

1 **Evaluation of the capability of the simulated dual energy X-ray**
2 **absorptiometry-based two-dimensional finite element models for**
3 **predicting vertebral failure loads**

4
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33 **Abstract**

34
35 Prediction of the vertebral failure load is of great importance for the prevention and early
36 treatment of bone fracture. However, an efficient and effective method for accurately
37 predicting the failure load of vertebral bones is still lacking. The aim of the present study
38 was to evaluate the capability of the simulated dual energy X-ray absorptiometry (DXA)-
39 based finite element (FE) model for predicting vertebral failure loads.

40 Thirteen dissected spinal segments (T11/T12/L1) were scanned using a HR-pQCT
41 scanner and then were mechanically tested until failure. The subject-specific three-
42 dimensional (3D) and two-dimensional (2D) FE models of T12 were generated from the
43 HR-pQCT scanner and the simulated DXA images, respectively. Additionally, the areal
44 bone mineral density (aBMD) and areal bone mineral content (aBMC) of T12 were
45 calculated. The failure loads predicted by the simulated DXA-based 2D FE models were
46 more moderately correlated with the experimental failure loads ($R^2 = 0.66$) than the aBMC
47 ($R^2 = 0.61$) and aBMD ($R^2 = 0.56$). The 2D FE models were slightly outperformed by the
48 HR-pQCT-based 3D FE models ($R^2 = 0.71$). The present study demonstrated that the
49 simulated DXA-based 2D FE model has better capability for predicting the vertebral
50 failure loads than the densitometric measurements but is outperformed by the 3D FE
51 model. The 2D FE model is more suitable for clinical use due to the low radiation dose
52 and low cost, but it remains to be validated by further *in vitro* and *in vivo* studies.

53
54 **Keywords:** Vertebral failure; finite element analysis; DXA; prediction capability; BMD

55

56 **1. Introduction**

57 Vertebral fracture is a major clinical problem associated with low back pain and
58 impaired quality of life [1]. Assessing the failure loads of vertebral bones is of great
59 importance for the prevention and early treatment of bone fracture. Vertebral fractures in
60 elderly people are strongly related to osteoporosis, which leads to the loss of bone mass
61 and the deterioration of bone microarchitecture [2]. Currently, monitoring of the changes
62 in the bone densitometric parameters such as bone mineral density (BMD) is the most
63 important clinical approach for assessing the risk of bone fracture. The commonly used
64 BMD measurements include the areal bone mineral density (aBMD) measured by dual
65 energy X-ray absorptiometry (DXA) and the volumetric bone mineral density (vBMD)
66 measured by quantitative computed tomography (QCT). However, QCT cannot be
67 performed routinely due to its high radiation dose [3]. In addition, only approximately 50%
68 of the variability in the vertebral failure load can be predicted by these BMD
69 measurements, which cannot provide information about bone microarchitecture and BMD
70 distribution [4 - 6]. By contrast, DXA can be used routinely and frequently because of its
71 low radiation dose and low cost [7]. However, the aBMD obtained from DXA does not
72 contain information about the material microarchitecture or any mechanical properties of
73 the bone tissues. Therefore, it is necessary to develop advanced DXA-based techniques
74 for the accurate prediction of bone failure loads that can be easily transferred into routine
75 clinical use [3, 8].

76 In recent years, the use of subject-specific finite element (FE) models to predict
77 vertebral failure loads has attracted increasing attention, because the FE models account
78 for the vertebral geometry, the BMD distribution and the mechanical properties of bone
79 tissues [9 - 12]. Three-dimensional (3D) FE models have been demonstrated to be more
80 reliable for predicting vertebral failure loads than aBMD [13] and vBMD [14]. However,
81 it is very challenging to apply the subject-specific 3D FE models in clinical use due to the
82 invasive QCT imaging and the complexity of 3D image segmentation that are required to
83 construct the 3D FE models, and the high cost of performing the 3D FE simulations.
84 Because of the low radiation dose and low cost associated with DXA scans and the high

85 efficiency of the construction of 2D FE models, DXA-based two-dimensional (2D) FE
86 models have the potential for application in clinical use as an efficient tool to predict
87 vertebral failure loads. However, no previous studies have evaluated the capability of the
88 DXA-based 2D FE models for predicting the vertebral fracture risk.

89 The aim of the present study was to assess the capability of the simulated DXA-based
90 2D FE model for predicting vertebral failure loads by comparing its predictions with
91 experimentally measured failure loads and by comparing its predictive power with those
92 of the methods based on bone densitometric measurements and the quantitative computed
93 tomography (QCT)-based 3D FE model.

94

95 **2. Materials and methods**

96 **2.1. Specimen preparation, HR-pQCT imaging and mechanical testing**

97 To validate the predictions of the simulated DXA-based 2D FE models, spinal
98 segments were harvested, dissected, imaged and mechanically tested until failure. The
99 detailed procedures of the dissection, HR-pQCT imaging and mechanical testing of the
100 vertebral specimens are described in previous studies [6, 9]. Briefly, thirteen T11/T12/L1
101 spinal segments, which did not have any fracture or osteophytes, were harvested from
102 postmenopausal female donors (mean age of 79.9 ± 7.9 years). The segments were
103 scanned while frozen using a HR-pQCT scanner (XtremeCT, Scanco Medical AG,
104 Bruettisellen, Switzerland) with an isotropic voxel size of $82.0 \times 82.0 \times 82.0 \mu\text{m}^3$. The
105 spinal facet joints were removed to allow for the loading transferred only through the
106 vertebral bodies and failures of T11 and L1 were avoided by replacing all of the cancellous
107 bones in T11 and L1 with polymethylmethacrylate (PMMA) (see **Fig. 1** in [6]). The
108 specimens were embedded in the metal cups with the application of a fixation frame to
109 ensure that the mid-transverse planes of T12 were horizontal and in the neutral posture
110 (no bending) [9, 15]. Then, the embedded specimens were mounted on the material testing
111 machine (**Fig. 1e**). Failure loads of the T12 bodies were obtained using the loading
112 scenario of a quasi-static compression via the intervertebral discs (IVD). The
113 experimentally measured failure loads of T12 were used as the reference for validating

114 the predictions from the simulated DXA-based 2D FE models.

115 **2.2. Finite element analysis and calculation of bone failure load**

116 The 2D FE models, including the T12 vertebra and the adjacent IVDs, were created
117 by converting each pixel in the simulated DXA images into a 2D 4-node plane stress
118 element (PLANE182). The following steps were used to obtain the simulated DXA images.
119 First, the HR-pQCT image data of each T12 vertebral body were rotated to align the spinal
120 cranio-caudal and anterior-posterior axes along the Z- and Y-axes, respectively. The image
121 voxel size was then coarsened to $1.002 \times 1.002 \times 1.002 \text{ mm}^3$ in order to match the resolution
122 of a clinical lumbar DXA scan. Simulated DXA images were then obtained by projecting
123 the 3D images onto the frontal plane of T12 (i.e., along the spinal anterior-posterior
124 direction) (**Fig. 1a**). All of these image processing steps were performed using Amira
125 (v5.4.3, FEI Visualization Sciences Group, France).

126 In the simulated DXA-based 2D FE models, heterogeneous material properties were
127 defined for T12 using the following two steps. First, the grayscale image datasets were
128 smoothed using a Gaussian filter (sigma = 1.2, support = 2.0) to reduce the influence of
129 image noise. Second, the image grayscale values were converted into vBMD values based
130 on the linear calibration equation provided by the HR-pQCT scanner. The vBMD values
131 were further converted into bone ash density according to the relationship reported in the
132 literature [16]. After matching the phantom type and anatomic site, the relationship of
133 $\rho_{ash} = 0.877 \times \rho_{HA} + 0.079$ (ρ_{HA} is the HA-equivalent vBMD) was chosen. It should
134 be noted that if clinical DXA images and aBMD values were available, the vBMD values
135 could be obtained by dividing the aBMD by the subject-specific constant thickness [3].

136 Young's modulus of each bone element was calculated from the bone ash density
137 based on the exponential density-modulus relationship reported in the literature [16].
138 Considering that some image pixels may have artificially high grayscale values that could
139 lead to unrealistically high bone densities, an upper threshold value of 1200.00 mg/cm^3 ,
140 which is the maximum bone ash density value [16], was defined in the density-modulus
141 relationship [17]. On the other hand, a lower threshold value of the bone ash density of
142 400.00 mg/cm^3 was adopted in the density-modulus relationship to avoid the

143 unrealistically low moduli in the FE models. Young's moduli for the elements with the
 144 bone ash density lower than 400.00 mg/cm³ were set to 0.0104 MPa [17]. In summary,
 145 after matching the anatomic site (i.e., vertebra), the following exponential density-
 146 modulus relationship was used in the present study [18]:

$$147 \quad E = \begin{cases} 0.0104 & \rho_{ash} < 400 \\ a \times \rho_{ash}^b & 400 \leq \rho_{ash} \leq 1200 \\ a \times 1200^b & \rho_{ash} > 1200 \end{cases} \quad (1)$$

148 where a and b are constants (a = 0.1127, b = 1.746 in the present study), *E* is Young's
 149 modulus (MPa) and ρ_{ash} is the bone ash density (mg/cm³).

150 Poisson's ratio for the bone elements was set to 0.30. The material with the bone ash
 151 density lower than 400 mg/cm³ was regarded as bone marrow, and the corresponding
 152 Poisson's ratio was set to 0.49 [14]. The heterogeneous FE models were generated by
 153 mapping the elastic modulus calculated at each image pixel onto the FE mesh using an in-
 154 house developed MATLAB (R2017a, MathWorks, Natick, Massachusetts, U.S.A.) code
 155 [19].

156 The intervertebral discs were added into the 2D FE T12 models in order to enable
 157 the definition of consistent loading condition in the models (Fig. 1b). The IVDs in the 2D
 158 FE models were simplified as one material and no differentiation of the nucleus pulposus
 159 and annulus fibers was made in the 2D IVD models. An incompressible isotropic Mooney-
 160 Rivlin material model was used to describe the mechanical behavior of the 2D IVDs, with
 161 C_{10} , C_{01} and D were set to 0.10 MPa, 2.50 MPa and 0.30 MPa⁻¹, respectively [20]. The
 162 thickness of the IVDs was based on the average thickness of human IVDs, i.e., it was
 163 approximately 8.00 mm. The FE meshes of IVDs were created by converting each image
 164 pixel into PLANE182, and thus the IVDs were fully bounded with T12 at the interface. A
 165 mesh convergence study was performed by refining the PLANE182 elements until the
 166 predictions (failure loads) were not affected by the mesh size, resulting in approximately
 167 5,128 elements per 2D FE spinal model. In the 2D FE models, a uniform displacement of
 168 2.00 mm was applied on the topmost layer of the IVD, while all degrees of freedom were
 169 fixed for the nodes in the bottom layer. This boundary condition was defined because it
 170 can be easily applied and transferred into clinical use.

171 The failure load of T12 vertebra predicted from the simulated DXA-based 2D FE
172 models was defined as the load under which at least 5% of the bone elements in the 2D
173 model experience stress/strain that exceeds the failure threshold [21]. Because there is
174 currently still no consensus on which failure criterion should be used for bone tissues, and
175 to investigate the influence of the failure criterion on the 2D FE predictions, four different
176 failure criteria were considered in the present study including the principal stress, the
177 principal strain, the von Mises stress and the von Mises strain. The yield stresses in each
178 bone element were related to Young's modulus using the empirical linear equations [22]:

$$179 \quad S_t = 0.0039 \times E + 0.33 \quad (2)$$

$$180 \quad S_c = 0.0062 \times E - 0.41 \quad (3)$$

181 where S_t is the tensile yield stress (MPa), S_c is the compressive yield stress (MPa) and E
182 is Young's modulus (MPa).

183 The von Mises yield stress for bone tissues was defined as the average value of the
184 tensile and compressive yield stresses. The tensile and compressive yield strains for bone
185 tissues were set to 7300.00 $\mu\epsilon$ and 10400.00 $\mu\epsilon$, respectively [22]. The von Mises yield
186 strain was set to the average value of the tensile and compressive yield strains.

187 To investigate the influence of the failure criterion on the fracture initiation, the
188 failure ratios in the 2D FE models were calculated using different failure criteria. The
189 failure ratio using the failure criteria of principal stress (or strain) was defined as the
190 larger value of the ratio of tensile stress (or strain) to tensile yield stress (or strain) and
191 the ratio of compressive stress (or strain) to compressive yield stress (or strain), while
192 the failure ratio using the failure criterion of von Mises stress (or strain) was defined as
193 the ratio of the von Mises stress (or strain) to the von Mises yield stress (or strain). The
194 region in the 2D model where the highest failure ratio occurred was considered the
195 fracture initiation region. All of the DXA-based 2D linear FE models were solved using
196 Ansys (Release 15.0, ANSYS, Inc., Canonsburg, PA, U.S.A).

197 The capability of the simulated DXA-based 2D FE models for predicting vertebral
198 failure loads was assessed by comparing their prediction with those of the corresponding
199 3D FE models (Fig. 1c). The calculation of the failure loads of T12 from the 3D FE models

200 was performed as described in a previous study [9]. Briefly, the 3D FE models, including
201 the T12 vertebral body and two adjacent IVDs, were generated from the HR-pQCT images.
202 Quadratic wedge (C3D15) elements were defined for the cortex, and quadratic tetrahedral
203 elements (C3D10) were defined for the trabecular bone and the IVD. A mesh convergence
204 study was performed to ensure that the predicted failure loads were not affected by the
205 mesh size, resulting approximately 35,874 elements per 3D FE spinal model. The
206 anisotropic elastic-plastic-damage model [23] was used to simulate the mechanical
207 behavior of bone elements until failure. The Mooney-Rivlin model was defined for the
208 nucleus pulposus, and the fiber-reinforced hyperelastic model was chosen for the annulus
209 fibrosus. The *in vitro* loading scenario was simulated, i.e., the bottom nodes from the
210 inferior IVD were fully constrained, and the loading condition of a 4° forward bending
211 followed by an axial displacement of 4.0 mm was applied on the cranial nodes of the
212 superior IVD. The failure loads of T12 were computed from the 3D FE models as the
213 maximal force obtained from the nonlinear FE analyses.

214 **2.3. Measurements of bone densitometric parameters**

215 The predictive power of the simulated DXA-based T12 FE model was compared to
216 that of the aBMD and areal bone mineral content (aBMC) of T12. The aBMD and aBMC
217 of T12 were calculated from the simulated DXA images (i.e., the projected images from
218 the HR-pQCT) (Fig. 1d). To calculate the aBMD and aBMC of T12, the simulated DXA
219 images were first smoothed using a Gaussian filter (convolution kernel = [3 3 3], standard
220 deviation = 0.65) to reduce the influence of image noise. Then, the grayscale images were
221 binarized using a threshold that was equal to 25.5% of the maximal grayscale value [24],
222 and bone masks (regions occupied by bone voxels) were defined in the binary images.
223 The image threshold values applied were equivalent to an average BMD of 433.00 ± 14.00
224 mg HA/cm^3 (range from $401.00 \text{ mg HA/cm}^3$ to $447.00 \text{ mg HA/cm}^3$) and corresponded to
225 the valley region between the two peaks in the BMD histograms. All of the segmentations
226 were visually evaluated to ensure the proper application of the threshold values selected.
227 Then, the HA-equivalent volumetric BMD (vBMD) values in the bone voxels (bone mask
228 regions) were calculated from the CT grayscale values using the calibration law provided

229 by the manufacturer of the HR-pQCT scanner. The HR-pQCT scanner was calibrated
230 weekly using the phantom provided by the manufacturer. The bone minerals in each bone
231 pixel were calculated from the corresponding vBMD by multiplying the vBMD by the
232 volume of the image voxel, i.e., $1.002 \times 1.002 \times 1.002 \text{ mm}^3$. Then, the aBMC of T12 was
233 calculated as the total bone minerals over the masked bone regions, and the aBMD of T12
234 was obtained by dividing the aBMC of T12 by the total area of T12.

235 **2.4. Statistical analysis**

236 The normal distribution of the parameters was evaluated by the Shapiro-Wilk test and
237 by visually inspecting the normal probability plots. If a normal distribution was fulfilled,
238 the Pearson's correlation coefficients (r) were calculated to quantify the correlations
239 among the failure loads predicted by the DXA-based 2D FE models using different failure
240 criteria. Regression equations, coefficients of determination (R^2) and root mean squared
241 errors (RMS) were computed to determine the linear correlations between the
242 experimentally measured vertebral failure loads and the prediction from the simulated
243 DXA-based 2D FE models, and between the 2D and 3D FE models. Statistical analyses
244 were performed using MATLAB. The probability of type I error was set as $\alpha = 0.05$,
245 i.e., $p < 0.05$ was considered to be statistically significant.

246

247 **3. Results**

248 The mean \pm standard deviation (SD) values of the failure loads of T12 predicted by
249 the simulated DXA-based 2D FE models using the failure criteria of principal stress, von
250 Mises stress, principal strain and von Mises strain were $540.00 \pm 144.00 \text{ N}$, $460.00 \pm$
251 120.00 N , $952.00 \pm 249.00 \text{ N}$ and $792.00 \pm 201.00 \text{ N}$, respectively. The vertebral failure
252 loads predicted by the simulated DXA-based 2D FE models using different failure criteria
253 were highly correlated with each other, and the Pearson's correlation coefficients (r) were
254 all significant (all $r > 0.99$, $p < 0.001$) (**Table 1**). The distributions of the failure ratios and
255 the fracture initiation regions calculated using different failure criteria were similar (**Fig.**
256 **2**). Therefore, in the following analysis, only the results from the failure criteria of the

257 principal strain are reported.

258 Linear correlations of the experimentally measured failure loads of T12 (F_{Exp}) with
259 the aBMD, the aBMC and the failure loads predicted by the simulated DXA-based 2D FE
260 models (DXA_{FE}) were all significant ($p < 0.005$). The failure loads predicted by the
261 DXA-based 2D FE models (DXA_{FE}) were more moderately correlated with the
262 experimental failure loads ($R^2 = 0.66$) than the aBMD ($R^2 = 0.56$) and the aBMC ($R^2 =$
263 0.61) (**Fig. 3 and Fig. 4a**). The DXA-based 2D FE models were slightly outperformed by
264 the HR-pQCT-based 3D FE models ($R^2 = 0.71$ for the correlation with the experimental
265 data). Moderate correlations were found between the failure loads predicted by the DXA-
266 based 2D FE models and the HR-pQCT-based 3D FE models ($HR-pQCT_{FE}$) ($R^2 = 0.70$,
267 $p < 0.001$) (**Fig. 4b**). Compared to the experimentally measured failure loads (2.09 ± 0.48
268 kN), the failure loads of T12 predicted by the FE models were 74% lower in the DXA-
269 based 2D FE models (0.54 ± 0.14 kN, $p < 0.001$) and 12% lower in HR-pQCT-based 3D
270 FE models (1.84 ± 0.47 kN, $p < 0.001$).

271 Using a computer with an i7 processor and 8G RAM, it typically took less than
272 15 minutes to perform the DXA-based 2D FE simulation, while the segmentation and
273 simulation of the HR-pQCT-based 3D FE model required approximately 420 minutes
274 (each calculation took approximately 190 minutes). The number of degrees of freedom
275 was approximately 10,848 for the DXA-based 2D FE models and approximately 194,467
276 for the HR-pQCT-based 3D FE models.

277

278 **4. Discussion**

279 The goal of the present study was to assess the capability of a simulated DXA-based
280 2D FE model for predicting the vertebral failure loads by comparing its predictions with
281 the experimentally measured vertebral failure loads and by comparing its predictive power
282 with the predictive powers of the vertebral densitometric measurements and of the HR-
283 pQCT-based 3D FE model. It was demonstrated that the simulated DXA-based 2D FE
284 models are more reliable for predicting the failure loads of T12 ($R^2 = 0.66$) than the
285 densitometric measurements including the aBMD ($R^2 = 0.56$) and the aBMC ($R^2 = 0.61$)

286 that are currently used in clinical practice. Although the 2D FE models are outperformed
287 by the HR-pQCT-based 3D FE models ($R^2 = 0.71$) in predicting the failure loads of T12
288 [9], the 3D approach requires the use of a high radiation dose and the construction of the
289 3D FE models has a high computational cost. By contrast, the DXA-based 2D FE
290 modeling approach is highly efficient (requiring only a few minutes to run the simulation),
291 requires the use of only a low radiation dose and has a low cost, making it more suitable
292 for clinical use.

293 The present study is an extension of our previous study [9], in which it was found
294 that up to 71% of the variability in the vertebral failure loads can be predicted using the
295 HR-pQCT-based 3D FE models including the T12 vertebral body and the adjacent
296 intervertebral discs [9]. However, the main issue associated with the 3D models is the
297 need for a high radiation dose and the long time that is normally needed to create and
298 solve the 3D FE models, which pose considerable challenges for making the 3D modeling
299 approach readily available in clinical use. Therefore, an efficient 2D FE modeling
300 approach based on the simulated DXA images was developed in the present study. It
301 should be noted that only a moderate correlation ($R^2 = 0.70$) was found between the
302 simulated DXA-based 2D models and the HR-pQCT-based 3D FE models, implying that
303 the 3D FE models contain some additional information that contributes to the 5% increase
304 (Fig. 4a) in the prediction accuracy of vertebral failure loads.

305 It was demonstrated that the failure loads predicted by the simulated DXA-based 2D
306 FE models are more moderately correlated with the experimentally measured failure loads
307 than the densitometric measurements (aBMD and aBMC). This finding may be because
308 the biomechanical features of T12 (including the heterogeneous mechanical properties,
309 geometry and boundary conditions, etc.) that are important for the prediction of failure
310 loads can be reflected in the 2D FE models to some extent [25]. By contrast, the
311 densitometric measurements only contain the information regarding the average bone
312 mineral density and bone mass and are not directly related to the mechanical behavior of
313 the bones. Therefore, densitometric measurements have limited capability for predicting
314 bone failure loads. The fact that the failure load is more moderately correlated with the

315 aBMC than with the aBMD may be because the bone failure load is a non-normalized
316 parameter and can be influenced by the bone dimension. It should be noted that in addition
317 to the 2D FE model, the trabecular bone score (TBS) can also be derived from the DXA
318 images. TBS is a texture index and can provide information that is complementary to the
319 information provided by BMD, motivating many investigations of its predictive capability
320 in the recent years [26, 27]. Indeed, numerous studies have shown that lower TBS values
321 are associated with increased risk for major osteoporotic fracture [26]. However, our
322 previous study showed that the TBS is a poor surrogate for vertebral strength [27],
323 suggesting that further research on the relationship between TBS and vertebral strength is
324 necessary.

325 It should be noted that although several bone material models have been developed
326 previously, there is still no consensus regarding which model can best describe the
327 mechanical behavior of bone. Zysset et al. has developed a complex anisotropic elastic-
328 plastic-damage model [23] to simulate the mechanical behavior of human vertebrae [28,
329 29]. On the other hand, Viceconti et al. has predicted the ultimate loads of the bone based
330 on a linear elastic material model [3, 30, 31]. In the 2D FE models developed in the present
331 study, Viceconti's approach is adopted. However, it is unclear which failure criterion
332 should be used to accurately predict the bone failure loads. In previous studies [3, 31, 32],
333 the failure criteria of the principal stress, principal strain, von Mises stress and von Mises
334 strain were all widely used. Therefore, these four failure criteria were assessed in the 2D
335 FE models developed in the present study. It was found that the failure loads predicted by
336 the DXA-based 2D FE models using different failure criteria are strongly correlated with
337 each other, demonstrating that adoption of different failure criteria has a minimal influence
338 on the results of the 2D FE models.

339 Several limitations of the present study need to be noted. First, the DXA-based 2D
340 FE models are generated from the simulated DXA images, i.e., the 2D coarsened
341 projections of the HR-pQCT images. The reasons for using the simulated DXA images
342 are that the image datasets from our previous studies are used making it possible to
343 validate the model and make comparisons with 3D models using these data. It should be

344 noted that in the present study, the vertebral posterior elements and surrounding tissues
345 (ribs, etc.) were removed when projecting the HR-pQCT images, and consequently, the
346 simulated DXA represents the best case condition for DXA imaging, which is expected to
347 have lower quality in the clinical practice. Although the quality of the simulated DXA
348 images was compared with the quality of the clinical images and it was found that aBMD
349 can be simulated from HR-pQCT images of the distal radius [33], the comparison using
350 the spinal segment has not been performed and furthermore, the results of the FE models
351 obtained from the simulated and clinical spinal DXA images have not been evaluated.
352 Therefore, in the future, the methodology developed in the present study should be
353 validated directly using the clinical DXA scans. Second, the nonlinear behavior of bone
354 prior to failure is not considered in the DXA-based 2D FE models. However, experimental
355 data showed that bone is a brittle material [34] and plastic behavior has a minimal effect
356 on the calculation of bone failure loads. Third, the sample size used in the present study
357 is small ($N = 13$), and the bone samples are obtained only from old female donors (mean
358 age of 79.9 ± 7.9 years), which may hinder the application of these findings to a wider
359 range of vertebral bones in different conditions, in particular to younger individuals with
360 higher BMD values. However, it is very challenging to harvest a sufficient number of
361 vertebral specimens from young donors.

362 The present study is the first to assess the capability of simulated DXA-based 2D FE
363 models for predicting the compressive failure loads of vertebral bodies. In conclusion, the
364 present study showed that the simulated DXA-based 2D FE model is a better predictor
365 than the densitometric measurements for predicting the compressive failure loads of
366 vertebral bodies in elderly women with osteoporosis. Although the 2D FE model is not as
367 capable as the 3D FE model for predicting the vertebral failure loads, the construction of
368 the 2D model requires a markedly shorter period, less expertise and a much shorter
369 computational time. Additionally, the DXA scan requires the use of a low radiation dose
370 and incurs a low cost. However, only simulated DXA images were used in the present
371 study, and this approach remains to be further validated for clinical applications by
372 evaluating its performance *in vitro* and *in vivo* directly using clinical DXA images.

373

374 **Conflict of interest**

375 The authors declare there is no conflict of interest

376

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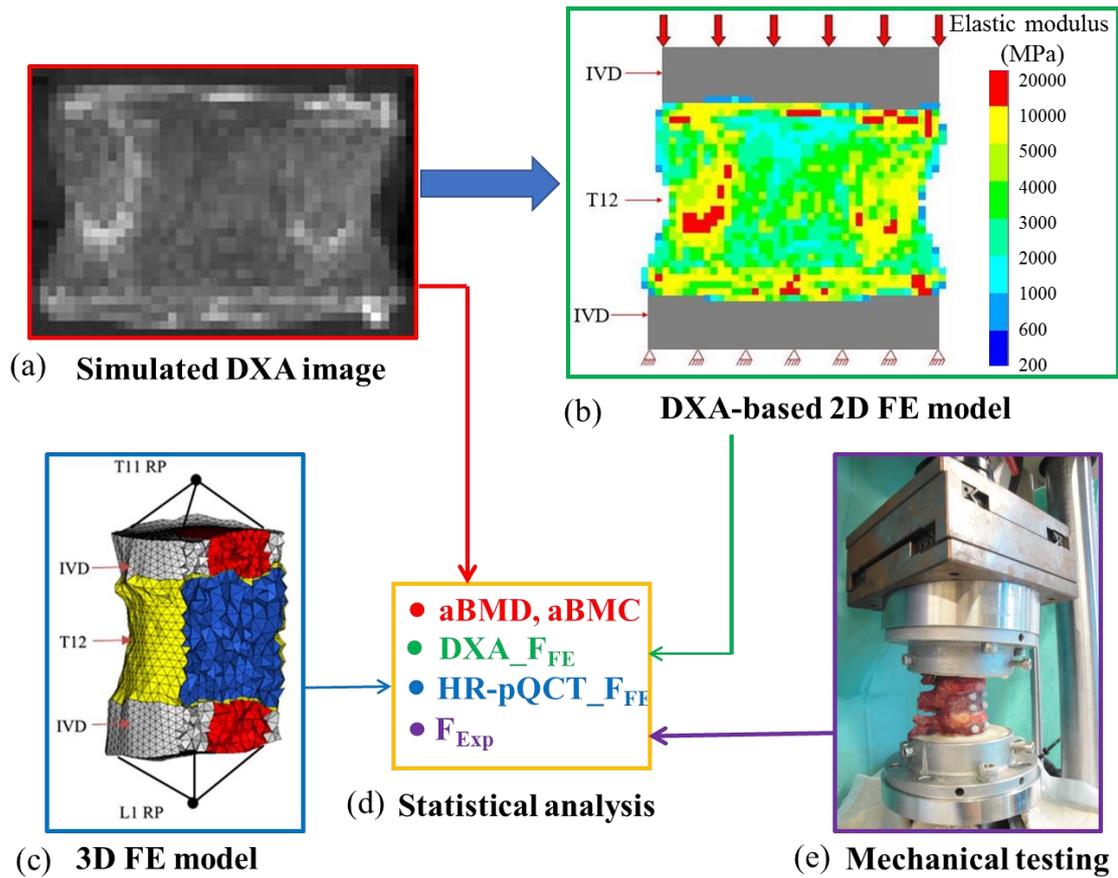
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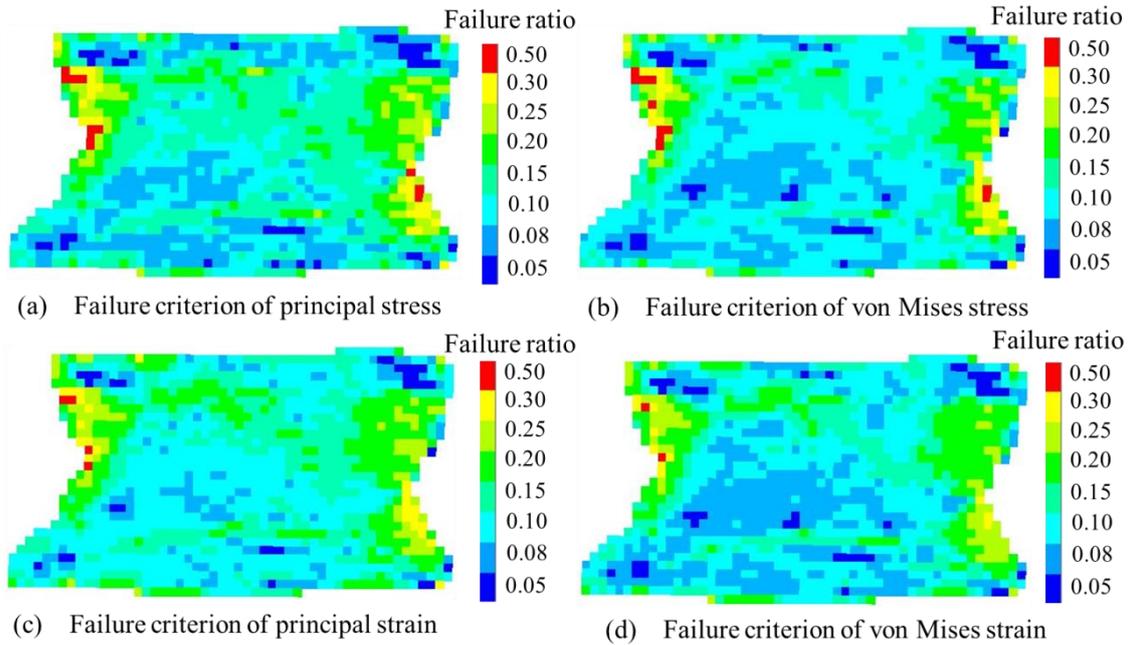
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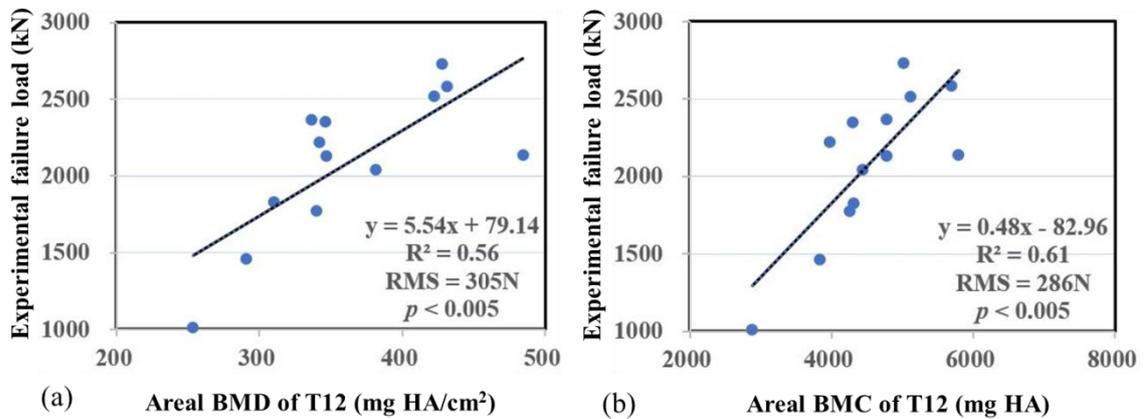
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Fig. 1. Overview of the methods used in the present study: (a) aBMD and aBMC were calculated from the simulated DXA images of T12; (b) and (c) the simulated DXA-based 2D and the HR-pQCT-based 3D FE models were generated; (d) and (e) thirteen spinal segments (T11/T12/L1) were mechanically tested until failure (F_{Exp}) and statistical analysis was performed on these parameters.



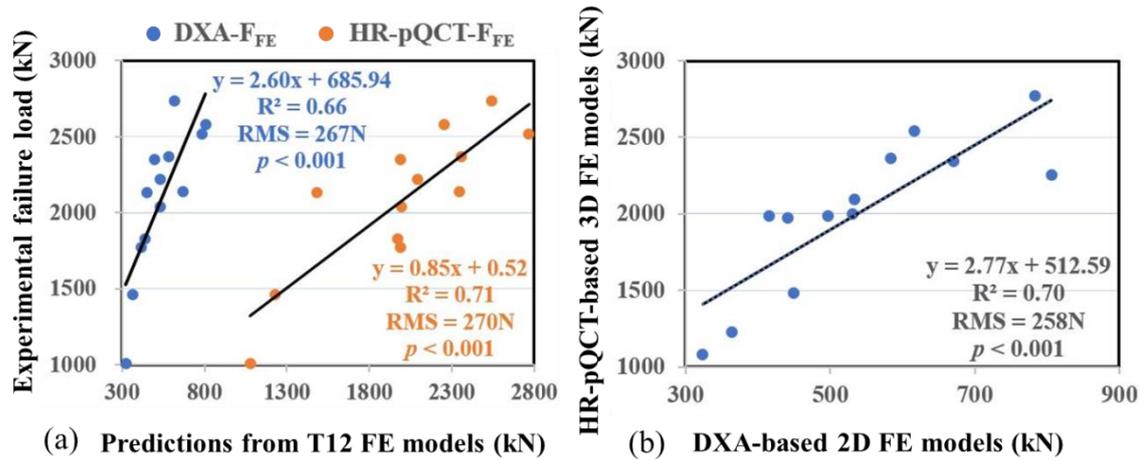
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Fig. 2. Distribution of the failure ratios in the simulated DXA-based 2D FE models using different failure criteria: (a) principal stress, (b) von Mises stress, (c) principal strain and (d) von Mises strain.



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Fig. 3. Linear regressions of the experimentally measured failure loads of T12 as a function of (a) the aBMD of T12 and (b) the aBMC of T12.



508

509 **Fig. 4.** (a) Linear regression of the experimentally measured failure loads of T12 as a
 510 function of the failure loads predicted by the FE models and (b) linear correlation between
 511 the failure loads of T12 predicted by the HR-pQCT-based 3D FE models (HR-pQCT-F_{FE})
 512 and the simulated DXA-based 2D FE models (DXA-F_{FE}).

513

514 **Table 1.** Pearson's correlation coefficients (*r*) among the failure loads of T12 predicted
 515 by the simulated DXA-based 2D FE models using different failure criteria (*p* < 0.001)

	Principal stress	von Mises stress	Principal strain	von Mises strain
Principal stress	-	-		
von Mises stress	0.999	-		
Principal strain	0.999	0.999	-	
von Mises strain	0.997	0.995	0.995	-

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