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About the inevitable compromise between spatial resolution and accuracy of strain measurement for bone tissue: A 3D zero-strain study

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ABSTRACT

The accurate measurement of local strain is necessary to study bone mechanics and to validate micro computed tomography (μCT) based finite element (FE) models at the tissue scale. Digital volume correlation (DVC) has been used to provide a volumetric estimation of local strain in trabecular bone sample with a reasonable accuracy. However, nothing has been reported so far for μCT based analysis of cortical bone. The goal of this study was to evaluate accuracy and precision of a deformable registration method for prediction of local zero-strains in bovine cortical and trabecular bone samples. The accuracy and precision were analyzed by comparing scans virtually displaced, repeated scans without any repositioning of the sample in the scanner and repeated scans with repositioning of the samples.

The analysis showed that both precision and accuracy errors decrease with increasing the size of the region analyzed, by following power laws. The main source of error was found to be the intrinsic noise of the images compared to the others investigated. The results, once extrapolated for larger regions of interest that are typically used in the literature, were in most cases better than the ones previously reported. For a nodal spacing equal to 50 voxels (498 μm), the accuracy and precision ranges were 425–692 με and 202–394 με, respectively. In conclusion, it was shown that the proposed method can be used to study the local deformation of cortical and trabecular bone loaded beyond yield, if a sufficiently high nodal spacing is used.

1. Introduction

Osteoporotic fractures increase morbidity and mortality, reduce the quality of life, and affect the economy of our ageing society (Kanis and Johnell, 2005). A deep understanding of bone mechanical properties at the different dimensional scales is necessary to develop new diagnostic methods and drug treatments that can be used to reduce the negative outcomes of bone pathologies. In particular, the investigation of the mechanical properties of bone biopsies (10^{-3}–10^{-2} m) is needed in order to understand how much they depend on bone quantity (e.g. bone mineral density, bone volume fraction) and quality (e.g. microarchitecture, morphology, etc.) (Bouxsein, 2003).

At that dimensional scale a number of studies have investigated the relationships between trabecular and cortical bone apparent mechanical properties and their volume fraction, mineral density and microarchitecture (Kaneko et al., 2003; Kopperdahl and Keaveny, 1998; Li et al., 2013; Nyman et al., 2009; Ohman et al., 2007; Wolfram et al., 2011), by means of mechanical testing and micro computed tomography (μCT) scanning. However, little is known about the local distribution of stress and strain of bone under certain loads, information necessary to study how bone structure and its local mechanical competence are related. At the organ level strain gages (Cristofolini et al., 2010; Trabelsi and Yosibash, 2011) and digital image correlation (DIC) techniques (Amin Yavari et al., 2013; Dickinson et al., 2011) have been used to perform strain measurement on a limited portion of the external surface of the tested bone. However, these methods cannot be used at the biopsy level, where the space is limited and 3D volumetric information becomes essential due to the complex microstructure.

Yet, another approach that combines repeated μCT images and digital volume correlation (DVC) techniques has been developed recently to study the mechanical behaviour of whole vertebrae (Hussein et al., 2012), trabecular bone (Bay et al., 1999; Bremand et al., 2008; Gillard et al., 2014; Liu and Morgan, 2007; Zauel et al.,

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2006), scaffolds (Madi et al., 2013) and bone implant interface (Basler et al., 2011). These deformable registration approaches can provide an estimation of the distribution of displacements and strains between two 3D images of the sample before and after a certain deformation is applied. The information obtained can be used not only to estimate the relationships between bone morphological properties and local deformations, but also to validate the local prediction of μCT based FE models. In this context, it is of fundamental importance to carefully measure the accuracy and precision of this experimental method before any direct application. The precision of the measured displacement and strains with a number of DVC approaches is reported by a number of studies. Conversely, the accuracy is only reported by a few of them (please see the exhaustive literature review by Roberts et al. (2014) and the paper published recently by Gillard et al. (2014)). The different DVC methods applied to trabecular bone led to wide ranges of accuracy and precision for displacement measurements: 0.004–0.272 voxels and 0.005–0.115 voxels (Liu and Morgan, 2007; Zauel et al., 2006), respectively. For strain, the range reported in the literature for accuracy and precision are 20–~1280 με and 39–~630 με (Gillard et al., 2014; Liu and Morgan, 2007; Zauel et al., 2006), respectively (the "~" indicates that the data were extracted from the graphs of the referenced papers). Usually these parameters are estimated by registering repeated scans of the same sample to include errors related to the registration procedure as well as from the intrinsic noise in the μCT image. The large differences in results was probably due to different DVC methods used (such as the dimension of the region of interest, the optimization criterion, the interpolation function, etc.) (Roberts et al., 2014), and the different samples analysed (anatomical site, dimension, etc.) (Liu and Morgan, 2007; Roberts et al., 2014). In particular, it seems that there is a strong dependency between the dimension of the sub-region of interest and both accuracy and precision of the method.

Surprisingly, little is known about the reliability of the method in predicting the local strain of a more homogeneous material such as cortical bone. In fact, in the authors' knowledge, there is only one study where the accuracy of the method is reported for a small portion of the diaphysis of mice femora based on high resolution Synchrotron radiation scans (Christen et al., 2012). However, that study focused on a smaller dimensional scale and did not report accuracy and precision of the method based on repeated measurements. In fact, Christen et al. (2012) found an accuracy close to zero but a very large precision error (up to 13,000 με), by comparing an original image and its virtual translation of 0.5 voxels along each direction. Therefore, such methodology probably underestimates the error introduced in a real case where two different scans are registered, and therefore where the intrinsic noise of the images might play a significant role during the deformable registration. For these reasons, this study was not directly compared to the results of the present study.

The goal of this study was to evaluate the accuracy and precision of a deformable registration method previously used for soft tissues to investigate the local displacements and strains in cortical and trabecular bone samples, in the particular case of zero-strain.

2. Material and methods

The accuracy of the proposed method to estimate the local strains in μCT images of cortical and trabecular bone samples was estimated by analyzing simulated and real displacement and zero-strain fields (Liu and Morgan, 2007) (Fig. 1). In total each sample was scanned three times. After the first original scan (Scan1), the second and third scans were performed without (Scan2) and with (Scan3) repositioning of the sample holder in the machine. The analysis of a simulated displacement was based on the comparison between Scan1 and Scan1 after a virtual translation of two voxels in each direction. This experiment was used to estimate the predicted local total displacement (that should be 3.464 voxels) and the local strains (that should be 0) in an ideal case. Moreover, the accuracy of the method in predicting real strains was estimated by performing two further analyses. Scan1 and Scan2 were compared to estimate the accuracy and precision of the method by including the effect of the noise of the images for repeated scans. Furthermore, Scan2 and Scan3, rigidly registered to Scan2, were compared to evaluate the accuracy by including also a rigid registration (and therefore interpolation) error. In all cases accuracy and precision of the displacement and of the strain were estimated with the mean and standard deviation of the difference between the imposed and measured variables.

2.1. Sample preparation and scanning

Samples were extracted from a bovine femur, collected from animal that was killed for alimentary purposes. Two sections were cut with a precision diamond saw (*Isomet1000, Buehler, USA*) from the greater trochanter (12 mm in thickness) and diaphysis (20 mm in thickness) of the femur. A diamond core drill tool mounted on a drilling machine was used to extract under constant water irrigation a 3 mm in diameter cylindrical cortical bone sample and an 8 mm in diameter cylindrical trabecular bone sample. The samples were then scanned in saline solution with a μCT (*Skyscan 1172, Bruker*) with the parameters reported as following. X-Ray detector: 10 Megapixel 12-bit digital cooled ORCA-HR CCD, 2000 × 1048 pixel. Voltage equal to 59 kV and to 70 kV were used for the trabecular and cortical bone, respectively. All the other parameters were the same for both bone types: power equal to 10 W, voxel size equal to 9.96 μm (spatial resolution equal to 5 μm), exposure time equal to 1180 ms, rotation step equal to 0.7°, total rotation equal to 180°, images averages × 2, 1 mm Aluminum beam hardening filter, height scan 9.323 mm.

2.2. Image processing

After image reconstruction, a parallelepiped with square cross section of 180 × 180 voxels and height equal to 932 voxels (9.28 mm) was cropped in the central portion of each sample. These dimensions were chosen to fit in the volume of the smaller cortical bone sample (CORT). For comparison with the literature, also a larger region in the trabecular sample was cropped (cube with 430 voxels in each side, equivalent to 4.28 mm side length, similar to the one reported by Liu and Morgan, 2007).

To evaluate the effect of a masking operation, the trabecular bone sample (TRAB) was also segmented as following. A mask (binary image with value one for bone voxel and zero elsewhere) was created from the original images by applying first a Gauss filter to reduce the noise (sigma equal to 1.5) followed by a single level threshold chosen according to the histograms (Tassani et al., 2011). The quality of the mask was checked by visual inspection. The obtained mask was multiplied to the original image, obtaining a masked trabecular bone sample (TRAB-Masked) with the original greyscale value in the bony pixels, and zero elsewhere.

For the first comparison (Scan1, simulated displacement) a bounding box of ten voxels was added around the sample that was virtually translated of two voxels in each direction. All cropping and translating steps were done with the free imaging processing toolkit *MeVisLab* (*MeVis Medical Solutions AG*, http://www.mevislab.de/). For the third comparison (Scan2 vs Scan3) the repositioned scan was rigidly registered by using the *MERIT* script in *MeVisLab*. This 3D multi-resolution rigid registration script is based on Sum of Squared Differences (SSD) as similarity measure, and the parameters of the rigid registration were chosen after a proper optimization performed on two 3D images of cortical and trabecular bone virtually rotated and translated of a known quantity (unpublished data).

2.3. Registration and evaluation of displacements

In this study a deformable image registration toolkit (*ShIRT*) (Barber and Hose, 2005; Barber et al., 2007; Khodabakhshi et al., 2013), which was previously applied to soft tissues, was used. We report here only the main steps of the procedure and more details in Appendix A.

The procedure focuses on the recognition of identical features in the two 3D images (called the fixed and moved images). The problem can be translated into finding the displacement functions u, v and w that map each point in the fixed image (with coordinates x, y, z) into the ones in the moved image (with coordinated $x'=x+u$, $y'=y+v$, $z'=z+w$). In ShIRT the mapping function is computed in points of a homogeneous cubic grid superimposed to the images, with nodal spacing NS. The computed displacement functions are then interpolated (tri-linearly) to provide full 3D field estimations of displacement in each point of the image. In this study we have investigated the accuracy and precision of the estimated displacements and strains in function of NS, varied from 5 to 50 voxels (Table 1). For the larger images cropped from the trabecular bone sample, also NS equal to 125 and 150 voxels were analyzed.

2.4. Evaluation of strain

ShIRT computes the displacements at the nodes of the grid. Each grid was then converted into a reticular structure that was defined as a mesh for a FE model.