MATHEMATICAL ANALYSIS OF PHYSIOLOGICAL AND PATHOLOGICAL WOUND HEALING. APPLICATION TO DIABETIC FOOT ULCERS.

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Wound healing is a highly orchestrated process that takes place by means of the timely combination of strongly coupled biological, chemical and mechanical processes (Singer and Clark, 1999). Successful healing is crucial to maintain (or even recover) organ functionality and integrity. However, delayed cell migration and transport of biochemical factors or excessive wound contraction may result in impaired wound healing and chronic wounds, leading to a poor quality of life of the patient. For instance, wounds in the limbs of diabetic patients are an example of co-operative disease that, due to insufficient oxygen supply, a poor supply of immune cells (leukocytes, phagocytes) and a lack of pressure sensibility, leads to repeated failure of healing and eventually requires surgical intervention (Blakytny and Jude, 2006).

In this work we extend a classical wound healing model, see for instance (Javierre et al, 2009), with a formalism for the immune response, which allows us to consider the influence of an deficient immune response. In our formalism of the immune response, the diabetes-impaired capillary stiffness is incorporated through a reduction of supply of oxygen and the decreased flux of immune cells (leukocytes, phagocytes). These immune cells neutralize infectious agents and harmful bacteria, which compete with other cell types on oxygen and nutrients. This competition finally results into a decrease of the motility of the constituting fibroblasts and thereby wound healing is impaired. If the supply of immune cells is insufficient to neutralize the bacteria and harmful agents, then a wound heals less efficiently, or, even becomes chronic. In our work, we present a way to incorporate the deficient immune response into wound healing models and quantitatively show the implications on the impaired immune response on the kinetics of wound healing. The model is formulated in terms of a coupled set of nonlinear partial differential equations, which are solved in a finite-element framework.

References

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