Modeling Tissue Expansion With Isogeometric Analysis: Distinguishing True *Skin Growth* From Elastic *Skin Stretch*

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Purpose: The optimal rate of tissue expansion has been debated, including several "rapid expansion" protocols. However, the distinction between true *skin growth* and elastic *skin stretch*, and the relative effect of each during the process of tissue expansion, has not been objectively studied. Our porcine model utilizes isogeometric analysis (Figure 1), a computational approach to analysis of thin membranes, which allows the first precise calculation of both stretch and growth of any point of an expanded skin patch. This type of analysis allows us to correlate these factors with assessments of molecular and cellular responses of the skin.

Materials and Methods: Two minipigs were each implanted with tissue expanders under tattooed skin grids, with unexpanded patches as internal controls. One pig was expanded maximally over 35 days (slow protocol), and the second over 15 days (rapid protocol). Multiview stereo was used to create 3-dimensional models of skin patches *in vivo* and *ex vivo*. Isogeometric analysis was performed to calculate skin growth due to expansion and purely elastic deformation (stretch). Epidermal/dermal thickness was evaluated by histology. Immunohistochemistry was performed to assess cellular proliferation (Ki-67), vascularity (CD31), and activation of ERK1/2, a biomarker implicated in mechanotransduction.

Results: Total deformation of skin patches was similar (1.66 for rapid, 1.76 for slow, p=0.271). This deformation was more attributable to elastic stretch in rapid (1.40) than in slow expansion (1.12, p<0.001). Conversely, skin growth from tissue expansion was much higher (1.52) in slow expansion than in rapid (1.07, p<0.001). Epidermal thickness, dermal thinning, and keratinocyte proliferation were correlated with both tissue growth and stretch (p<0.001). Vascularity was correlated with skin growth. ERK1/2 activation was positively correlated with growth but negatively with stretch (p<0.001).

Conclusions: While rapid tissue expansion is capable of deforming skin to a similar level as slower filling, the majority of this deformation is attributable to elastic skin *stretch*. Our data suggests that skin *growth* appears to require a longer expansion protocol. Further work is needed to delineate how quickly skin grows in response to a given stretch. In the skin area over a tissue expander, histologic and cellular changes are variable and correlate to the growth and stretch at a given point.

Legend:

Figure 1. Example of isogeometric analysis to calculate deformation (φ) in an expanded skin patch.