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

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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 \( \approx 150 \, \mu m \)) 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% CO\(_2\) (figure 1). Unloaded samples (C) and samples loaded with a small plate of negligible weight (PC) were used as control.

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\(\alpha\). The levels of IL-1\(\alpha\) 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\(\alpha\) 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\(\alpha\) release increased with magnitude of loading (figure 2b).

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\(\alpha\), may have potential for effective clinical identification and prevention of pressure ulcers.

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References: