

Preprint

Validation of Composite Finite Elements Efficiently Simulating Elasticity of Trabecular Bone

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Patient specific analyses of the mechanical properties of bones become increasingly important for the management of patients with osteoporosis. The potential of Composite Finite Elements (CFEs), a novel FE technique, to assess the apparent stiffness of vertebral trabecular bone is investigated in this study.

Segmented volumes of cylindrical specimens of trabecular bone are compared to measured volumes. Elasticity under uniaxial loading conditions is simulated, apparent stiffnesses are compared to experimentally determined values. Computational efficiency is assessed and recommendations for simulation parameters are given.

Validating apparent stiffnesses results in concordance correlation coefficients $0.69 \leq r_c \leq 0.92$ for resolutions finer than $168 \mu\text{m}$ and an average error of 5.8% between experimental and numerical results at $24 \mu\text{m}$ resolution.

To show the potential, the code was used to compute local, macroscopic stiffness tensors for the trabecular structure of a lumbar vertebra (L4).

The presented technique allows for computing stiffness using smooth FE meshes at resolutions that are well achievable in peripheral high resolution quantitative CTs. Therefore, CFEs could be a valuable tool for the patient-specific assessment of bone stiffness.

Keywords: apparent stiffness; composite finite elements; linearised elasticity; nanoindentation; trabecular bone; validation

1. Introduction

Osteoporosis-related fractures represent a major public health problem. Predicting fracture load from high resolution CT datasets could be very useful for osteoporosis management. It was shown that fracture load can be predicted with large scale μFE models based on μCT datasets (Pistoia et al. 2002). Such an approach necessitates efficient algorithms to setup reliable μFE models and compute the fracture load of the structure of interest.

To investigate mechanical properties of trabecular bone *in silico*, voxel-based μFE models are usually used (Faulkner et al. 1991; Müller et al. 1994; Guo and Kim 2002; van Rietbergen et al. 2003; Morgan et al. 2005; Thurner et al. 2006; Woo et al. 2007; Chevalier et al. 2007). Disadvantages of those models are the nonsmooth meshes and their dependence on high resolutions (Verhulp et al. 2008; Wolfram et al. 2010). Smoothing of meshes obtained directly from μCT voxel data (Boyd and Müller 2006) can remedy non-smoothness in the surface representation but may lead to distorted

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elements. Tetrahedrisations of the scanned objects suitable for FE simulations are not obtained trivially (Bern and Eppstein 1992; Teng and Wong 2000; Shewchuk 2002). Furthermore, computational efficiency suffers from their inherently unstructured nature.

In classical μ FE models, the geometric complexity of trabeculae is represented in the mesh. To overcome the aforementioned disadvantages in classical μ FE models, composite finite elements (CFEs) were introduced (Hackbusch and Sauter 1997a,b, 1998). Their key property is that they use the hexahedral mesh given immediately by the voxel image data and represent the geometric shape with sub-pixel accuracy in adapted basis functions (Liehr et al. 2009; Schwen 2010).

As any computational method, CFEs should be validated against *in vitro* experiments before they can be used in biomechanical analyses. Therefore, the goals of this study are 1) to validate the segmentation approach used for the CFE construction; 2) to validate the CFE simulation of uniaxial compression and tension experiments using linearised elasticity; and 3) to assess computational efficiency and to determine simulation parameters such as imaging resolution and solver accuracy. As a final application, we show simulation and numerical homogenisation results obtained for the trabecular core of a lumbar vertebra.

2. Materials and Methods

2.1 Volume Measurement

For the validation of the segmentation approach, six bovine (age between 6 and 9 months), six porcine (age between 6 and 9 months), six young σ human (37 y) and six old φ human (92 y) cylindrical trabecular bone specimens of 8×12 mm were obtained from vertebrae of the thoraco-lumbar region. The endplates of the vertebrae were removed using a high precision band saw (Exakt Apparatebau, Norderstedt, Germany). The cylinders were cored from the remaining vertebral plates using a dental trepan (229XL 080, Hager & Meisinger, Neuss, Germany) and freed from marrow using a pulsed water-jet (Braun Oral-B Professional Care 6500, Kronberg, Germany). Thereafter, the cylinders were scanned in a μ CT (XCT FAN Beam μ -Scope, Stratec Medizintechnik GmbH, Pforzheim, Germany) at a spatial resolution of 30 μ m.

Sample volume was experimentally measured using a gas micro-pycnometer (helium gas micro-pycnometer, AccuPyc 1330, Micromeritics, Norcross, USA). Samples were submerged in helium and the volume was determined from the ousted gas volume. *In silico*, the volumes were determined from the reconstructed and thresholded CT dataset by a) counting voxels or b) determining the interior in the CFE construction described below. The threshold needed for both these was determined according to (Ridler and Calvard 1978). This threshold, which in general is not integer-valued, is later referred to as τ .

To later investigate the dependence of the apparent mechanical properties on the image resolution, μ CT datasets were coarsened by an integer factor c . Coarsening was performed by averaging blocks of c^3 voxels of the original scan, possibly dropping excess slices at the boundary. The threshold previously determined for the finest resolution was used for all downsampled resolutions.

2.2 Mechanical Tension and In Vitro Compression Tests

For the validation of the CFE-method against mechanical tests, experimental data from a previous validation study (Wolfram et al. 2010) were used. Briefly, the material

consisted of 16 fresh frozen vertebrae (T6 to L2; 7 ♂, 3 ♀ donors) with a median age of 51 y (range: 37 to 84 y). After preparation, 20 cylindrical samples with 8 mm diameter and, depending on the vertebral height, 18 to 25 mm height were cored from the vertebra and endcapped so that an approximately 12 mm free gage length was obtained. The cylinders were scanned in a different μ CT (μ CT 40, SCANCO Medical AG, Brüttisellen, Switzerland) at a spatial resolution of 12 μ m. The scanner software provides a segmentation threshold for the specimens considered here by a method similar to the one (Ridler and Calvard 1978) used above. Voxel-based and CFE-based volumes were determined as before.

Prior to apparent testing, cylindrical samples were rehydrated in 0.9% physiological buffered solution. Aluminium rods were attached to the endcaps using cyanoacrylate and an extensometer was applied to the PU endcaps spanning the free testing length after mounting the specimen on the testing system (Mini-Bionix MTS system, Milwaukee, MN, USA). Testing was performed under moist conditions. The samples were (mechanically) preconditioned with three cycles to $\varepsilon = 0.4\%$ strain at a strain rate of $\dot{\varepsilon} = 0.4\%s^{-1}$. Subsequently, the specimens were loaded up to $\varepsilon = 0.004$ strain at a strain rate of $\dot{\varepsilon} = 0.2\%s^{-1}$ (Wolfram et al. 2010). Stresses were calculated from the force and strain curves by dividing the obtained forces by the initial cross section area of the bounding cylinder.

2.3 Tissue Material Parameters

Tissue material parameters for the samples designated for mechanical testing were obtained from the surrounding tissue using nanoindentation (Wolfram et al. 2010). After coring the cylinders, a 5 mm thick trabecular slice was obtained from the surrounding trabecular tissue using a high precision band saw (Exakt Apparatebau, Norderstedt, Germany). Subsequently, a mild preparation protocol was applied to conserve tissue mechanical properties (Wolfram et al. 2010). After curing, the samples were embedded in epoxy resin (Struers A/S, Ballerup, Denmark), polished with increasing grades of silicon carbide paper (P1000, P1400, P2000, P2500, P4000 – Hermes Schleifmittel GmbH & Co. KG, Hamburg, Germany) and finished with 1 μ m diamond paste on a polishing cloth. Prior to testing, the samples were rehydrated in 99% saturated Hank’s Balanced Salt Solution (HBSS) for 1.5 h. Indentations were performed on samples submerged in HBSS using a pyramidal Berkovich diamond tip mounted in a depth-sensing nanohardness tester additionally equipped with a wet cell (CSM Instruments SA, Peseux, Switzerland). Indentations were driven to 2.5 μ m depth at 0.002 Ns^{-1} . Load was maintained for 30 s to prevent creep influences. Subsequently, the samples were unloaded at 0.002 Ns^{-1} . Six indentations were performed on three axial trabecular cross-sections providing 18 indentation measurements per cylindrical specimen. A Poisson’s ratio of 0.32 was assumed for the bone tissue (Rho et al. 1997; Hengsberger et al. 2003). Tissue elastic moduli were determined (Oliver and Pharr 1992) and averaged over all 18 indentations per sample.

2.4 Composite Finite Element Simulations

CFEs use a level set representation (Osher and Sethian 1988) of the object of interest. This is obtained from the μ CT voxel image g using the thresholds τ described above using the affine transformation of the grey values $g_\tau = -g + \tau$. The trabecular structure is then represented by $[g_\tau < 0]$, i.e. trabecular bone corresponds to negative values of g_τ and the zero isosurface of g_τ represents the bone pore interface. It has to be mentioned that this transformation of grey values is compatible with (and actually commutes with) the resampling described above. Figure 1 shows the CFE

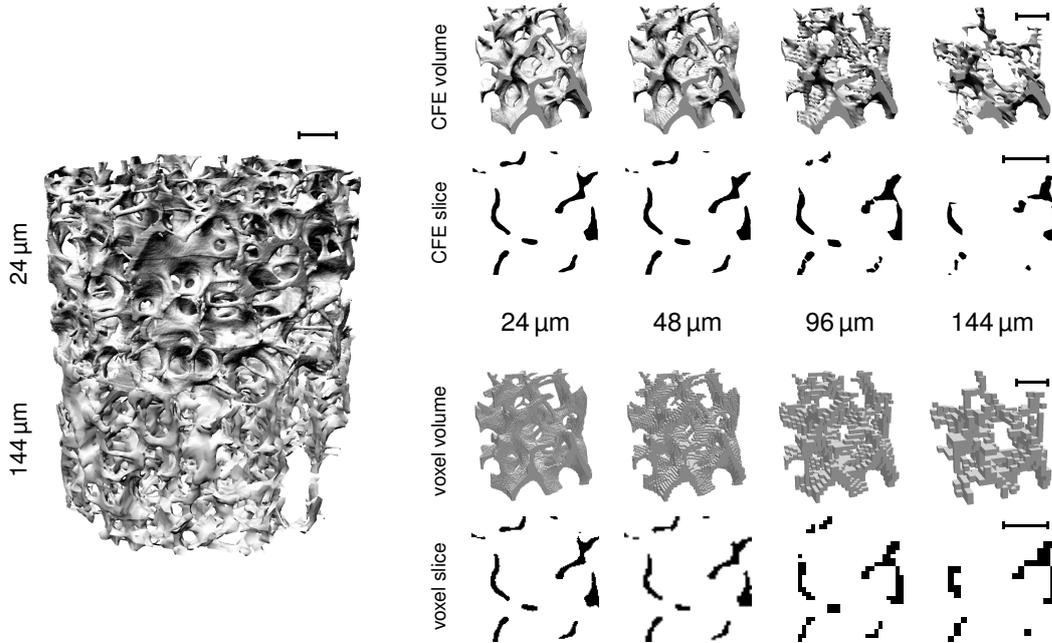


Figure 1: On the *left*, the CFE interface of one human trabecular specimen used in our simulations is shown at resolution $24\ \mu\text{m}$ (*upper half*) and $144\ \mu\text{m}$ (*lower half*). On the *right*, a small subset of the specimen is considered. The shape of the object and one slice in the CFE representation is shown for decreasing μCT resolution. For comparison, the corresponding voxel-based volumes and slices are shown below. Notice that, at fixed resolution, the CFE and voxel-based simulations use the same set of degrees of freedom associated to the hexahedral (voxel) computational mesh. The CFEs, via sub-pixel adaption of basis functions, are capable of capturing more geometric detail as the voxel size approaches the trabecular thickness. Black bars corresponding to $1\ \text{mm}$ length indicate the different scales in the visualisation.

representation of one of the cylindrical specimens and the influence of the imaging resolution on the geometric accuracy of the CFE representation compared to a voxel-based model.

The CFE construction for complicated domains (Liehr et al. 2009; Schwen 2010) basically works as follows. Each hexahedron in the grid defined by voxel midpoints is subdivided in six tetrahedra in such a way that edges on the faces of neighbouring cubes coincide. Finding the zero crossings of the level set function on these tetrahedral edges (by affine interpolation) allows restricting standard affine-linear FE basis functions on the tetrahedra to the approximate interior. Hence, no additional DOF are introduced except for those associated to vertices in the hexahedral voxel grid.

A standard conjugate gradient solver using SSOR (numerical) preconditioning (Hackbusch 1994) was used for solving the systems of equations arising from this type of simulation, as indicated by a solver performance comparison in (Schwen 2010).

Tension or compression by $0.1\ \text{mm}$ was simulated assuming isotropic, linearised elasticity of the trabecular tissue with the parameters as described above. The corresponding force was subsequently evaluated and the apparent elastic moduli were determined (Wolfram et al. 2009).

2.5 Statistical Analysis

Statistical analyses were performed with R (R Development Core Team 2008). The agreement between experiment and simulation with respect to the volume measurements and apparent stiffness was evaluated with concordance correlation

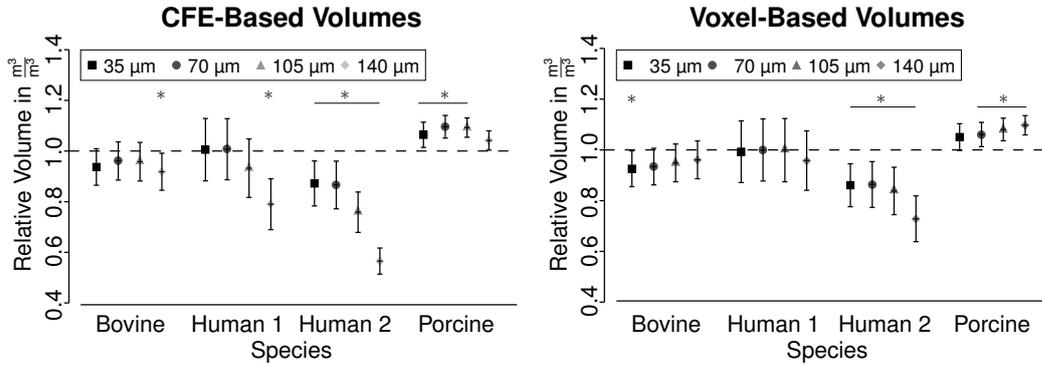


Figure 2: Volume segmentation depending on the image resolution. The relative volume was computed by dividing the volume determined *in silico* by the experimentally measured volume. The black horizontal line and the asterisk indicate relative volumes significantly different from one, which would indicate specimen wise concordance with the experimental data.

coefficients r_c (Lin 1989). The models were considered valid if $r_c > 0.90$. Due to linear quantile-quantile plots the t -test was used to compare groups applying a significance level of $p < 0.05$.

2.6 Application: Numerical Homogenisation in the Vertebral Core

As an application example, local stiffness tensors are computed for the trabecular core of a ♀ human lumbar vertebra (58 y). The posterior structures were removed using a band saw. The vertebra was wrapped in foil and scanned in a μ CT (Skyscan 1172, Skyscan, Kontich, Belgium) at a spatial resolution of 30 μ m.

From the scan, a slice of 21 mm thickness was selected and resampled by a factor of 3, resulting in 90 μ m image resolution. By the same procedure as before, the vertebral slice was used in a compression simulation by 0.1 mm, assuming isotropic elasticity properties with $E = 13$ GPa and $\nu = 0.32$. Moreover, 59 cubes of 6 mm edge length (200^3 voxels) of the vertebral core were selected, smoothed using Gaussian smoothing ($\sigma = 2$ voxels) and resampled to resolution 150^3 using multilinear interpolation. For these subsets of the trabecular bone, effective elasticity properties were determined numerically by a method described previously (Rumpf et al. 2010). In summary, deformations by elementary displacements are simulated and the respective stresses are evaluated on an interior subdomain (to avoid boundary stiffening artifacts) so that the effective elasticity tensor is determined. Microscopic material isotropy combined with geometric anisotropy then results in anisotropic effective material properties.

3. Results

3.1 Validation of Segmented Volumes

The segmentation of the volumes indicates for small resolutions a better volume determination of the CFE approach in comparison to the voxel-based determination of the volumes (Figure 2). Both the CFE-based and voxel-based approach underestimated the bone volume of the elderly female donor. In contrast, both methods overestimated the volume of the porcine specimens. In case of the bovine specimens and the specimens of the young human donor, the CFE-based volume determination was able to detect the volume correctly for resolutions smaller than 140 μ m. This was not reproduced by the voxel-based volume determination.

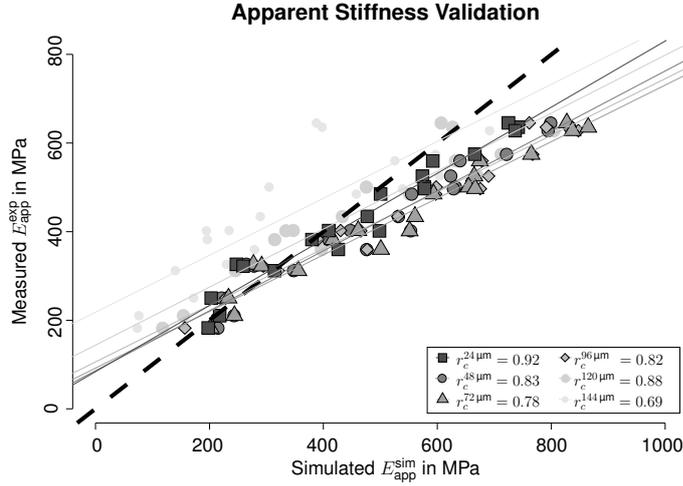


Figure 3: Concordance correlation straight for resolutions below $168 \mu\text{m}$ were statistically significant ($p < 0.05$) and indicate a moderate but acceptable concordance between experiment and simulation (apparent stiffnesses $E_{\text{app}}^{\text{exp}}$ and $E_{\text{app}}^{\text{sim}}$, respectively). Ideal concordance would have been given by a correlation straight falling together with the black, dashed line.

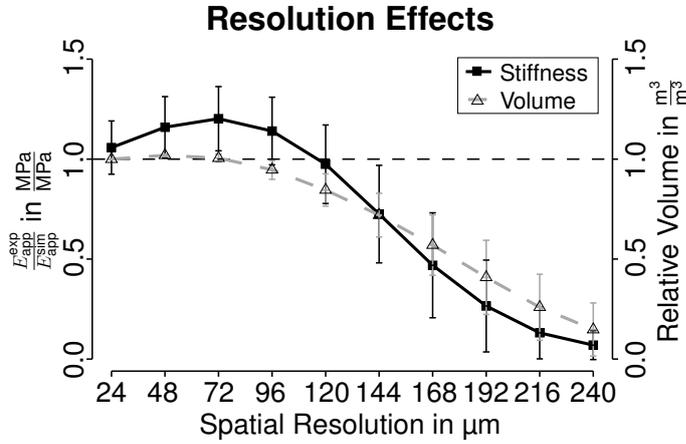


Figure 4: Relative apparent stiffness (computed stiffness $E_{\text{app}}^{\text{sim}}$ divided by experimentally determined stiffness $E_{\text{app}}^{\text{exp}}$) indicates that resolutions up to $120 \mu\text{m}$ allow to correctly determine mean apparent stiffnesses. Relative volumes (current volume divided by the volume calculated on the finest resolution) show a different evolution with resolution than relative apparent stiffness.

3.2 Validation of Apparent Stiffnesses

The comparison of the compression and tension experiments with the respective simulation yielded concordance correlation coefficients of $r_c < 0.9$ but $r_c \geq 0.78$ for resolutions below $168 \mu\text{m}$ (Figure 3). The best concordance was achieved for a resolution of $120 \mu\text{m}$. Interestingly, this was slightly smaller than the $140 \mu\text{m}$ that were the boundary for accurate prediction of the volume (Section 3.1). Nevertheless, the concordance correlation coefficients were all smaller 0.95. Thus, CFE-models did not deliver valid results comparing experiments and simulations in a one-to-one fashion.

The inclination fashion of the concordance straight (Figure 3) indicates that CFEs are at least well capable of providing correct mean results. This is further corroborated by comparing the mean relative apparent stiffness (Figure 4). Here a slight overestimation was found for resolutions $\{24, 48, 72, 96, 120\} \mu\text{m}$. At the same resolutions the relative volume of the samples did not change significantly.

Table 1: For one compression case and one tension case, the table shows the computational workload (wall clock time) of the system solver and resulting effective force F_{eff} for different solver thresholds ϵ_{tol} .

ϵ_{tol}	compression case			tension case		
	# iter	F_{eff} in N	time in s	# iter	F_{eff} in N	time in s
10^{-2}	32	119.474	82.4	31	10.726	68.0
10^{-3}	185	190.755	513.1	189	133.462	408.3
10^{-4}	589	188.338	1512.2	686	128.096	1592.7
10^{-5}	939	188.125	2056.9	1137	127.971	2580.5
10^{-6}	1573	188.147	3303.0	2231	127.959	4553.3
10^{-7}	2282	188.149	5076.1	2735	127.958	5599.3
10^{-8}	2889	188.149	6140.3	3587	127.958	7139.3

Table 2: For one compression case and one tension case, computational parameters (number of degrees of freedom, iterations of the system solver and its wall clock time duration) for simulations at different image resolutions are shown.

resolution	compression case			tension case		
	# DOF	# iter	time in s	# DOF	# iter	time in s
48 μm	$3 \times 957\,370$	1573	3303.0	$3 \times 734\,963$	2231	4553.3
72 μm	$3 \times 360\,093$	956	658.2	$3 \times 269\,857$	1231	815.0
96 μm	$3 \times 177\,282$	1132	374.9	$3 \times 133\,618$	1129	340.8
120 μm	$3 \times 99\,265$	1217	206.9	$3 \times 75\,380$	1088	170.2

3.3 Computational Performance

To assess the computational performance of the CFE method described, the system solver accuracy needed for robust results was investigated first. The results in Table 1 (for one of the compression and tension simulations, respectively) indicate that a stopping criterion of reduction of the residuum norm by six orders of magnitude is sufficient for computing the apparent stiffness in a robust manner. In the implementation (C++ code compiled with gcc 4.5.2 on Ubuntu 10.04, using OpenMP for some simple parallelisation and allowing up to four threads), 5 995 and 5 189 MiB of memory were needed and the simulations took about 55 and 76 minutes, respectively, on a 2.8 GHz Intel Core i7 CPU using IEEE double floating point accuracy, averaging 2.29 and 2.36 threads. For the simulations at 24 μm resolution, a compute server was necessary due to larger memory requirements.

Table 2 shows, for the solver accuracy described above, to what extent problem sizes and computational workloads decrease for coarser image resolutions of the same datasets and loading cases as before.

3.4 Simulation on a Whole Vertebra

The result of the compression simulation on an almost complete vertebra ($608 \times 487 \times 233$ computational grid) is shown in Figure 5. The force corresponding to a compression of the object by 0.1 mm is 17 688.5 N.

Figure 5 moreover shows the the resulting effective elasticity tensors on different cubic subsets of the vertebral dataset. These were visualized (at the respective location inside the vertebra) as deformed and colored spheres according to (He and Curnier 1995; Cazzani and Rovati 2003) so that elongation encodes uniaxial compressive stiffness and color encodes the bulk modulus.

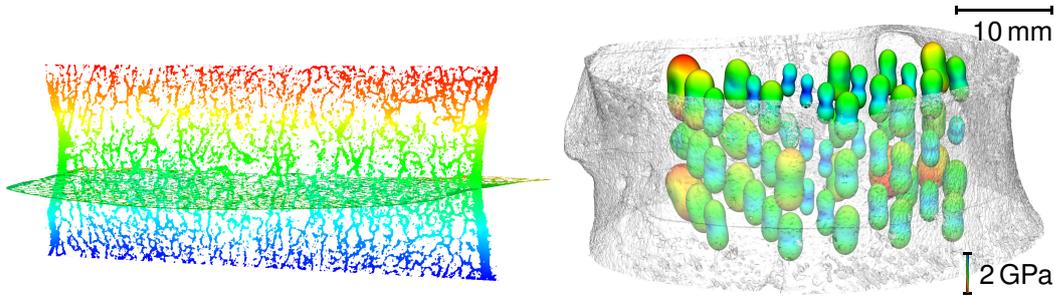


Figure 5: The *left* image shows the deformations obtained on two slices through a dataset of a vertebra subject to compression, color-coded from blue to red (maximum downward displacement). On the *right*, effective elasticity tensors obtained by numerical homogenisation on cubic subspecimens of the same vertebra are visualized. This shows both the anisotropy induced by the geometric microstructure and the inhomogeneity of macroscopic elasticity properties.

4. Discussion

The paper is concerned with the validation and application of a promising FE-tool that allows to directly set up sooth μ FE models of complicated domains such as trabecular bone. First, it is possible to accurately segment given volumes using an established segmentation technique and a CFE volume mesh. Second, CFEs allow to predict the apparent modulus of elasticity with a moderate but acceptable concordance coefficient. Third, computational efficiency was assessed to show that μ FE-models of trabecular bone where usually compute servers are employed can be solved on a desktop PC using CFEs. In our case approximately one hour.

The volume measurements for the evaluation of the capabilities of the segmentation technique used for setting up the CFE-models could only be performed at a comparable coarse resolution of $35\ \mu\text{m}$. This due to the fact that no better μ CT-scanner was available at that time. Different species with distinct bone morphology were selected to be able to test the segmentation on different measurement targets and because of a better availability of animal material. The good volume prediction in case of the bovine and young human specimens indicate that the resolution of the scanner was sufficient for these measurements. However, in case of the elderly female donor, low bone volume fraction and trabecular thickness could have led to partial volume effects which could have influenced the volume measurements. Parts of the volume could have been systematically segmented as background which led to the underestimation of the volume. The slight overestimation in case of the porcine samples could have been due to the higher bone volume fraction and the lower trabecular spacing. The indifferent volume prediction in case of the voxel-based volume determination may be an artifact caused by the non-smooth nature of the bone surface. Both the CFE-based and the voxel-based volume measurements showed only small errors at resolutions up to $105\ \mu\text{m}$ in comparison to the experimental gas micro-pycnometer measurements. This experimental method was considered as gold standard since its measurement error is several orders of magnitude smaller than that of the used CT. Besides the resolution of the μ CT, the segmentation technique (Ridler and Calvard 1978) used could have been a further source of error to these measurements. The advantage of the single-level threshold is its capability to provide an optimal threshold in an iterative procedure. This should ensure the best possible volume segmentation. For voxel-based μ FE-models it is known that their capabilities to predict stiffness decreases dramatically with resolutions greater $60\ \mu\text{m}$ (Verhulp et al. 2008; Bevill and Keaveny 2009) due to their non-smoothness. In providing an equally good volume segmentation CFEs could be a candidate to circumvent this disadvantage.

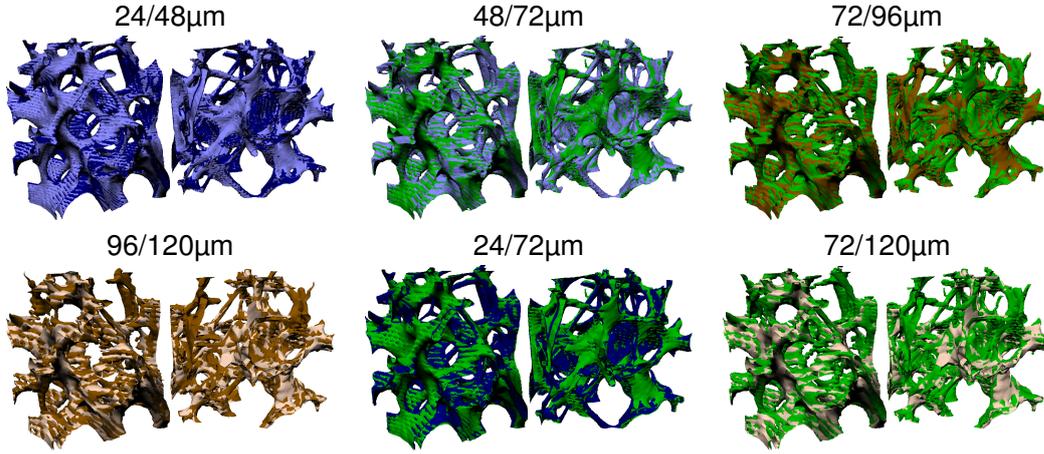


Figure 6: CFE models at different resolutions, front and back view of the same sub-structures each. Stiffer structures such as plates or junctions could have been over-segmented with increasing resolutions. At the same time more compliant structures such as rods could have been under-segmented. This could have led to the diverging evolutions of stiffness and volume (Figure 4). The effect seems to reverse at 72 μm . Dark blue denotes the interface at 24 μm , light blue at 48 μm , green at 72 μm , brown at 96 μm and light brown at 120 μm .

The stiffnesses determined *in silico* using CFEs correspond on average to those determined *in vitro*. The comparison in a one-to-one fashion delivered moderate but acceptable concordance to the *in vitro* measurements. However, compared to a similar study (Wolfram et al. 2010) that employed an already existing μFE -code (Arbenz et al. 2008) on the same samples, r_c and, thus, the one-to-one concordance between simulation and experiment was approximately 10 % worse. Since the same threshold was used on the same datasets at similar resolutions this disagreement could be due to the nature of the CFEs or their implementation.

It was observed that different resolutions lead to larger differences in stiffness than the corresponding volume changes suggest (Figure 4). This could have been due to over- or underestimation of local volume elements such as plates and rods. CFE model generation could have led to a local increase of volume in stiffening elements such as plates and locally decreasing volumes in rather unnecessary structures or vice versa. In that way total volume could have been almost constant while the stiffness could have been increased (Figure 6). In fact, it seems that CFEs produce concavities in thin rod-like structures which could be compensated for by convexities in other structures such as junctions (Schwen 2010). Thicker trabeculae which are mainly oriented along the main loading axis could over-proportionally benefit from such a thickening. At the same time other structures could have thinned and, thus, compensated the volume change without compensating for the apparent stiffness. These effects require further investigation and maybe an adaption of the CFE construction for structures only a few voxels thick.

The linear models deliver acceptable results at resolutions where other studies (Bevill and Keaveny 2009) suggested the usage of nonlinear FE models. Furthermore acceptable results in comparing simulations to experiments are obtained at resolutions which are coarser than those that can be obtained with state-of-the-art high resolution peripheral quantitative CTs (HRpQCT) (XtremeCT, SCANCO Medical AG, Brüttisellen, Switzerland). Hence, the presented technique allows computing stiffness and strength in combination with a failure load analysis based on linear FE models (Pistoia et al. 2002) at resolutions that are well achievable *in vivo*.

Assessing the influence of additional image processing techniques is beyond the scope of this study. Hence, in order to avoid influences the simulation results, no image denoising (e.g. isotropic, Perona-Malik (Perona and Malik 1990), or anisotropic

(Nemitz et al. 2007) diffusion, or more advanced techniques (Buades et al. 2005)), no more elaborate segmentation algorithms (Pal and Pal 1993; Pham et al. 2000), or joint denoising-segmentation approaches (Mumford and Shah 1989; Chan and Vese 2001) were used. Furthermore, the datasets were coarsened as described in Section 2.1 instead of scanning the samples at different resolutions. This would exclude possible volume losses caused in the scans due to partial volume effects. However, for illustrating the capabilities of CFEs, coarsened datasets were considered sufficient.

The anisotropy and inhomogeneity of the effective elasticity properties of the trabecular bone indicate that the cancellous bone should not be modelled as a homogeneous continuum. The results illustrate that it is necessary to incorporate the anisotropy of the trabecular core using either fabric-based material models or two-scale models.

5. Conclusions

Smooth valid μ FE-models of vertebral trabecular bone can be generated and efficiently solved using CFEs. Resolutions of 48 μm resolve the microstructure sufficiently. Simulated apparent stiffness of the bone samples delivered an average error of 5.8 % compared to experimental results, for which the computational effort is about one hour on a desktop PC. Coarser models are solved faster and the error in comparison to the experiment considered here is still acceptable at a spatial resolution of 120 μm , despite the fact that the microstructure is not resolved properly anymore. However, the resolution is coarser than those currently achieved with HRpQCTs. Setting up smooth meshes based on the natural voxel grid of the image instead of tetrahedral meshing could be particularly interesting for applications on such CTs in clinical use.

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