Linking collagen CLSM and immune-system cell-migration to predict the outcome of chronic leg wounds

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Chronic wound care is being transformed from a subjective visual inspection to an evidence based treatment track. This is driven by the needs of a demographically increasing proportion of aging persons that live longer, a dwindling younger generation and the need for sustainable costs. Here we present longitudinal quantification of closure of individual chronic lower leg venous ulcers (70% of total) and foot ulcers which are often diabetes related. Both linear and non-linear optical non-invasive Confocal Laser Scanning Microscopy (CLSM) is a monitoring method of choice.

Imaging modalities from thermal to acoustic are currently world-wide being implemented on a macro (leg / foot), micro and nanoscopic scale (cell / single molecule or nanoparticle ). What is actually needed however, is Point-Of-Care (home / community clinic) fast mesoscopic non-invasive digital imaging which allows bridging overview (macro) and detail (micro/nano). Suitable chronic wound 3D characterization methods include (in)elastic (in)coherent backscatter to obtain biophysical (structures of collagen, ExtraCellular Matrix (ECM), Extracellular Polymeric Substance (EPS), morphology) and biochemical tissue fingerprinting (Raman), biomarker detection (example: Matrix MetalloProteases, MMPs) and biofilm properties. These methods (e.g. SHG) allow imaging of long term dynamics and extend as such fluorescence based techniques.

Ensemble based models are presented. They describe on a molecular level collagen production by the host and breakdown by the bacterial biofilm. On a cellular level they aim to describe biofilm and neutrophil, fibroblast, macrophage oxygen concentration dependent interactions. Chronic wound / tissue level observed failure-to-heal probabilities allow creating an individualized hazard function. Examples are shown. Statistically significant influences of co-morbidities, environmental factors, effects of personal habits can be factored in. In the course of the research it has become clear that implementation of at least best practice guidance and standardization of reporting via an Electronic Health Record (EHR) will benefit the coupling of the outcome of basic research (non-invasive non-linear CLSM methods) via modeling with personalized predictive characterization of chronic wound healing expectations. Such a practice may contribute to obtaining larger cohorts. Complementary benefits include long term monitoring eg. of nanoparticle toxicity as used in smart wound dressings, and training opportunities.