

## Wearable biocompatible sensors for dialysis monitoring

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### Introduction and Key Question

- 50,000 dialysis patients (France) Sessions 2-5/week for 5 hours.
- Clinical issue: Rebound in biomarke n (urea and potassium) in blood after dialysis.

Clinical stakes: Understanding the evolution of potassium and urea concentration in dialysis patients during and between dialysis sessions in order to improve treatment.

### Technical solution

- Hypothesis: the blood concentration rebound is due to abolite release by the tissues.
- Technical solution: Continuous monitoring in real time urea and potassium concentration in the interstitial flu (ISF). ISF is a blood "filtrate" in which cells are bathed:
- No coagulation for continuous monitoring. · Monitoring as close as possible to the tissues

### Objectives and implementation method

Development of wearable devices combining microneedles and potentiometric ion-selective electrodes (ISE) as electrochemical sensors for the monitoring of biomarkers in ISF.

### Technical and scientific challenges:

- Formulate membranes sensitive to potassium ions  $(K^+)$  and urea using biocompatible materials.
- Integrate electrodes with microneedles to continuous potassium and urea in interstitial fluid and in real time.





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# Enzymatic layer (urea sensor only): Hydrolyses urea into ammonium then detect

sulating layers: In

### Ion sensor - Sensitive layer: Manufacturing and characterisation

Open Circuit Potential (OCP) characterisation with ion addition. Sensitivity S is determined by Nernst equation ( $S_{theorical limit} \approx 59 \, \text{mV} \, at \, room \, temperature \, for$ 

 $E_{electrode} = E_0 + S \log(a_{i^+}), a_{i^+} ion activity$ 



Potassium monitoring measuren different sensitive layers

Advantage over conventional

formulations

• 3D formatting compatibility,

• Biocompatibility: reduced amount

### Urea sensor - Enzymatic layer: Strategies to entrap urease

- Micro-encapsulation → no interest in Micro-encapsulation → no interest in using solid membranes.
   Cross-linking → highly likely to inhibit enzyme activity.
   Adsorption → no long-term stability.
   Covalent bonding → No functional groups on lon Selective membrane.
   Choice\_Entrapment in a hydrogel.

+ Non-crosslink alginate no long-term stability. -\psi Alginate vinylsulfone crosslinking with PEG-bis(thiol); long-term stability without pH Alginate vinylsulfone crosslinking with PEI: mid-term stability with pH control.

### Potassium Selective Membranes:

Blocompatibility assessment:
Story of the Compatibility assessment of the Cytotoxicity test carried out in accordance with the ISO10993 standard on Potassium equivalent to 2 working electrodes (WST test).

Poliminiary userill 95% visibility 1787

Integration of electrodes with microneedles:
Production of the first potassium-sensitive Production of microneedles.



### **Conclusions and Perspectives**

Biocompatible materials can replace conventional ISM materials. The membranes developed are highly sensitive, low in plasticizers and non-cytotoxic. They can be used to create 3D electrodes and, in our case, micro-needles directly in the sensitive material (no coating is required).

The enzymatic membrane is still under development, with questions remains the controlling the pH of the membrane to promote the production of  $NH_4^+$ . Future work will assess the robustness of the formulation and optimize the shape of microneedle for monitoring potassium and urea in dialysis using microneedles.





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