Release of IL-1a upon epidermal loading

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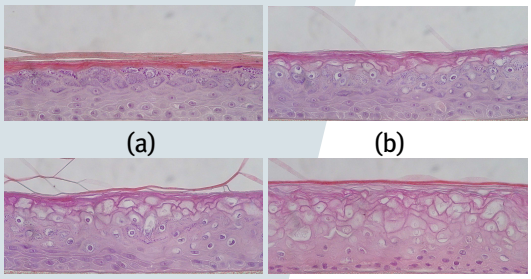
Introduction

A pressure ulcer is a degeneration of soft tissues due to sustained loading. Currently, pressure ulcer detection techniques are limited and mostly based on subjective measures. Hence, we aim at an objective non-invasive way of risk assessment. *In vitro*, the release of biochemical damage markers (e.g. interleukin-1α (IL-1α)) into the tissue supernatant due to mechanical loading is studied. A numerical model is developed to determine the release from the cells inside the culture. The release of IL-1α is also assessed *in vivo* in a clinical study.

Experimental study

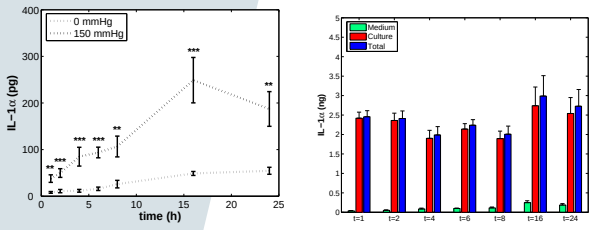
Engineered epidermal equivalents (EpiDerm, MatTek, USA) were loaded with 0 and 150 mmHg in a custom-built loading device. After 4h of loading, the first signs of structural tissue damage appeared and the damage increased in time (fig 1).



(a) (b) (c) (d)

Fig 1: *Histology of unloaded (0 mmHg) EpiDerm cultures (a) and of cultures loaded with 150 mmHg for 4 h (b), 8 h (c) and 24 h (d).*

After only 1 h of loading, a significant increase in IL-1α release into the culture supernatant was found (fig 2a), which further increased in time. The release pattern of the unloaded control groups (0 mmHg) only slightly increased in time.



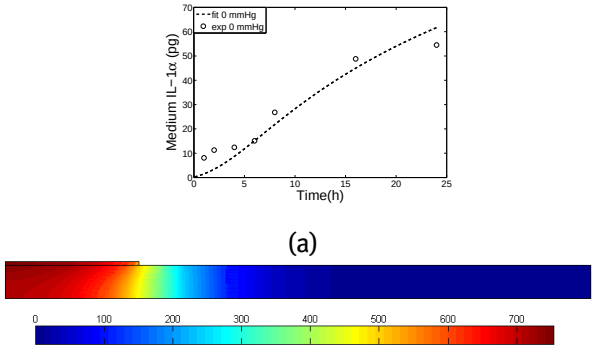
(a) (b)

Fig 2: *(a) The release (mean $\pm$ SEM) of IL-1α into the culture supernatant after applying 0 and 150 mmHg for various loading times. ** indicates P<0.01, and *** indicates P<0.001 compared to the control group. (b) The medium, culture, and total amount (mean+SEM) of IL-1α after applying a pressure of 150 mmHg for various loading times.*

Since the total amount of IL-1α (i.e. the sum of the amount in the medium and in the culture) did not change in time, there was no production of IL-1α (fig 2b). IL-1α seemed to be stored intracellularly, since the amount inside the epidermal tissue is much larger than the amount in the culture supernatants for all time periods.

Numerical study

The transport of IL-1α was described using the diffusion equation and equations for binding to and release from receptors. Release from the cells at 0 mmHg was estimated to be $f = 11e^{-2.5 \cdot 10^{-6} t}$ by fitting the calculated medium concentration to the experimental results (fig 2a). The 150 mmHg still has to be fitted. The numerical calculation fitted the experimental data reasonably well (fig 3a). The distribution of the IL-1α after 24 hours is depicted in figure 3b.



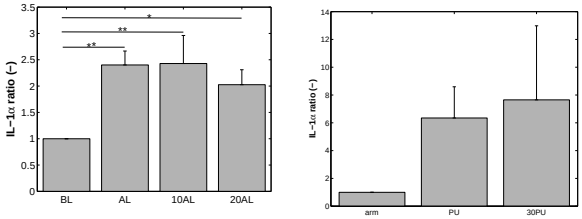
(a)

(b)

Fig 3: *(a) The numerical fit of the IL-1α release into the medium after loading with 0 mmHg. (b) The distribution of free IL-1α after 24 hours in the control situation. The left upper rectangle represents the EpiDerm culture and the large rectangle represents the surrounding medium.*

Clinical study

The release of IL-1α was measured *in vivo* both in healthy volunteers after loading the forearm for 2 hours with 100 mmHg and in patients with a grade 1 pressure ulcer at the sacrum. In both situations, the release of IL-1α was increased after mechanical loading and the release remained increased after unloading for a short period of time (fig 4).



(a) (b)

Fig 4: *(a) The ratio of IL-1α release (after loading/before loading) after applying 150 mmHg for 2 hours, directly after unloading (AL), and after 10 (10AL) and 20 (20AL) minutes unloading. * indicates P<0.05, and ** indicates P<0.01. (b) The ratio of IL-1α release (arm/sacrum) at grade 1 pressure ulcers, directly after unloading (PU), and after 30 minutes unloading (30PU)*

Conclusion

- IL-1α seems suitable for the early detection of mechanically-induced epidermal damage.
- IL-1α release from the cells decreased in time.
- IL-1α is released *in vivo* after mechanical loading.

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