Flexible electronics for implantable medical devices: the Optogenerapy case and beyond.

A project coordinated by

eurecat

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EuroNanoForum 2019

Bucarest, 12th June 2019

About the Horizon 2020 funded project:

Optogenetic Protein Therapy for Multiple Sclerosis

Acronym: OPTOGENERAPY

Call – Topic: NMBP-09-2016 Biomaterials for diagnosis and treatment of demyelination disorders of the Central Nervous System.

Duration: 36 Months (1st January 2017 to 31st January 2020)

Budget: 6.233.258 € (EU contribution: 4.777.258 €)

- **11 partners** from 7 European countries:
  - **4 SMEs:** TWO, NEOS and Ultrasion (ES); geneXplain (DE);
  - **LE:** BOSTON Scientific (IE)
  - **5 RTOs:** EURECAT (ES); ETHZ (CH); INSERM (FR); TUL (PL) and ERASMUS (NL)
  - **1 Standardization body**: UNE (ES)

The need: reliable Multiple Sclerosis therapies

700.000 people have Multiple Sclerosis in Europe

Affects people most frequently between the **ages of 20 and 40**

About **2/3** of the people affected are women

By 2010 the market revenue of MS therapies was **€2.3 billion** in Europe

Optogenerapy project summary

Context

Multiple Sclerosis (MS) is a potentially disabling disease of the brain and spinal cord (Central Nervous System).

700.000 people has Multiple Sclerosis in Europe.

By 2010 the market revenue of MS therapies was €2.3 billion in Europe.

70% are diagnosed during working years.

IFN-β therapies represent 45% of total MS therapies market.

Up to 35% of MS patients using IFN-β are non-adherent.

More than 50% of the patients and their relatives suffer steep income loss within a few years.

Objectives

Develop and validate a new optogenetic implant for controlled beta interferon (IFN-ß) protein delivery for treating patients with Multiple Sclerosis.

Quality of life of patients with MS will be improved by:

- Eliminating short and long term effects of serial injections

- Increased therapeutic efficiency due to medication adherence.

Inputs

To develop Optogenerapy and to bring it to the market, requires the following budget:

- H2020 programme will fund the project with €4,8M

- BOSTON SCI will be in charge of industrialisation and launch onto market, which cost is €20-25M

Activities

These main activities will be conducted:

1) Implant technological development

2) Cell-based therapy

3) Manufacturing & Sterilisation

4) Preclinical Validation

5) Regulatory and social impact

6) Communication campaign

Expected outputs

The following outputs are expected:

1) Optogenerapy Implant

2) Disability and Quality of Life impact Assessment

3) Validation from Biocompatibility & performance tests

4) Implementation of pre-clinical regulatory

Expected impacts

- Increasing by 20% patient satisfaction, improving the quality of life according to EuroQoL 5D questionnaire

- 2% reduction of total MS in EU28 expenditure

- Time to market reduction of 30% vs other cell therapies.

- Improve of compliance with evidence-based treatments

- Engaging MS society, patients and clinical associations, such as: European Multiple, Sclerosis Platform (EMSP), Multiple Sclerosis Society.

General Objectives

To develop and demonstrate a new optogenetics implant for controlled beta interferon (IFN-ß) protein delivery for treating patients suffering from multiple sclerosis.

It is a **new bio-electronic cell based implant device to be implanted subcutaneously** providing controlled drug production and release during at least 6 months, up to pre-clinical stage.

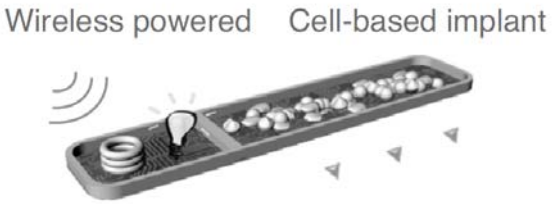
It is a **wireless powered optogenetics device** where light controls the cellular response of genetically engineered cells that produce the drug in safe conditions, combining:

- **Polymeric biomaterials** with strong optical, biocompatibility and barrier requirements.
- **Optoelectronics** miniaturization, autonomy and optical performance.
- **Cellular engineering** design for stability and performance of the synthetic optogenetic gene pathway over long-term implantation.
- **Micro moulding** enabling optoelectronics embedding for safety and minimal invasiveness: in-mold electronics in micro implantable devices.

Concept

Optogenetic Implant, consisting of:

- Drug delivery **cell chamber**: composed of a frame of biocompatible optical polymer with the upper and lower surfaces closed by flat membranes, and a lateral filling port to load cells in the cell chamber.
- **Optoelectronics module**: a micro-power energy harvesting antenna and rectifying circuit controling a NIR-LED, packaged in long term hermetic and stable material and then embedded in moulded polymer.



First prototypes by ETHZ, with conventional electronics

Benefits

- A reliable **ON/OFF switch** to start and interrupt the drug delivery:
  - With external control possible.
  - Steady drug flow: eliminating serum peak levels.
- Cell-produced IFN-β **not causing immune reaction** in the long-term.
  - Health gain and increased **patient satisfaction of 20%.**
- Minimal invasive device: ambulatory surgery.
  - Help to improve adherence and persistence.
  - Reduce side and long term effects.
- Save the costs of non-adherence to the healthcare system: direct and indirect**: 2% reduction** of total MS EU expenditure.

Consortium

Optogenerapy

eurecat
Centre Tecnològic de Catalunya

ETH zürich

Politechnika Łódzka

Erasmus University Rotterdam

geneXplain

ase Optics Europe
A Rochester Precision Optics Company

NEOS SURGERY

ultrasion
Innovative Ultrasonic Solutions

Boston Scientific
Advancing science for life™

Instituts thématiques Inserm
Institut national de la santé et de la recherche médicale

UNE
Normalización Española

Flexible electronics as a key enabler in Optogenerapy

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Printed flexible electronics as a key enabler in Optogenerapy

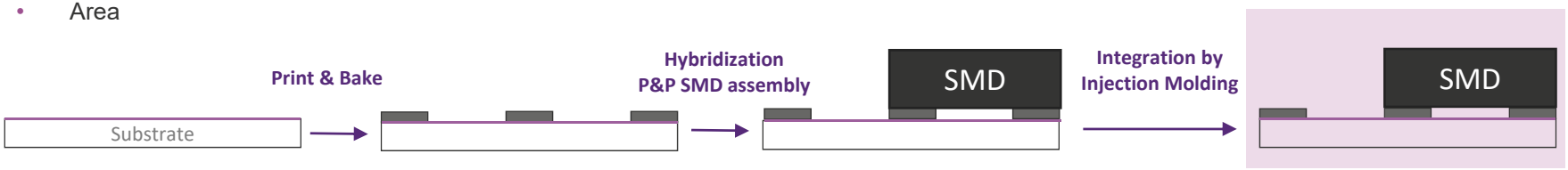
Printed Electronics is the technology able to fabricate electronic circuits in all range of substrates and soft materials due it's low temperature inks & processes

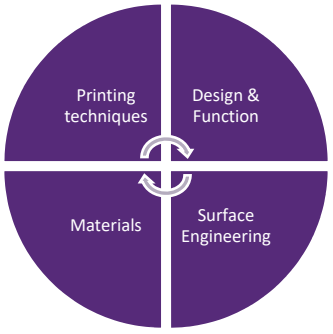
Challenges

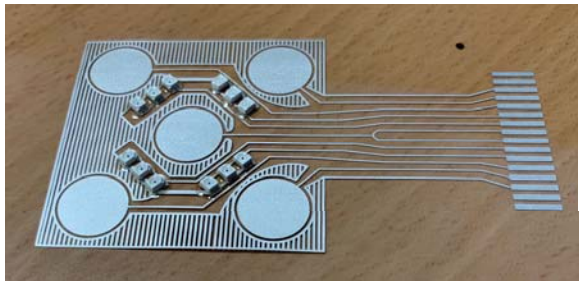
- Reliability
- Robustness
- Area

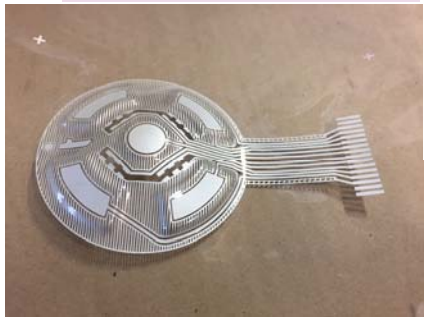
Advantages

- Flexibility/thickness
- Compatible technology
- Low weight
- Cost reduction
- Robustness
- Large area fab





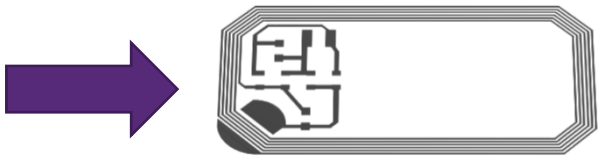




Hybrid Printed Electronics concept

Challenges

- Provide a good mechanical adhesion of the components on the film.
- Achieve a good electrical contact (minimizing the electrical contact resistance).
- Deposit conductive paste drops with high-precision to avoid short circuits caused by a bad deposition.



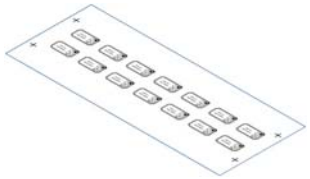
Copper tracks in rigid conventional PCB: High temperature processing

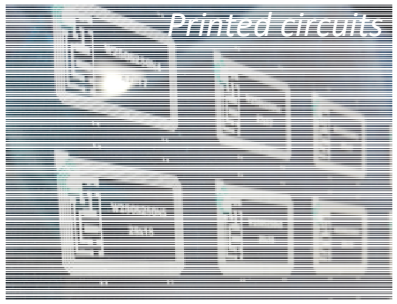
Printed silver tracks on flexible polymer foil: Low temperature materials & techniques

Invasiveness KPIs	PCB electronics	Hybrid printed electronics
Implant weight, g	3	2,1
Implant thickness, mm	6,9	4

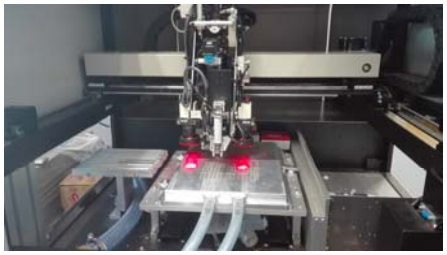
Optoelectronic Device Manufacturing Workflow

1. Screenprinting & Curing

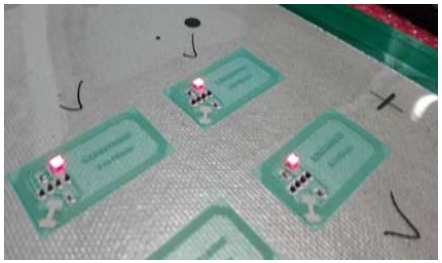




2. Hybridization by P&P SMD assembly & curing



P&P Adhesive and SMD chip



Hybrid printed circuit

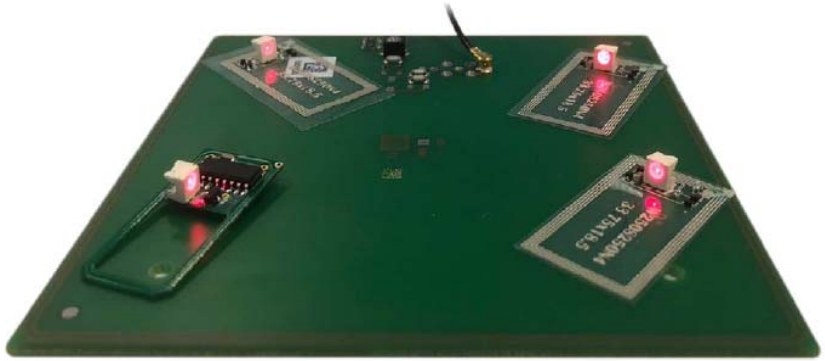
3. Silicone Molding

Molded Hybrid printed circuit

Flexible electronics for a cell-based bio-electronic implant

External Controlling Module

- **ON / OFF external LED switch**
- **Emitter electromagnetic antenna**: to power the electronics encapsulated in the implant by electromagnetic energy.



Implant flexible electronics

- **Optoelectronics unit**: electronic circuit of the implant in flexible electronics and hybridized LED, which controls the generation of the IFN-β drug by the cells within the chamber.
- **Compact low-resistance screen-printed flexible NFC antennas** of high quality factor with the footprint and interconnections on which the components are hybridized. NFC enables the exchange of data between two devices and smaller Q factor antennas than with PCB.

The flexibility and miniturization of the antenna play an important role in implants, but can also be applied to packaging and payment solutions.

Flexible electronics for medical devices, beyond Optogenerapy

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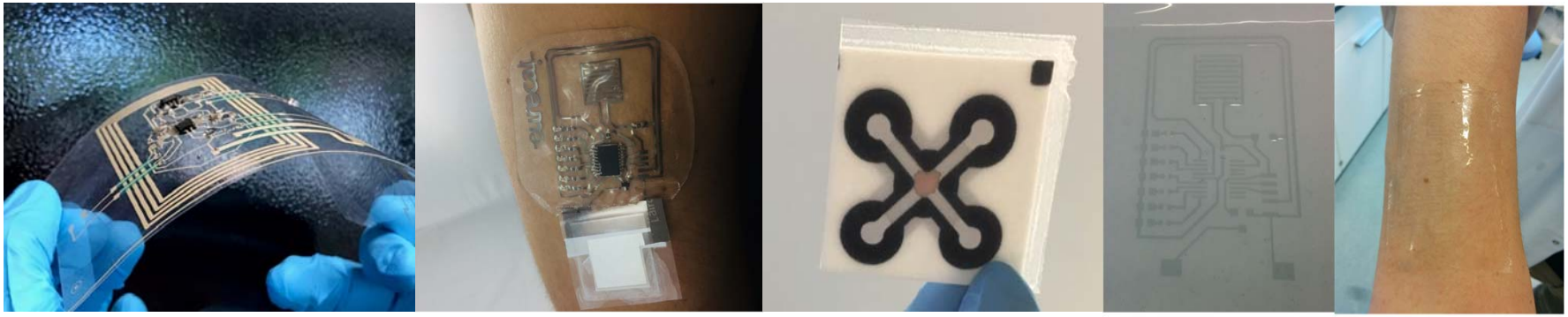
Flexible electronics for medical devices, beyond Optogenerapy



Epidermal electronics, Point of Care devices & Robotic Skin

Autonomous & Self-Powered Smart Patches with Printed Sensors & Biosensors

Flexible electronics and Injection Moulding in medical devices

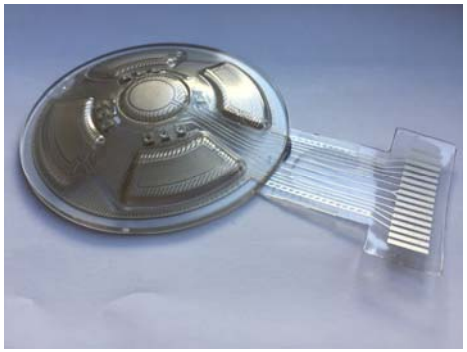
In Optogenerapy: In-mould integration of printed electronics and silicone (or other biocompatible polymer)

Benefits

- Simplification of the device arquitecture: thin & lightweight parts: minimally invasive devices
- Multifunctionality
- Integration of LEDs and optical functionalities in the plastics to perform as lenses.
- Encapsulated and protected printed electronics with overmoulded plastic.
- Compatible with curved 3D shapes.

Applications

- Smart medical devices
- Bio-electronics
- Opto-genetics
- Microfluidics
- Biosensors



Thank you!

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This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 720694