CT-BASED MULTISCALE ELASTICITY OF HYDROXYAPATITE GRANULES FOR REGENERATIVE MEDICINE

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Motivation

Investigation of micro- and nanomechanical characteristics of HYDROXYAPATITE GRANULES for regenerative medicine

Porous hydroxyapatite (HA) globules [1] have proven as a successful tissue engineering strategy to handle bone defects in vivo, as was shown in studies on human mandibles (see Figure 1). These granules need to provide enough porous space for bone ingrowth, while maintaining sufficient mechanical competence (stiffness and strength), in this highly load-bearing organ. This double-challenge motivates to scrutinize deeper into the micro- and nanomechanical characteristics of such globules, as to identify possible optimization routes [2].

Methods – µCT, polycrystal micromechanics, Finite Element Analysis

Micro CT imaging

SKYSCAN 1172 micro computed tomography (µCT)

Stack of 583 8-bit grey-scaled images, each consisting of 748x748 pixels

Image processing

• Segmentation
• Thresholding
• Decrease number of voxels: merging algorithm
• Translation of voxels into cubic Abaqus finite elements

Simulation of voxel-specific porosity and Young’s modulus of the globule in Abaqus

Attenuation-to-nanoporosity conversion

Considering the average rule for X-ray attenuation coefficients of composite materials [3, 4], which in our case read as:

\[ \mu_{\text{HA}}(x) = \rho \mu_{\text{HA}}(x) + \rho \mu_{\text{air}}(x) \]

we derive the voxel-specific nanoporosity from voxel-specific grey values:

\[ \phi_{\text{HA}}(x) = \frac{\rho \mu_{\text{HA}}(x) - \rho \mu_{\text{air}}(x)}{\mu_{\text{HA}}(x) - \rho \mu_{\text{air}}(x)} \]

\[ \mu_{\text{HA}}(x) \]

… voxel-specific nanoporosity

\[ \rho \mu_{\text{HA}}(x) \]

… attenuation of a voxel entirely filled with hydroxyapatite

\[ \rho \mu_{\text{air}}(x) \]

… attenuation of a voxel entirely filled with air

\[ \rho(x) \]

… probability density function of \( \rho \)

\[ X_{\text{HA}} \]

… volume concentration of HA

\[ X_{\text{air}} \]

… volume concentration of air

\[ X_{\text{globule}} \]

… volume concentration of globule, \( \phi_{\text{HA}} \), which is accessible from mass and volume measurements:

\[ X_{\text{HA}} = \frac{\int \rho \mu_{\text{HA}}(x) dx}{\int \rho(x) dx} \]

No phantom calibration necessary!

Nanoporosity-to-elasticity conversion

Continuum micromechanics representation:

Porous polycrystals built up by HA crystals oriented in all space directions [5].

Model input:

- Hydroxyapatite stiffness [6] (bulk modulus 83 GPa, shear modulus 45 GPa)
- Nanoporosity

Translation of finite element-specific nanoporosities to finite element-specific elastic properties.

Finite Element Analysis

Uniaxial compression test:

- Forces at the poles by prescribed displacement of 0.1% of the globule’s diameter “BC1” (physiologic strain)
- Fixed displacements perpendicular to the loading direction “BC2”
- Zero displacement at “BC3” (Realized in SIMULIA Abaqus v6.7-2)

Aim: decipher the mechanical behavior of the globule through comparison of three differently precise models:

1) Finite Element model with voxel-specific elastic properties
2) Finite Element model with homogeneous elastic properties of solid voxels, related to the average nanoporosity
3) Analytical sphere model of Lurie [7], considering nano- and micropores, but no cracks

Results

Voxel-specific elasticity

Probability density functions of the finite element-specific elastic material properties, namely Young’s modulus and Poisson’s ratio, over all finite elements:

Maximum principal stresses

Results of Finite Element simulation, with (element-specific) heterogeneous [3]-[6] and homogeneous [6]-[9] elastic properties: maximum principal stresses, in three perpendicular cross-sections through the center of the globule. The cross-sections are parallel to the y-z (g), x-z (h) and y-x (i) planes. About 95.5% of all values lie between +/- 3MPa (see color legend (j)).

Effect of heterogeneity and cracks

Neglection of heterogeneity of nanopores (and corresponding voxel-specific elastic properties) leads to a stiffness overestimation of about 5% [comparison of pore forces in models 1 and 2], while the negligence of crack morphology results in a stiffness overestimation by a factor of around 80 [comparison of pore forces in models 1, 2, and 3].

Outlook

Currently, we extend this type of analysis to strength properties [5], providing a path finally leading to fully patient-specific analysis of organ-biomaterial compounds in regenerative orthopedics and dentistry.

References: