

Development of an animal-free methodology for mechanical performance assessment of engineered skin substitutes

Original

Development of an animal-free methodology for mechanical performance assessment of engineered skin substitutes / Audenino, Alberto; Bignardi, Cristina; Massai, Diana; Terzini, Mara; Aldieri, Alessandra. - In: BIOMEDICAL SCIENCE AND ENGINEERING. - ISSN 2531-9892. - 3:s3(2020), pp. 1-2. [10.4081/bse.2019.103]

Availability:

This version is available at: 11583/2804794 since: 2020-03-20T12:01:58Z

Publisher:

PAGEpress

Published

DOI:10.4081/bse.2019.103

Terms of use:

This article is made available under terms and conditions as specified in the corresponding bibliographic description in the repository

Publisher copyright

(Article begins on next page)

Development of an animal-free methodology for mechanical performance assessment of engineered skin substitutes

Alessandra Aldieri, Mara Terzini,
Diana Massai, Cristina Bignardi,
Alberto Audenino

Polito^{BIO}Med Lab, Department of
Mechanical and Aerospace Engineering,
Politecnico di Torino, Turin;
Interuniversity Center for the promo-
tion of the 3Rs principles in teaching
and research, Italy

Abstract

Functional substitutes for the treatment of skin wounds are nowadays widely available thanks to the progress in skin tissue engineering. However, the performance of the existing substitutes in terms of mechanical behavior, which is a determinant for their success, still does not match the native tissue. Since the mechanical behavior of skin is governed by dermis, an in-depth investigation of human dermis mechanics would be pivotal for integrating the design and validation of skin substitutes. In the perspective of reducing and replacing animal experiments through validated alternative tools, an accurate *in silico* constitutive model describing the human dermis mechanics is presented. Biaxial tests were performed on human dermis samples, and resulting data were used for setting the constitutive parameters of the model, able to reliably describing the mechanical proper-

ties of the native tissue, and to be compared with the mechanical behavior of skin substitutes attainable through the same procedure.

Introduction

Progress in skin tissue engineering has led to the development of functional substitutes for the treatment of acute and chronic skin wounds. However, the performance of the existing substitutes in terms of mechanical behavior still does not match native human skin.¹ Since the mechanical behavior of skin strongly depends on dermis, an in-depth investigation of the human dermis mechanics would be essential for supporting the design and the validation of skin substitutes.² In the perspective of reducing and replacing animal experiments thanks to validated alternative tools, here we present an accurate *in silico* constitutive model describing the human dermis mechanics. Biaxial tests were performed on human dermis samples, and resulting data were used for setting the constitutive parameters of the model adopted for faithfully describing the mechanical behavior of dermis under load.

Materials and Methods

Dermis samples were harvested from the lower back of a human donor, coherently with the anatomical orientations³ (cranio-caudal-CC and mediolateral-ML). Planar equi-biaxial tests were performed using a purpose-built fixture⁴ mounted on a uniaxial testing machine (loading rate = 0.16 mm/s) (Figure 1a). Results were reported in terms of Cauchy stresses *vs* engineering strains, computed by tracking the average distance along the CC and ML directions of

Correspondence: Mara Terzini, Polito^{BIO}Med Lab, Department of Mechanical and Aerospace Engineering, Politecnico di Torino, Turin, Italy.

E-mail: mara.terzini@polito.it

Key words: Human dermis; anisotropy; biaxial test; finite element; GOH model.

Conference presentation: this paper was presented at the Second Centro 3R Annual Meeting - 3Rs in Italian Universities, 2019, June 20-21, University of Genoa, Italy.

Received for publication: 28 October 2019.

Accepted for publication: 11 November 2019.

This work is licensed under a Creative Commons Attribution NonCommercial 4.0 License (CC BY-NC 4.0).

©Copyright: the Author(s), 2019

Licensee PAGEPress, Italy

Biomedical Science and Engineering 2019; 3(s3):103
doi:10.4081/bse.2019.103

four central markers drawn on the sample surface.⁴ Since dermis exhibits a highly nonlinear behavior, with anisotropic and heterogeneous responses during loading,³ the Gasser-Ogden-Holzapfel (GOH) model (Eq. 1, for parameters details see Aldieri *et al.*⁵) was selected. Its constitutive parameters, describing the anisotropic hyperelastic response of dermis, were extracted from experimental data through a minimization procedure.

$$W = \frac{c}{2} (\bar{I}_1 - 3) + \frac{k_1}{2k_2} [e^{k_2[\kappa \bar{I}_1 + (1-3\kappa)\bar{I}_4 - 1]^2} - 1] + \frac{k_3}{2k_4} [e^{k_4[\kappa \bar{I}_1 + (1-3\kappa)\bar{I}_6 - 1]^2} - 1] \quad (1)$$

The GOH model was validated by repli-

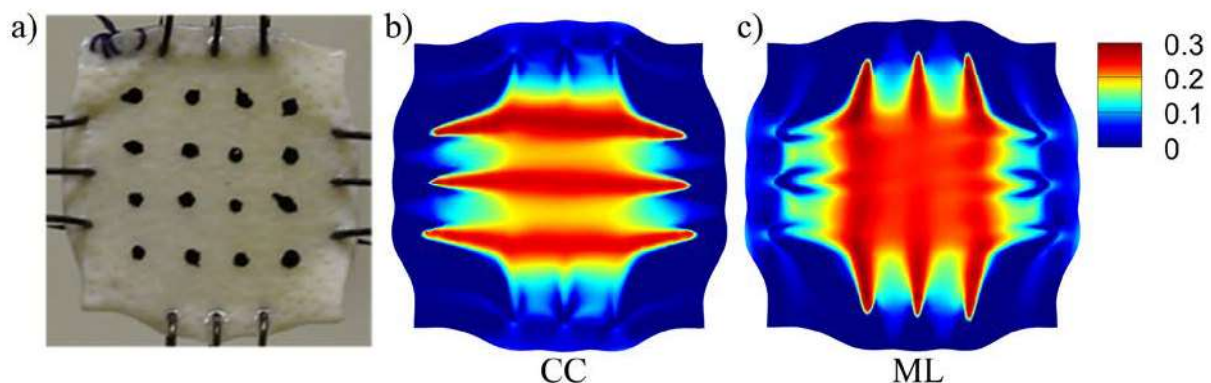


Figure 1. Human dermis sample during equi-biaxial test (a), and contour plots of engineering strains along the CC (b) and ML (c) loading directions.

cating experimental tests through Finite Element (FE) analyses and computing the normalized mean square error (NMSE) between numerical and experimental displacement magnitudes of the central markers.

Results

The obtained GOH constitutive parameters ($k_1=90.3$ kPa, $k_3=50.6$ kPa, $k_2=11.0$, $k_4=8.0$, $c=1.2$ kPa, $\kappa=0.0005$) were implemented in the FE model. Figure 1b and c shows the contour plots of engineering strains along the CC and ML directions, respectively. The numerical displacement magnitudes of the central markers were in good agreement with the experimental ones (average NMSE = 0.908), and, in accordance with experimental evidences,^{3,4} a higher degree of deformation was achieved along the ML direction. This confirmed that the FE model outcomes accurately

described the sample biaxial response, mirroring the experimental anisotropy.

Conclusions

In this work biaxial characterization and FE analyses on human dermis samples were combined to identify the GOH constitutive parameters for dermis mechanical description. The proposed animal-free methodology enables to investigate the mechanical performance of engineered skin substitutes with a combined *in vitro/in silico* approach, representing a powerful tool for selecting the optimal engineered substitute to be *in vivo* tested, with consequent reduction of animal testing.

References

1. Sander EA, Lynch KA, Boyce S.

Development of the mechanical properties of engineered skin substitutes after grafting to full-thickness wounds. *J Biomech Eng* 2014;136:051008.

2. Li W. Modelling methods for In Vitro biomechanical properties of the skin: A review. *Biomed Eng Lett* 2015;5:241-50.
3. Terzini M, Bignardi C, Castagnoli C, et al. Dermis mechanical behaviour after different cell removal treatments. *Med Eng Phys* 2016;38:862-9.
4. Terzini M, Aldieri A, Zanetti EM, et al. Native human dermis versus human acellular dermal matrix: A comparison of biaxial mechanical properties. *Australas Med J* 2018;11:434-42.
5. Aldieri A, Terzini M, Bignardi C, et al. Implementation and validation of constitutive relations for human dermis mechanical response. *Med Biol Eng Comput* 2018;56:2083-93.