Advanced wound dressings and models for their preclinical validation

Ing. Rossella Laurano, Ph.D.

Politecnico di Torino, Dipartimento di Ingegneria Meccanica e Aerospaziale

Chronic skin wounds affect more than 40 million patients worldwide and represent a severe burden for both the society and the healthcare systems

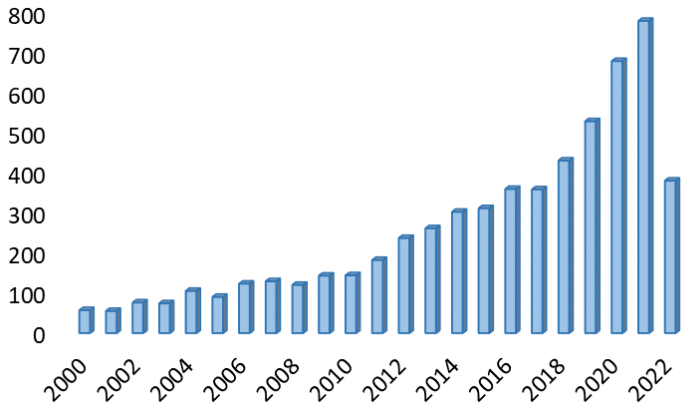
Patients

Society

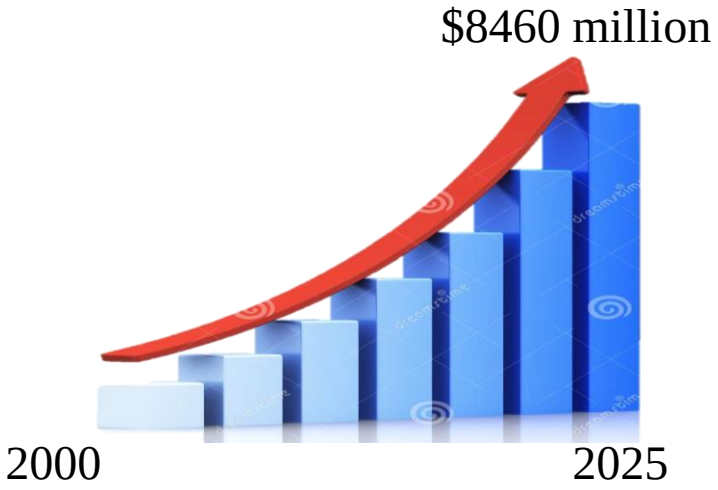
Healthcare System

Great efforts have been devoted to the development of treatments and wound care products able to effectively enhance the wound healing process

Number of publications per year on "advanced wound dressing development"[1]

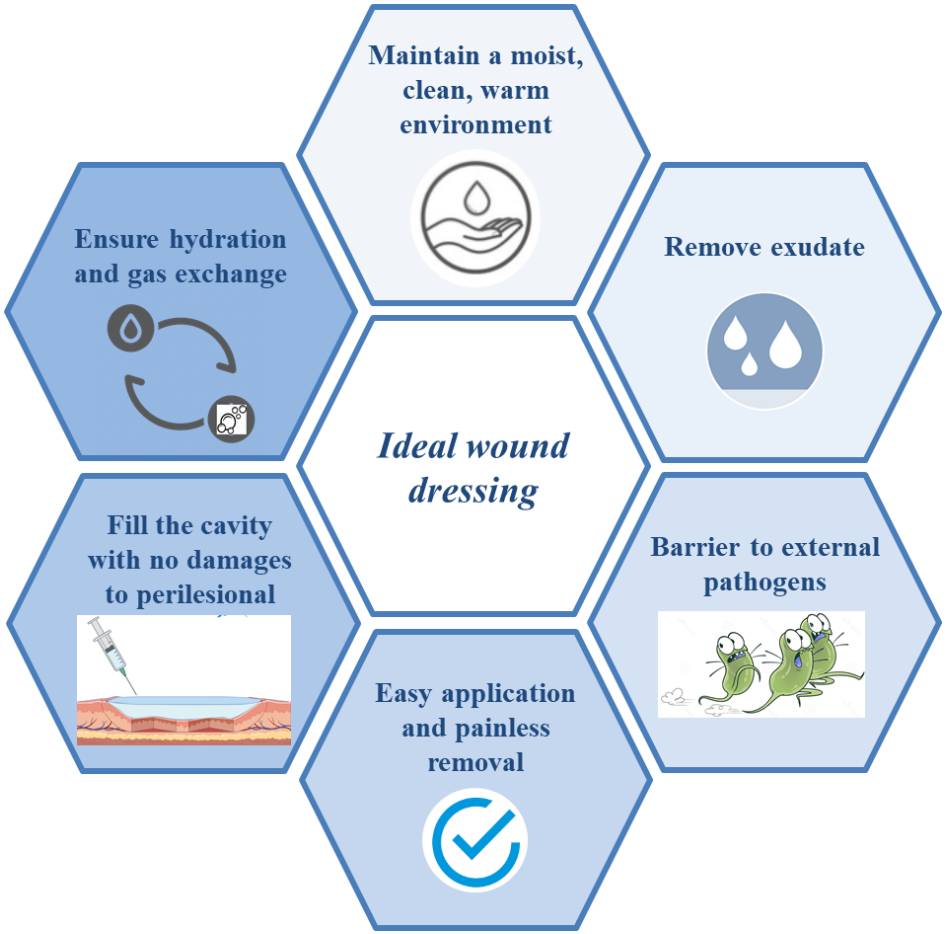


Global market size of wound dressings[2]



[1]Data from PubMed database
[2]Data from www.fortunebusinessinsigth.com

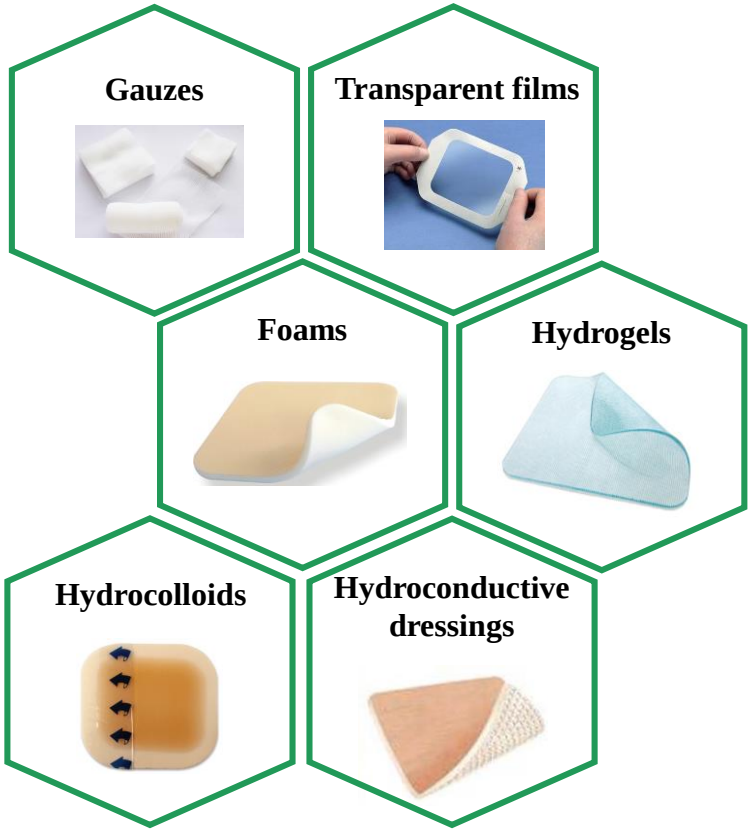
The most influencing concept guiding the design of wound care products has been the moist wound healing theory postulated by Prof Winter in 1962[1]



[1]G. D. Winter, *Nature* **1962**, *193*, 293-294

Centro 3R

Traditional Wound Dressings | Medicated Wound Dressings | Advanced Wound Dressings



- Frequent changes
- Need of a secondary wound dressing
- Passive wound dressings

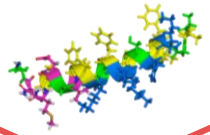
Traditional Wound Dressings | **Medicated Wound Dressings** | Advanced Wound Dressings

Functional wound dressings able to actively take part to the wound healing process

Bioactive wound dressings

Bioactive macromer

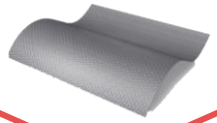
Antimicrobial Peptides



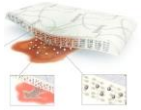
Natural antiseptics

Drug-loaded wound dressings

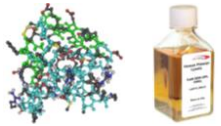
Anti-bacterial agents



Anti-inflammatory and analgesic drugs



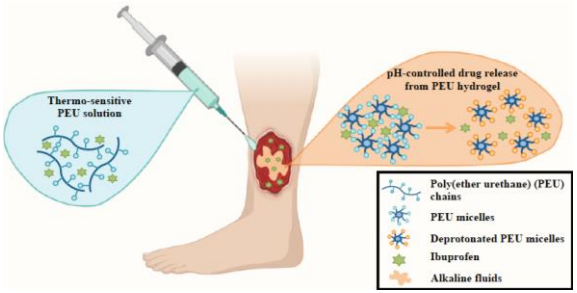
Biological factors



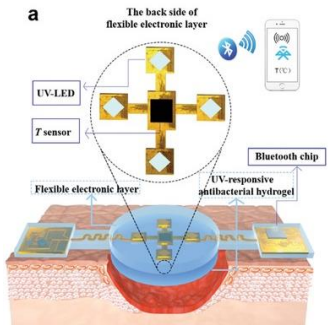
- No control over payload release kinetics

Traditional Wound Dressings | **Medicated Wound Dressings** | **Advanced Wound Dressings**

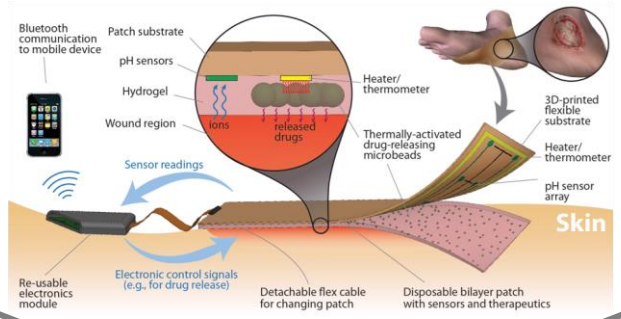
Self-responding drug-releasing wound dressings[1]



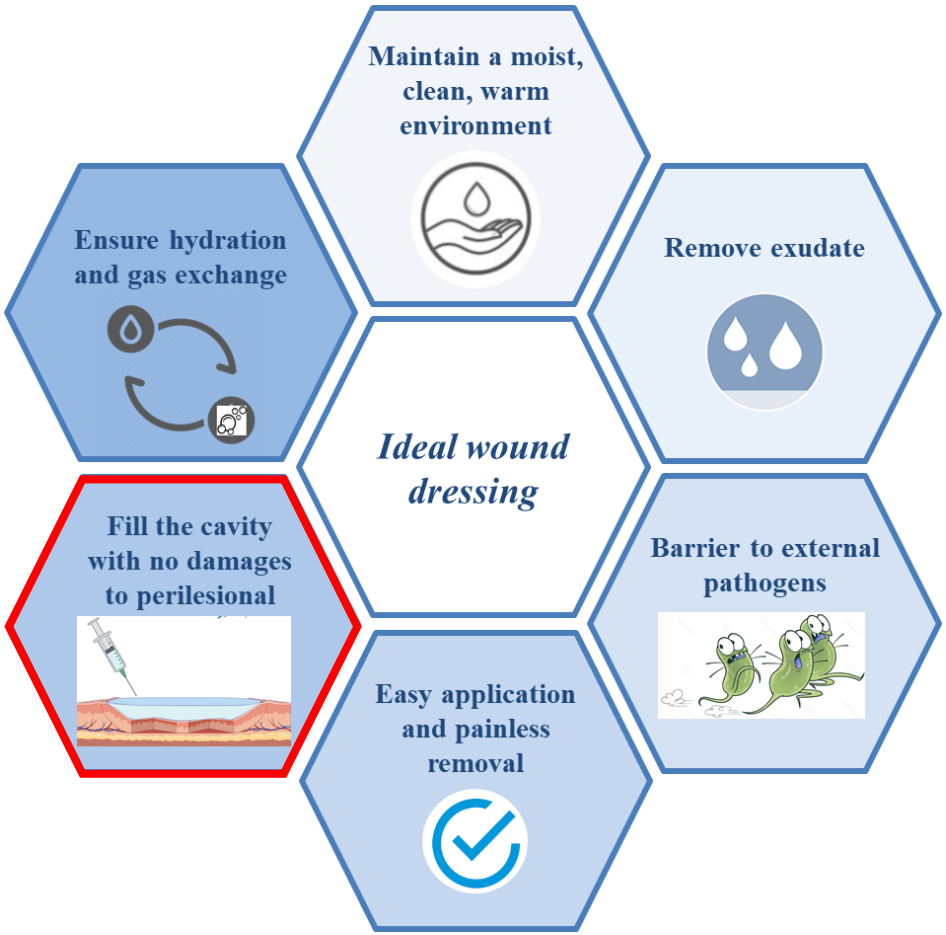
Externally-triggered drug-releasing wound dressings[2]



Automated drug-releasing wound dressings[3]



[1]R. Laurano et al., *Bioactive Materials* **2021**, *6*, 3013-3024
[2]Q. Pang et al., *Adv. Sci.* **2020**, *7*, 1902673-1902683
[3]P. Mustafalu et al., *Small* **2018**, *1*, 1703509-1703518



G. D. Winter, *Nature* **1962**, *193*, 293-294

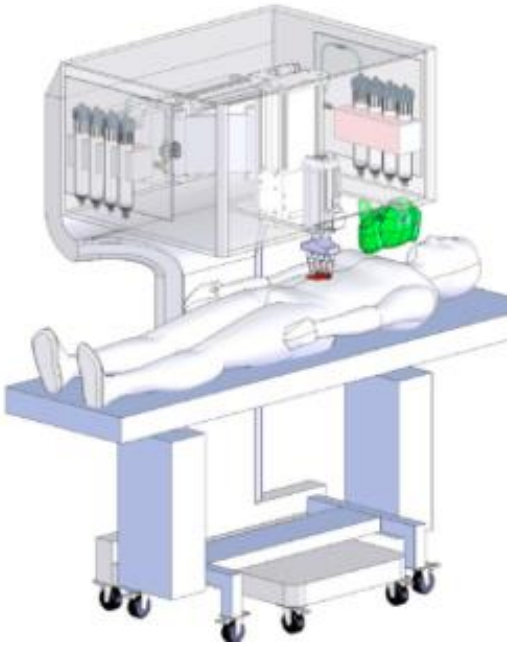
Each wound shows a unique morphology

→ need of personalized patient's specific wound dressings

Personalized patient's specific wound dressings

Portable electrospinning[1]

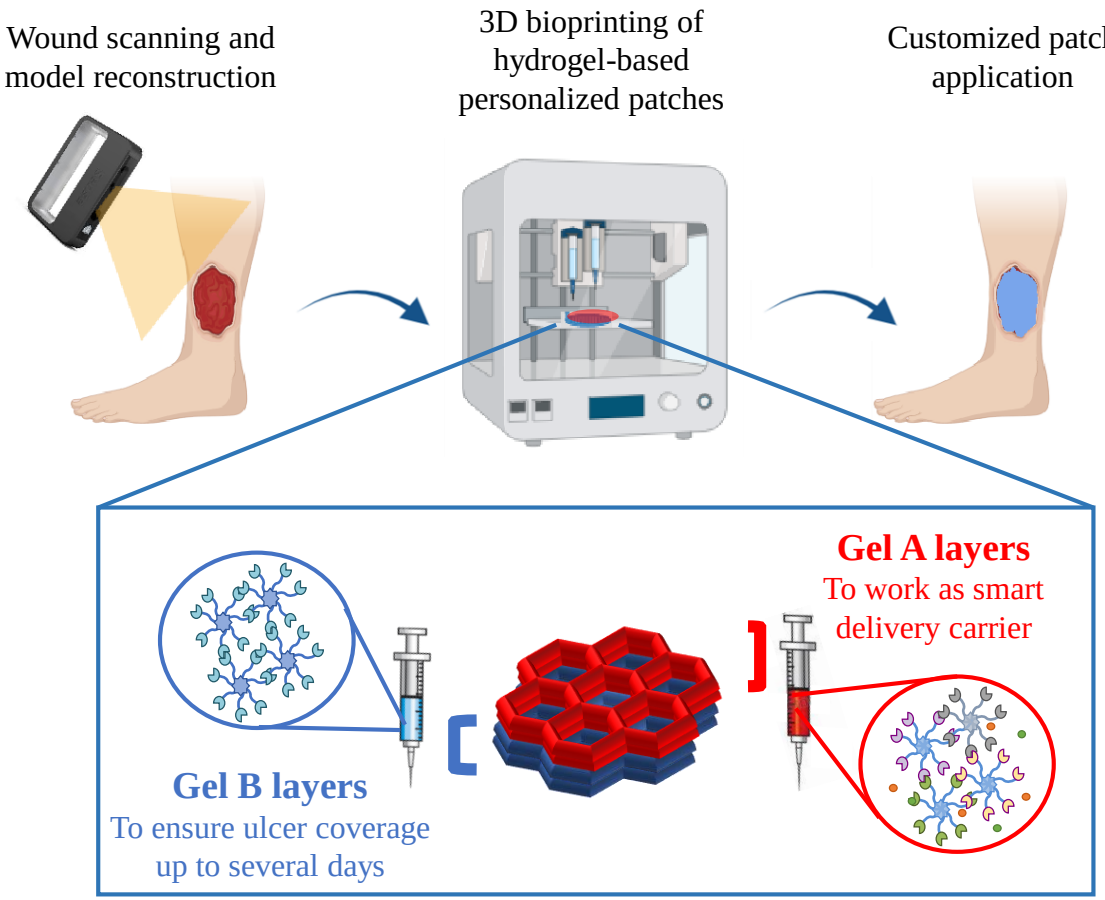
***In situ* bioprinting[2]**



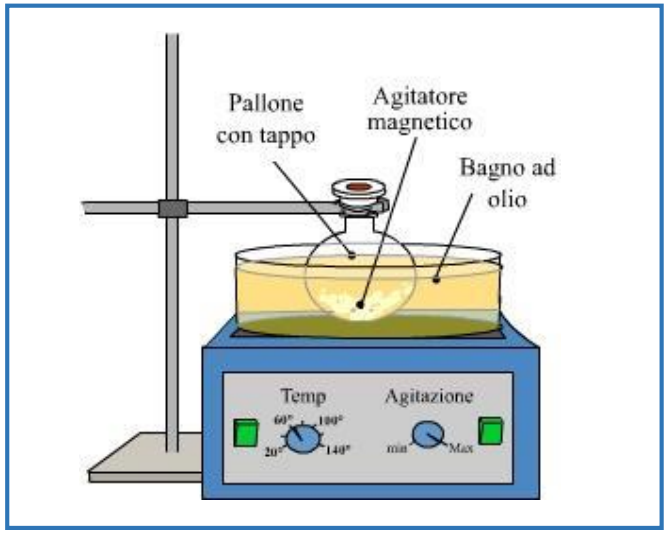
[1]R.H. Dong et al., *Nanoscale* **2016**, *00*, 1-6
[2]M. Albanna et al., *Sci. Reports* **2019**, *9*, 1856-1871

Case study at PoliTO

Design of a patient-personalized patch able to encapsulate different therapeutic agents (e.g., hydrophobic and hydrophilic drugs, therapeutic ions, biomolecules) and control their release through wound-triggered stimuli (e.g., alkalinity of wound exudate)

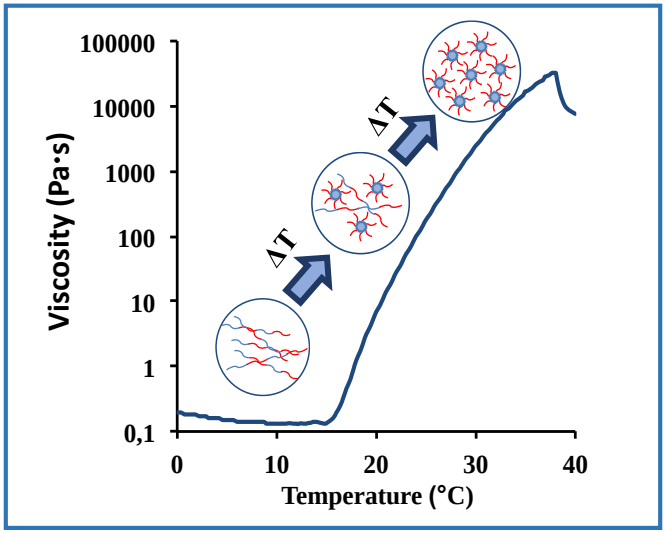


Synthesis of amphiphilic poly(ether urethane)s (PEUs)



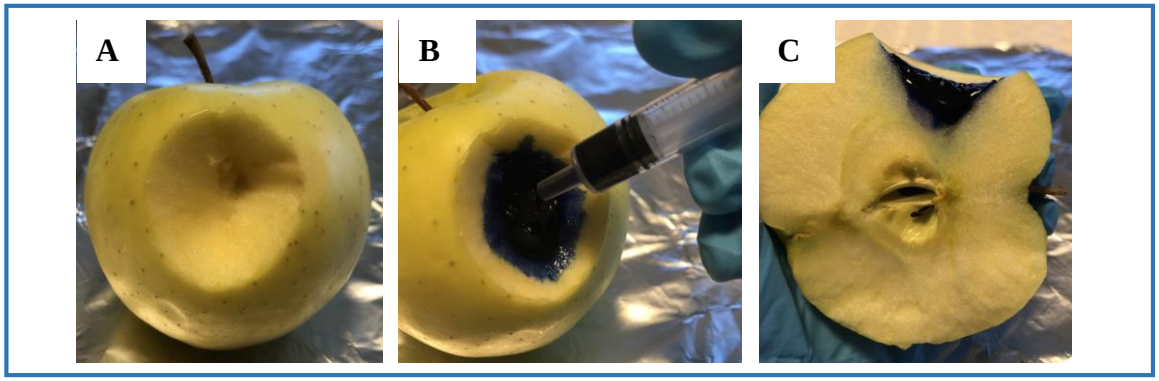
M. Boffito et al., *Polymer International*, **2016**, 65:756-769

Design of temperature-induced gelling formulations

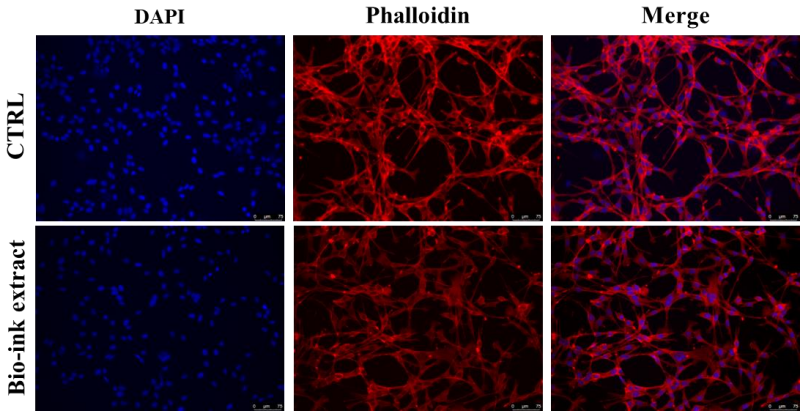


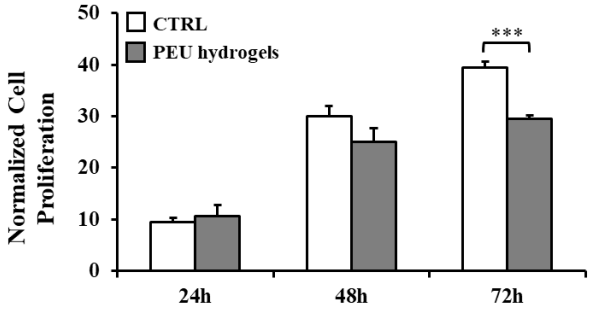
R. Laurano et al., *Frontiers in Materials*, **2020**, 7:1-15

Assessment of hydrogel injectability and shape retention

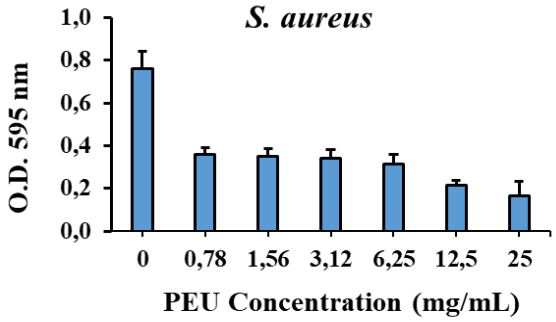


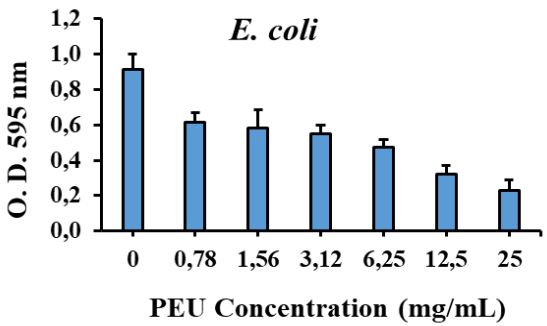
R. Laurano et al., *Engineered Regeneration*, **2021**, 2, 263-278

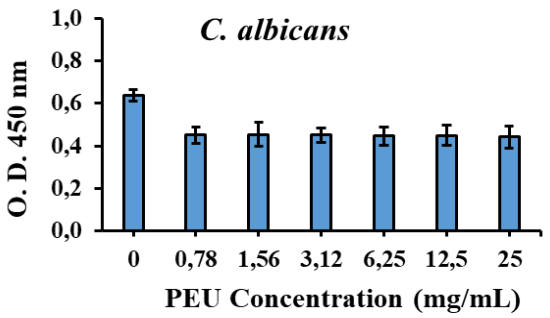




Hydrogel biocompatibility tested according to ISO 10993-5 regulation and capability to support NIH-3T3 murine fibroblast proliferation





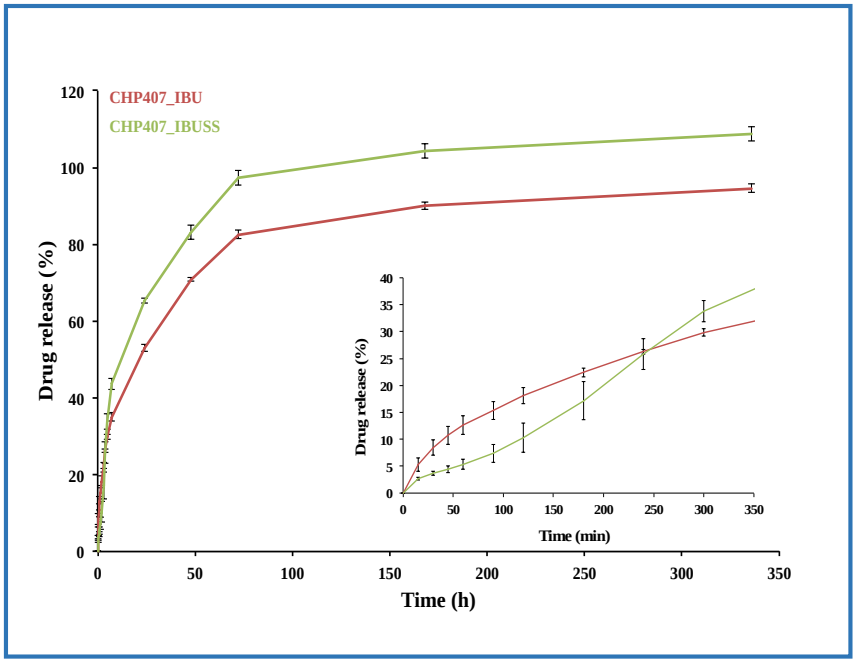


Remarkable concentration-dependent antibacterial and antifungal activity due to the amphiphilic nature of bio-ink constituent polymer[1]

[1]In collaboration with Prof Letizia Fracchia, Università del Piemonte Orientale

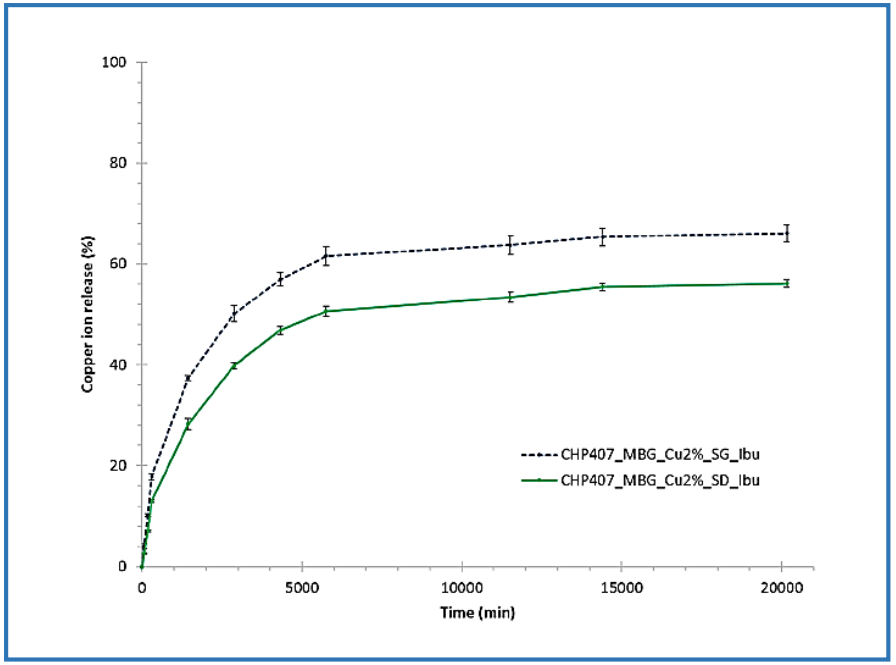
R. Laurano et al., *Engineered Regeneration*, **2021**, 2, 263-278

Hydrogel capability to encapsulate and release both hydrophobic and hydrophilic drugs with different kinetics based on their nature

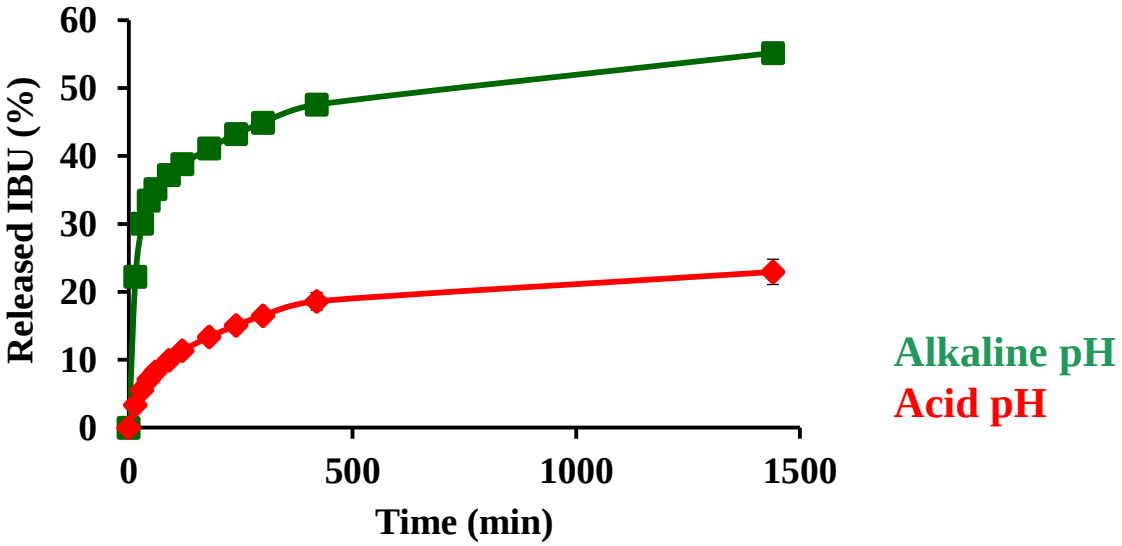


R. Laurano & M. Boffito, *Frontiers in Bioengineering and Biotechnology*, **2020**, 708:1-14

Hydrogel capability to embed ion-doped mesoporous silica nanoparticles and release therapeutic ions avoiding burst release phenomena

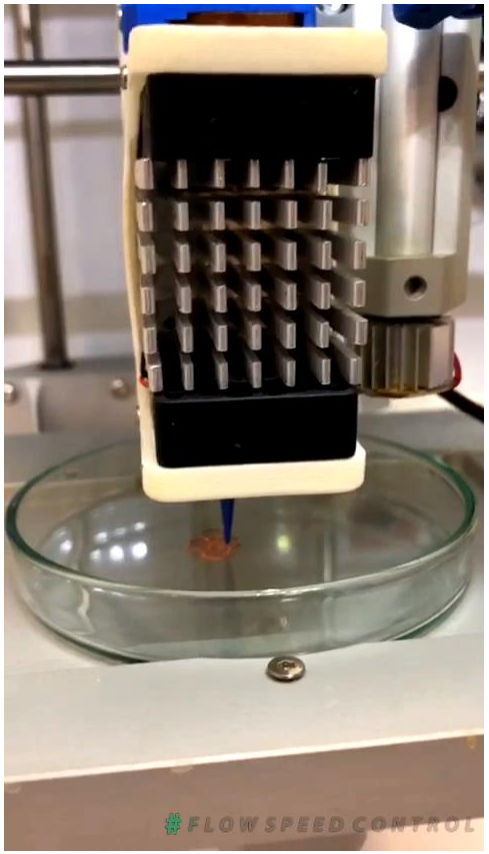


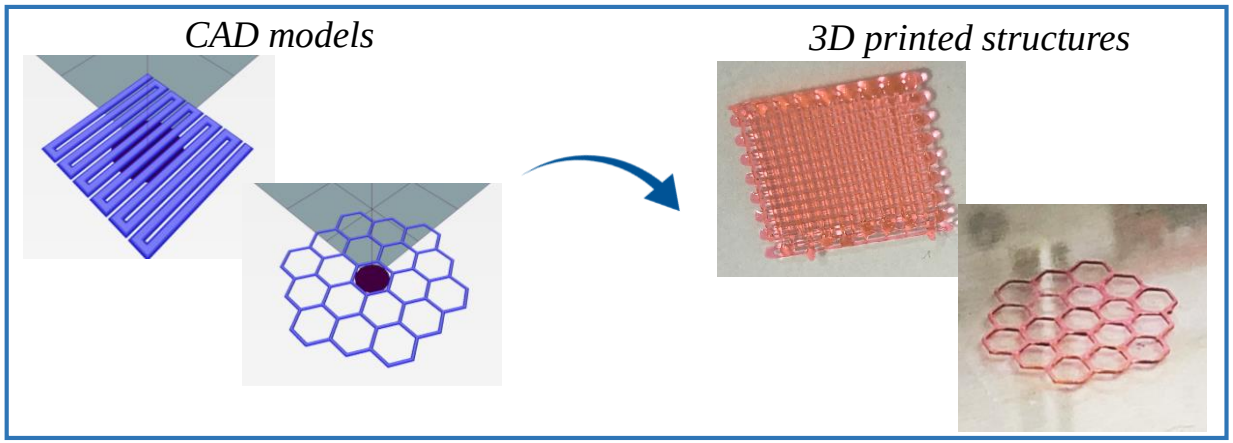
M. Boffito and C. Pontremoli et al., *Pharmaceutics*, **2019**, 11:501-521

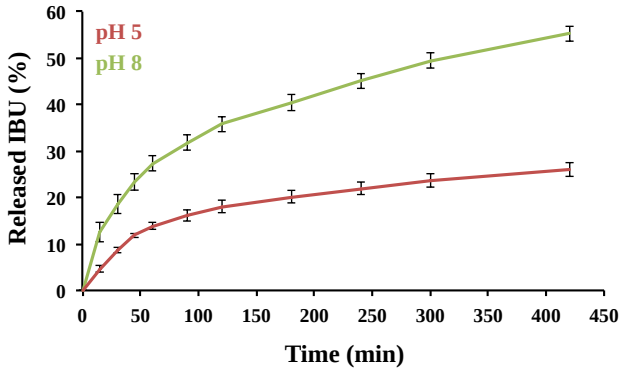


Payload release triggered by the absorption of fluids characterized by an alkaline pH (e.g., exudate of infected chronic wounds)

R. Laurano & Boffito M. et al., *Polymers*, **2019**, 11:2109
R. Laurano & Boffito, M. et al., *Bioactive Materials*, **2021**, 6:3013-3024





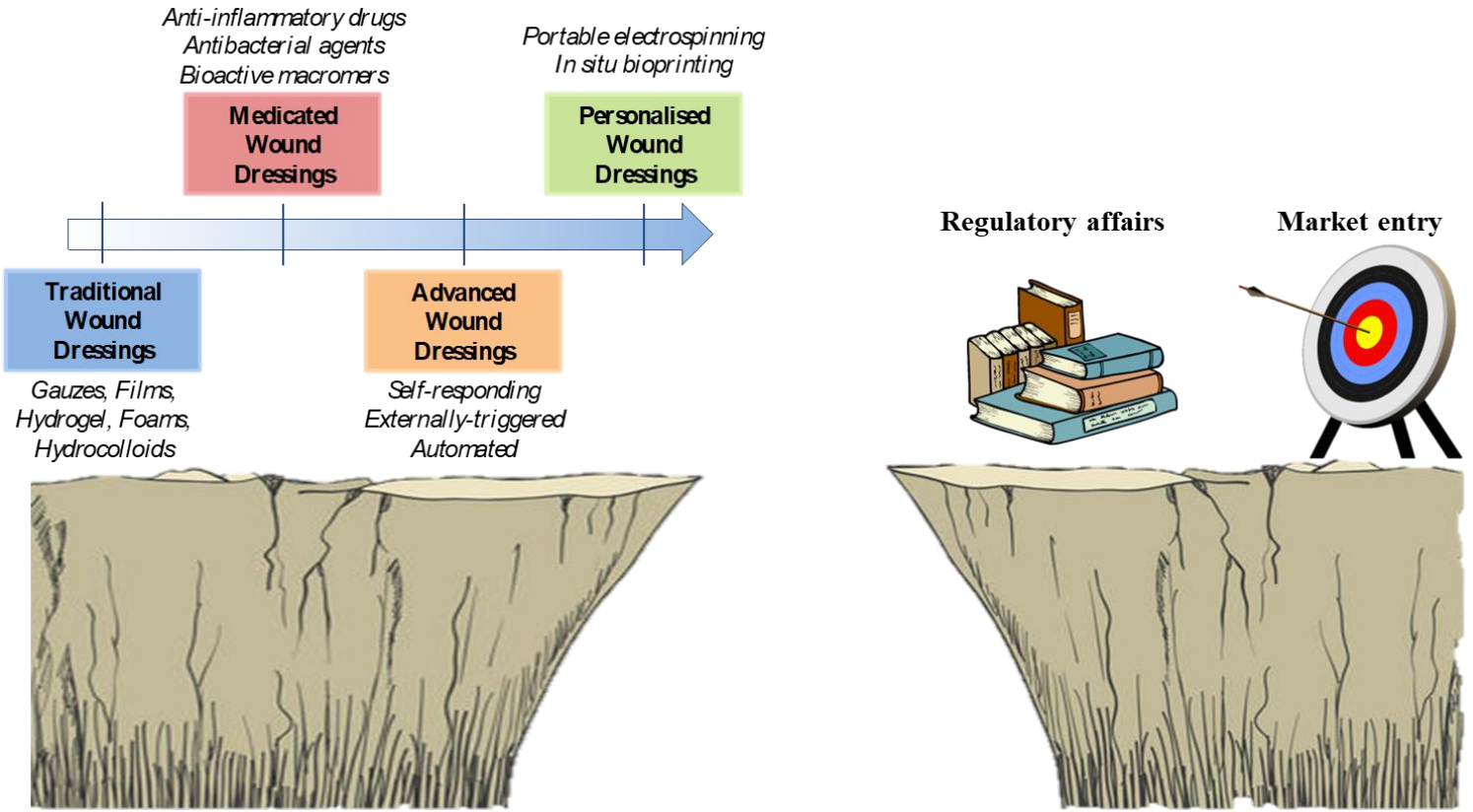


Hydrogel retained capability to control payload release via a pH-controlled mechanism upon irradiation with Vis light

R. Laurano et al. *(in preparation)*

Despite this wide literature on smart and personalized wound care formulations an ideal wound dressing does not exist on the market!

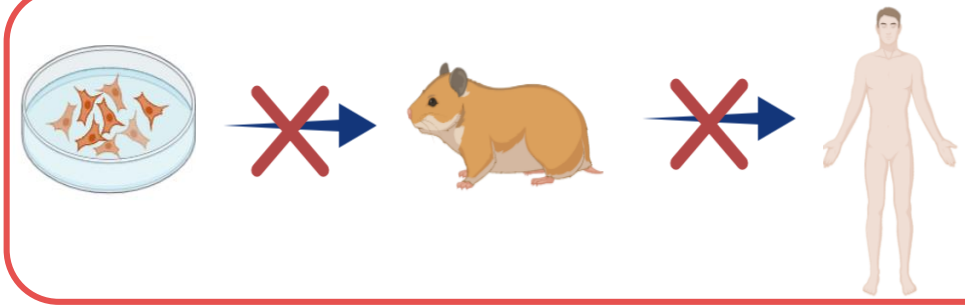
The challenges of wound dressings



R. Laurano et al., *Engineered Regeneration*, **2022**, *3*, 182-200

Key factors limiting the quick market entry of advanced wound dressings

Regulatory concerns
to assess the safety and functionality of complex and multicomponent devices



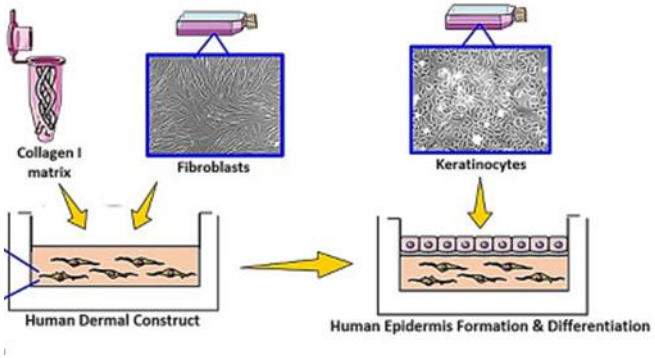
Technical issues
Complex identification of standardized procedures to prove the superior effectiveness of advanced wound dressings compared to traditional ones

Need to get funds for technological readiness level increase
requiring preclinical animal tests and then clinical trials

R. Laurano et al., *Engineered Regeneration*, **2022**, *3*, 182-200

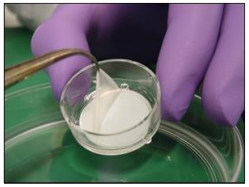
In this regards, the development of *in vitro* human skin models for preclinical validation of drug and therapies could help in reducing time- and cost-to the market of products for wound treatment/healing

Research products



A. Idrees et al., *4Open*, **2021**, *4*, 1-21

Commercial products



EPISKIN

MatTek IN VITRO LIFE SCIENCE LABORATORIES

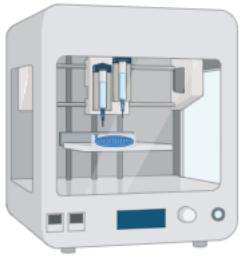
New preclinical validation methods have been developed and other are in progress, as underlined in the periodic reports by EU Reference Laboratory for alternatives to animal testing[1]

[1] https://ec.europa.eu/growth/sectors/cosmetics/ban-animal-testing_it

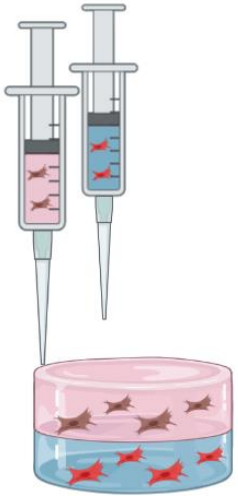
Case study at PoliTO

Development of an *in vitro* 3D skin wound model to preclinically evaluate the effectiveness of advanced and personalized wound dressings under the 3Rs principles

Biomaterial synthesis

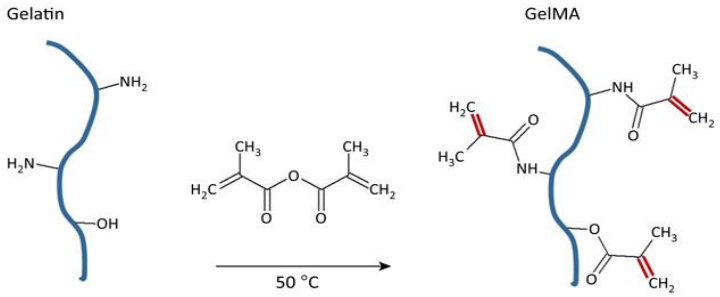


Green processing techniques

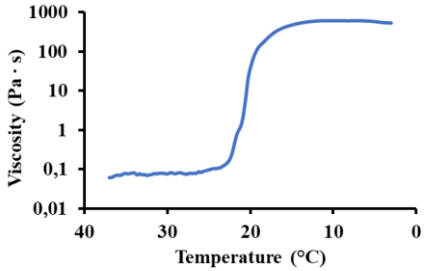


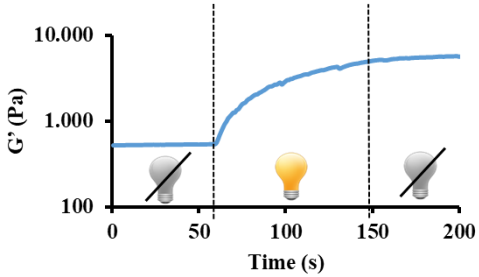
3D chronic wound models able to replicate relevant clinical conditions in terms of morphology, thickness and infections

Polymer functionalization

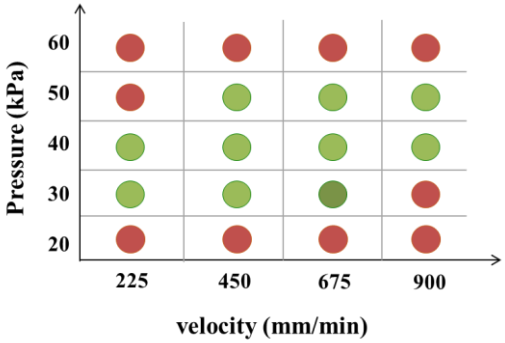


Bio-ink characterization

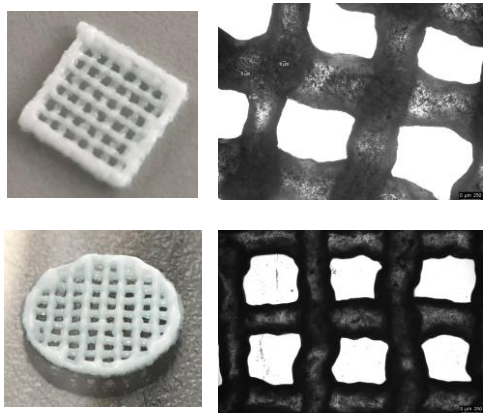




Printability evaluation



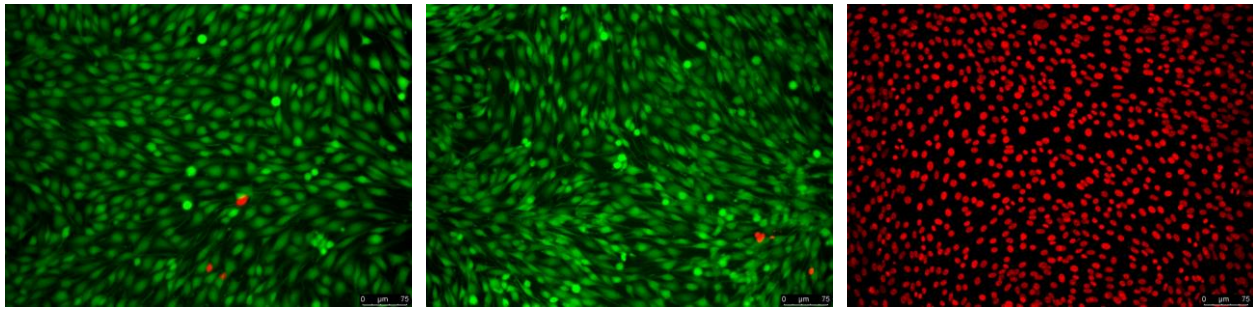
3D model development



R. Laurano et al. *(in preparation)*

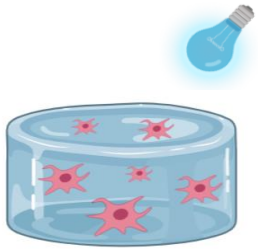
NIH-3T3 murine fibroblast encapsulation in the bio-ink

Negative control | **GelMA extracts** | **Positive control**

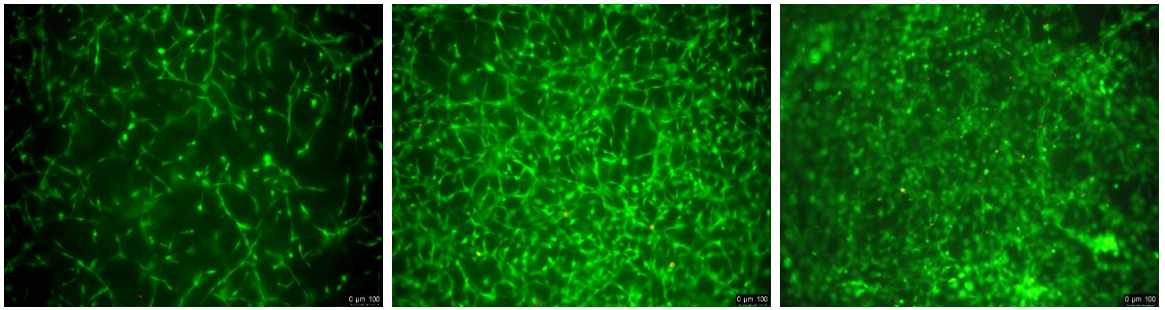


Cytocompatibility of GelMA extracts according to the DIN EN ISO 10993:5 regulation

Visible light



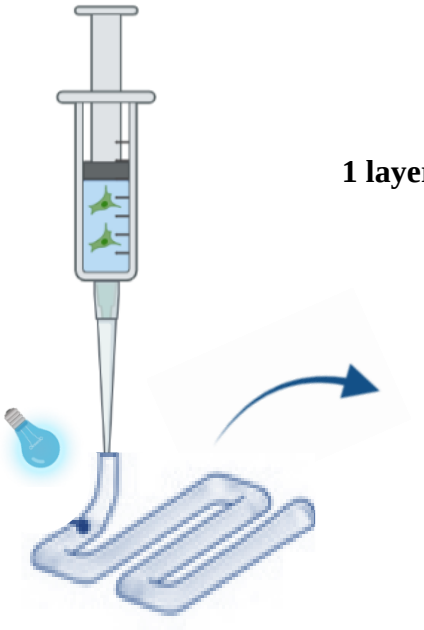
2 days | **4 days** | **7 days**



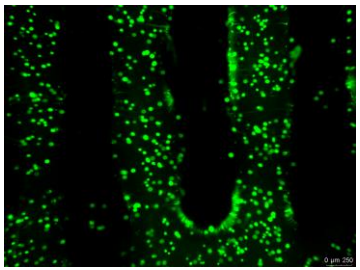
Absence of cell detrimental effects induced by construct irradiation with visible light and strong proliferation observed up to 7 days of culture in static conditions

R. Laurano et al. *(in preparation)*

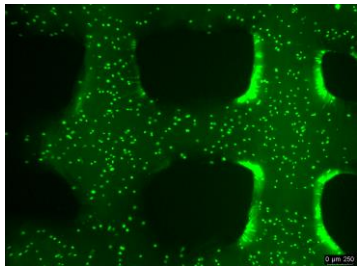
NIH-3T3 murine fibroblast encapsulation in the bio-ink



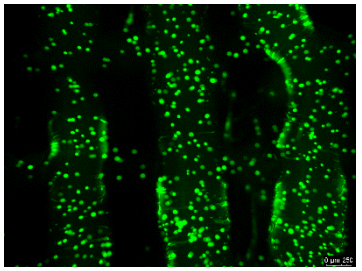
1 layer



2 layers



4 layers



Homogeneous cell dispersion within the bio-ink and absence of extrusion-induced cell damages.
Cell proliferation observed up to 7 days of culture in static conditions

R. Laurano et al. *(in preparation)*

Take home message

A great deal of effort towards the development of effective wound dressings has been registered within the scientific community during the last decades

Currently, an ideal wound dressing able to promptly manage wound treatment does not exist

Several regulatory affairs, technical and economical issues are strongly limiting the clinical translation of advanced research platforms

The development of *in vitro* wound models as preclinical validation tool can speed the product market-entry up, reduce costs and replace the need of animal experimentation

This work has been financially supported by the European Union's Horizon 2020 research and innovation program under grant agreement No. 685872-MOZART (www.mozartproject.eu).

Prof. Gianluca Ciardelli
Prof. Valeria Chiono
Dr. Monica Boffito

Dr. Claudio Cassino
Prof. Letizia Fracchia

Dr. Rossella Laurano
rossella.laurano@polito.it