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Micro-finite-element method to assess elastic properties of trabecular bone at micro- and macroscopic level

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Abstract

34 *Objective of the study:* The objective of the present study is to assess the mechanical behavior
35 of trabecular bone based on microCT imaging and micro-finite-element analysis. In this way
36 two methods are detailed: i) Direct determination of macroscopic elastic property of trabecular
37 bone; ii) Inverse approach to assess mechanical properties of trabecular bone tissue.

38

39 *Patients:* Thirty-five females and seven males (forty-two subjects) mean aged (\pm S.D.) 80 ± 11.7
40 years from hospitals of Assistance Publique-Hôpitaux de Paris (APHP) diagnosed with osteo-
41 porosis following a femoral neck fracture due to a fall from standing were included in this study.

42

43 *Materials and methods:* Fractured heads were collected during hip replacement surgery. Stand-
44 ardized bone cores were removed from the femoral head's equator by a trephine in a water bath.
45 MicroCT images acquisition and analysis were performed with CTan® software and bone vol-
46 ume fraction () was then determined. Micro-finite-element simulations were performed using
47 Abaqus 6.9-2 ® software in order to determine the macroscopic mechanical behaviour of the
48 trabecular bone. After microCT acquisition, a longitudinal compression test was performed and
49 the experimental macroscopic Young's Modulus was extracted. An inverse approach based on
50 the whole trabecular bone's mechanical response and micro-finite-element analysis was per-
51 formed to determine microscopic mechanical properties of trabecular bone.

52

53 *Results:* In the present study, elasticity of the tissue was shown to be similar to that of healthy
54 tissue but with a lower yield stress.

55

56 *Conclusion:* Classical histomorphometric analysis form microCT imaging associated with an
57 inverse micro-finite-element method allowed to assess microscopic mechanical trabecular bone
58 parameters.

59

60 **Résumé**

61 *Objectif de l'étude:* Déterminer le comportement mécanique de l'os trabéculaire à l'aide d'une
62 acquisition micro-tomographique par rayons X et d'une analyse par la méthode des micro-élé-
63 ments finis: i) Détermination directe du module d'élasticité macroscopique de l'os trabéculaire
64 ; ii) Approche inverse pour déterminer les propriétés mécaniques du tissu trabéculaire.

65

66 *Patients:* 35 femmes et 7 hommes d'âge moyen (\pm D.S.) 80 ± 11.7 ans de l'Assistance Publique
67 des Hôpitaux de Paris (APHP) diagnostiqués ostéoporotiques suite à une fracture de l'extrémité
68 supérieur du fémur due à une chute.

69

70 *Matériels et méthodes:* Suite à une arthroplastie, des carottes osseuses ont été extraites au som-
71 met de la tête fémorale à l'aide d'un trépan. Une acquisition micro-tomographique par rayons
72 X et une analyse des paramètres histomorphométriques ont ensuite été effectués. Par la suite,
73 le comportement macroscopique de l'os trabéculaire a été déterminé par la méthode des micro-
74 éléments-finis sur le logiciel Abaqus 6.9-2 ®. Un essai de compression longitudinal a ensuite
75 été réalisé afin de mesurer le module d'élasticité macroscopique. Enfin une analyse inverse
76 basée sur le comportement mécanique expérimental macroscopique combiné à la méthode des
77 micro-éléments-finis a permis de déterminer le comportement microscopique de l'os tra-
78 béculaire.

79

80 *Résultats:* Les résultats ont montré que les propriétés élastiques de l'os trabéculaire présentaient
81 les mêmes caractéristiques que chez des patients sains mais avec une limite élastique plus faible.

82

83 *Conclusion:* La méthode classique d'histomorphométrie combinée à une méthode inverse des
84 micro-éléments-finis permet de remonter aux propriétés élastiques microscopiques de l'os tra-
85 béculaire.

86

87 **Keywords:** Mechanical properties; Micro-computed tomography; Micro-finite-element;
88 Trabecular bone; Inverse method

89 **1. Introduction**

90 Bone mechanical properties are affected by bone loss and modification of bone quality. The
91 term “bone quality” refers to a complex definition that involves intrinsic microstructural
92 properties [1,2]. A definition of bone quality was proposed by Bouxsein [3] as “the totality of
93 features and characteristics that influence a bone’s ability to resist fracture”. In fact, human
94 bone is a composite material whose mechanical properties depend on its hierarchical
95 organization [4–6]. Despite extensive research, a mechanistic framework to describe how the
96 microstructure affects the mechanical behaviour of bone has not been established. The major
97 difficulty lies in intrinsic properties of bone, a tissue which can adapt both structurally and
98 architecturally to its mechanical environment through bone remodeling [7]. For instance, on the
99 microscopic scale local properties of the cortical bone emphasizes the importance of cement
100 lines as an efficient structural component to ensure internal movement at the material level and
101 to prevent the progression of localization damage zones and cracks [8,9].

102 Bone remodelling is a multi-cellular phenomenon that is not fully understood. Bone cells such
103 as osteocytes transduce mechanical and biochemical information into bone adaptation signals
104 [10,11] triggering microstructural and material modifications through osteoblast and osteoclast

105 activity. Thanks to the development of micro-computed tomography (microCT), the trabecular
106 bone microarchitecture has been extensively studied. New histomorphometric indicators are
107 now available to characterize bone pathology and remodeling process [12,13]. However,
108 developing knowledge of the mechanical behaviour of the trabecular bone tissue, *i.e.*, the
109 effective material constituting the trabecular bone is still a challenging issue.

110 Trabecular bone mechanical properties can be studied on two different scales. On a macroscopic
111 scale, the compression of a trabecular bone sample is characterized by a three-stage stress-strain
112 curve composed of the following parts: i) a linear elastic regime that corresponds to cell edge
113 deformation, ii) an ultimate yield stress followed by a plateau corresponding to cell collapse
114 due to fracture of trabeculae and iii) the densification stage [14]. Clearly, macroscopic
115 mechanical parameters such as Young's modulus and ultimate yield stress, which take into
116 account both the microarchitecture and trabecular bone tissue properties, depend on anatomic
117 location and function [15]. However, in all cases macroscopic mechanical properties of the
118 trabecular bone are weaker than mechanical features of the trabecular bone tissue [16].

119 An alternative approach to direct measurements at the tissue level is to use micro- finite-element
120 models derived from micro-computed tomography (microCT) imaging. This approach
121 combines experimental results obtained at the sample level with large finite-element
122 computations to calibrate effective properties of the tissue [17]. However, due to edge artefacts
123 and microCT imaging treatments [18,19], most of these studies report low values of calibrated
124 effective tissue moduli compared to experimental results. Two studies [20,21] on bovine tissue
125 and one on a small number of cadavers [22] found values of trabecular bone tissue Young's
126 moduli that are close to cortical values. Moreover, large finite-element analysis performed on
127 trabecular bone samples using specific trabecular tissue elasticities obtained by nanoindentation
128 technique gives a good approximation of the experimental Young's modulus value of bone
129 sample [23,24].

130 The main objective of the present study is to assess the mechanical behaviour of the trabecular
131 bone based on microCT imaging and micro-finite-element analysis. Therefore, two methods are
132 detailed on a cohort of osteoporotic patients: i) direct determination of macroscopic elastic
133 properties of the trabecular bone, ii) inverse approach to assess mechanical properties of the
134 trabecular bone tissue.

135 **2. Patients**

136 Thirty-five females and seven males (forty-two subjects) mean aged (\pm S.D.) 80 ± 11.7 years
137 from hospitals of Assistance Publique-Hôpitaux de Paris (APHP) were included in this study.
138 All subjects were diagnosed with osteoporosis following a femoral neck fracture due to a fall
139 from standing. Fractured heads were collected during hip replacement surgery. Subjects with a
140 medical history of neoplastic disease, a radiologic aspect compatible with a pathological
141 fracture or a refusal to participate were excluded.

142 **3. Materials and methods**

143 3.1. Samples

144 Standardized bone cores of 7 mm diameter were removed from the femoral head's equator by
145 a trephine in a water bath. The two extreme surfaces were polished (grit #1200) to obtain a
146 fresh, standard, cylindrical sample of human trabecular bone with a mean radius of 3.5 mm and
147 a mean length of 8.7 mm as depicted in Figure 1a.

148 (FIGURE 1)

149

150 3.2. MicroCT imaging

151 Standardized bone cores were placed into a cryotube (10 mm inner diameter and 86 mm length)
152 filled with phosphate-buffered saline (PBS) solution to prevent desiccation. The tubes were set
153 onto a brass spigot made to fit cryotubes and were examined with a Skyscan 1172 microCT
154 (Skyscan, Aartselaar, Belgium) using the cone-beam method. Projection images on the CCD

155 camera were obtained at 60 kV and 100 μ A with a 0.5-mm aluminium filter at 35x magnification
156 for which the voxel size was 8 microns in all three spatial directions. A 0.25° rotation was
157 applied between successive image acquisitions to provide a series of 720 projection images.
158 From this series of projection images, a stack of 2D sections was reconstructed for each bone
159 sample (Figure 1b) and stored as .bmp files with indexed grey levels ranging from 0 (black) to
160 255 (white). The number of sections needed for the entire core height was close to 1100. 3D
161 reconstruction and analysis was performed using microCT results in CTan software. NRecon
162 (v.1.6.6, Skyscan) and CT-analyser (v.1.12, Skyscan) and bone volume fraction (BV/TV) was
163 then determined.

164 3.3. Finite-element meshing

166 For each sample, a finite-element mesh was generated based on the images acquired during
167 initial microCT. A special treatment was performed on the microCT images to carefully build
168 an accurate tetrahedral finite-element mesh that was representative of the sample's
169 microarchitecture. First, the micro-scanned images were converted to an exploitable 8-bit image
170 format in axial slices with 256 grey-levels as the procedure described in Figure 2. The images
171 were then smoothed using a 3D median filter to reduce the noise generated during image
172 acquisition (Figure 2a). Afterwards, the images with 256 grey levels were segmented (Figure
173 2b) using a threshold defined as the minimum of the %pixel on grey-level histogram of all slices
174 [25,26]. All voxels with a grey level higher than the defined threshold were considered to
175 represent bone. Subsequently, a 3D surface mesh based on the segmented images was generated
176 by the software Avizo fire® (Figure 2c). Because the initial large number of edges was not
177 directly exploitable, a simplified model of the surface contour was built. (Figure 2d). The last
178 step is the creation of a finite-element mesh of the 3D volume using tetrahedral elements (Figure
179 2e). All islands formed by unconnected regions of the mesh were deleted prior to mesh

180 generation. This procedure led to a mesh composed of approximately 250 000 nodes and
181 800 000 elements on average.

182 (FIGURE 2)

183

184 3.4. Mechanical compression test

185 After acquisition of the histomorphometric parameters, each sample was placed horizontally
186 into a customised micro-compression device [27,28] run by the software LabVIEW 7.1® to
187 load the cylinder along its long axis. A preload of 10 N was applied to immobilize the sample.
188 In the first step, a compression loading-unloading cycle (10N-60N) was applied at constant
189 velocity (1 $\mu\text{m/s}$). Then, the compression test was performed until the plastic stress plateau was
190 reached; this was followed by an unloading step. The force-displacement curves were recorded
191 at a rate of one point per second to determine the experimental macroscopic Young's Modulus
192 E_s^{exp} during the unloading step as depicted in the right hand side of the Figure 1c. Afterwards,
193 the cylindrical sample was placed back into the tube sample holder to undergo a second
194 microCT acquisition.

195

196 3.5. Macromechanical finite element analysis

197

198 For the purpose of this study, finite-element simulations were performed using the software
199 Abaqus 6.9-2 ®. The constitutive law used for bone tissue was isotropic, linear-elastic/ideally-
200 plastic and characterised by three parameters: the Young's modulus E_{Tr} , the Von Mises yield
201 Stress σ_{Tr} and Poisson's ratio ν_{Tr} . The subscript Tr corresponds to the trabecular tissue to
202 contrast with the subscript s characterizing the sample macroscopic values. Poisson's ratio was
203 set to the regular value of 0.3 [19]. The Young's modulus E_{Tr} for trabecular bone tissue
204 corresponds to a full filled trabecular bone sample, i.e. $\text{BV/TV} = 100\%$. Micro- finite-element

205 simulations were performed with a bone tissue Young's modulus $E_{Tr} = 20$ GPa for the linear
206 elastic/ideally plastic behaviour law usually given for cortical bone in the literature. Boundary
207 conditions were defined to reproduce the boundary conditions of the experimental compression
208 test in a realistic manner. A uniform displacement was imposed on nodes located on the
209 sample's top axial surface in the bone core axis. Displacements and rotations of the nodes
210 located on the opposite (bottom) axial surface were blocked in the bone core axis direction.
211 After the finite element analysis of the axial compression test, the macroscopic stress-strain
212 curve enabled the determination of the macroscopic Young's modulus E_s^{num} of the trabecular
213 bone sample (Figure 1d).

214 3.6. Inverse micro-finite-element method

215

216 Based on finite element analysis, the trabecular bone tissue modulus E_{Tr} and yield stress σ_{Tr}
217 were determined using an inverse method already detailed in several studies [17,22]. In this
218 method, trabecular bone tissue properties were obtained by calibrating the mechanical
219 behaviour-law parameters of the micro-finite-element model to match the sample's
220 macroscopic experimental measurements (Figure 1c-d).

221 In a first numerical step using micro-finite-element analyses, compression tests were simulated
222 with an arbitrary tissue modulus of 20 GPa. The macroscopic Young's moduli of specimens
223 E_s^{num} were extracted from their numerical stress-strain curves. As the macroscopic Young's
224 modulus varies linearly with trabecular bone tissue modulus in the elastic domain, the trabecular
225 bone tissue modulus E_{Tr} can be derived directly as the ratio between the experimental and
226 numerical macroscopic Young's modulus of the sample E_s^{exp} and E_s^{num} as expressed by the
227 equation (1).

$$E_{Tr} = 20 \times \frac{E_s^{exp}}{E_s^{num}} \quad (1)$$

228 In a second numerical step, the specific-subject trabecular tissue Young's modulus E_{Tr}
229 previously determined from linear analyses was used in each simulation. The value of the
230 trabecular tissue yield stress σ_{Tr} was then calibrated to reproduce the nonlinearity observed on
231 the macroscopic experimental force-displacement curves. Calibration was performed with a
232 manual trial-and-error procedure.

233

234 3.7. Statistical analysis

235 Successive linear regressions were performed to assess possible correlations among the
236 different studied parameters. A value of $\alpha=0.05$ was used as the threshold of statistical
237 significance. Every result with $p<0.05$ was considered to be statistically significant. All
238 statistical analyses were performed with the freeware R 2.13.2.

239

240 4. Results

241 4.1. Experimental macroscopic mechanical behaviour assessment

242

243 For the forty-two bone specimens BV/TV mean value was $22\pm 4.6\%$ with a range from 14.5%
244 to 32.1%.

245 For each subject, macroscopic Young's modulus E_s^{exp} and yield stress σ_s^{exp} were measured on
246 the load deflection curve of the micro-compression test. The mean (\pm S.D.) value of macroscopic
247 Young's modulus E_s^{exp} measured for the forty-two bone specimens was 1.55 ± 0.67 GPa with a
248 range from 0.43 MPa to 3.02 GPa. The mean (\pm S.D.) yield stress σ_s^{exp} was 4.8 ± 2.41 MPa with
249 a range from 1.46 MPa to 12 MPa.

250 No significant linear correlations between any macroscopic mechanical parameters and age was
251 found ($R^2=0.0045$ and $p=0.7$ for E_s^{exp} vs. age, $R^2=0.0273$ and $p=0.3$ for σ_s^{exp} vs. age). However,
252 the macroscopic Young's modulus and stress yield σ_s were significantly correlated with bone
253 volume fraction ($R^2=0.5779$ and $p<0.05$, $R^2=0.4955$ and $p<0.05$, respectively), see Figure 3.

254

255

256

257

258

(FIGURE 3)

259 4.2. Numerical macroscopic mechanical behaviour assessment based on microCT images

260

261 From the numerical test, macroscopic Young's modulus E_s^{num} was determined. The results are
262 depicted in Figure 4 and compared to the experimental Young's modulus E_s^{exp} determined
263 previously. The mean (\pm S.D.) value of the macroscopic Young's modulus E_s^{num} obtained from
264 the simulation for the forty-two bone specimens was 1.71 ± 0.71 GPa with a range from 0.6 GPa
265 to 3.5 GPa. The Young's modulus obtained from the experimental tests and the simulations
266 were comparable ($p=0.3$).

267

(FIGURE 4)

268

269 Linear correlations between the numerical macroscopic Young's modulus E_s^{num} and either age
270 or bone volume fraction BV/TV was also investigated. No significant linear correlation with
271 age was found ($R^2=0.0045$ and $p=0.7$). However, E_s^{num} was significantly correlated with bone
272 volume fraction ($R^2=0.6195$, $p<0.05$) as depicted in Figure 5.

273

(FIGURE 5)

274

275

276 4.3. Trabecular bone tissue Young's modulus and yield stress assessment based on microCT
277 images and experimental compression test

278 4.3.1. Trabecular bone tissue modulus using an inverse method

279 The results of the simulations (E_s^{num}) and the experimental tests (E_s) were implemented into
280 equation (1). Mean (\pm S.D.) value of 18.92 ± 5.43 GPa with a range from 9 GPa to 29 GPa for
281 the trabecular bone tissue modulus E_{Tr} was computed for the forty-two bone specimens (Figure
282 6).

283 (FIGURE 6)

284

285 4.3.2. Trabecular tissue yield property using nonlinear micro-finite-element analyses

286 The mean (\pm S.D.) value of trabecular bone tissue yield stress σ_{Tr} for the forty-two specimens
287 was 86.5 ± 16.51 MPa with a range from 65 MPa to 160 MPa (Figure 6).

288

289 **5. Discussion**

290

291 In this study, trabecular bone samples of forty-two subjects diagnosed with osteoporosis
292 following a femoral neck fracture due to a fall from standing were analyzed. Macroscopic and
293 microscopic mechanical properties were investigated using micro-finite-element analysis
294 coupled to an inverse approach. This method assess how macroscopic and microscopic
295 mechanical properties of trabecular bone can be determined based only on its microarchitecture.
296 The determination of the trabecular bone tissue elasticity by this method has been reported in
297 numerous studies, but to our knowledge only one has used this approach to assess the Young's
298 modulus of trabecular bone specimens from women with and without femoral neck fractures

299 [29]. Computed numerical macroscopic Young's modulus and yield stress are significantly
300 correlated with bone volume fraction and comparable to the experimental measurements.
301 Trabecular bone tissue Young's modulus mean value is consistent with experimental
302 measurements from nanoindentation technique found in the literature. Moreover, this method
303 shows how to identify the trabecular bone tissue yield stress to reproduce the nonlinearity
304 observed on the macroscopic experimental force-displacement curve. Altogether in accordance
305 with the literature, results of this study show that the elasticity of the trabecular bone tissue is
306 similar to that of healthy one but with the yield stress lower than in cortical tissue.

307 At the macroscopic scale, the mean (\pm S.D.) value of bone volume fraction for the forty-two
308 specimens was $22\pm 4.6\%$ with a range from 14% to 32%, which is in good agreement with
309 several studies [23,30]. Moreover, macroscopic Young's modulus and yield stress were
310 significantly correlated with bone volume fraction. As described previously in other studies,
311 bone volume fraction was relevant to quantify bone quality [31]. From a mechanical point of
312 view, whole bone properties strongly vary between anatomic sites [15]. Indeed, bone quality is
313 greater for human proximal tibial bone than for the human greater trochanter. For instance,
314 trabecular bone retrieved from the ilium, which is not a common site of fragility fractures,
315 differs completely from trabecular bone extracted from the femoral head. In this context, exact
316 values of the mean macroscopic mechanical parameters are difficult to compare, and we can
317 only claim that our experimental and numerical results are of the same order of magnitude as
318 values found in the literature [23,32,33].

319 Macroscopic mechanical property of trabecular bone can be determined based only on its
320 microarchitecture. Linear elastic finite-element analysis, with homogeneous mechanical
321 behaviour of trabecular tissue, performed on high-resolution microCT images converted into a
322 micro-finite-element mesh provided the relationship between bone stress and bone strain. This
323 method was also validated by Chevalier *et al.* [20] and recently by Wolfram *et al.* [24], who

324 directly used microscopic Young's modulus obtained from nanoindentation measurements in
325 finite-element computations. Likewise in our study, numerical and experimental macroscopic
326 elasticities were quite comparable. Nevertheless, several studies have investigated the effect of
327 heterogeneous mineral distributions on the mechanical response [34–39] leading to non-
328 homogeneous mechanical parameters distribution. They showed that “mineral heterogeneity
329 has only a minor influence on the macroscopic elastic properties of human cancellous bone”.
330 Therefore, it is reasonable to assume homogeneous mechanical behaviour of trabecular tissue.

331 In this study, microscopic mechanical properties of trabecular bone are determined by an
332 inverse approach based on the whole trabecular bone's mechanical response and micro-finite-
333 element analysis as first used by Rietbergen *et al.* in 1995 [17]. Since that study, the
334 determination of trabecular bone tissue elasticity by this method has been reported in numerous
335 studies, but to our knowledge only Homminga *et al.* [29] used this approach to assess the
336 Young's modulus of trabecular bone specimens from women with and without femoral neck
337 fractures. In this study, Homminga *et al.* concluded that no significant difference in the elasticity
338 of trabecular tissue between osteoporotic and healthy specimens was observed, and they
339 determined a Young's modulus value of 10 GPa. This result, two times less than cortical bone
340 values, was in concordance with several studies based on this method [35,40,41] but in direct
341 contradiction with experimental measurements performed by ultrasonic and nanoindentation
342 techniques. To explain the very low values obtained using the micro-finite-element method,
343 several authors highlighted the end artefacts, the boundary conditions of the simulation and the
344 thresholding method [42,43]. Especially, the global threshold value chosen can greatly
345 influence the finite-element analysis through the estimation of bone volume fraction [44], which
346 has been shown to be correlated with macroscopic mechanical behavior and relevant to quantify
347 bone quality [31]. Studies that successfully eliminated these artefacts found modulus values
348 similar to the values for cortical bone [21,22]. In the present study to avoid the mentioned

349 artefacts, the whole experimental bone sample was meshed, boundary conditions that simulate
350 experimental conditions were applied and an automatic threshold described by Chappard *et al.*
351 [25] was used. Application of this method to samples from osteoporotic patients gave a mean
352 (\pm S.D.) trabecular bone tissue Young's modulus of 18.92 ± 5.43 GPa. This value is almost two
353 times greater than results obtained by Homminga *et al.* [29] on a similar population, but very
354 close to experimental measurements from nanoindentation technique. For instance, Turner *et*
355 *al.* [45] retrieved trabecular bone tissue Young's moduli from the distal femoral condyle using
356 ultrasonic and nanoindentation techniques of 17.5 GPa and 18.14 GPa, respectively. Also,
357 femoral cortical bone microscopic Young's moduli in the transverse and longitudinal directions
358 were 15-17 GPa and 21-24 GPa, respectively due to the anisotropy [45,46]. Therefore, the
359 consensus today is that the elastic modulus of trabecular bone tissue is similar to that of cortical
360 bone. Altogether, this results indicate that osteoporotic population trabecular bone tissue
361 elasticity is fully comparable to those of healthy population.

362 Microscopic trabecular bone tissue yield stress identification for the elastic/ideally-plastic
363 behavior law can be performed with a manual trial-and-error procedure on an inverse micro-
364 finite-element analysis. Since, yield stress due to trabecular bone tissue damage is difficult to
365 assess, Bayraktar *et al.* [22] were the first to propose this method on elderly trabecular bone
366 samples and found a mean (\pm S.D.) value of 84.9 ± 11.2 MPa in compression. The authors
367 concluded that compressive and tensile yield stress was higher by 20-30 % for cortical bone in
368 [22,47]. In the present study, the mean (\pm S.D.) value of the yield stress on an osteoporotic
369 population was 85.6 ± 16.7 MPa, which also indicates that the yield stress of osteoporotic
370 trabecular bone tissue is lower compared to healthy cortical tissue.

371

372 **6. Conclusion**

373

374 In conclusion, a study of forty-two patients with fractured femoral necks was undertaken to
375 evaluate the mechanical behaviour of trabecular bone in the femoral head at different scales. At
376 the macroscopic scale, the bone volume fraction plays an important role in the determination
377 of bone quality. Macroscopic mechanical property of trabecular bone can be determined based
378 only on its microarchitecture by high-resolution microCT images and micro-finite-element
379 analysis. The method gives macroscopic trabecular bone Young's modulus comparable to
380 experimental results. Microscopic mechanical properties of trabecular bone can be assessed by
381 an inverse approach based on the whole trabecular bone's mechanical response and micro-
382 finite-element analysis. The results obtained by this method support the hypothesis that
383 osteoporotic population trabecular bone tissue elasticity is comparable to those of healthy
384 population. However, it indicates that the yield stress of osteoporotic trabecular bone tissue is
385 lower compared to healthy cortical tissue. Consequently, micro-finite-element analysis can be
386 used as an additional method to classical histomorphometric analysis in order to characterize
387 bone quality by macroscopic and microscopic trabecular bone mechanical properties
388 identification. The framework presented in the current study is suitable to assess bone
389 biomechanical performance from patients with osteoarthritis or those undergoing treatment
390 with anti-resorptive agents.

391

392

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397 **Conflicts or disclosures**

398 Romain Rieger, Jean Charles Auregan and Thierry Hoc declare that they have no conflict of
399 interest.

400 **Figures legend**

401 Figure 1 : Schematic approach for the estimation of the trabecular bone microscopic and
402 mechanical properties using micro-finite-element methods. (a) Bone retrieval procedure and
403 imaging, (b) finite-element meshing and trabecular bone tissue linear elastic/ideally plastic
404 behaviour law definition, (c) experimental compressive test performed at the sample scale, and
405 (d) Finite element compressive test. E_s^{exp} : Experimental macroscopic Young's modulus ; E_s^{num} :
406 Numerical macroscopic Young's modulus ; σ_s^{exp} : Experimental macroscopic yield stress ;
407 σ_s^{num} : Numerical macroscopic yield stress ; Y_s : Macroscopic ultimate compressive stress ;
408 E_{Tr} : Trabecular bone tissue Young's modulus ; σ_{Tr} : Trabecular bone tissue yield stress.

409

410 Figure 2 : Finite element meshing process from microCT images in 8 bits format (256 grey
411 levels) performed on Avizio Fire®. (a) Smoothing using 3D median filter; (b) Segmentation by
412 defining a threshold; (c) 3D surface mesh generation (4.10^7 facets); (d) 3D surface mesh
413 simplification (400 000 facets); (e) 3D tetrahedral meshing (250 000 nodes and 800 000
414 elements).

415

416 Figure 3 : Evolution of the macroscopic mechanical parameters versus bone volume fraction
417 BV/TV . E_s^{exp} corresponds to the macroscopic Young's modulus and σ_s^{exp} to the yield stress.

418

419 Figure 4 : Macroscopic Young's modulus E_s from experimental test compared to the one
420 obtained from micro-finite-element analysis E_s^{num} with a default trabecular bone tissue Young's
421 modulus of 20 GPa.

422

423 Figure 5 : Evolution of macroscopic Young's modulus E_s^{num} versus bone volume fraction
424 BV/TV .

425

426 Figure 6 : Trabecular bone tissue Young's modulus E_{Tr} and yield stress σ_s obtained from
427 inverse micro-finite-element analysis.

428

429 **Légendes des figures**

430 Figure 1 : Schéma décrivant l'approche de détermination des propriétés mécaniques
431 microscopique et macroscopique à l'aide de la méthode des micro-éléments-finis. (a) Extraction
432 des échantillons osseux et imagerie, (b) maillage éléments-finis et loi de comportement linéaire
433 élastique/plastique parfait, (c) Essai de compression expérimentale sur l'échantillon, and (d)
434 Essai de compression par éléments-finis. E_s^{exp} : Module de young macroscopique expérimental ;
435 E_s^{num} : Module de young macroscopique numérique ; σ_s^{exp} : Limite d'élasticité macroscopique
436 expérimental ; σ_s^{num} : Limite d'élasticité macroscopique numérique ; Y_s : Contrainte limite

437 macroscopique en compression ; E_{Tr} : Module d'élasticité du tissu osseux trabéculaire ; σ_{Tr} :
438 Limite d'élasticité du tissu osseux trabéculaire.

439

440 Figure 2 : Maillage éléments finis obtenus par micro-tomographie aux rayons X au format 8 bits (256
441 niveaux de gris) réalisé à l'aide du logiciel Avizio Fire®. (a) Lissage à l'aide d'un filtre médian ; (b)
442 Segmentation par seuillage ; (c) Génération d'un maillage surfacique 3D ($4 \cdot 10^7$ faces) ; (d)
443 Simplification du maillage surfacique 3D (400 000 faces) ; (e) Maillage tétraédrique 3D (250 000 nœuds
444 and 800 000 éléments).

445

446 Figure 3 : Evolution des paramètres mécaniques macroscopiques en fonction de la fraction volumique
447 BV/TV . E_s^{exp} correspond au module d'élasticité macroscopique et σ_s^{exp} à la limite d'élasticité.

448

449 Figure 4 : Module d'élasticité macroscopique E_s obtenue lors de l'essai expérimental et comparé à
450 celui obtenu à l'aide de l'analyse par micro-éléments-finis E_s^{num} simulé avec un module d'élasticité
451 local de 20 GPa.

452

453 Figure 5 : Evolution du module d'élasticité macroscopique E_s^{num} en fonction de la fraction volumique
454 BV/TV .

455

456 Figure 6 : Module d'élasticité E_{Tr} et limite d'élasticité σ_s du tissu trabéculaire obtenu par la
457 méthode inverse d'analyse par micro-éléments-finis.

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459 References

460

- 461 [1] Chappard D, Baslé MF, Legrand E, Audran M. New laboratory tools in the assessment of
462 bone quality. *Osteoporos Int* 2011;22:2225–40. doi:10.1007/s00198-011-1573-6.
- 463 [2] Hernandez CJ, Keaveny T. A biomechanical perspective on bone quality. *Bone*
464 2006;39:1173–81. doi:10.1016/j.bone.2006.06.001.
- 465 [3] Bouxsein ML. Bone quality: where do we go from here? *Osteoporos Int* 2003;14:118–
466 27. doi:10.1007/s00198-003-1489-x.
- 467 [4] Cowin S. *Bone Mechanics Handbook*, Second Edition. CRC Press 2001.
468 [https://www.crcpress.com/Bone-Mechanics-Handbook-Second-](https://www.crcpress.com/Bone-Mechanics-Handbook-Second-Edition/Cowin/p/book/9780849391170)
469 [Edition/Cowin/p/book/9780849391170](https://www.crcpress.com/Bone-Mechanics-Handbook-Second-Edition/Cowin/p/book/9780849391170) (accessed January 25, 2017).
- 470 [5] Katz JL. The structure and biomechanics of bone. *Symp Soc Exp Biol* 1980;34:137–68.
- 471 [6] Hamed E, Jasiuk I, Yoo A, Lee Y, Litzka T. Multi-scale modelling of elastic moduli of
472 trabecular bone. *J R Soc Interface* 2012;9:1654–73. doi:10.1098/rsif.2011.0814.
- 473 [7] Currey JD. How Well Are Bones Designed to Resist Fracture? *J Bone Miner Res*
474 2003;18:591–8. doi:10.1359/jbmr.2003.18.4.591.
- 475 [8] Budyn É, Hoc T. Analysis of micro fracture in human Haversian cortical bone under
476 transverse tension using extended physical imaging. *Int J Numer Methods Eng*
477 2010;82:940–65. doi:10.1002/nme.2791.
- 478 [9] Budyno E, Hoc T. Multiple scale modeling for cortical bone fracture in tension using X-
479 FEM. *Eur J Comput Mech* 2007;16:213–36. doi:10.3166/remn.16.213-236.
- 480 [10] Rieger R, Hambli R, Jennane R. Modeling of biological doses and mechanical effects on
481 bone transduction. *J Theor Biol* 2011;274:36–42. doi:10.1016/j.jtbi.2011.01.003.
- 482 [11] Hambli R, Rieger R. Physiologically based mathematical model of transduction of
483 mechanobiological signals by osteocytes. *Biomech Model Mechanobiol* 2012;11:83–93.

- 484 doi:10.1007/s10237-011-0294-2.
- 485 [12] Stauber M, Müller R. Age-related changes in trabecular bone microstructures: global and
486 local morphometry. *Osteoporos Int* 2006;17:616–26. doi:10.1007/s00198-005-0025-6.
- 487 [13] Ding M, Hvid I. Quantification of age-related changes in the structure model type and
488 trabecular thickness of human tibial cancellous bone. *Bone* 2000;26:291–5.
489 doi:10.1016/S8756-3282(99)00281-1.
- 490 [14] Gibson LJ. Biomechanics of cellular solids. *J Biomech* 2005;38:377–99.
491 doi:10.1016/j.jbiomech.2004.09.027.
- 492 [15] Goldstein SA. The mechanical properties of trabecular bone: Dependence on anatomic
493 location and function. *J Biomech* 1987;20:1055–61. doi:10.1016/0021-9290(87)90023-
494 6.
- 495 [16] Choi K, Goldstein SA. A comparison of the fatigue behavior of human trabecular and
496 cortical bone tissue. *J Biomech* 1992;25:1371–81. doi:10.1016/0021-9290(92)90051-2.
- 497 [17] van Rietbergen B, Weinans H, Huiskes R, Odgaard A. A new method to determine
498 trabecular bone elastic properties and loading using micromechanical finite-element
499 models. *J Biomech* 1995;28:69–81. doi:10.1016/0021-9290(95)80008-5.
- 500 [18] Jacobs CR, Davis BR, Rieger CJ, Francis JJ, Saad M, Fyhrie DP. The impact of
501 boundary conditions and mesh size on the accuracy of cancellous bone tissue modulus
502 determination using large-scale finite-element modeling. *J Biomech* 1999;32:1159–64.
503 doi:10.1016/S0021-9290(99)00115-3.
- 504 [19] Keaveny TM, Pinilla TP, Crawford RP, Kopperdahl DL, Lou A. Systematic and random
505 errors in compression testing of trabecular bone. *J Orthop Res* 1997;15:101–10.
506 doi:10.1002/jor.1100150115.
- 507 [20] Chevalier Y, Pahr D, Allmer H, Charlebois M, Zysset P. Validation of a voxel-based FE
508 method for prediction of the uniaxial apparent modulus of human trabecular bone using
509 macroscopic mechanical tests and nanoindentation. *J Biomech* 2007;40:3333–40.
510 doi:10.1016/j.jbiomech.2007.05.004.
- 511 [21] Niebur GL, Feldstein MJ, Yuen JC, Chen TJ, Keaveny TM. High-resolution finite
512 element models with tissue strength asymmetry accurately predict failure of trabecular
513 bone. *J Biomech* 2000;33:1575–83. doi:10.1016/S0021-9290(00)00149-4.
- 514 [22] Bayraktar HH, Morgan EF, Niebur GL, Morris GE, Wong EK, Keaveny TM.
515 Comparison of the elastic and yield properties of human femoral trabecular and cortical
516 bone tissue. *J Biomech* 2004;37:27–35. doi:10.1016/S0021-9290(03)00257-4.
- 517 [23] Ciarelli TE, Fyhrie DP, Schaffler MB, Goldstein SA. Variations in Three-Dimensional
518 Cancellous Bone Architecture of the Proximal Femur in Female Hip Fractures and in
519 Controls. *J Bone Miner Res* 2000;15:32–40. doi:10.1359/jbmr.2000.15.1.32.
- 520 [24] Wolfram U, Wilke H-J, Zysset PK. Valid μ finite element models of vertebral trabecular
521 bone can be obtained using tissue properties measured with nanoindentation under wet
522 conditions. *J Biomech* 2010;43:1731–7. doi:10.1016/j.jbiomech.2010.02.026.
- 523 [25] Chappard C, Marchadier A, Benhamou CL. Side-to-side and within-side variability of
524 3D bone microarchitecture by conventional micro-computed tomography of paired iliac
525 crest biopsies. *Bone* 2008;43:203–8. doi:10.1016/j.bone.2008.02.019.
- 526 [26] Cruel M, Granke M, Bossier C, Audran M, Hoc T. Chronic alcohol abuse in men alters
527 bone mechanical properties by affecting both tissue mechanical properties and
528 microarchitectural parameters. *Morphologie* 2017;101:88–96.
529 doi:10.1016/j.morpho.2017.03.001.
- 530 [27] Hoc T, Henry L, Verdier M, Aubry D, Sedel L, Meunier A. Effect of microstructure on
531 the mechanical properties of Haversian cortical bone. *Bone* 2006;38:466–74.
532 doi:10.1016/j.bone.2005.09.017.
- 533 [28] Devulder A, Puel G, Bensidhoum M, Sedel L, Hoc T. Determination of the mechanical

- 534 behaviour of the human cortical bone using micro-extensometry technique. *Osteoporos*
535 *Int* 2010;21:1104–7. doi:10.1007/s00198-010-1175-8.
- 536 [29] Homminga J, McCreadie BR, Ciarelli TE, Weinans H, Goldstein SA, Huiskes R.
537 Cancellous bone mechanical properties from normals and patients with hip fractures
538 differ on the structure level, not on the bone hard tissue level. *Bone* 2002;30:759–64.
539 doi:10.1016/S8756-3282(02)00693-2.
- 540 [30] Zhang Z-M, Li Z-C, Jiang L-S, Jiang S-D, Dai L-Y. Micro-CT and mechanical
541 evaluation of subchondral trabecular bone structure between postmenopausal women
542 with osteoarthritis and osteoporosis. *Osteoporos Int* 2010;21:1383–90.
543 doi:10.1007/s00198-009-1071-2.
- 544 [31] Newitt DC, Majumdar S, Rietbergen B van, Ingersleben G von, Harris ST, Genant HK,
545 et al. In Vivo Assessment of Architecture and Micro-Finite Element Analysis Derived
546 Indices of Mechanical Properties of Trabecular Bone in the Radius. *Osteoporos Int*
547 2002;13:6–17. doi:10.1007/s198-002-8332-0.
- 548 [32] Morgan EF, Keaveny TM. Dependence of yield strain of human trabecular bone on
549 anatomic site. *J Biomech* 2001;34:569–77. doi:10.1016/S0021-9290(01)00011-2.
- 550 [33] Öhman C, Baleani M, Perilli E, Dall’Ara E, Tassani S, Baruffaldi F, et al. Mechanical
551 testing of cancellous bone from the femoral head: Experimental errors due to off-axis
552 measurements. *J Biomech* 2007;40:2426–33. doi:10.1016/j.jbiomech.2006.11.020.
- 553 [34] Harrison NM, McDonnell PF, O’Mahoney DC, Kennedy OD, O’Brien FJ, McHugh PE.
554 Heterogeneous linear elastic trabecular bone modelling using micro-CT attenuation data
555 and experimentally measured heterogeneous tissue properties. *J Biomech* 2008;41:2589–
556 96. doi:10.1016/j.jbiomech.2008.05.014.
- 557 [35] van der Linden JC, Birkenhäger-Frenkel DH, Verhaar JAN, Weinans H. Trabecular
558 bone’s mechanical properties are affected by its non-uniform mineral distribution. *J*
559 *Biomech* 2001;34:1573–80. doi:10.1016/S0021-9290(01)00146-4.
- 560 [36] Jaasma MJ, Bayraktar HH, Niebur GL, Keaveny TM. Biomechanical effects of
561 intraspecimen variations in tissue modulus for trabecular bone. *J Biomech* 2002;35:237–
562 46. doi:10.1016/S0021-9290(01)00193-2.
- 563 [37] Renders GAP, Mulder L, Langenbach GEJ, van Ruijven LJ, van Eijden TMGJ.
564 Biomechanical effect of mineral heterogeneity in trabecular bone. *J Biomech*
565 2008;41:2793–8. doi:10.1016/j.jbiomech.2008.07.009.
- 566 [38] Renders GAP, Mulder L, van Ruijven LJ, Langenbach GEJ, van Eijden TMGJ. Mineral
567 heterogeneity affects predictions of intratrabecular stress and strain. *J Biomech*
568 2011;44:402–7. doi:10.1016/j.jbiomech.2010.10.004.
- 569 [39] Gross T, Pahr DH, Peyrin F, Zysset PK. Mineral heterogeneity has a minor influence on
570 the apparent elastic properties of human cancellous bone: a SR μ CT-based finite element
571 study. *Comput Methods Biomech Biomed Engin* 2012;15:1137–44.
572 doi:10.1080/10255842.2011.581236.
- 573 [40] Hou FJ, Lang SM, Hoshaw SJ, Reimann DA, Fyhrie DP. Human vertebral body apparent
574 and hard tissue stiffness. *J Biomech* 1998;31:1009–15. doi:10.1016/S0021-
575 9290(98)00110-9.
- 576 [41] Ladd AJC, Kinney JH, Haupt DL, Goldstein SA. Finite-element modeling of trabecular
577 bone: Comparison with mechanical testing and determination of tissue modulus. *J*
578 *Orthop Res* 1998;16:622–8. doi:10.1002/jor.1100160516.
- 579 [42] Pahr DH, Zysset PK. Influence of boundary conditions on computed apparent elastic
580 properties of cancellous bone. *Biomech Model Mechanobiol* 2008;7:463–76.
581 doi:10.1007/s10237-007-0109-7.
- 582 [43] Bevill G, Eswaran SK, Farahmand F, Keaveny TM. The influence of boundary
583 conditions and loading mode on high-resolution finite element-computed trabecular

- 584 tissue properties. *Bone* 2009;44:573–8. doi:10.1016/j.bone.2008.11.015.
- 585 [44] Tassani S, Korfiatis V, Matsopoulos GK. Influence of segmentation on micro-CT images
586 of trabecular bone. *J Microsc* 2014;256:75–81. doi:10.1111/jmi.12159.
- 587 [45] Turner CH, Rho J, Takano Y, Tsui TY, Pharr GM. The elastic properties of trabecular and
588 cortical bone tissues are similar: results from two microscopic measurement techniques.
589 *J Biomech* 1999;32:437–41. doi:10.1016/S0021-9290(98)00177-8.
- 590 [46] Rho JY, Zioupos P, Currey JD, Pharr GM. Microstructural elasticity and regional
591 heterogeneity in human femoral bone of various ages examined by nano-indentation. *J*
592 *Biomech* 2002;35:189–98. doi:10.1016/S0021-9290(01)00199-3.
- 593 [47] Burstein AH, Reilly DT, Martens M. Aging of bone tissue: mechanical properties. *J*
594 *Bone Jt Surg - Ser A* 1976;58:82–6.

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