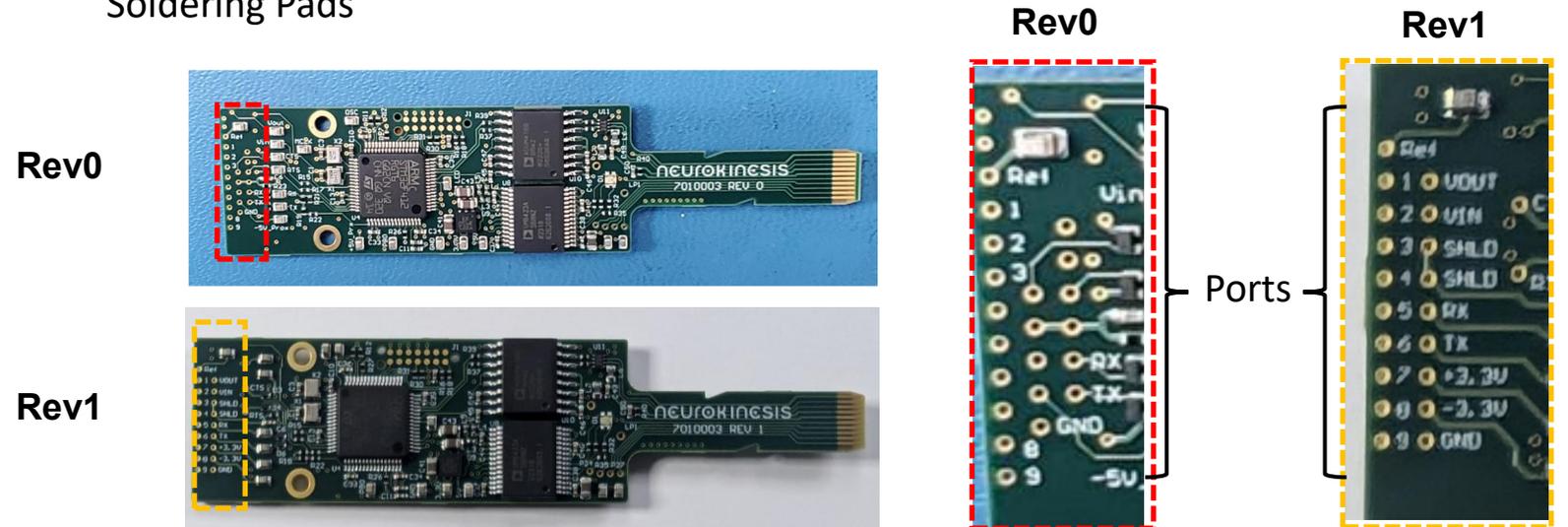
Rev1 Improvements – Flex Board

- Merge proximal flex board with distal flex board
- Reduces width of board for easier insertion into catheter shaft
- Reduce hole in bonding pads to improve bond strength with wires
- Upgrade components to increase speed and reduce noise
 - 8x1 multiplexer
 - 3x low noise voltage regulators



Rev1 Improvements – Handle Board

- Improve alignment of connection ports and add labels to reduce wiring error rate during manufacturing



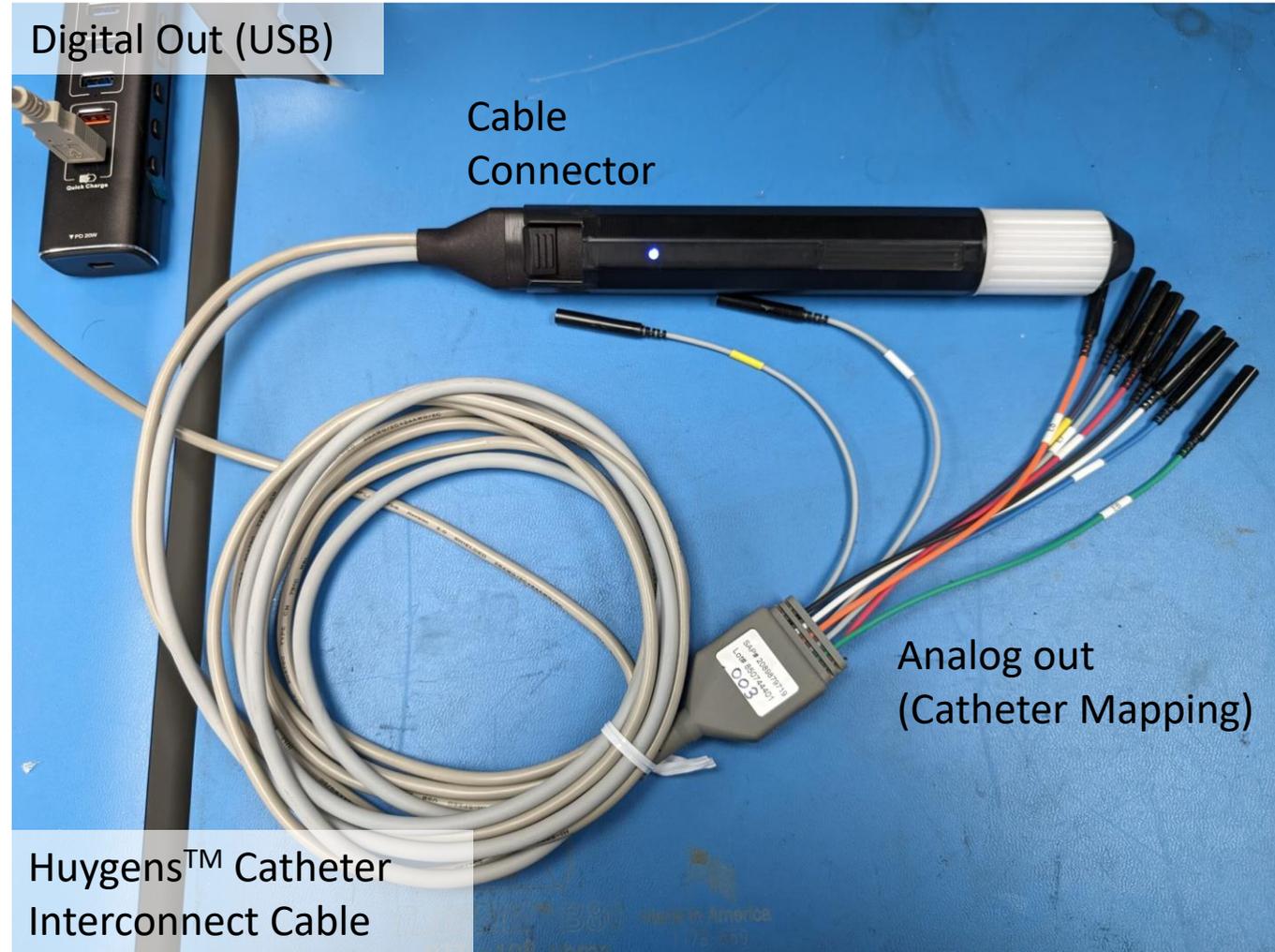
Huygens™ Catheter Interconnect Cable

Custom cable developed by
Phillips Molex Corporation

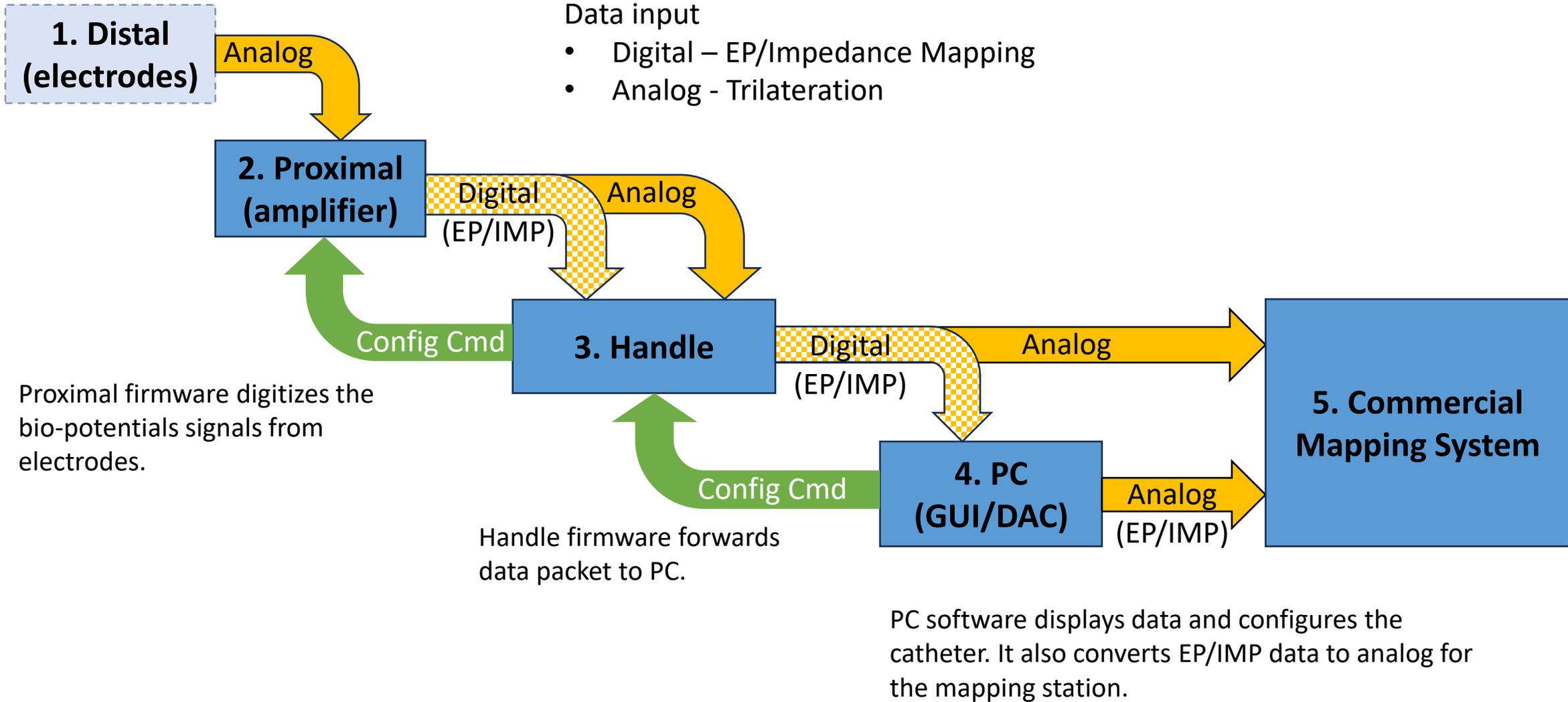
Analog out for catheter
mapping

Digital out for EP and
conductivity signals

Powers the Huygens
Catheter electronics by USB



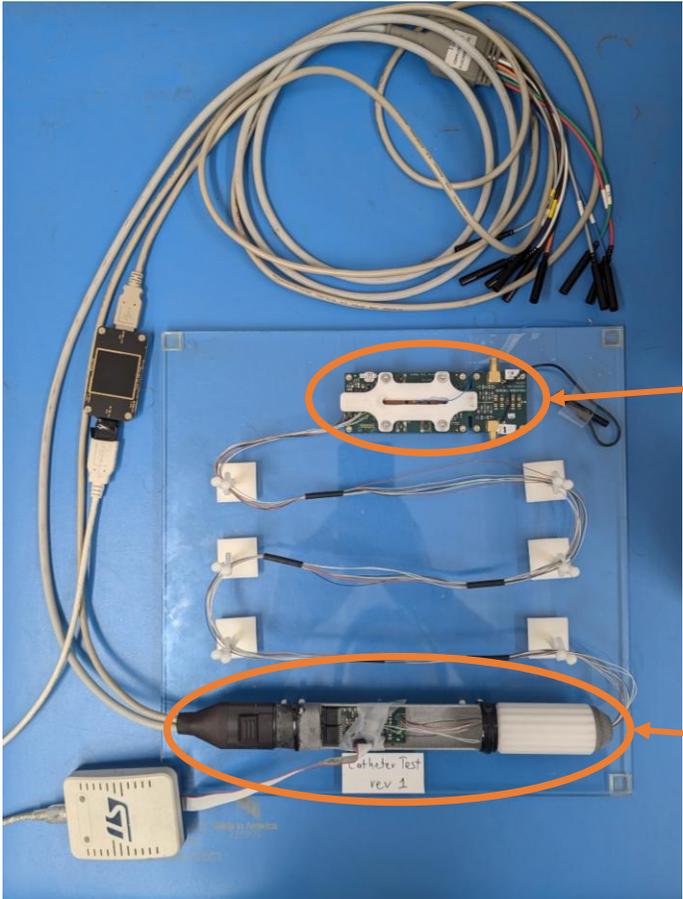
Huygens™ Catheter Firmware



THE USE OF LOCAL AMPLIFIERS AND A HUYGENS SENSOR ARRAY IN MEASURING BIOELECTRIC SIGNALS AND CLINICAL APPLICATIONS THEREOF, Patent PCT/US2022/030399

Huygens™ Catheter Prototype Functional Testing

Firmware is downloaded into electronic boards to test electronics

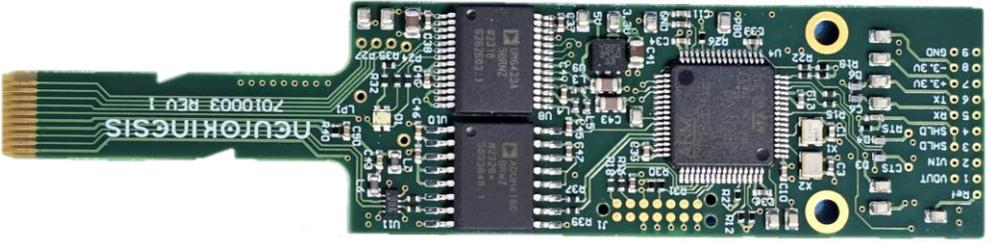


USB Power Cable

Programmer

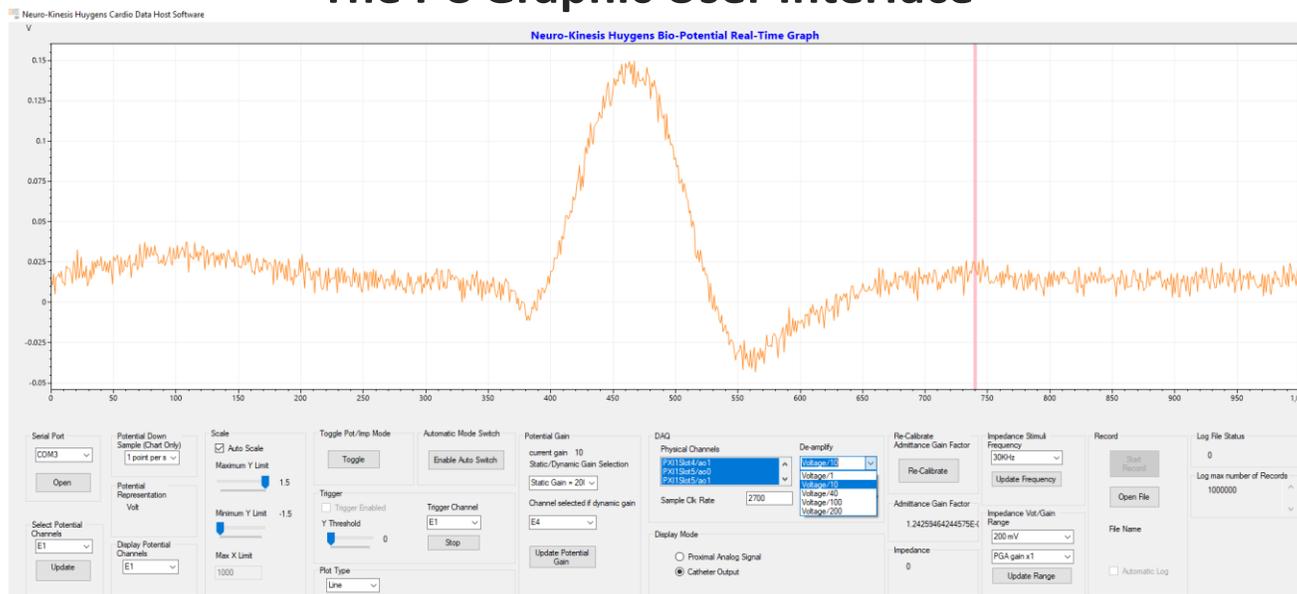
Flex Board Test Fixture

Handle Rev1 Test Fixture



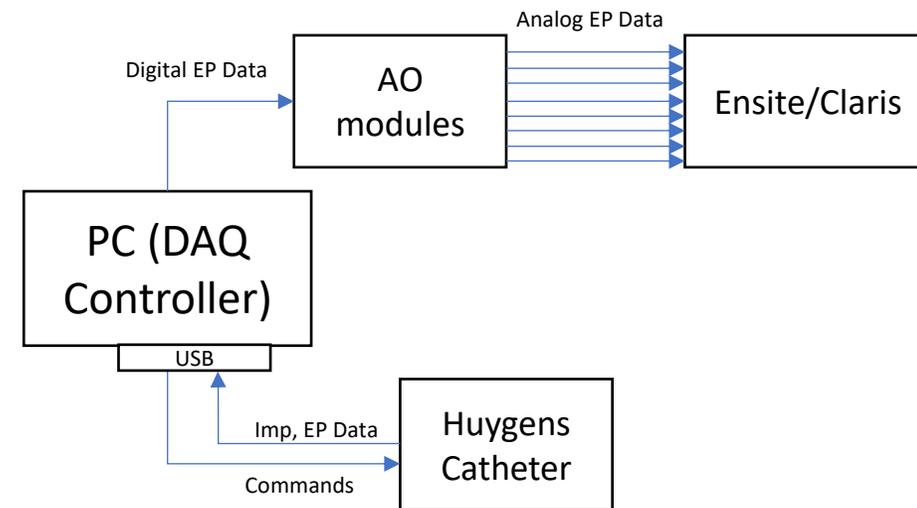
Huygens™ Catheter Software Test Platform

The PC Graphic User Interface

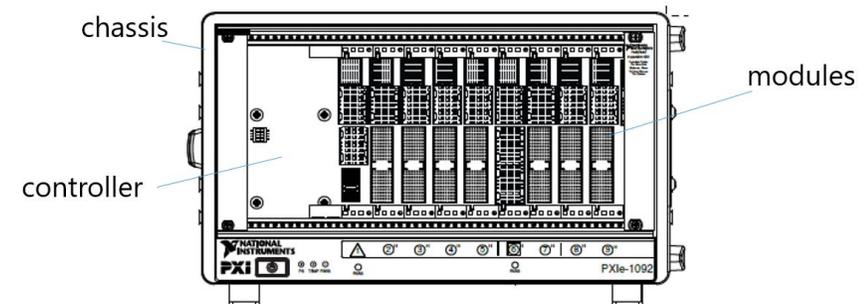


The data acquisition unit (DAQ) is used to convert the digitized EP data back to analog signals which is fed into the Abbot Ensite and Claris switches to compare the signal quality against the conventional analog based catheters. The PC software runs on the DAQ controller takes the EP data through USB from the handle board and forward them to the analog output modules. The output of the analog ports are fed to the Abbot catheter electrode switch panels. The graphic user interface allows the operator to change cardiac potential analog input gain, measure impedance, log results to the hard drive, and so forth. It also displays the EP data on the computer screen in real time.

The PC(DAQ Controller) and System Blocks



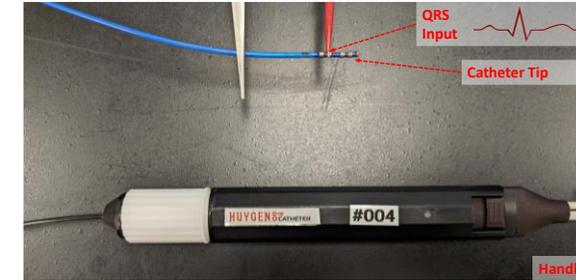
Data Acquisition Unit (DAQ)



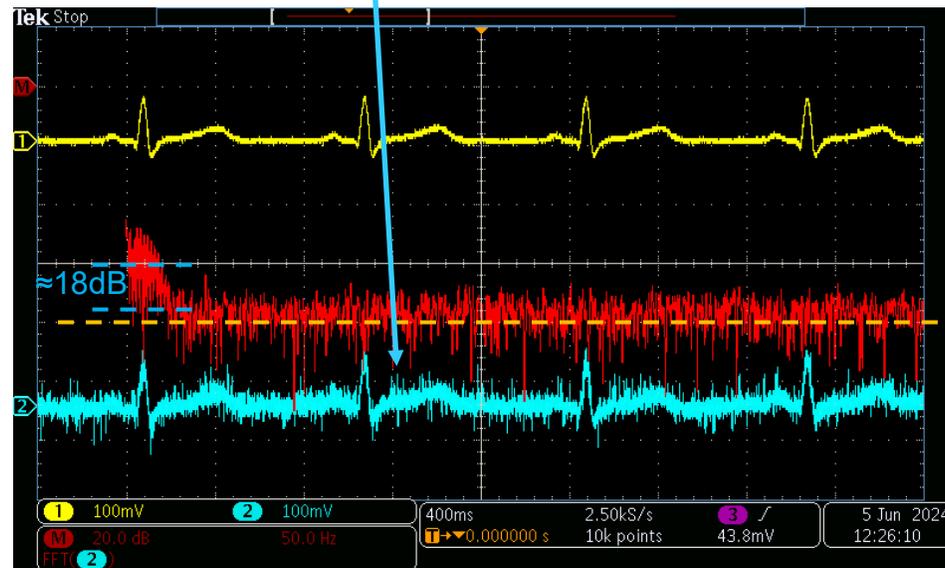
THE USE OF LOCAL AMPLIFIERS AND A HUYGENS SENSOR ARRAY IN MEASURING BIOELECTRIC SIGNALS AND CLINICAL APPLICATIONS THEREOF, Patent PCT/US2022/030399

Huygens™ Catheter Test Results

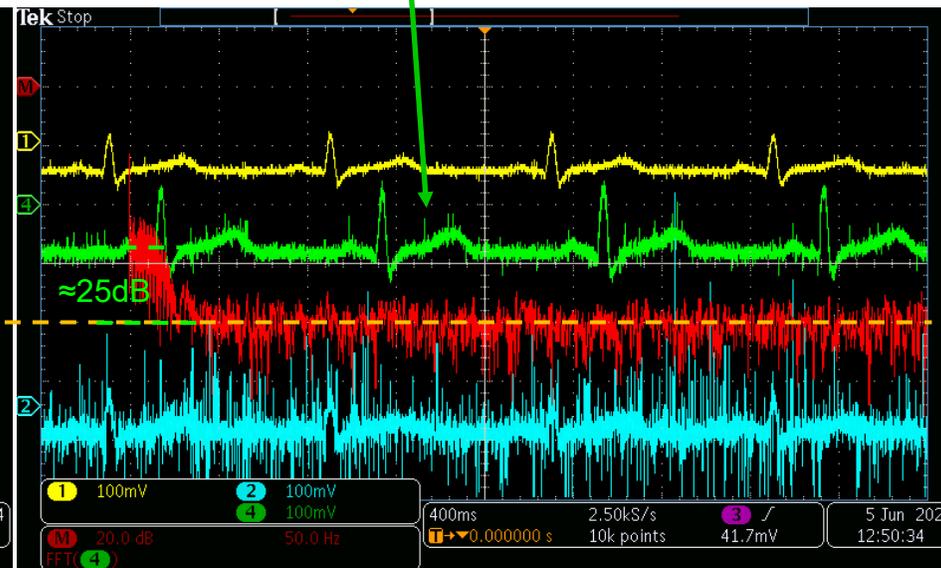
Applying the same ECG QRS (yellow) input signal for both catheters, we obtain from 18 to 25dB, thus 2.2x better signal to noise ratio on the NKC digital catheter.



Analog catheter output SNR 18dB



NKC Catheter digital output SNR 25dB



Legend:

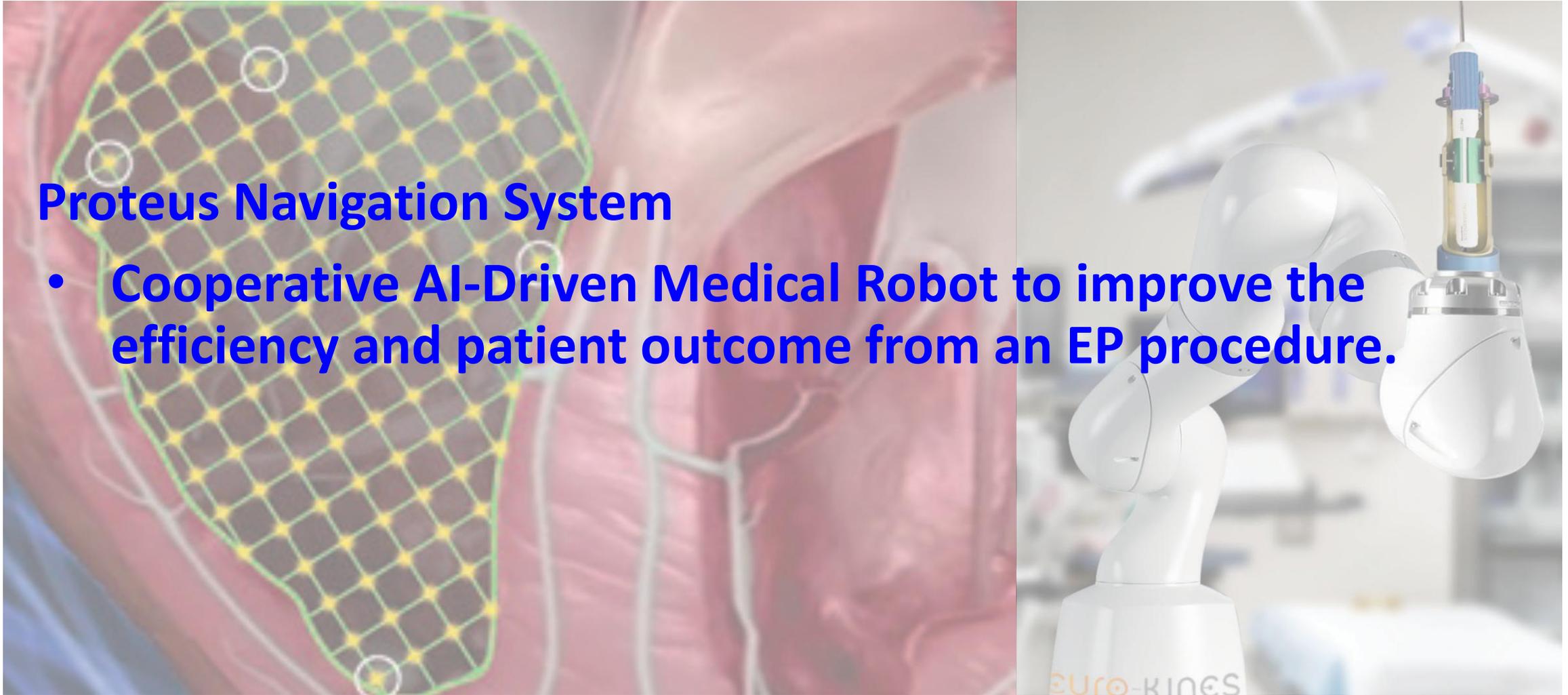
- Yellow: ECG QRS signals at electrode.
- Red: FFT frequency domain of the blue for analog and green for digital.
- Blue: Analog catheter output signal.
- Green: Digital catheter output (DAC output signal)

- NKC catheter has 7dB SNR improvement over commercial EP catheters
- Further improvement in performance is anticipated with a direct digital connection.

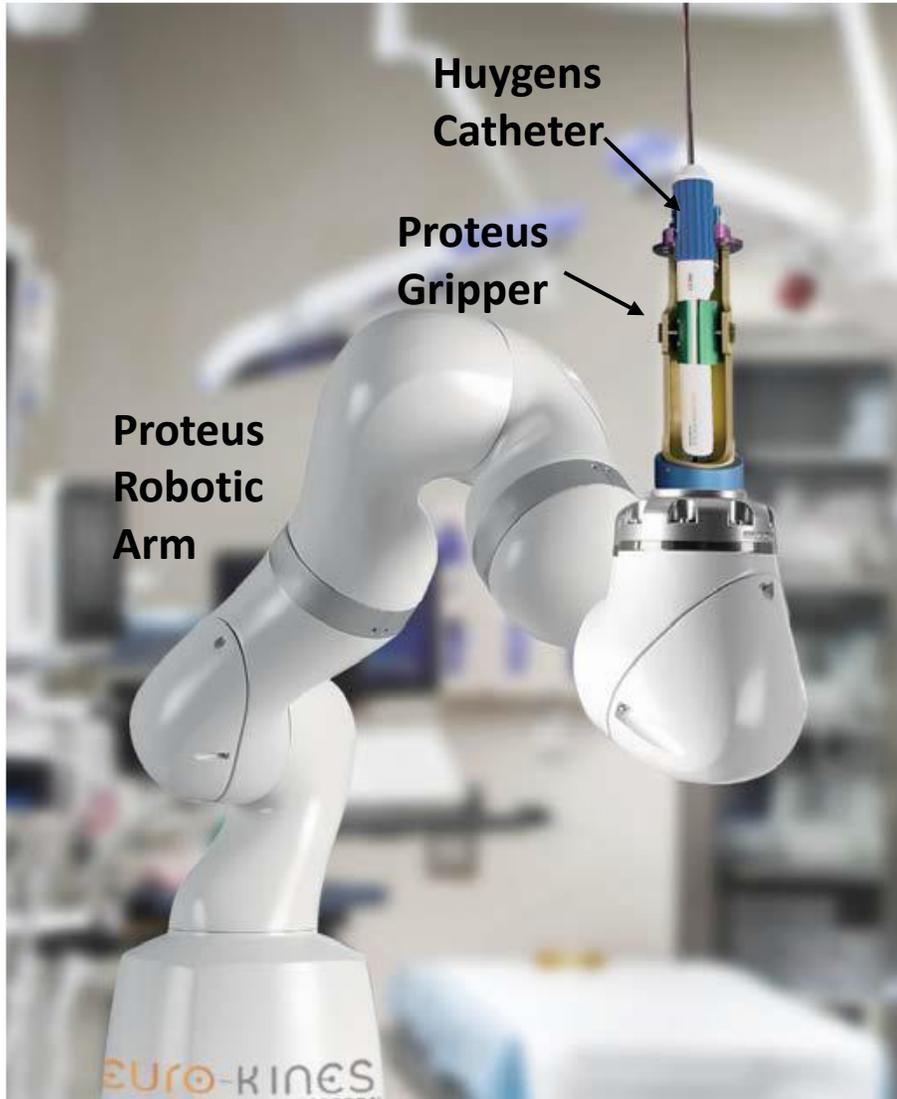
THE USE OF LOCAL AMPLIFIERS AND A HUYGENS SENSOR ARRAY IN MEASURING BIOELECTRIC SIGNALS AND CLINICAL APPLICATIONS THEREOF, Patent PCT/US2022/030399

Proteus Navigation System

- Cooperative AI-Driven Medical Robot to improve the efficiency and patient outcome from an EP procedure.



Proteus™ Navigation System



- Based on a Medical Grade Cobot technology FDA-approved for use in precision surgical procedures.
- Designed in compliance with IEC 60601-1.
- Can be integrated with external end effectors and controllers for remote operation.

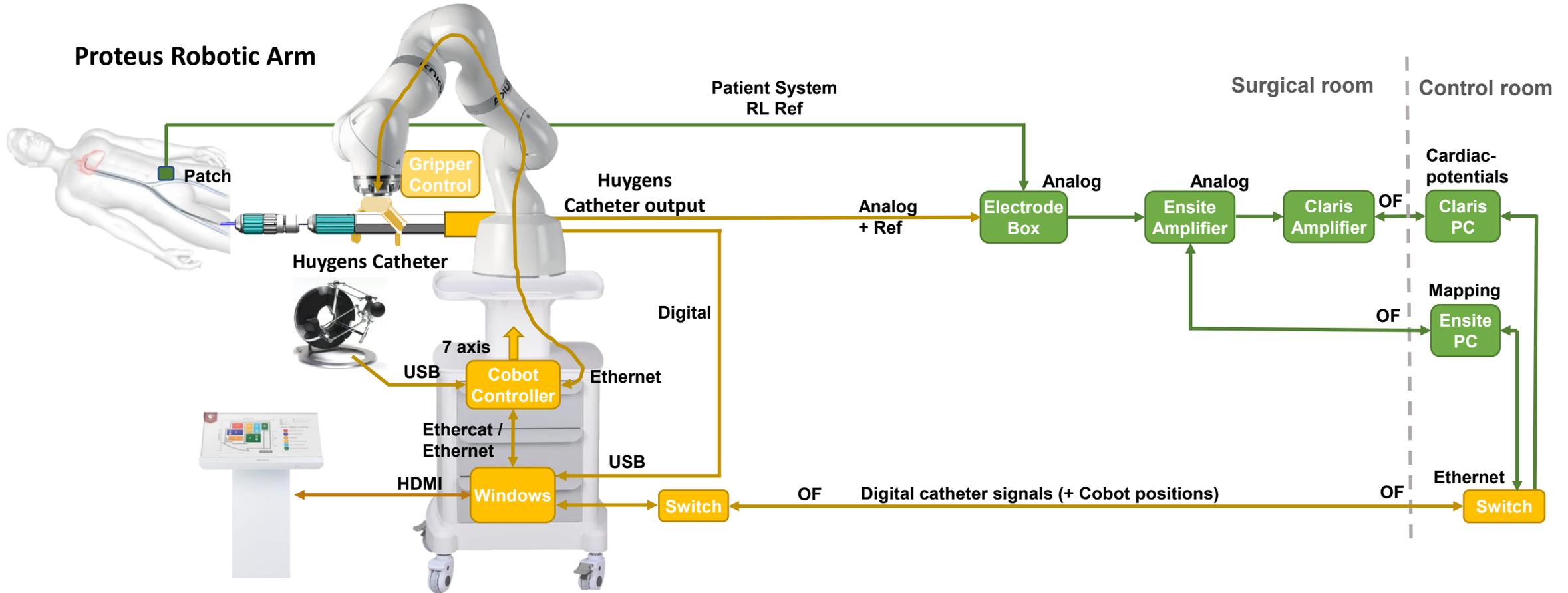


Robotically Controlled Electrophysiology Catheter With Closed Loop Control, Patent # WO2023/038682 A1

Proteus™ Navigation System

Need	Proteus Solution
Adaptive, flexible, and easy to use.	<p>Modular system that easily adapts to any commercial mapping station.</p> <p>Gripper end effector adapts to any commercial EP or ablation catheter.</p> <p>Cooperative (cobot) mode allows for manual positioning of the robot arm for easy patient prep.</p>
Precision and Accuracy	<p>Remote haptic joystick control that enables switching between different operational modes.</p> <p>Positioning logging to return the catheter to points of interest for follow up procedures such as pacing and ablation.</p>
Speed	<p>Automated mapping procedures programmed into the Proteus System as macros that can be run to reduce procedure times from hours to minutes.</p>
Safe to use	<p>Alert system that provides the surgeon with warnings and automatically shuts down in the event of a failure.</p> <p>Force-feedback control system alerts the user of a potential harm to the patient.</p> <p>Robot stops when path is obstructed.</p> <p>Cobot is medical device qualified.</p>

Proteus™ System Overview



Proteus is seamlessly integrated into an EP workstation using a PC-based control station

Robotically Controlled Electrophysiology Catheter With Closed Loop Control, Patent # WO2023/038682 A1

Proteus™ System Operation

Catheter Implantation:

- The EP physician manually moves the **Huygens™ Catheter** into position through the femoral artery and into the right atrial chamber of the patient's heart.

Positioning:

- Once the catheter is in position, the **Proteus™ Robotic Arm** is put in COBOT Mode where it can be manually moved into operational position in order for the **Huygens™ Catheter** handle to be inserted.

Proteus Attachment:

- The **Huygens™ Catheter Handle** is secured into the gripper of the **Proteus™ Robotic Hand**. The catheter handle clamp is secured and the rotating clamp is engaged with the deflection ring.

Navigation:

- The physician performs mapping from a remote control station
- In the future, **NKC** is working to add the capability of the **Proteus™** to handle advanced navigational routines such as grid mapping and automatic return-to-point ablation procedures.

Catheter Implantation



Proteus Positioning



Proteus Attachment



Navigation



Robotically Controlled Electrophysiology Catheter With Closed Loop Control, Patent # WO2023/038682 A1

Proteus™ Gripper

Adaptable:

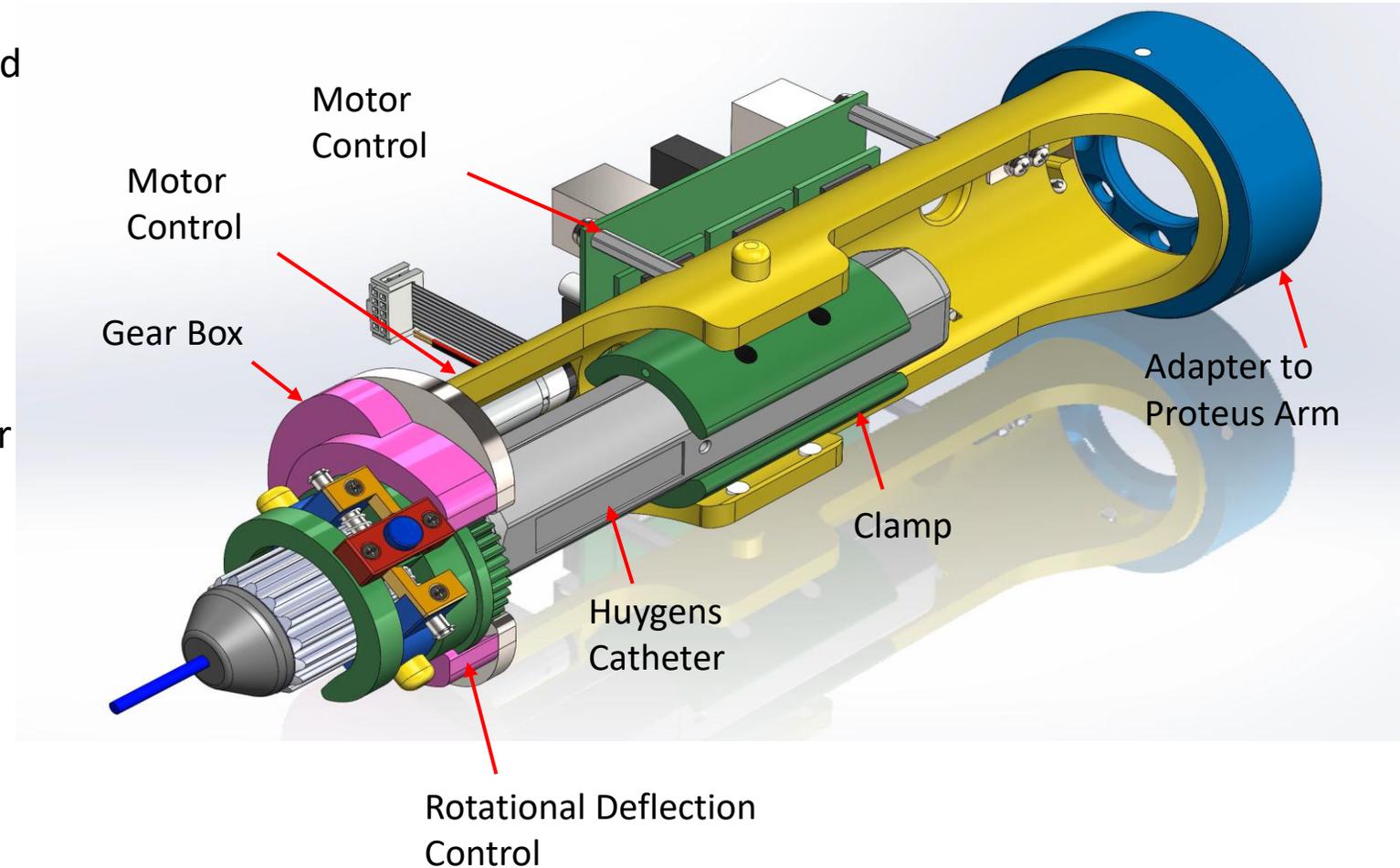
- Adjustable clamps at the center and tip of the catheter handle is designed to accommodate mapping and ablation catheters on the market

Proteus Attachment:

- The **Huygens™ Catheter Handle** is secured into the gripper of the **Proteus™ Robotic Arm**. The catheter handle clamp is secured and the rotating clamp is engaged with the deflection ring

Deflection:

- Motor driven rotational deflection control system rotates the catheter knob to control deflection of the catheter tip



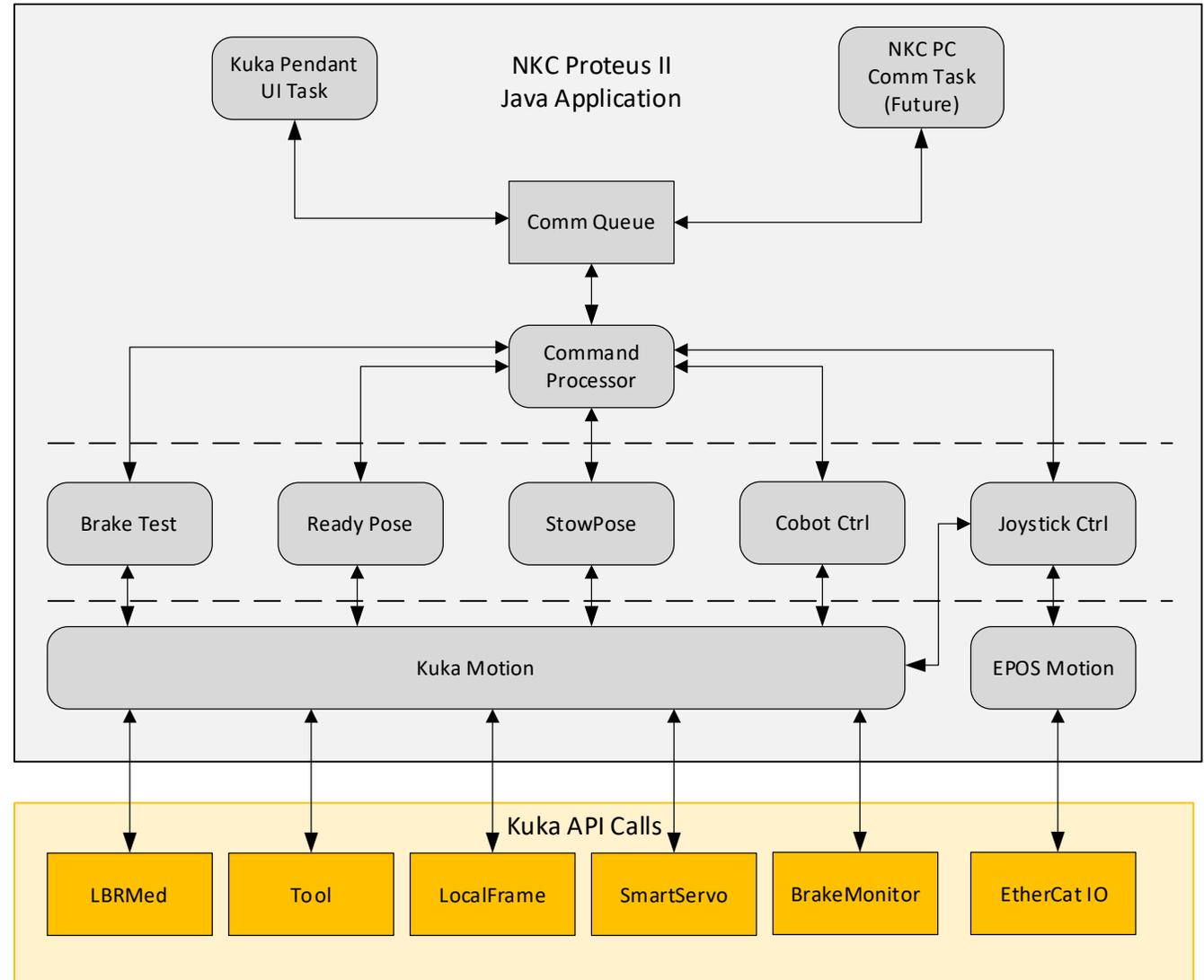
Robotically Controlled Electrophysiology Catheter With Closed Loop Control, Patent # WO2023/038682 A1

Proteus™ Software

The Proteus™ control system runs on a software platform designed in accordance with IEC 62304

Cobot arm positioning by remote control:

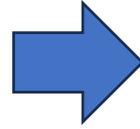
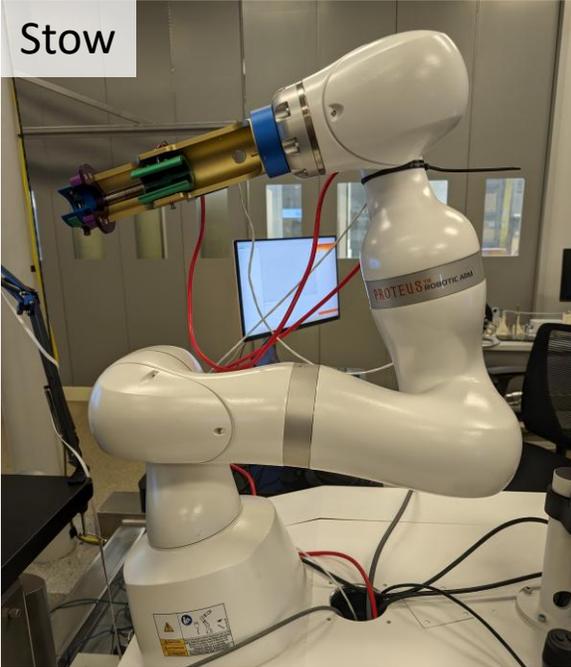
Position	Function
Stow	Storage
Ready	Brings the robot arm to the patient for preparation for use
Cobot	Enables the physician to position the robot against the patient for loading of the catheter
Navigation	Enables high precision rotation, translational, and deflection movements required for navigation during a mapping procedure



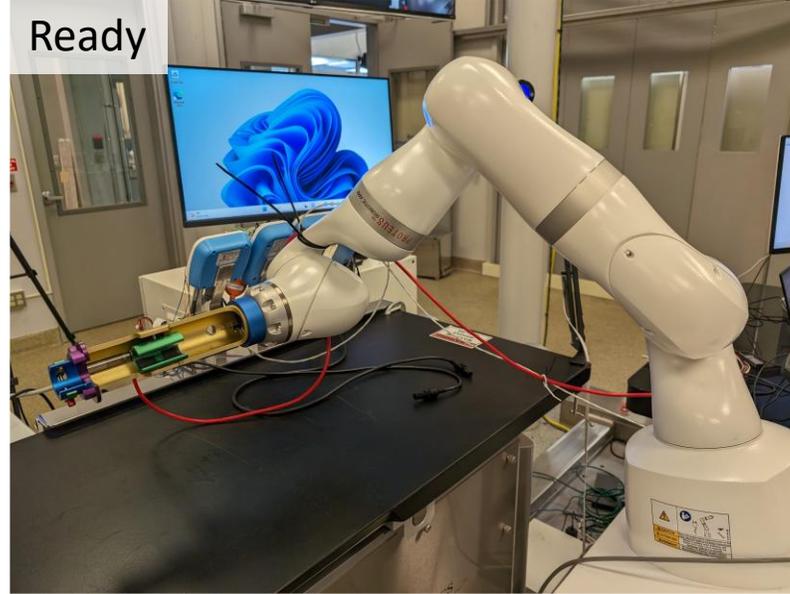
Robotically Controlled Electrophysiology Catheter With Closed Loop Control, Patent # WO2023/038682 A1

Proteus™ Operational Positions

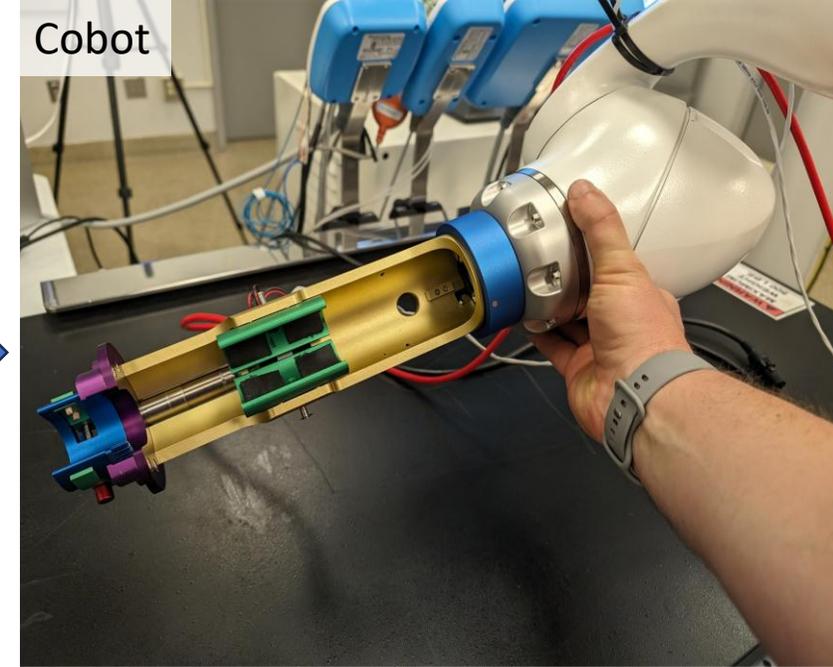
Stow



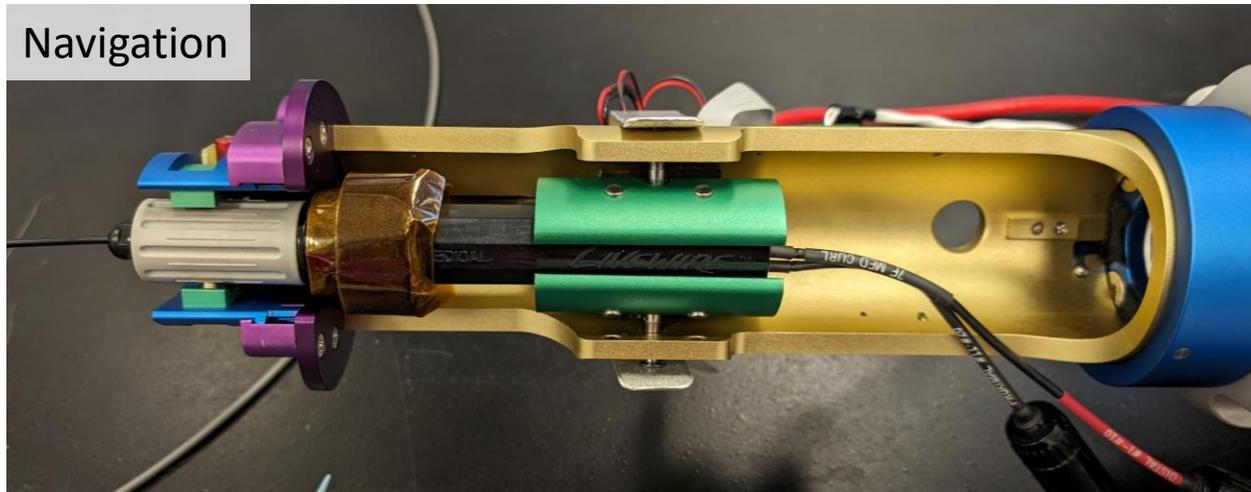
Ready



Cobot



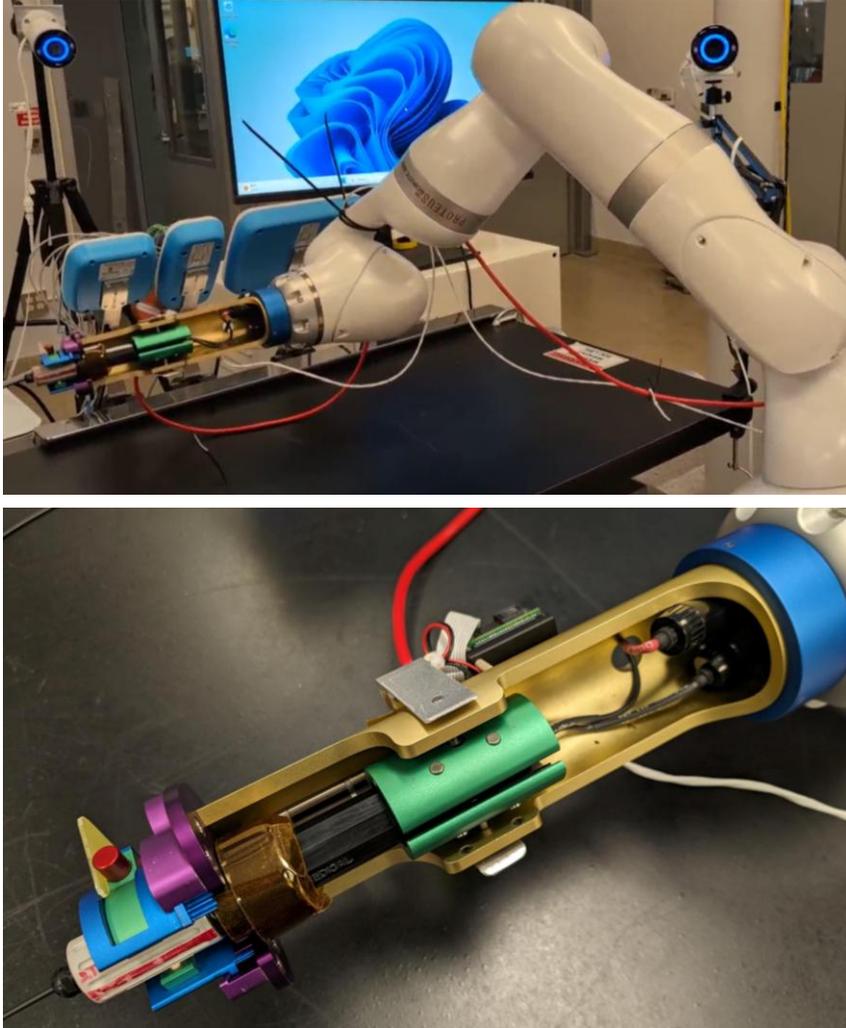
Navigation



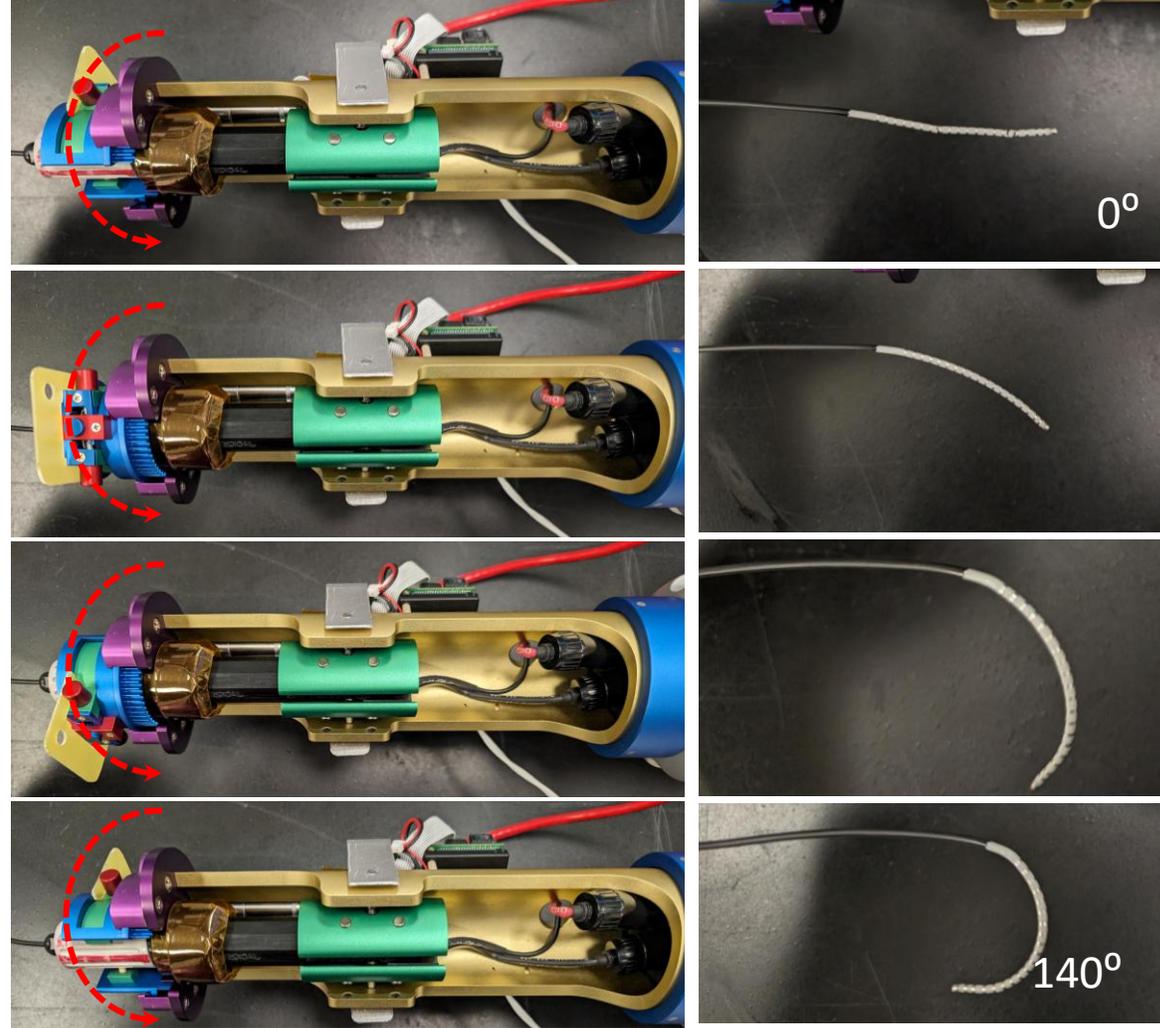
Robotically Controlled Electrophysiology Catheter With Closed Loop Control, Patent # WO2023/038682 A1

Proteus™ Prototype Testing

Catheter loading



Deflection



Robotically Controlled Electrophysiology Catheter With Closed Loop Control, Patent # WO2023/038682 A1

Appendix A : NKC IP Portfolio

NKC Patent portfolio recent

Patent Number	Name
US 2020/0375541 A1	Optically Coupled Catheter And Method Of Using The Same
WO 2020/242753 A1	Optically Coupled Catheter And Method Of Using The Same
IL 288156 A	Optically Coupled Catheter And Method Of Using The Same
Europe 20814810.6	Optically Coupled Catheter And Method Of Using The Same
PCT/US22/30399	Robotically Controlled Electrophysio-logy Catheter with Closed Loop Control
US 18/608388	Robotically Controlled Electrophysio-logy Catheter with Closed Loop Control
EP 22867852.0	Robotically Controlled Electrophysio-logy Catheter with Closed Loop Control
WO 2023/038682 AI	Robotically Controlled Electrophysio-logy Catheter with Closed Loop Control

NKC Patent portfolio recent

Patent Number	Name
PCT/US22/39798	The Use of Local Amplifiers and Huygens™ Sensor Array in Measuring Bioelectric Signals and Clinical Applications Thereof
CA 3192059	<u>The Use Of Local Amplifiers And A Huygens Sensor Array In Measuring Bioelectrical Signals And Clinical Applications Thereof</u>
Europe 22867870.02	<u>The Use Of Local Amplifiers And A Huygens Sensor Array In Measuring Bioelectrical Signals And Clinical Applications Thereof</u>
US 18/188980	<u>The Use Of Local Amplifiers And A Huygens Sensor Array In Measuring Bioelectrical Signals And Clinical Applications Thereof</u>
WO 2023/038748 A1	The Use Of Local Amplifiers And A Huygens Sensor Array In Measuring Bioelectrical Signals And Clinical Applications Thereof

NKC Patent portfolio recent

Patent Number	Name
US 2022/0047202 A1	Catheter for Cardiac and Renal Nerve Sensing and Mediation
EP 4 144 294 A1	A Catheter for Cardiac and Renal Nerve Sensing and Mediation

NKC Patent portfolio

Patent Number	Name
US 2010/7,769,427B2	<u>APPARATUS AND METHOD FOR CATHETER GUIDANCE CONTROL AND IMAGING</u>
US 2011/331,781	<u>System and method for controlling movement of a surgical tool</u>
US 2010/331,944	<u>Apparatus and method for generating a magnetic field</u>
US 2011/7,873,401	<u>SYSTEM AND METHOD FOR A MAGNETIC CATHETER TIP</u>
US 2007/7,280,863	<u>SYSTEM AND METHOD FOR RADAR-ASSISTED CATHETER GUIDANCE AND CONTROL</u>
US 2011/7,873,402B2	<u>SYSTEM AND METHOD FOR RADAR-ASSISTED CATHETER GUIDANCE AND CONTROL</u>
US 2011/8,027,714B2	<u>APPARATUS AND METHOD FOR SHAPED MAGNETIC FIELD CONTROL FOR CATHETER, GUIDANCE, CONTROL, AND IMAGING</u>
US 2012/0143,127A1	<u>APPARATUS AND METHOD FOR SHAPED MAGNETIC FIELD CONTROL FOR CATHETER, GUIDANCE, CONTROL, AND IMAGING</u>

NKC Patent portfolio

Patent Number	Name
HK1123959	Apparatus for Magnetically Deployable Catheter with MOSFET Sensor and Method for Mapping and Ablation
US 2007/0197891 A1	Apparatus for Magnetically Deployable Catheter with MOSFET Sensor and Method for Mapping and Ablation
US 2009/0248014 A1	Apparatus for Magnetically Deployable Catheter with MOSFET Sensor and Method for Mapping and Ablation
US 2011/7,869,854 B2	Apparatus for Magnetically Deployable Catheter with MOSFET Sensor and Method for Mapping and Ablation
WO 2007/100559A2	Apparatus for Magnetically Deployable Catheter with MOSFET Sensor and Method for Mapping and Ablation
EP 1 986 560 A0	Apparatus for Magnetically Deployable Catheter with MOSFET Sensor and Method for Mapping and Ablation
CA 2 637 622	Apparatus for Magnetically Deployable Catheter with MOSFET Sensor and Method for Mapping and Ablation

NKC Patent portfolio

Patent Number	Name
US 2013/0006100A1	<u>METHOD AND APPARATUS FOR CONTROLLING CATHETER POSITIONING AND ORIENTATION</u>
US 2008/0297287A1	<u>MAGNETIC LINEAR ACTUATOR FOR DEPLOYABLE CATHETER TOOLS</u>
US 2012/0310111A1	<u>MAGNETIC LINEAR ACTUATOR FOR DEPLOYABLE CATHETER TOOLS</u>
US 2009/0253985A1	<u>APPARATUS AND METHOD FOR LORENTZ-ACTIVE SHEATH DISPLAY AND CONTROL OF SURGICAL TOOLS</u>
US 2012/0289822 A1	Apparatus and Method for Lorentz-Active Sheath Display and Control of Surgical Tools
WO 2009/126575 A1	Apparatus and Method for Lorentz-Active Sheath Display and Control of Surgical Tools
9730100.6	Apparatus and Method for Lorentz-Active Sheath Display and Control of Surgical Tools
US 2009/0275828A1	<u>APPARATUS AND METHOD FOR LORENTZ-ACTIVE SHEATH DISPLAY AND CONTROL OF SURGICAL TOOLS</u>
9739407.6	Apparatus and Method for Lorentz-Active Sheath Display and Control of Surgical Tools
CN 102065746 A	Apparatus and Method for Lorentz-Active Sheath Display and Control of Surgical Tools

NKC Patent portfolio

Patent Number	Name
US 11/362,542	Apparatus For Magnetically Deployable Catheter With MOSFET Sensor And Method For Mapping And Ablation
HK1123959	Apparatus for Magnetically Deployable Catheter with MOSFET Sensor and Method for Mapping and Ablation
US 2009/0275828	<u>Method and Apparatus for Creating a High Resolution Map of the Electrical and Mechanical Properties of the Heart</u>
US 2012/031066 A1	<u>Method and Apparatus for Creating a High Resolution Map of the Electrical and Mechanical Properties of the Heart</u>
US 2011/0092808A1	<u>METHOD FOR ACQUIRING HIGH DENSITY MAPPING DATA WITH A CATHETER GUIDANCE SYSTEM</u>
US 2012/0316431A1	<u>METHOD FOR ACQUIRING HIGH DENSITY MAPPING DATA WITH A CATHETER GUIDANCE SYSTEM</u>
US 2011/0091853A1	<u>METHOD FOR SIMULATING A CATHETER GUIDANCE SYSTEM FOR CONTROL, DEVELOPMENT AND TRAINING APPLICATIONS</u>
US 2012/0288838A1	<u>METHOD FOR SIMULATING A CATHETER GUIDANCE SYSTEM FOR CONTROL, DEVELOPMENT AND TRAINING APPLICATIONS</u>

NKC Patent portfolio

Patent Number	Name
WO 2009/134605	Method and Apparatus for Creating a High Resolution Map of the Electrical and Mechanical Properties of the Heart
US 2014/0018792 A1	Method And Apparatus For Magnetically Guided Catheter For Renal Denervation Employing Mosfet Sensor Array
US 9,381,063 B2	<u>Method And Apparatus For Magnetically Guided Catheter For Renal Denervation Employing Mosfet Sensor Array</u>
US 2012/9,220,425.	<u>Method And Apparatus For Measuring Biopotential And Mapping Ephaptic Coupling Employing A Catheter With Mosfet Sensor Array</u>
US 2014/0081114 A1	Method And Apparatus For Measuring Biopotential And Mapping Ephaptic Coupling Employing A Catheter With Mosfet Sensor Array
US 9,220,425 B2	Ephaptic Coupling Employing A Catheter With Mosfet Sensor Array

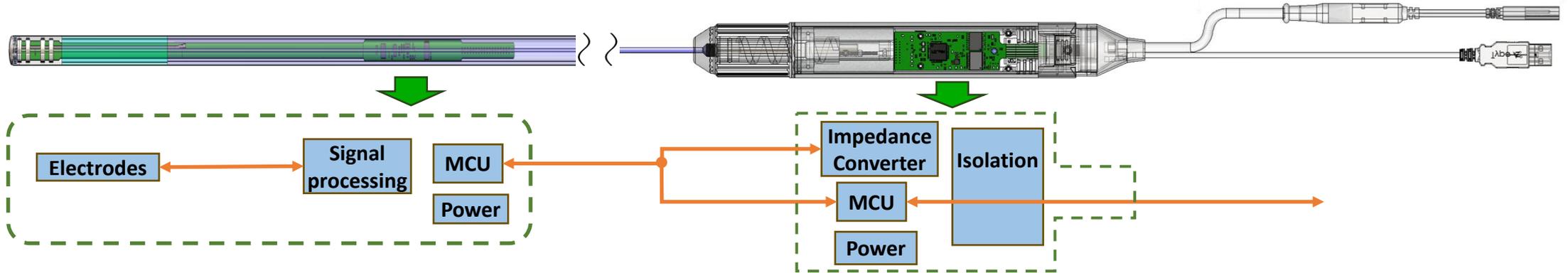
NKC Patent portfolio

Patent Number	Name
US 2010/0130854 A1	System and Method for a Catheter Impedance Seeking Device
US 8,457,714 B2	System and Method for a Catheter Impedance Seeking Device
PCT/US2010/052696	System and Method for a Catheter Impedance Seeking Device
WO 2010/065267 A1	System and Method for a Catheter Impedance Seeking Device
US 2012/9,655,539	SYSTEM AND METHOD FOR TARGETING CATHETER ELECTRODES
US 2011/0112396A1	SYSTEM AND METHOD FOR TARGETING CATHETER ELECTRODES
US 2012/314,273	MAGNETICALLY MANEUVERABLE IN-VIVO DEVICE
US 2013/966,526	MAGNETICALLY MANEUVERABLE IN-VIVO DEVICE
US 2014/8684010B2	DIAGNOSTIC AND THERAPEUTIC MAGNETIC PROPULSION CAPSULE AND METHOD FOR USING THE SAME

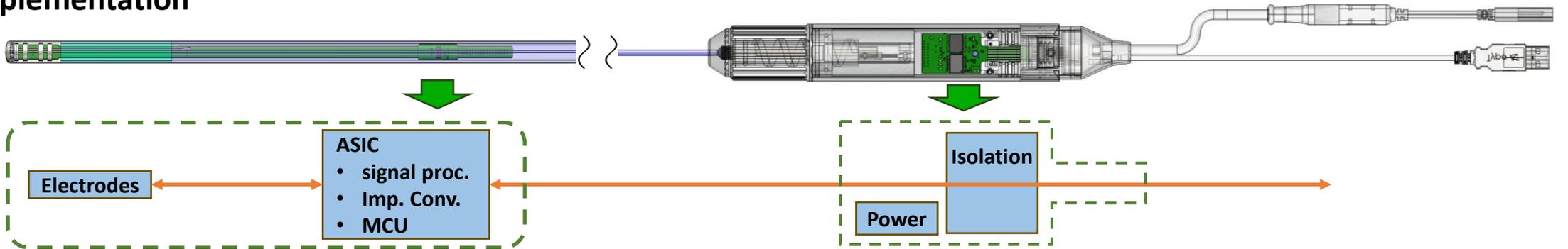
Appendix B : NKC Huygens ASIC ongoing development

Optimize Performance through ASIC Integration

Current



ASIC implementation



ASIC implementation Advantages:

- Compact, smaller
- Cheaper
- Better performances
- More reliable
- IP protection
- Less Power consumption

Optimize Performance through ASIC Integration

ASIC implementation Advantages:

- Application specific electronic, integration optimization, shorter routing lines, power planes, less electrical noise,....
- Fewer electrical components, smaller PCB area, less components to assemble, **reducing power** consumption.
- As all functionalities are embedded into one micro-chip, reverse engineering is very difficult, thus **guaranteeing IP** protection.

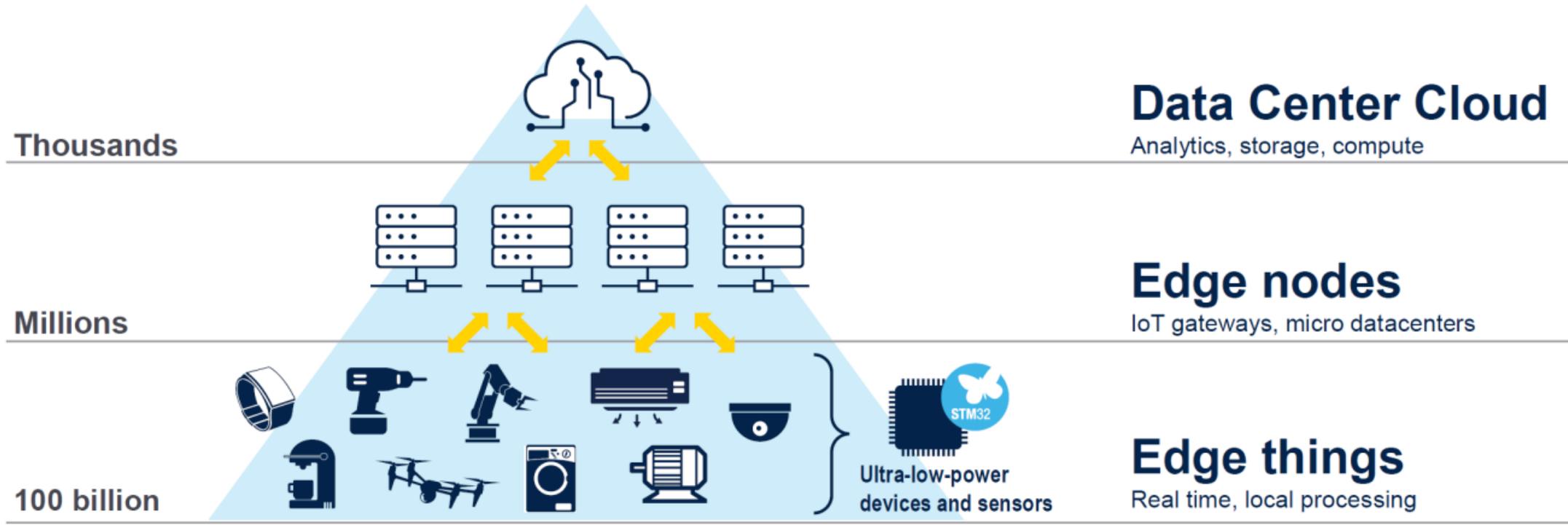
All these advantages gives the possibility to produce smaller catheter from Fr9 to Fr7, Fr5,...
Furthermore, **cheaper**, more **reliable**, and with better **performances**.



Appendix C : NKC AI ongoing development

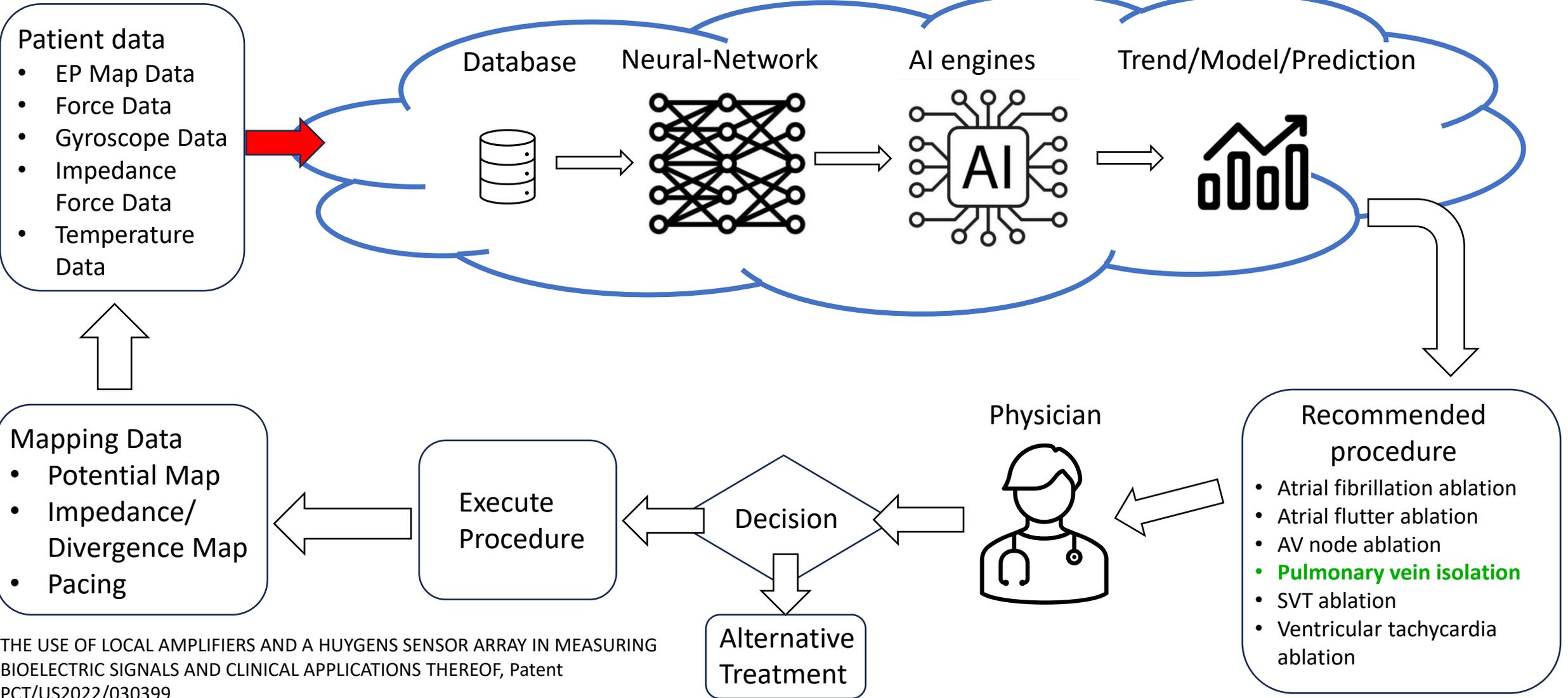
Enhanced by AI: The Future of EP with the Huygens™ Catheter

Layered AI Approach



Enhanced by AI: The Future of EP with the Huygens™ Catheter

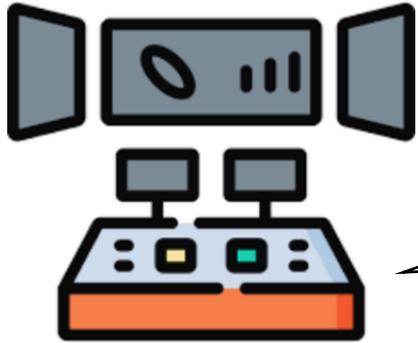
Data Center Cloud Layer



THE USE OF LOCAL AMPLIFIERS AND A HUYGENS SENSOR ARRAY IN MEASURING BIOELECTRIC SIGNALS AND CLINICAL APPLICATIONS THEREOF, Patent PCT/US2022/030399

Enhanced by AI: The Future of EP with the Huygens™ Catheter

Edge Nodes Layer



- GPU/CPU Machine Learning from potential/impedance maps :
- real-time pattern recognition
 - Rotor/Flutter source identification

Edge Things Layer



- MCU Machine Learning Core:
- Estimate catheter tip force
 - Signal-to-noise ratio
 - Conductivity
 - Initial-measurement unit

Advantages:

- Improved accuracy
- Reduced data transmission speed
- Ultra-low latency
- Enhanced privacy and security
- Power efficiency

Appendix D : NKC Renal Denervation RD

EP Mapping and Renal Denervation – The Huygens solution

Recording and localizing sympathetic nerve activity in renal arteries in patients with difficult to treat hypertension, the success of such procedure depend on the ability of mapping the appropriate nerve ending and firing sequence within a patient.

The problem with the current art is the **variability** of the anatomical distribution as shown in pathological cross section of nerve ending arborization.

Each patient has its own “fingerprint” *distribution* of the dominant nerve ending where clinical study indicates that to terminate the command emanating from the ganglia, we need to identify which of the nerve endings are significant. Through the identification of an apparatus such as define by the Huygens catheter, the physician will be able to measure the amplitude and frequency of the nerve ending firing sequence.

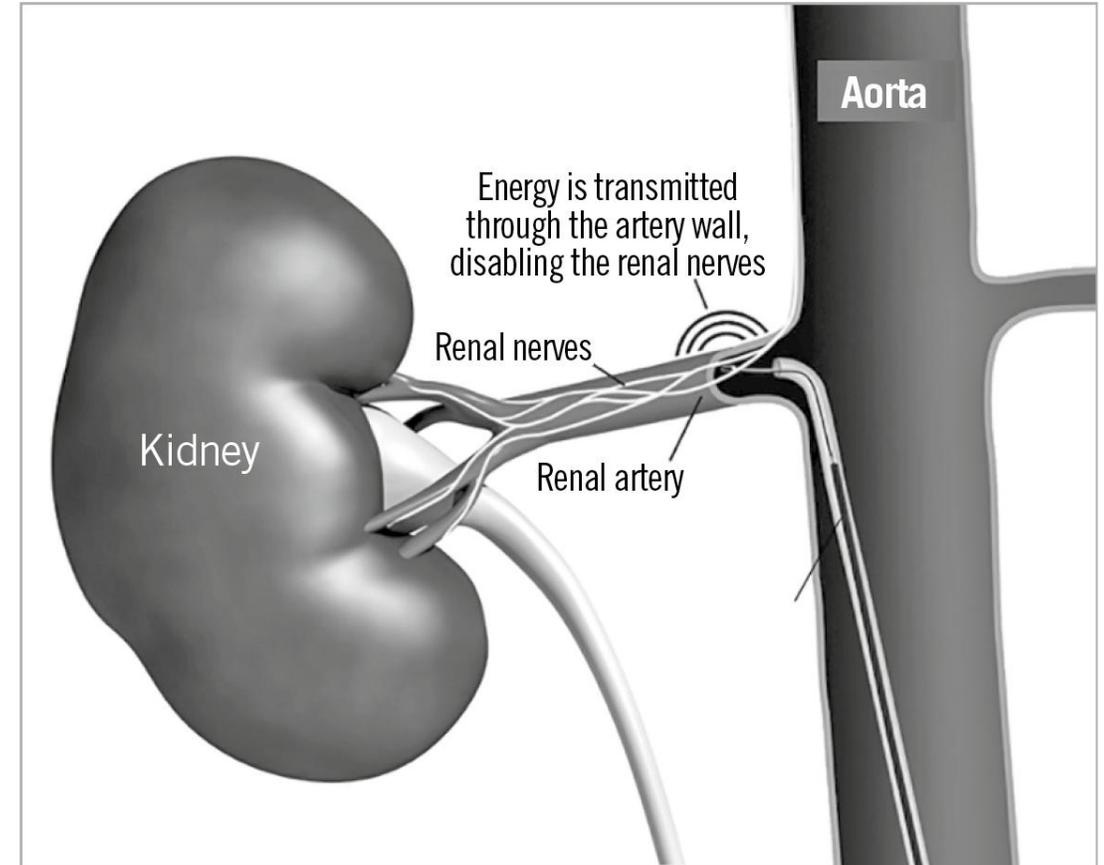
To achieve such detection, the catheter must have a high sampling rate of at least 10 times the nerve pulse width, thus the Huygens digital sampling rate of 30kHz will suffice to address this limitation in the current art and thereby provide a necessary detection capability to specifically address the therapeutic target detection needs.

Ref: <https://www.asiaintervention.org/article/renal-denervation-therapy-for-hypertension-truths-and-half-truths/>

EP Mapping and Renal Denervation

RD Ablation as a Therapy for Hypertension

- Health complications associated with high blood pressure put a tremendous strain on the healthcare system.
- In some patients with persistent hypertension, medication and lifestyle change fail to reduce blood pressure.
- One possible cause is dysregulation of the release of renin, a hormone that elevated release of renin and persistent high blood pressure.
- Under normal function, the kidneys control the release of renin
- RD is a procedure that aims to turn off this biochemical switch through deactivated ablation of the renal nerves in the kidney

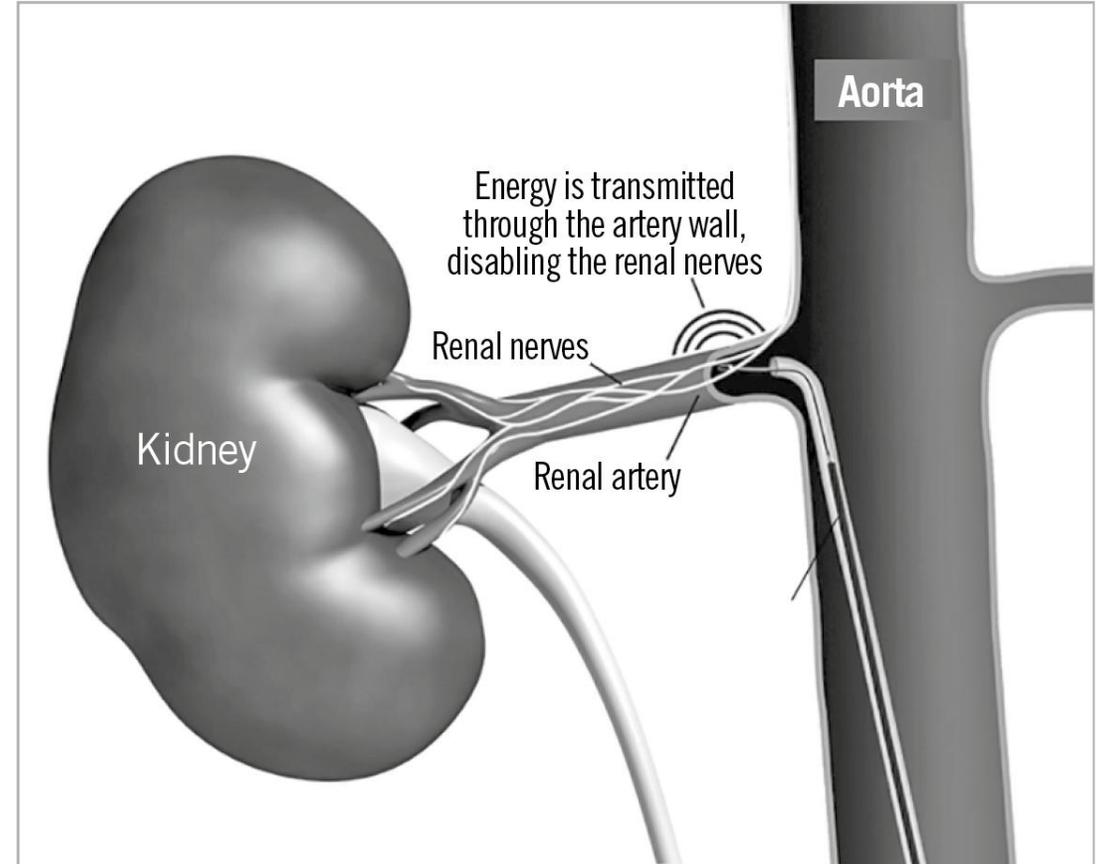


Ref: <https://www.asiaintervention.org/article/renal-denervation-therapy-for-hypertension-truths-and-half-truths/>

EP Mapping and Renal Denervation

Current RD procedure

- The ablation catheter is routed from the aorta into the renal artery and to renal plexus.
- RF ablation is performed to sever the nerve connection, deactivating the mechanism that releases renin into the blood stream
- The targeting of the nerve must be precise to maximize therapeutic adverse effect.
- Currently, there is limited long term success of RD when compared with existing remedies such as medication and lifestyle change.



The concept of catheter-based renal denervation.

Ref: <https://www.asiaintervention.org/article/renal-denervation-therapy-for-hypertension-truths-and-half-truths/>

EP Mapping and Renal Denervation

Limitations to overcome

- Renal nerve formations in the kidney are individualized to each person
- Electrical impulses occur when a biological event occurs that triggers the nerve to signal the brain
- Electrical signals are very high frequency and of short duration, making detection for mapping difficult.

Challenge:

How do you generate an electroanatomical map to identify a location for ablation when the electrical signal occurs randomly and it's difficult to detect when it does?

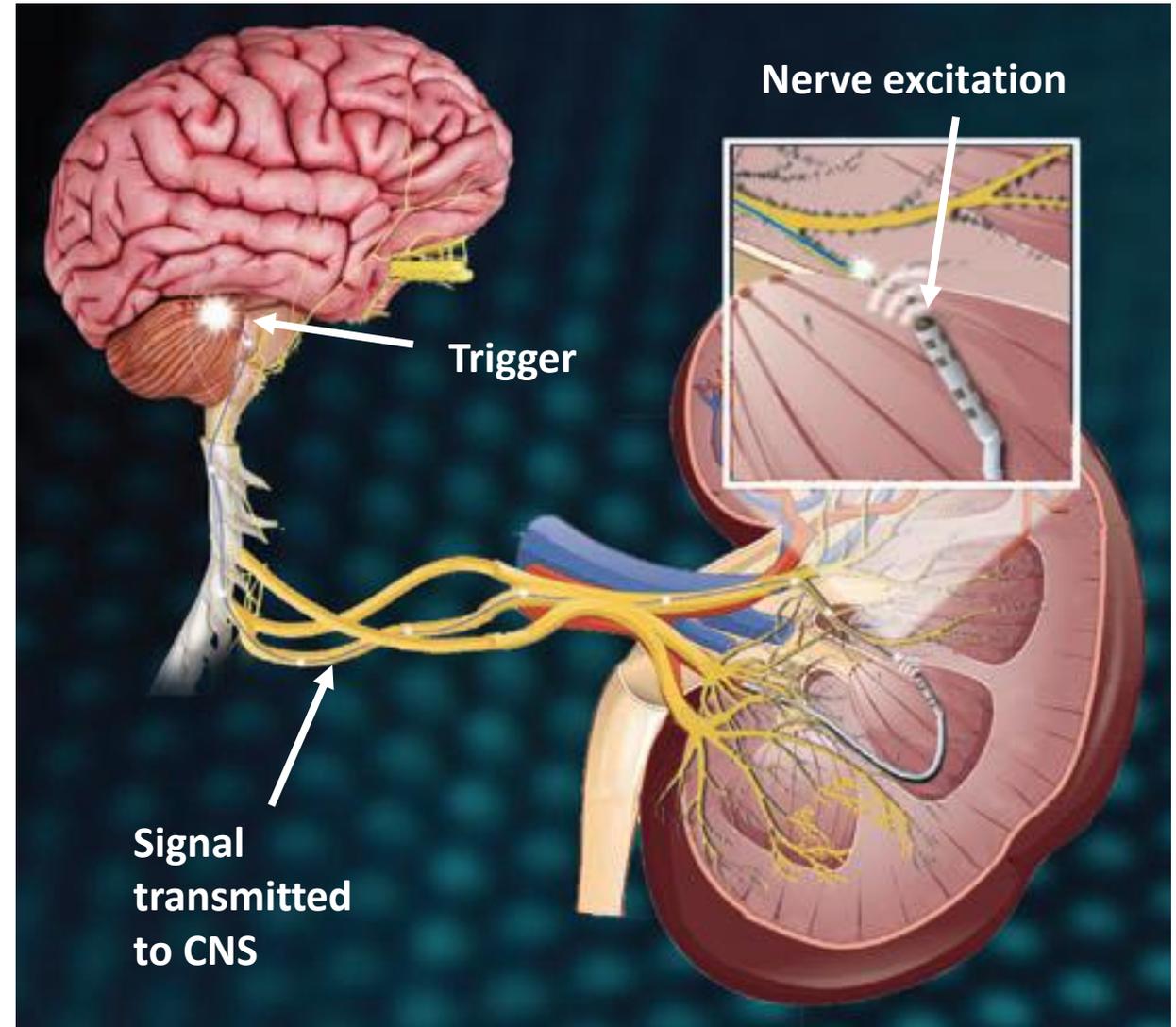


Nerve bundle of the Renal Plexus

Renal Plexus Mapping with the Huygens™ Catheter

Step 1: Turn on the light

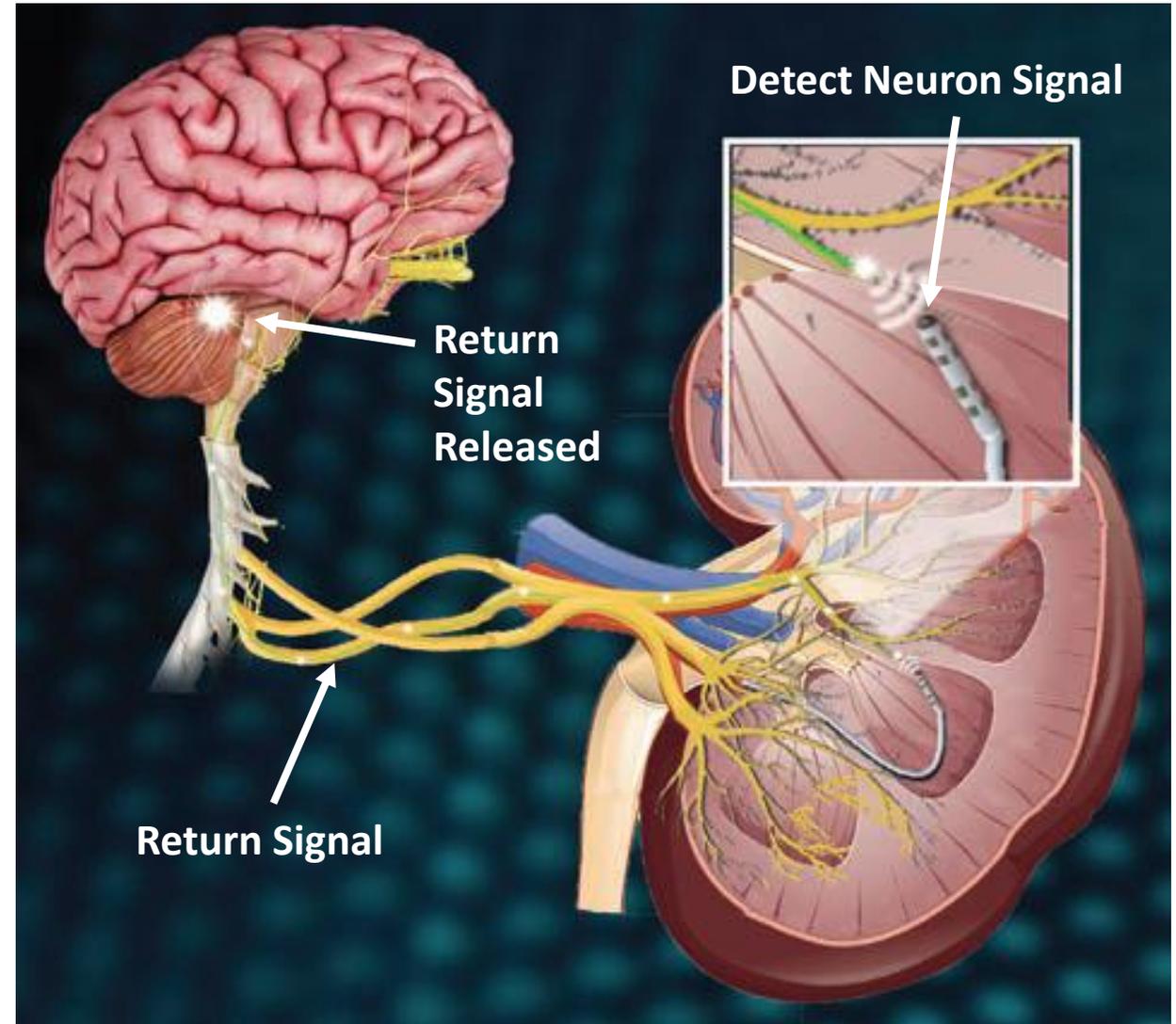
- Once the Huygens Catheter tip is in contact with the renal plexus, an AC pulse is delivered from the electrode array to the nerve tissue.
- A depolarization wave is initiated.
- The signal is transmitted to the brain.
- The brain releases a response signal.

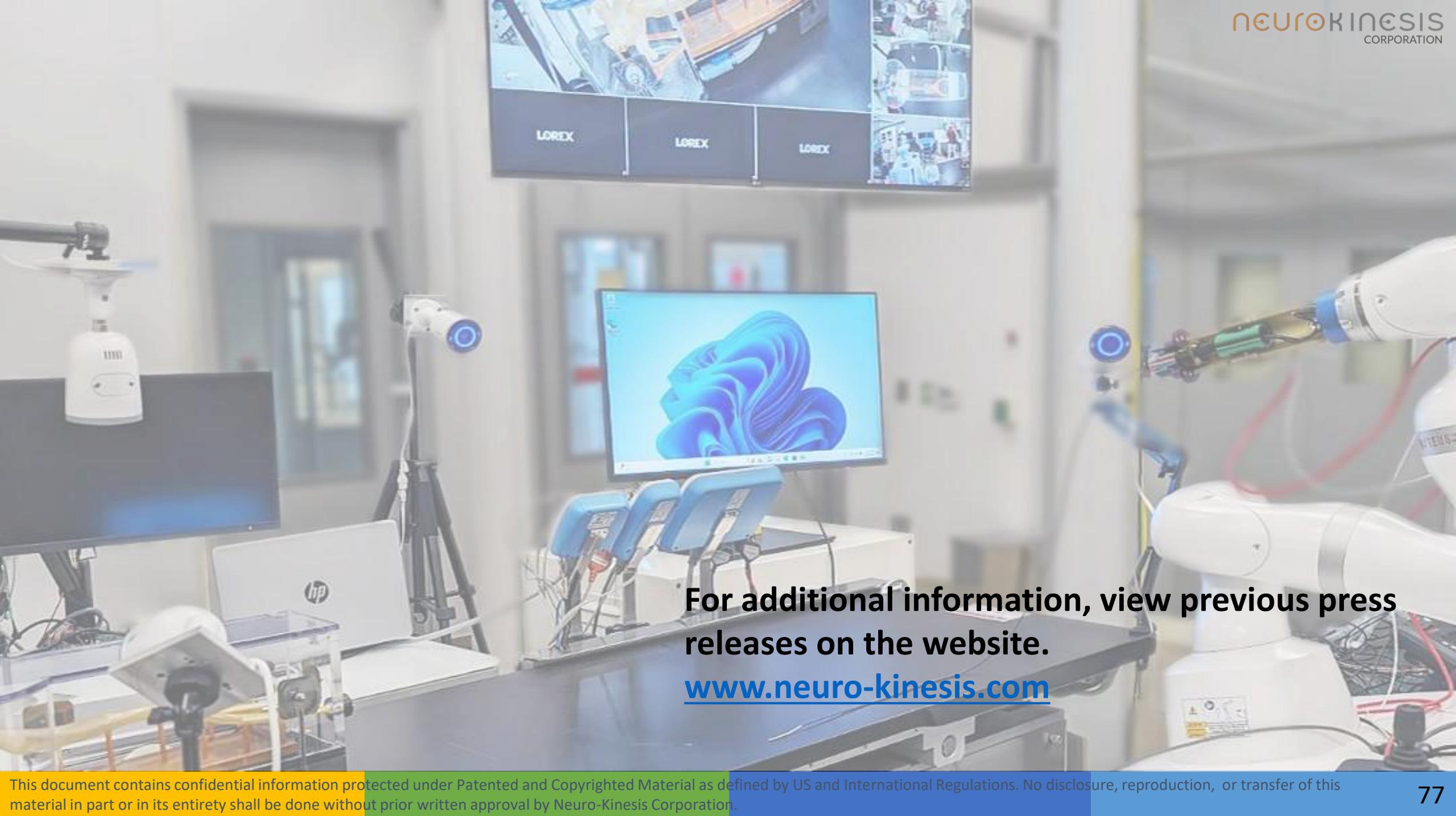


Renal Plexus Mapping with the Huygens™ Catheter

Step 2: Detect the Light

- The return signal from the brain depolarizes the renal nerve, lighting up the termination point in the Renal Plexus.
- The electrical activity at the termination point is detected by the Huygens Catheter.
- This process is repeated at the desired points to generate an EP map of the Renal Plexus.





For additional information, view previous press releases on the website.
www.neuro-kinesis.com