# AN UNCERTAINTY QUANTIFICATION OF IN-SILICO TRIALS FOR THE USE CASE OF NON-UNION TREATMENT

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## Introduction

Virtualization and *in-silico* trials in the clinical context offer numerous advantages and will be a useful addition to today's established methods. Firstly, they are faster and more cost-effective. Secondly, they are safe and do not put human subjects or animals at risk. Additionally, *in-silico* trials allow for infinite variations in simulation conditions and parameters, enabling a comprehensive exploration of different scenarios especially if they are not feasible for ethical or legal reasons. Finally, *in-silico* trials are a valuable tool for data analysis and modeling, providing insights into the underlying mechanisms and processes. Nevertheless, simulations are subject to many factors that affect reliability and accuracy, and an understanding of these factors is necessary to evaluate results and to address their limitations.

## Methods

The basis of the simulations for the *in-silico trial* and the uncertainty quantification is our established workflow consisting of model generation by segmentation of clinical imaging data combined with a musculoskeletal simulation based on the patient's motion capturing data, cf. [1]. Based on the collected patient data, new data sets are generated by varying the identified parameters and their influence on the results is analyzed. Thereby, the main outcome variables are local fracture gap mechanics, cf. [2] and implant stress. The varied parameters in the geometry and model generation, respectively, are the mesh fineness and the advantages of adaptive meshing to avoid local geometric singularities, as well as the mapping of the grayscale values from the CT data to local bone material properties. For the biomechanical simulations, a stochastic concept was chosen for the application of the boundary conditions in order to vary both the magnitude of the applied forces and their direction. This reflects different possibilities for performing individual movements and allows conclusions to be made about the probability of healing, cf. [3]. To generate new data sets, bones from a statistical bone model are augmented with fractures generated in a free-form software and virtually treated with CAD-based implant models. These virtually generated data sets are then also assigned with boundary conditions using the stochastic concept.

## **Results and Discussion**

Within the framework of our concept for the generation of virtual data sets and associated boundary conditions,

simple models of fractured bones with a corresponding treatment can be generated. These models are provided with stochastically applied boundary conditions and simulated. This allows to analyze the generated models under realistic motions and to make conclusions about possible healing potentials. The major advantage of this concept is the analysis of real and virtual patient data sets under motion sequences that could not be reflected in a clinical trial. For example, one can virtually test different partial weight-bearing recommendations for lower extremity injuries and get an indication of what this would mean for a patient. The same is applicable for different loading scenarios or rehabilitation exercises for the upper extremity. Figure 1 illustrates the overall framework, musculoskeletal simulations, stress-strain distribution of implant and fracture gap, material parameter identification via calibration phantoms and different meshing strategies.



Figure 1: Illustration of our implemented simulation workflow: musculoskeletal simulation based on patients' motion capture data, finite element simulation of a treated fracture of the humerus, segmented bone from a CT scan with a six-rod calibration phantom and a adaptive meshing example representing a fracture in higher resolution.

#### References

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