

Effects of exudate physical, chemical and thermal conditions on collective migration of tissue-repairing cells: Mechanobiological studies

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Aim: As a result of the increased vascular permeability which is part of the natural inflammatory process, fluids continuously enter the wound bed. These fluids, termed exudate, may contain proteins, nutrients, inflammatory mediators, digestive enzymes, growth factors, waste products, immune cells (primarily neutrophils and macrophages) and platelets. The exudate plays several critical roles in healing, specifically in: (i) protecting the wound bed from drying out, (ii) facilitating diffusion and transport of nutrients, signaling molecules and growth factors, and (iii) allowing migration of tissue-repairing cells. Related to the latter point, our objective was to determine how collective cell migration is affected by the conditions and properties of the exudate.

Methods: We used a cell culture model to determine the effects of low temperature (35°C versus 37°C), low glucose (1g/L versus 4.5 g/L) and low pH (6.7 versus 7.6) which are common in exudates, on collective migration patterns of tissue-repairing cells. We studied NIH3T3 fibroblasts, 3T3L1 preadipocytes and C2C12 myoblasts which are associated with the tissues affected by chronic wounds, i.e. skin, adipose and skeletal muscle, respectively. Cell migration into a local damage site in the cultures, produced by crushing cells under a micro-indentor, was monitored over a day under the above altered conditions, using our dedicated image processing technology for analyzing collective migration. Work to integrate these altered physical, chemical and thermal conditions that are characteristic to chronic wounds with a custom-made, instrumented cell stretching device (CSD) which simulates deformation effects of negative pressure wound therapy (NPWT) at a cell level, is underway.

Results: The present mechanobiological approach and methodologies, combining the CSD apparatus and image processing algorithms, are powerful in identifying the ideal conditions and properties of exudates. First, migration rates and times differ significantly across cell types. Second, under static culture conditions, which do not incorporate mechanical stimuli by NPWT, acidic exudate conditions significantly impede collective migration of fibroblasts, and consistently delay the times for onset and end of the en mass migration of these cells. The effects of low temperature and glucose, however, were not significant on any cell type under the static loading mode. Recent preliminary data shows that simulated NPWT conditions impact proliferation and migration rates of the aforementioned cells, depending on the magnitude and waveform of the applied deformations.

Conclusion: Wound exudate should not be seen as merely a clinical management problem. The exudate has key functions in the healing process, and its composition and properties specifically influence migration of tissue-repairing cells in the wound bed. The mechanobiological research approach and the methods described above are able to provide objective, quantitative and standardized indicators of whether the composition and properties of specific exudates are conducive to healing.

Clinical relevance: Moist wound healing is warranted, but the exudate needs to have optimal properties for efficient tissue repair. Future exudate management should focus on proactively altering the composition and properties of the exudate in the wound bed, if and as needed, e.g. to accelerate cell migration towards epithelization and formation of granulation tissue, in order to promote healing. This can be done by means of 'active' smart dressings, which can be used for more than just fluid retention, that is, dressings may tune the patient-specific physical, chemical and thermal conditions in the exudate as needed.

Ideal dressing characteristics in exudate management of diabetic foot ulceration

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Aim: This presentation will look at the key issues relating to the choice of dressings when controlling moisture balance in the diabetic foot. It will use case studies to examine the effects of appropriate and inappropriate dressing regimens.

Key Points: Exudate plays a key role in wound healing; however, it can delay healing when there is too much or too little or it is in the wrong composition. Effective assessment and, crucially, effective management of exudate is therefore key to ensuring timely wound healing with less risk of complications. This is of increasing importance in the management of diabetic foot ulceration where failure to manage moisture balance increases the risk of limb-threatening infection.

Dressings are the mainstay of exudate management. Dressing selection should be individual to the patient and the location of the wound. The foot is notoriously difficult to dress with issues regarding adhesion, conformability and adaptation under weightbearing having an impact.

Conclusions: As discussed in the World Union of Wound Healing Societies (2019) position document on exudate management, many factors will affect dressing selection, including wound bed tissue type, exudate level, wound depth, infection/biofilm and odour. In practice, dressing/device availability, reimbursement issues, clinician familiarity and patient preference are also likely to play important roles.