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A model system to study the damaging effects of prolonged mechanical loading of the epidermis

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Biomechanics and Tissue Engineering, Materials Technology

Introduction

Pressure ulcers are areas of soft tissue breakdown that result from sustained mechanical loading of the skin and underlying tissues. Today, little is known with respect to the aetiology of these ulcers. This study introduces an *in vitro* model system to study the effects of clinically relevant loading regimes on damage progression in the epidermis, the uppermost skin layer.

Material and methods

Engineered epidermal equivalent

A commercially available human epidermal equivalent, EpiDerm (EPI-200, MatTek Corporation, Ashland, MA, USA), was used as an *in vitro* model of the epidermis in this study. This model (diameter = 8 mm and thickness $\approx 150 \mu\text{m}$) consists of human-derived epidermal keratinocytes, which have been cultured at the air-liquid interface to form a multilayered, differentiated model of the human epidermis [1]. Four different batches of EpiDerm samples were used in this study.

Loading of epidermal equivalents

EpiDerm samples were subjected to 6.7 (LP) and 13.3 kPa (HP) for either 2 or 20 h using a custom-built loading device, which was placed in an incubator at 37°C and 5% CO₂ (figure 1). Unloaded samples (C) and samples loaded with a small plate of negligible weight (PC) were used as control.

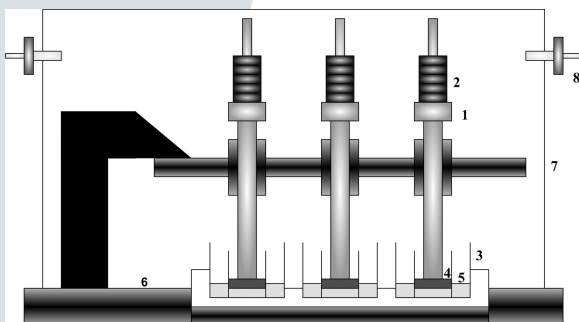


Figure 1. Schematic side-view of the custom-built loading device. In this representation (1) indicates an indenter, (2) the weights, (3) a 6-well plate, (4) an EpiDerm sample, (5) culture medium, (6) the stainless-steel frame, (7) the cover, and (8) an air-filter.

Damage assessment

After loading, tissue damage was assessed by histological examination (H&E and Pyronine-Y staining) [2] and by the release of a pro-inflammatory mediator, interleukin-1 α . The levels of IL-1 α in the medium of all EpiDerm samples were determined by a quantitative sandwich enzyme immunoassay technique (Quantikine, R&D systems, Uithoorn, NL).

Results

Loading the EpiDerm samples for a period of 2 h increased the IL-1 α release (figure 2a), although no visible tissue damage was observed. However, in the 20 h loading experiments visible tissue damage (figure 3) and a small decrease in tissue viability were observed (data not shown). Tissue damage was histologically characterized by cell swelling, a decrease in cytoplasmic RNA, necrosis, and by loss of distinguishable epidermal layers. Furthermore, in these experiments the IL-1 α release increased with magnitude of loading (figure 2b).

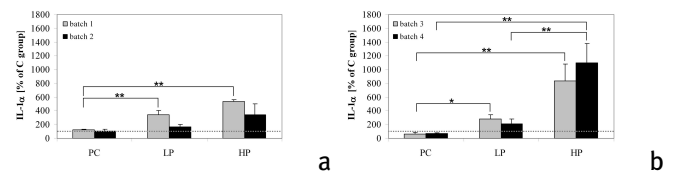


Figure 2. IL-1 α release (mean + SEM) of the PC, LP, and HP group, expressed as percentage of the C group (dashed line), after 2 (a) and 20 h of loading (b). * represents $P < 0.05$ and ** represents $P < 0.005$.

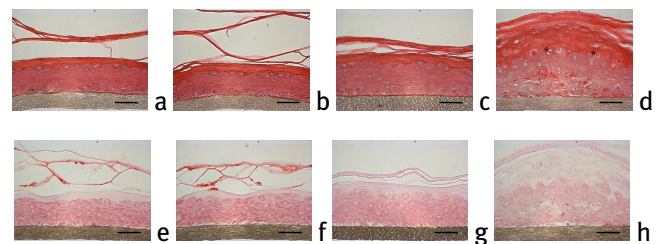


Figure 3. Epidermal histology of the C (a, e), PC (b, f), LP (c, g) and HP group (d, h) after the 20 h loading period. Images were obtained within the loading region. H&E (a-d) and Pyronine-Y (e-h) staining are shown. * indicates cellular necrosis and the bars indicate a distance of 50 μm .

Discussion

This *in vitro* model system can be used to improve insight in the epidermal damage process as a result of prolonged mechanical loading. Furthermore, identification of early damage markers, such as IL-1 α , may have potential for effective clinical identification and prevention of pressure ulcers.

Acknowledgement

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References:

- [1] CANNON, C.L., et al: *Toxicol. In Vitro* 1994; 8: 889-891
- [2] SPIEKSTRA, S.W., et al: *Exp Dermatol* 2005; 14: 109-116