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Using the Geometry of Parameter Space to Find the Most Influential Factors in the Healing of Diabetic Foot Ulcers.

The treatment of chronic wounds has long been a challenge to wound care professionals and presents a substantial economic burden to healthcare systems globally. Over 50 billion is spent annually on the treatment of chronic wounds. To combat this issue, a mathematical model describing the interactions between matrix metalloproteinases (MMPs), their regulators (TIMPs), fibroblasts, and the extracellular matrix (ECM) was developed and analyzed to find the most influential factors, or parameters, in the healing process of diabetic foot ulcers. Using the differential equation model with de-identified patient data, the three-dimensional geometry of parameter space was visualized for all combinations of the twelve parameters in the model to see how these parameters affect the biological system. Knowledge of the identifiability of parameters can streamline treatment by allowing us to individualize treatment. This approach plots two parameters against the sum of squares errors to generate a three-dimensional graph. By analyzing the minimum of the graph, we can conclude if a parameter is identifiable and thus important in the healing response. This research shows that the parameters associated with the regulators of MMPs (TIMPs) are the most influential in a wound-healing model. (Received August 14, 2020)