Multimaterial-printed *in vitro* 3D skin model using a hybrid melt electrowriting and extrusion bioprinting technique

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1 Background

Skin acts as the body's primary barrier against physical, microbial, and environmental damage. To better understand skin biology and wound repair, physiologically relevant human skin models are needed. Although 3D *in vitro* skin models offer a promising alternative to animal studies, many current models still lack sufficient mechanical strength, structural organization, and reproducibility.

In this study, we developed a composite skin equivalent combining melt electrowritten (MEW) PCL with bioprinted GelMA to improve structural support, biological relevance, and scalability.

2 Methodology

2.1 Skin model fabrication process

Melt electrowriting

MEW PCL mesh was fabricated to mimic dermal architecture and provide mechanical support.

Dermal layer bioprinting

Human foreskin fibroblasts (HFF)-laden GelMA was bioprinted into the PCL scaffold using an extrusion bioprinter and blue-light crosslinked.

Epidermal layer bioprinting

The construct was rotated, then a thin keratinocytes (N/TERT-1)-laden GelMA layer was printed on top and crosslinked to form the epidermis.

2.2. Characterizations

PCL

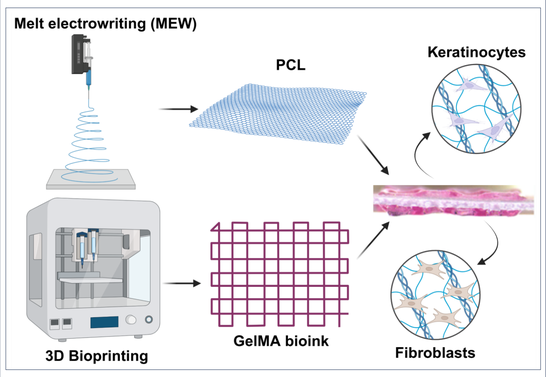
Microcomputed tomography (μCT), Mechanical behavior

GelMA

Rheological behavior, Swelling test

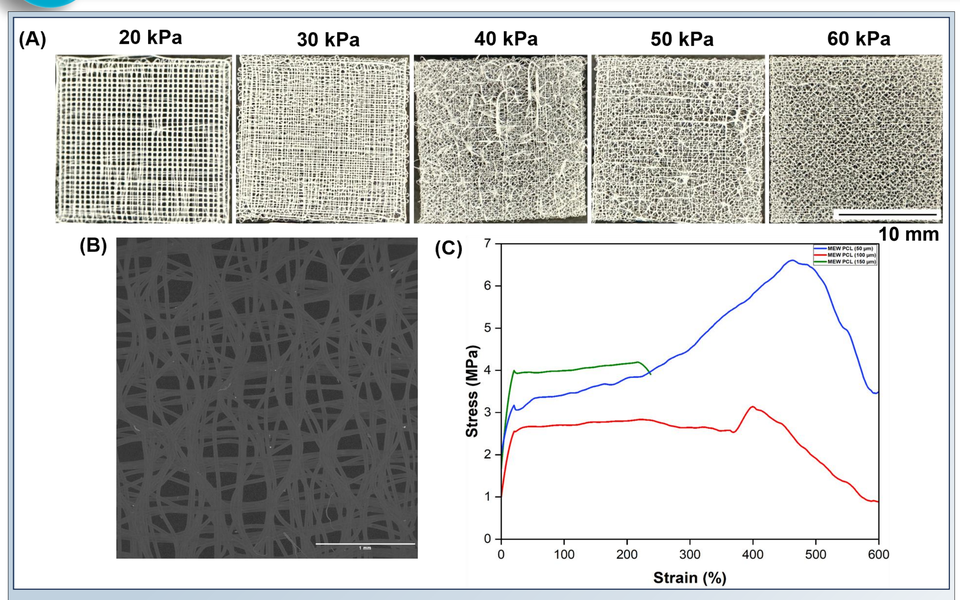
Skin model

Live/Dead assay, Lucifer Yellow permeation test



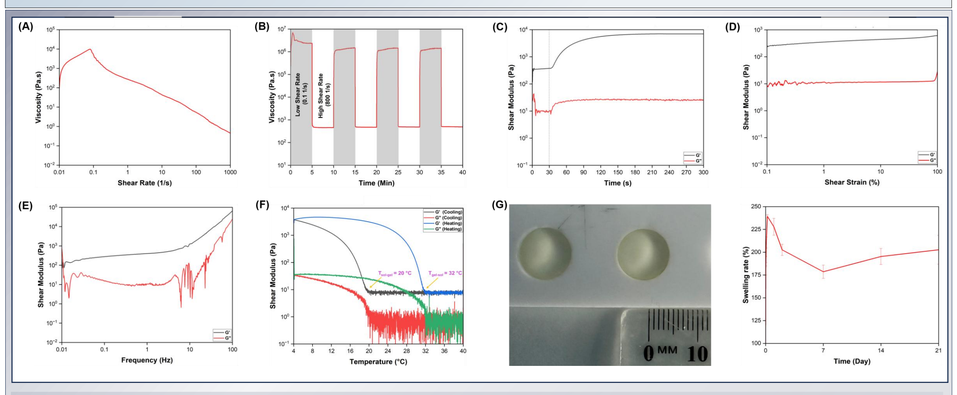
Schematic representation of the skin model fabrication process.

3 Results and Discussion



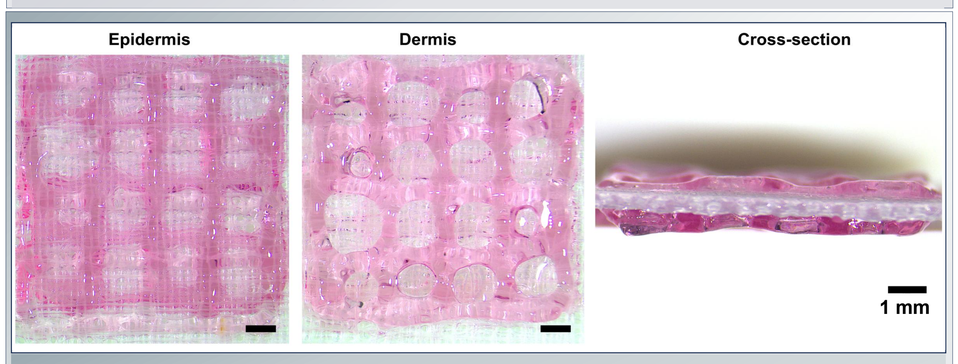
3.1. MEW PCL characterizations

- Higher pneumatic pressure improved fiber uniformity (**A**).
- The optimized scaffold showed ~70% porosity with nano-/microporous architecture (**B**).
- The 150 μm scaffold showed the most suitable mechanical performance for skin model applications (**C**).



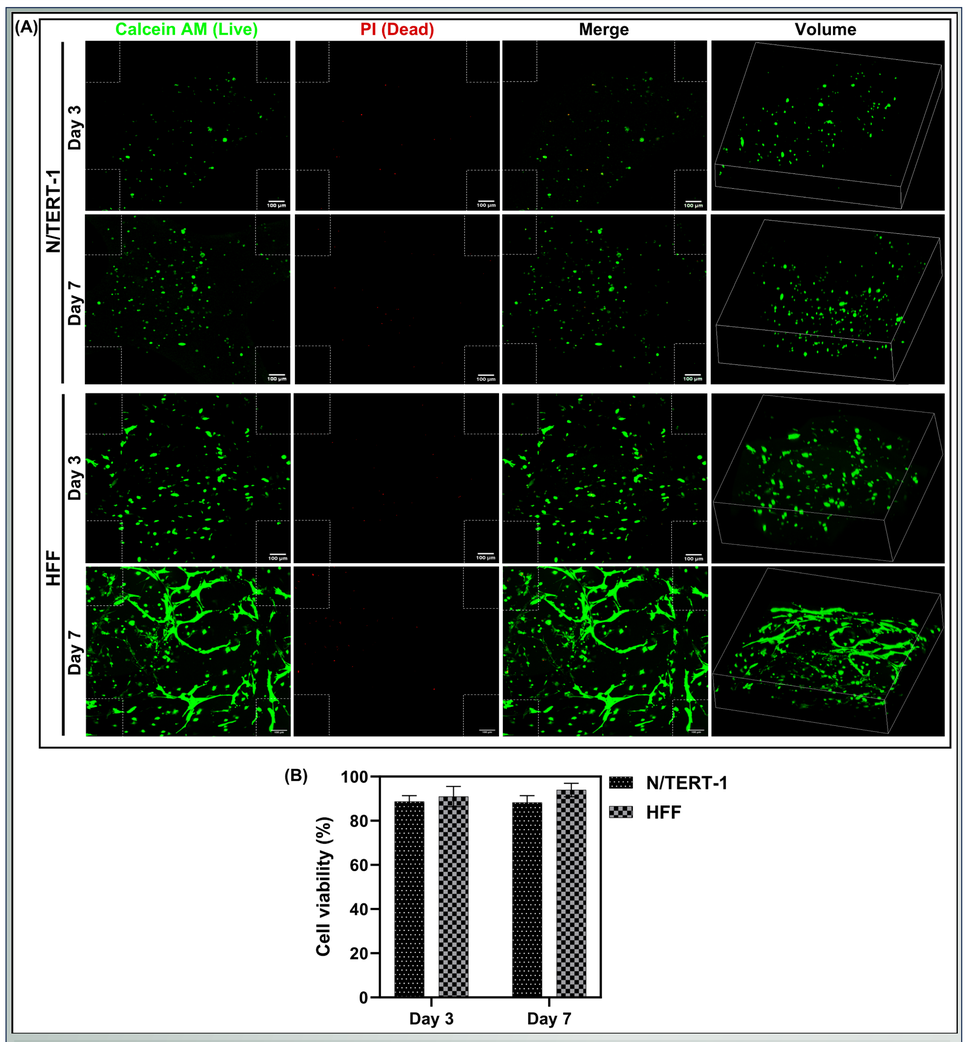
3.2. GelMA characterizations

- 7.5% GelMA showed suitable rheological properties for bioprinting.
- The hydrogel exhibited shear-thinning and reversible shear recovery, supporting printability and shape fidelity (**A and B**).
- Rapid blue light crosslinking increased storage modulus to ~9 kPa within 2 min (**C**).
- GelMA also showed stable viscoelastic and thermoresponsive behavior (**D–F**).
- Swelling rose rapidly to >235% within 5 h and remained relatively stable thereafter (**G**).



3.3. Skin model fabrication

- GelMA was successfully deposited on both sides of the MEW PCL scaffold to form epidermal and dermal layers.
- Cross-sectional imaging confirmed a well-integrated and distinct bilayer structure after culture.
- The hybrid construct showed early structural integrity and reproducibility.



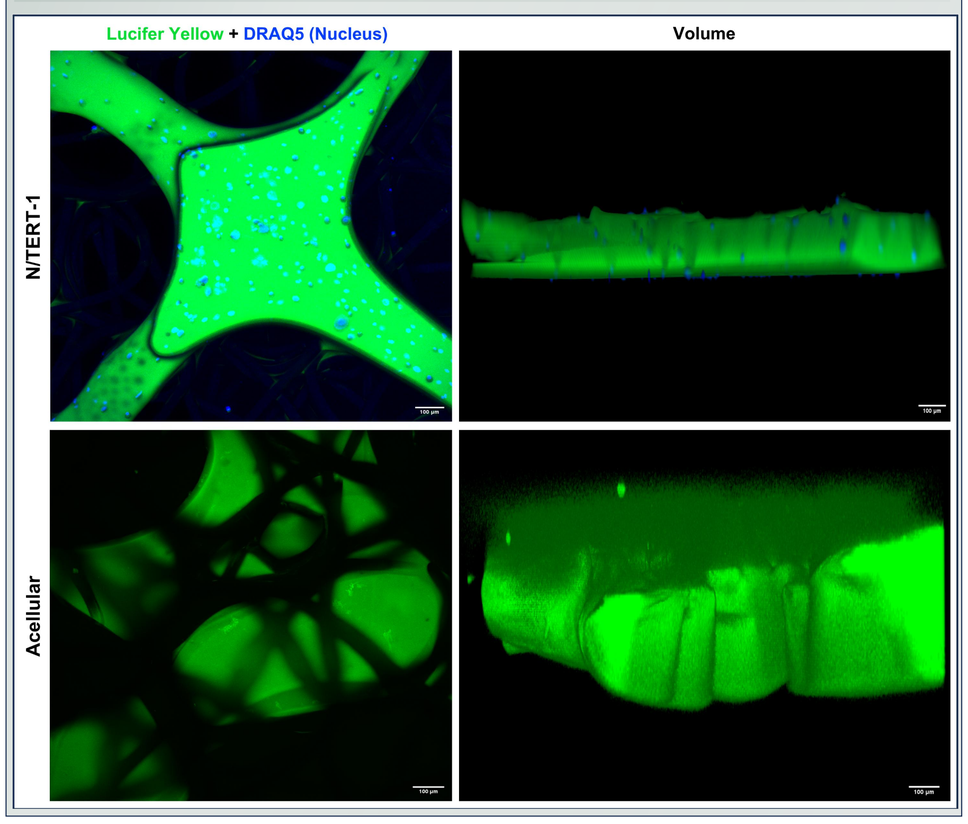
3.4. Skin model characterizations

Cytocompatibility

- Live/Dead imaging confirmed high viability in the bioprinted construct.
- Keratinocyte viability remained >88%, while HFF viability reached ~90–94% over 7 days.
- The hybrid construct supported sustained cell survival.

Barrier function

- Cellular skin models showed lower Lucifer Yellow penetration than acellular controls.
- Dye diffusion into the dermal layer was mainly observed in acellular constructs.
- These findings suggest development of barrier-like function.



4 Conclusion

We developed a fully automated hybrid MEW–bioprinted 3D skin model that reproducibly mimics key structural, mechanical, and biological features of native human skin. The construct showed suitable scaffold and hydrogel properties, high viability of both keratinocytes and fibroblasts, and maintained a well-defined bilayer architecture. Importantly, this model indicated the development of a functional barrier resembling healthy skin. Overall, this platform shows strong potential for skin biology studies, therapeutic screening, and cosmetic testing.

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