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Bio-inspired brominated-resilin electrospun scaffolds for vascular wall modeling

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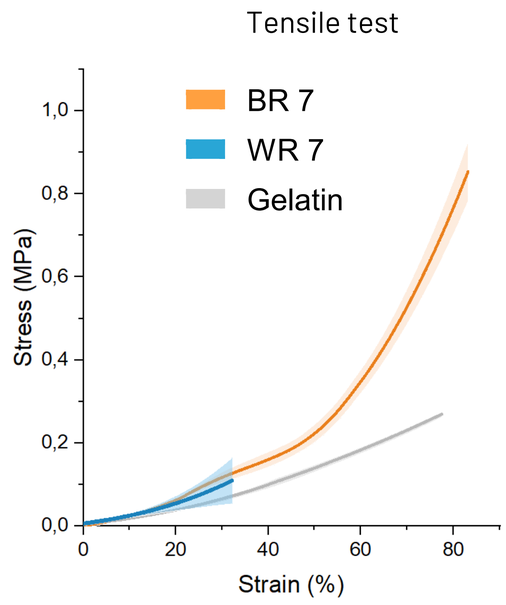
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Introduction

Cardiovascular diseases are currently among the leading causes of mortality worldwide. The urgency to study their onset and progression, as well as to evaluate potential treatments, has driven researchers to develop numerous ***in vitro* models** of blood vessels. Replicating the mechanics and layered organization of vessel walls remains a major challenge for vascular in vitro models [1].
Our aim is to develop and validate a compliant, stratified vascular microphysiological model with controllable porosity and stable co-culture of endothelial cells (ECs) and smooth muscle cells (SMCs), combining an innovative elastomeric peptide-based material with a bicompartmental versatile device.

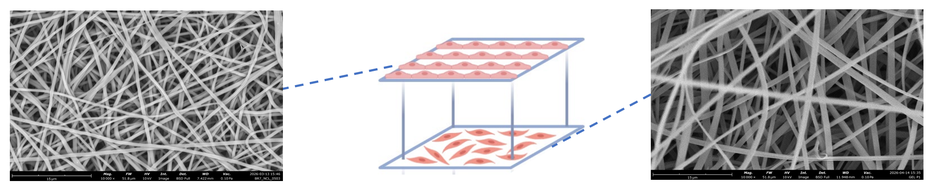
Brominated peptide-based scaffolds

Drawing on halogenation strategies found in nature, we engineered an elastomeric electrospun scaffold in which a brominated resilin-derived peptide provides elasticity and strain-stiffening, while gelatin supports fiber formation and handling. Matrices with three different compositions were produced and characterized: brominated peptide/gelatin 70/30% wild type peptide /gelatin 70/30 % (RW7) and Gelatin 100%. Tensile test confirmed that brominated matrices exhibits soft-tissue-like elastomeric behavior, making them suitable for mimicking vascular walls [2].



Multilayer design

By tuning electrospinning parameters, we aim to engineer a bilayer matrix mimicking the intima and media: a dense, low-porosity luminal layer to support endothelial monolayer formation, and a more porous layer to promote smooth muscle cell (SMC) infiltration.To date, the two layers have been fabricated separately. The dense layer has been characterized with endothelial cells, while the porous layer still requires biological validation with SMCs.

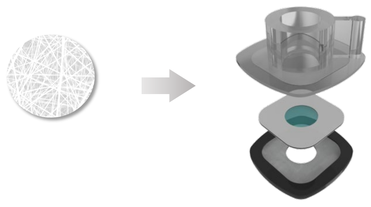


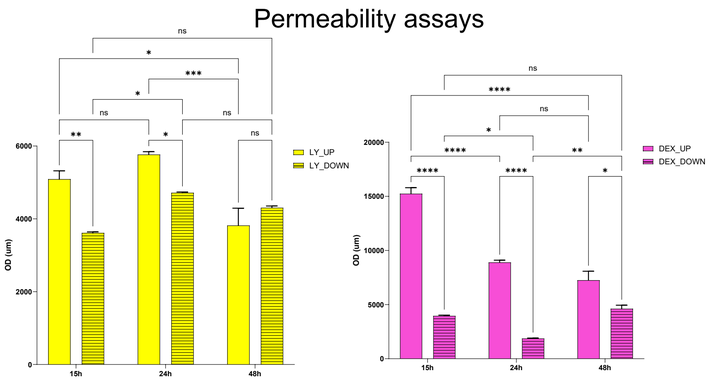
Biological characterization

For biological characterization, scaffolds have been integrated in an innovative cartridge-based bicompartmental platform (True Tissue on Platform) that facilitates handling, sample-retrieval and imaging [3].
Permeability assays with Dextran 40 and Lucifer Yellow on the dense layer confirm size-selective transport, supporting its potential as an intima-like barrier.

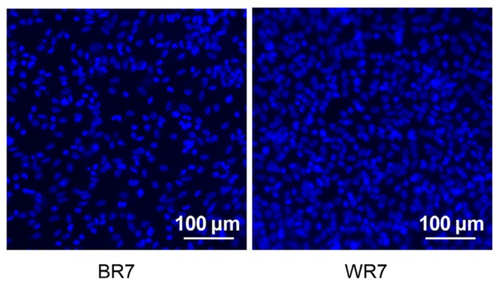
Resilin-based matrices demonstrated **biocompatibility** when tested with the EA.hy926 cell line, supporting **cell viability above 70%** with no significant differences between brominated and non-brominated samples, nor compared to gelatin and PC membranes used as controls.
Mid-term cultures confirmed good cell proliferation on resilin-based scaffolds, with **sustained biocompatibility over 21 days.**

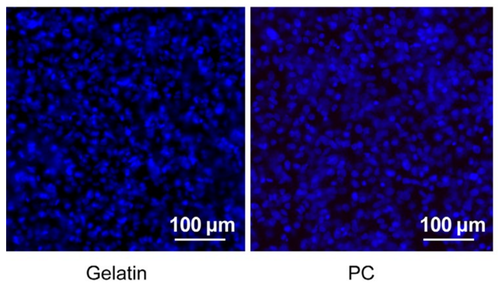
TToP device



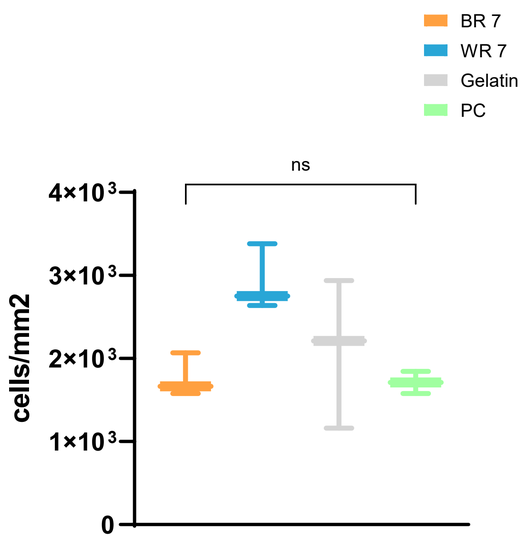


Nucleai staining (DAPI)

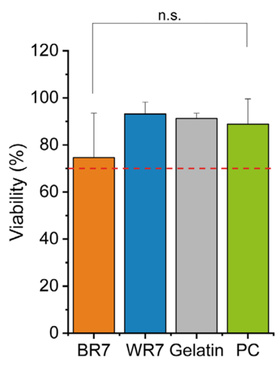


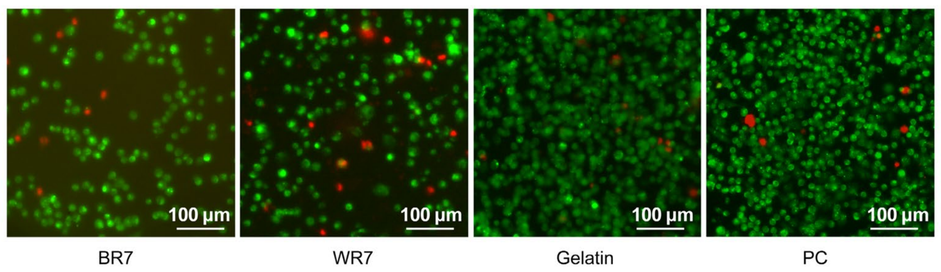


Cell density



Direct contact test - Live/dead assay
(Acridine Orange/Propidium Iodide)





Conclusions

Altogether, the combination of a compliant material and a layer-specific architecture delivers a microphysiological system closer to arterial reality: controllable permeability, guided cell organization, and long-term stability suitable for drug transport assays and mechanobiology readouts. Ongoing work translates this flat architecture into tubular constructs with prescribed fiber orientation to guide cell alignment, compatible with perfusion bioreactors, aiming at more complex 3D models and potential translation to implantable vascular grafts.

[1] He Z. et al. Appl. Sci. 2024;14:6780. doi:10.3390/app14156780
[2] Marelli E. et al. Adv. Funct. Mater. 2025;e18804. doi:10.1002/adfm.202518804
[3] Coppadoro L. et al. Adv. Mater. Technol. 2025. doi:10.1002/admt.202500065

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