THREE DIMENSIONAL MODELLING OF WOUND CONTRACTION

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INTRODUCTION
Skin is the largest human organ, covers all the external surface of the body, keeps the integrity of organs and avoids the transmission of infections and dehydration [1]. It is an elastic tissue that can support stresses under some limits. It is equally important its self-repairing capacity as a response to damage, with a perfect healing in most cases. Wounds can appear in the skin as a result of injury or surgery. Wound healing is a natural process where tissues are regenerated and several phenomena appear overlapped in time and which can be separated in four stages: inflammatory, proliferative, contraction and remodeling.

In this work, we have studied and simulated the contraction phase. During the contraction phase, the size of the wound is reduced, appearing mechanical stresses in both the wound and the surrounding skin.

During the past years a number of two-dimensional wound healing models have been proposed [2,3], but most of them take only into account biochemical factors, still lacking the mechanical stimulus as a regulator of cell function, which limits their predictive power. Those models describe the role of fibroblasts, myofibroblasts, a chemical growth factor and the extracellular matrix (ECM). More recently, this model has been implemented by Finite Element Method (FEM), adding the forces exerted by cells in function of the mechanical environment and also the evolution of the mechanical properties in the wound in function of the extracellular matrix production [4], incorporating the influence of mechanical stimulus.

METHODS
In this work, we have studied the contraction phase in three-dimensional wounds using a finite element analysis.

In this model the primary variables are the densities of fibroblasts, myofibroblasts, collagen, the concentration of a chemotactic growth factor and the ECM displacement vector.

We have studied the effect of wound shape and size on the contraction process extending the proposed numerical model by Javierre et al. (2009) [4] from 2D to 3D.

The influence of wound shape was analyzed comparing the contraction progress in three idealized wound shapes with the same characteristic dimensions (length, L; width, W and depth, D) but different shapes: rectangular, elliptical and ellipsoidal (Figure 1). As wounds were assumed symmetric we have just simulated a fourth of their total geometry, taking L=4 cm, W=1 cm and D=2 cm.

Figure 1: Wound geometries with different shape.

The effect of wound size was also analyzed on the contraction process. We chose the ellipsoidal wound and we considered two variations from the original geometry. In the first case, the depth was kept constant and the length was twice the original (i.e., 8 cm). In the second case the length was kept constant and the depth was reduced to half of the initial one (i.e., 1 cm) (Figure 2). In both cases we kept the width constant. We simulated the initial geometry and the two modifications comparing both results.

Figure 2: Wound geometries with different size.

The wound is simulated with the surrounding undamaged skin and both tissues are characterized by their mechanical properties, which can be found in [4]. The simulated skin was split into two parts: the wound and the undamaged skin. The undamaged skin was taken sufficiently large in order to avoid its size influence during the contraction process. The whole computational domain consists of a cube of side 10 cm.
The imposed boundary conditions were: no displacements at the boundary of the domain and no flux for every species through the boundary. We have also applied symmetry conditions where necessary. At the beginning of the contraction phase, myofibroblasts are still not present in any of the tissues, so its initial density is assumed zero in the whole domain. The initial concentration of growth factor is due to its accumulation during the inflammatory phase and it is higher in the wound part. Furthermore, as initial condition, we assume that in the wound domain there are not any cells, due to the injury, while its concentration does not decrease in the undamaged tissue. Collagen behaves in a similar way, but a low collagen density remains in the wound part. We have not considered the dermis strain prior to wound contraction.

RESULTS AND DISCUSSION
First we study the influence of wound shape in the contraction process. We compare the evolution of the normalized volume of the three wounds with different shape during the wound healing process (30 days). There are no significant differences in the evolution of the three wounds (Figure 3), with a contraction of 25% during the first half-period. The final volume respect the initial volume is similar in the three cases, near 70%.

![Figure 3: Temporal evolution of wound size for geometries with different shape.](image)

We have also studied the normalized volume variation along time in wounds with different size (Figure 4). It is clear from the results that deeper wounds contract at a lower rate. When the depth of the wound does not vary it is not possible to appreciate significant differences in the results, even if the length is reduced to half the original one.

![Figure 4: Temporal evolution of wound size for ellipsoidal wounds with different initial size.](image)

CONCLUSIONS
In this work we have used a previous model of wound contraction [4] based on the model developed by Olsen et al.[2] to simulate three-dimensional wounds. The model has been used to study the influence of wound shape and size in the contraction process.

We have observed that wound size influences both the rate and the extension of wound contraction, and deeper wounds contract percentage-wise less at a lower rate. The main reason why this happens is that the maximal growth factor concentration is located in the interface dermis-wound, so the deeper the wound is, the further this interface is located from the surface and the attraction that cells feel to it is weaker. As a result, the displacement of the surface wound-air is higher when the wound is less deep and the contraction that the wound suffers is higher.

This model is a first approach to advance in the understanding of wound contraction in wound healing, which will have a relevant impact in the treatment of chronic injuries, cosmetic surgery and others [5].

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REFERENCES