

# 1 **Femoral Fracture Type can be Predicted from Femoral Structure:**

## 2 **A Finite Element Study validated by Digital Volume Correlation Experiments.**

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18

19 **ABSTRACT**

20 Proximal femoral fractures can be categorised into two main types: neck and intertrochanteric  
21 fractures accounting for 53% and 43% of all proximal femoral fractures, respectively. The  
22 possibility to predict the type of fracture a specific patient is predisposed to would allow drug and  
23 exercise therapies, hip protector design and prophylactic surgery to be better targeted for this  
24 patient rendering fracture preventing strategies more effective. This study hypothesized that the  
25 type of fracture is closely related to the patient-specific femoral structure and predictable by finite  
26 element (FE) methods. Fourteen femora were DXA scanned, CT scanned and mechanically tested  
27 to fracture. FE-predicted fracture patterns were compared to experimentally observed fracture  
28 patterns. Measurements of strain patterns to explain neck and intertrochanteric fracture patterns  
29 were performed using a digital volume correlation (DVC) technique and compared to FE-predicted  
30 strains and experimentally observed fracture patterns. Although loaded identically, the femora  
31 exhibited different fracture types (6 neck and 8 intertrochanteric fractures). CT-based FE models  
32 matched the experimental observations well (86%) demonstrating that the fracture type can be  
33 predicted. DVC-measured and FE-predicted strains showed obvious consistency. Neither DXA-  
34 based BMD nor any morphologic characteristics such as neck diameter, femoral neck length or  
35 neck shaft angle were associated with fracture type. In conclusion, patient-specific femoral  
36 structure correlates with fracture type and FE analyses were able to predict these fracture types.  
37 Also, the demonstration of FE and DVC as metrics of the strains in bones may be of substantial  
38 clinical value, informing treatment strategies and device selection and design.

39

40 **Keywords:** neck; intertrochanteric; fracture; finite element analysis; digital volume correlation

41

42 **INTRODUCTION**

43 Proximal femoral fractures (PFF) can be categorised into two main types: femoral neck  
44 (intracapsular) and intertrochanteric (extracapsular) fractures accounting for 53% and 43%,  
45 respectively, of all PFF <sup>1</sup>. Each fracture type is treated with a specific type of operative treatment  
46 and has different potential complications to patients <sup>2</sup>. The ability to assess which fracture type a  
47 specific patient is predisposed to could aid fracture prevention strategies. It has been shown that  
48 by selecting specific exercise regimes <sup>3;4</sup> or drug treatments <sup>5</sup> specific parts of the femoral structure  
49 can be targeted and strengthened, potentially reducing the risk of this fracture type. Hip protectors  
50 could be designed to preferentially protect against the type of fracture the specific patient is prone  
51 to. More controversially, knowledge of the likely fracture type could aid prophylactic surgery.

52

53 Several studies have been performed to identify the factors that determine the fracture type <sup>6-16</sup>. A  
54 summary of these studies suggests that intertrochanteric fractures were associated with femora  
55 with lower bone mineral density (BMD) and thinner cortices while femoral neck fractures were  
56 associated with structural features such as a higher neck shaft angle (NSA) and a longer femoral  
57 neck length (FNL). However, these findings were not consistent, often reporting no significant  
58 effects, and some of the results were contradictory. Most of these studies were clinical studies  
59 involving patients who had suffered a fracture. The results of such studies are difficult to interpret  
60 in terms of the structural features of the femur associated with the fracture type as other factors,  
61 such as fall direction <sup>17</sup>, will also have an effect on the resulting fracture type.

62 To determine if the femoral structure alone predisposes a patient to a particular type of fracture  
63 this study aimed to isolate femoral structural features from other characteristics that may affect the

64 fracture type. To this end, cadaveric femora were tested under identical laboratory conditions,  
65 simulating a fall to investigate if these femora would exhibit different fracture types.

66

67 Any fracture has a degree of randomness resulting in a distribution of strength values. Thus the  
68 fracture type, may also have a seemingly random nature, the source of which may not be  
69 discernible from the overall structure assessed visually or from a CT scan. Hence, a CT based finite  
70 element (FE) analysis of each of the specimens was also carried out. The FE method is a frequently  
71 used tool for investigating femoral fracture load <sup>12; 17-22</sup> and its particular advantage in the context  
72 of our study is that it is entirely deterministic, containing no random elements. Thus, if the FE  
73 analysis predicts the experimental fracture types, then the fracture type is not determined by  
74 random effects but from features contained within the CT scan.

75

76 The hypothesis of this paper is that the femoral structure, including bone density distribution, as  
77 discernible from a CT-scan, determines if a patient is more predisposed to a femoral neck than to  
78 an intertrochanteric fracture. As part of the investigation it was assessed if the FE methodology  
79 could predict these fracture types. Thus, we assessed if FE may be used as a clinical tool for  
80 predicting the fracture type and aid in treatment planning. Finally, it was investigated if femoral  
81 characteristics, such as local BMD or femoral neck axis length, were associated with the fracture  
82 type.

83

## 84 MATERIAL AND METHODS

### 85 Femur Specimens and Preparation

86 Fourteen human cadaveric femora from eleven donors were obtained from Platinum Medical,  
87 Biological Resource Center, Phoenix, USA. The donors (mean age,  $66.5 \pm 14.5$  years; range: 42-86  
88 years) were four males, specimens M1 to M4, and seven females, specimens F1 to F10. This study  
89 was approved by the National Research Ethics Service (NRES) Committee London – London  
90 Bridge, United Kingdom (Ethics reference number: 12/LO/0797). The soft tissues were removed  
91 from the femora, and all femora were cut approximately 15 cm from the distal articular surface.  
92 The specimens were stored at  $-20^{\circ}\text{C}$  and thawed to room temperature for specimen preparation as  
93 well as prior to dual energy X-ray absorptiometry (DXA), CT scanning and mechanical testing.

94

### 95 Imaging Methods

96 The femora were radiographed, CT and DXA scanned. CT images were used for generating 3D  
97 FE models. Radiographs were used for measuring femoral geometrical characteristics while the  
98 DXA measurements were used to quantify BMD. Femora were scanned with a Philips, 64 slice  
99 CT scanner. The slice thickness was 1 mm. The settings were 120kV, 70mAs, and a 512 x 512  
100 pixels image matrix with pixel size between 0.8 to 1.0 mm. In-vitro DXA scans of the cadaveric  
101 femora, submerged in a water bath and positioned to replicate the routine clinical practice of supine  
102 patient position with the femur in  $20\text{-}25^{\circ}$  of internal rotation, were performed using GE Lunar  
103 Prodigy.

## 104 **In-Vitro Mechanical Testing**

105 The mechanical testing to fracture of the 14 femora was divided into two parts, twelve of the  
106 femora were tested in Part 1, while the remaining 2 femora, F7 and F10, were tested in Part 2. The  
107 mechanical set-up in Part 1 and Part 2 was conceptually the same (Figure 1), only the set-up in  
108 Part 2 was modified to be placed within a CT scanner, enabling CT scanning of the loaded  
109 specimen. In Part 1 the purpose was simply to record the fracture type and fracture load. In Part 2,  
110 in addition to recording to the fracture type and load, the specimen was CT-scanned at  
111 incrementally increasing loads until final failure. These CT scans were analysed using Digital  
112 Volume Correlation analysis (DVC) which measures the increasing strains within the femur during  
113 loading by tracking the grey scale patterns within the CT images as these patterns are deformed  
114 during loading. The main purpose of Part 2 was to provide strain fields close to fracture which  
115 could be used to further validate the FE fracture simulation.

116

### 117 **Part 1: In-Vitro Mechanical Testing within an Instron Test Machine**

118 To represent a sideways fall configuration each femoral shaft was positioned  $10^\circ$  from horizontal  
119 and the femoral neck axis internally rotated by  $15^\circ$  relative to a vertical axis (Figure 1)<sup>23-25</sup>. The  
120 femur was fixed at the distal end allowing the distal end to rotate freely around the axis normal to  
121 the plane of Figure 1. The medial aspect of the femoral head and the lateral aspect of the greater  
122 trochanter were covered with PMMA to prevent local crushing and simulating the effect of soft  
123 tissue cover<sup>24</sup>. Each femur was loaded to failure defined as the peak of the load-deformation curve  
124 using an Instron 8874 testing machine (Instron Corporation, Canton, MA). A constant vertical  
125 displacement of 6.6 mm/s was applied to the femoral head which rested on an x-y table to eliminate

126 any reaction forces. Load and displacement data were sampled at 1000 Hz. The load was measured  
127 using a uniaxial load cell. This load cell had a full-range of  $\pm 10$  kN and was accurate to 0.5% of  
128 the indicated load.

129

## 130 **Part 2: In-Vitro Mechanical Testing within a Clinical CT Scanner and DVC Strain Analysis**

131 In part 2 a CT-compatible custom-designed loading device was used. The set-up was conceptually  
132 the same as in Part 1 but the load was introduced by turning a Hex screw and measuring the load  
133 using a compression load cell (LBM-1000, Interface Force Measurements Ltd.) (Figure 1). The  
134 device was designed and positioned within the CT scanner in such a way that there were no metal  
135 components in the field of the CT scan thereby avoiding metal artefacts in the images. Patient scan  
136 settings of 120 kVp and 60 mAs were used. The compressive load was applied to the femoral head  
137 in increments of approximately 500 N. At the end of each increment a CT scan was performed. To  
138 reduce stress relaxation effects during the 4.4 seconds of the CT scan the specimen was held for 5  
139 minutes prior to scanning which allowed the load to stabilise and no change in load could be  
140 detected during the scan. This process of incremental loading and CT imaging was continued until  
141 final failure.

142

143 DVC uses digital image tracking to determine the displacement of patterns of voxel grey scale  
144 values in two sequential CT images of bone under increasing load. As the method utilises CT  
145 scans, the DVC method has the ability, uniquely amongst experimental methods, to assess the  
146 internal strains in bone<sup>26-28</sup>. Previous studies were based on micro-CT imaging and a novel aspect  
147 of this study was the use of DVC based on clinical CT images. The CT image files were imported

148 into commercial DVC software (DaVis 8.1.6, LaVision, Goettingen, Germany). Two scans were  
149 taken at zero load and confirmed that the maximum noise levels were 0.0003 and -0.0005 for  
150 the maximum and minimum strains, respectively, which had a negligible effect on the measured  
151 strain values. Software settings were: subvolume size sequences of 96x96x96, 76x76x76, and  
152 48x48x48 voxels/mm, 75% overlap and a correlation degree of 0.94. The software calculated the  
153 distribution of principal strains throughout the loaded femur. The DVC-measured strain  
154 distributions were compared with the FE-predicted strain patterns and the fracture patterns  
155 observed during mechanical testing.

156

### 157 **FE Model of Proximal Femur**

158 The CT dataset of the cadavers were segmented using medical image analysis software (Avizo,  
159 Version 6.3, Visualization Sciences Group, Burlington, MA, USA). The datasets had an average  
160 of 280 CT slices that covered the proximal head to about 25 cm down the shaft of the femur from  
161 the greater trochanter. Surface models were generated and exported to the FE software  
162 (Marc/Mentat 2013, MSC Software Corp., Santa Ana, CA, USA) to develop three-dimensional FE  
163 models of the femur. The models were meshed using linear 4-node tetrahedral solid elements.  
164 Mesh convergence analyses of three key results were performed: the load to initiation of failure  
165 (prior to deactivation of elements); the ultimate fracture load and the predicted fracture type. The  
166 converged meshes contained approximately 70,000 nodes and had an average element edge length  
167 of 1.3 mm (Figure 2).

168 Bone was modelled as a linear and isotropic material. The elastic modulus of each bone element  
169 was determined from the Hounsfield Units (HU) of the CT image using a previously established



170 procedure<sup>29</sup>. Specifically, the bone apparent density ( $\rho_{app}$  in  $\text{g/cm}^3$ ) was calculated using a linear  
171 relationship  $\rho_{app} = 0.00089 HU + 0.035$  and the Young's Modulus from  $E = 6.850 \rho_{app}^{1.49}$ . A  
172 Poisson's ratio of 0.3 was assumed.

173

174 The FE closely simulated the experimental set-up in Figure 1. The distal end was fixed apart from  
175 rotation around the axis normal to the plane of Figure 1. Nodes corresponding to the area covered  
176 by PMMA in the experiments (the trochanteric area) were constrained in the vertical direction.  
177 The vertical load applied to the surface of the femoral head was distributed on nodes over an area  
178 of approximately 3 cm in diameter. Femoral failure was predicted using maximum/minimum  
179 principal strain criteria. The maximum and minimum principal strains to failure used for both  
180 cortical and cancellous bone were 0.62% and -1.04%, respectively<sup>30; 31</sup>.

181

182 Assessing the FE-predicted fracture type based on just one element or a small area that first reaches  
183 the critical failure threshold was not considered sufficiently accurate since an initial failure may  
184 get arrested with subsequent failure initiating in another region of the femur. For these reasons a  
185 progressive FE failure simulation was adopted. Elements that met the principal strain failure  
186 criterion mentioned earlier were considered failed and automatically deactivated from the analysis  
187 during the iterative solution procedure (Figure 2). The use of iterative-level, load stepping  
188 constraints in Marc ensured convergence during the deactivation. A Newton-Raphson iterative  
189 scheme was used which meant that the onset of complete failure was numerically indicated by a  
190 reduced load in a subsequent increment.

191

## 192 **Definition of Fracture Types**

193 In both the physical experiment and in the FE models the specimens were tested until peak load  
194 which coincided with major but not complete fracture of the bone and as a result fractures were  
195 never displaced. A fracture that was contained within the intracapsular region (including subcapital  
196 and any variation of a fracture of the cervical neck) was defined as a neck fracture whilst a fracture  
197 that was contained within the extracapsular region (including fractures that were limited to or  
198 involved the greater trochanter, lesser trochanter, intertrochanteric region and subtrochanteric  
199 fractures) was defined as an intertrochanteric fracture. Fractures at the interface of the two regions  
200 (involving the basicervical region and extending outside the capsule into the intertrochanteric  
201 region running parallel to the basicervical region) were also categorised as intertrochanteric  
202 fractures due to these fractures being treated as extracapsular fractures in the clinical setting <sup>32</sup>.  
203 The classification of fractures was carried out blinded by three independent observers (MIZR, OB,  
204 & UNH); in cases of disagreement, the fracture type was classified according to the majority.

205

## 206 **Femoral Characteristics**

207 From DXA scans and 2D anterior-posterior radiographs (Figure 3) of the 14 specimens the total  
208 BMD, neck BMD, Ward's triangle BMD, greater trochanteric BMD, isthmus cortical index (CI),  
209 neck diameter (ND), femoral neck length (FNL) and neck shaft angle (NSA) were measured to  
210 determine which, if any, parameters were associated with fracture type.

211

## 212 **Statistical Analysis**

213 Inter-rater reliability was assessed using Fleiss' kappa <sup>33</sup>. All other data were analysed in SPSS  
214 (version 22, SPSS Inc., Chicago, Illinois) with the significance level set at  $p < 0.05$ . First, the  
215 correlation between the measured experimental fracture load and both BMD and FE-predicted  
216 fracture load was assessed with Pearson's product-moment correlation. Then the data were split  
217 into the two fracture groups, neck fracture or intertrochanteric and a Fisher's Exact Test was used  
218 to assess the association between the FE-predicted fracture types and the observed experimental  
219 fractures types. Finally, differences between specimen characteristics of the two fracture groups  
220 were analysed with unpaired t-tests.

221

## 222 **RESULTS**

223 The experimental and FE-predicted fracture loads and types are listed in Table 1 which also shows  
224 the total BMD values for each sample. Fracture load for specimen M4 was not recorded due to a  
225 technical error when collecting data and was not included for correlation statistics. Specimen M1  
226 was identified as a potential outlier as it had a BMD 1.5 times the interquartile range greater than  
227 the upper quartile of other specimens. A patient with such dense bone is unlikely to fracture and  
228 hence correlation data is presented both with and without this specimen. As expected, there was a  
229 strong correlation between increasing BMD and increasing experimental fracture load ( $r = 0.82$   
230 with M1,  $r = 0.63$  without M1,  $p < 0.029$  both with and without M1; Figure 4). There was an even  
231 stronger correlation between increasing FE-predicted fracture load and increasing experimental  
232 fracture load ( $r = 0.90$  with M1,  $r = 0.75$  without M1,  $p < 0.005$  both with and without M1, Figure  
233 4). The FE model predicted the experimentally observed fracture type 86 % of the time (Table 2,  
234 95 % CI: 65-100 %, Fisher's Exact  $p = 0.026$ ). The inter-rater reliability (Fleiss' kappa) for  
235 assessing these fracture types was 0.95.

236

237 The fracture types that occurred in the experimental rig were consistent with the FE-predicted and  
238 DVC-measured strain patterns (Figure 5). The two specimens that were used for this DVC analysis  
239 had notably different bone quality. F7 was osteopenic (T-score: -2.1) and F10 was osteoporotic  
240 (T-score: -4.3) and the two specimens exhibited different fracture types. The DVC strain  
241 measurements show the strain just prior to fracture and, consistent with the FE predictions and  
242 experimental fracture type, high strain concentrations can be noted in the neck and trochanteric  
243 regions, respectively. The FE and DVC assessments of strain were remarkably similar in regards  
244 to qualitative patterns as well as quantitative values. Thus, DVC strain measurements corroborated  
245 the FE predictions, both seemingly able to explain the fracture type.

246

247 No anatomic element was able to distinguish between fracture types in this small study (Table 3).  
248 No differences in any BMD measurements at any locations were detected between the fracture  
249 groups; neither for the entire group (all  $p \geq 0.08$ ), or for female only specimens (all  $p \geq 0.07$ ).  
250 However, there was a trend that specimens that fractured in the intertrochanteric region failed at  
251 lower loads, and had lower BMD than those that fractured at the neck. No other difference between  
252 the two fracture-groups were detected for any of the other variables: gender, age, height, weight,  
253 BMI, Isthmus CI, neck diameter, FNL and NSA; neither for the entire group (all  $p \geq 0.21$ ), nor for  
254 female-only specimens (all  $p \geq 0.21$ ).

255

256 **DISCUSSION**

257 This study investigated whether the femoral fracture type was random or if it could be predicted  
258 from the femoral structure based on a CT scan. Femora loaded in an identical manner resulted in  
259 a mix of fractures (6 neck fractures and 8 intertrochanteric fractures) reflecting clinical reality <sup>1</sup>,  
260 and giving credibility to the experimental set up. DXA-scores correlated well with the energy  
261 required to cause a fracture confirming the relevance of this imaging modality in the assessment  
262 of fracture risk. However, DXA was unable to distinguish between the types of fracture – no  
263 statistically significant differences were found between the fracture groups and BMD. In contrast,  
264 the FE model accurately predicted both the fracture load and the fracture pattern.

265

266 Keyak, et al. <sup>12</sup> and Pulkkinen, et al. <sup>9</sup> also reported a mix of fracture types when testing cadaver  
267 femora loaded in an identical manner (10 neck versus 4 intertrochanteric and 88 neck versus 51  
268 intertrochanteric fractures, respectively). Keyak, et al. <sup>12</sup> and Koivumaki, et al. <sup>8</sup> compared FE-  
269 predicted fracture types to in-vitro cadaver fracture types and found degrees of matching of 79%  
270 and 85%, respectively, supporting the predictive capability of FE found in our study.

271

272 In contrast to the FE modelling approaches by Keyak, et al. <sup>12</sup> and Koivumaki, et al. <sup>8</sup> our study  
273 modelled the progression of fracture from initiation to final failure. Keyak et al. predicted only the  
274 initial failure of a small area. If this area coincided with any part of the much larger experimentally  
275 observed fracture region it was considered a match. Such a strategy is likely to over-predict the  
276 degree of matching. Koivumaki et al. did not predict fracture but related the strain in the greater  
277 trochanteric region to the strain in the neck region. The region with the larger strain was predicted

278 to fracture. While our approach of simulating the progressing fracture and comparing like with  
279 like (fracture type with fracture type) did not vastly improve the degree of matching over those  
280 earlier studies it may arguably be more reliable.

281

282 The FE models statistically explained 57% of the variability seen in experimental fracture loads  
283 whereas DXA BMD-measurements were only able to explain 39% of the variability (Figure 4).  
284 These findings are consistent with Cody, et al. <sup>34</sup> and Orwoll, et al. <sup>35</sup> who also found FE to be  
285 superior in this aspect and to the findings of Cheng, et al. <sup>36</sup> who reported an  $R^2$  value of 0.76  
286 between total BMD and femoral strength. Cheng et al. also report femoral strengths ( $3.98\text{kN} \pm$   
287  $1.6\text{kN}$ ) which are comparable to the results of our study.

288

289 Mautalen, et al. <sup>15</sup>, in a comprehensive review of clinical studies, reports low BMD to be associated  
290 with intertrochanteric fractures. However, Dretakis, et al. <sup>37</sup> and Maeda, et al. <sup>7</sup> did not find a  
291 significant effect and Pulkkinen, et al. <sup>9</sup> reports lower strength (closely related to low BMD) to be  
292 associated with neck fractures. In our study, the intertrochanteric group had a nominally lower  
293 BMD (Table 3) which would be consistent with most previous studies, however, this result was  
294 not statistically significant. Our finding may be a type II statistical error due to the low power of  
295 the study as discussed below. The fact that the FE methodology, which includes any effect of low  
296 BMD, and despite the low power of the study exhibited a strong ability to predict the fracture types  
297 indicates the strength of this method over DXA.

298

299 Cheng, et al.<sup>36</sup> reported neck, Ward's triangle and greater trochanteric BMD values in females of  
300 0.676 g/cm<sup>2</sup>, 0.515 g/cm<sup>2</sup> and 0.612 g/cm<sup>2</sup>, respectively, which compares reasonably with the  
301 values found in our study (Table 3). Previous studies have reported an association between the  
302 location of BMD and the fracture type; low neck BMD being associated with neck fractures<sup>6</sup> and  
303 low trochlear BMD being associated with intertrochanteric fractures<sup>11; 15</sup>, while Maeda, et al.<sup>7</sup> did  
304 not find a significant association. In our study we also did not find such an association. Maeda, et  
305 al.<sup>7</sup> did find that a low Isthmus CI, suggested to reflect a general thinning of the cortices including  
306 the neck and trochanteric regions, was associated with intertrochanteric fractures. In our study we  
307 did not find such an association. However, the cortices at the isthmus were approximately 8 mm  
308 thick and considering the CT scan voxel dimension of ~ 1 mm it may be that the inaccuracy of our  
309 measurements prevented us from finding an association.

310

311 Pulkkinen, et al.<sup>9</sup> reported ND, FNL and NSA values for females with neck fractures of 3.06 cm,  
312 9.7 cm and 126°, respectively, which compares well with the values found here (Table 3). A wide  
313 and short femoral neck, and a low neck shaft angle all theoretically strengthen the femur against a  
314 femoral neck fracture and predispose the femur towards an intertrochanteric fracture. Such  
315 associations have been reported previously<sup>7; 11; 14</sup> although in other studies such associations were  
316 not found Dretakis, et al.<sup>37</sup>. In our study we did not find an association between these parameters  
317 and fracture type.

318 An important limitation affecting all the above findings was the limited number of samples.  
319 Notably, any differences in fracture strength and BMD values failed to differentiate statistically  
320 between the fracture groups. However, the p-values for these analyses were not far from the

321 statistical significance threshold of 0.05 (Table 3). Another limitation of the study was the  
322 subjective judgment made when classifying fractures into neck or intertrochanteric fracture.  
323 However, the three observers assessed the fracture types with inter-rater reliability of 0.95,  
324 suggesting that the reliability of the classification was not a severe limitation.

325

326 We used a loading rate of 6.6 mm/s comparable to that used in similar studies<sup>18; 38; 39</sup> but much  
327 lower than the loading rate during a sideways fall of  $\sim 100$  mm/s<sup>23</sup>. Courtney et al. (1994)<sup>23</sup> found  
328 that fracture load increased but energy to fracture was unaffected by loading rate. As the energy to  
329 fracture was unaffected it seems likely that also the fracture type would be unaffected by loading  
330 rate. Based on Courtney's work, we expect that our study underestimated the fracture load by about  
331 20% but did not change the fracture type.

332

333 There are several limitations of the FE modelling that may explain why 14% of fracture types were  
334 not predicted accurately. The FE model did not include features that are not captured by the CT  
335 image such as the presence of microcracks, differences in bone mineral crystallinity, or changes  
336 in bone collagen with age. The effect of such factors on the resulting fracture type will appear  
337 random in the context of the FE model used in this research. Another notable uncertainty involves  
338 details to reflect the real conditions of the impact to the greater trochanter during a fall (a  
339 complexity shared with the experimental set-up). However, too rigid or blunt a support would lead  
340 to high rates of trochanteric fractures which we did not find and may indicate that the effect of this  
341 limitation is minor. Finally, the fracture of bone is likely to be affected by the anisotropic  
342 mechanical properties of bone, including strength, which was not simulated.



343

344 Although initially introduced as a validation tool for the FE-predicted strains, the DVC component  
345 is an important additional outcome of the study. The DVC measured the strains throughout the  
346 bone and showed areas of critical strains indicating the location of imminent failure and showed  
347 remarkable agreement with the FE predictions in regards to both strain patterns and quantitative  
348 strain values. Interestingly, the DVC and FE assessments of F7 show that the strains in the regions  
349 of high tensile strain at the inferior aspect of the neck and high compressive strain at the superior  
350 aspect of the neck are both near the critical strain values of 0.62% and -1.04% for tension and  
351 compression, respectively. Hence, the femoral neck fracture may involve a complicated mix of  
352 tensile and compressive fracture.

353

354 Internal strains in bone have previously been measured using DVC <sup>28</sup> based on micro-CT images.  
355 However, in our study the analysis was based on images from a clinical CT-scanner. Prior to this  
356 study it was not clear that such an analysis would be possible. The feasibility of using clinical CT  
357 scans opens up the possibility of measuring internal bone strains also in patients and enables a  
358 great range of possible applications.

359

360 This study demonstrated that from an FE assessment of a patient's femoral structure it is possible  
361 to evaluate if the patient is prone to suffer a neck or an intertrochanteric fracture, thus, a hip  
362 protector, exercises or drug therapy that protects against the specific fracture type can be chosen.  
363 Also the study developed a novel DVC technique based on clinical CT scans which may have  
364 substantial clinical significance. The technique may be applied to measure the strains around

365 implants in patients, thereby monitoring the status of the fixation as part of patient follow-up or  
366 aid in the development of implants resulting in more benign stresses around the implant. Another  
367 major use of the DVC technique may be the assessment of the bone strains in patients under  
368 abnormal loading caused by, for example arthritis or bone deformities, providing unique  
369 information for the understanding and subsequent treatment of these pathologies.

370

### 371 **AUTHOR'S CONTRIBUTIONS**

372 Research design: MIZR, BP, JC, and UNH. Data analysis and interpretation: MIZR, CS, BP,  
373 RJvA, ABell, MK, AB, RB, OB, JC, and UNH. Drafting of manuscript: MIZR, BP, RJvA, OB,  
374 and UNH. Revision of manuscript: CS, ABell, MK, AB, RA, and JC. All authors have read and  
375 approved this manuscript.

376

### 377 **ACKNOWLEDGMENTS**

378 The authors would like to acknowledge assistance from Shirley Fetherston, Fiona Watson and  
379 Lesley Honeyfield of the Imperial College Healthcare NHS Trust for technical assistance. This  
380 work was sponsored by Malaysia-Imperial Doctoral Programme (MIDP).

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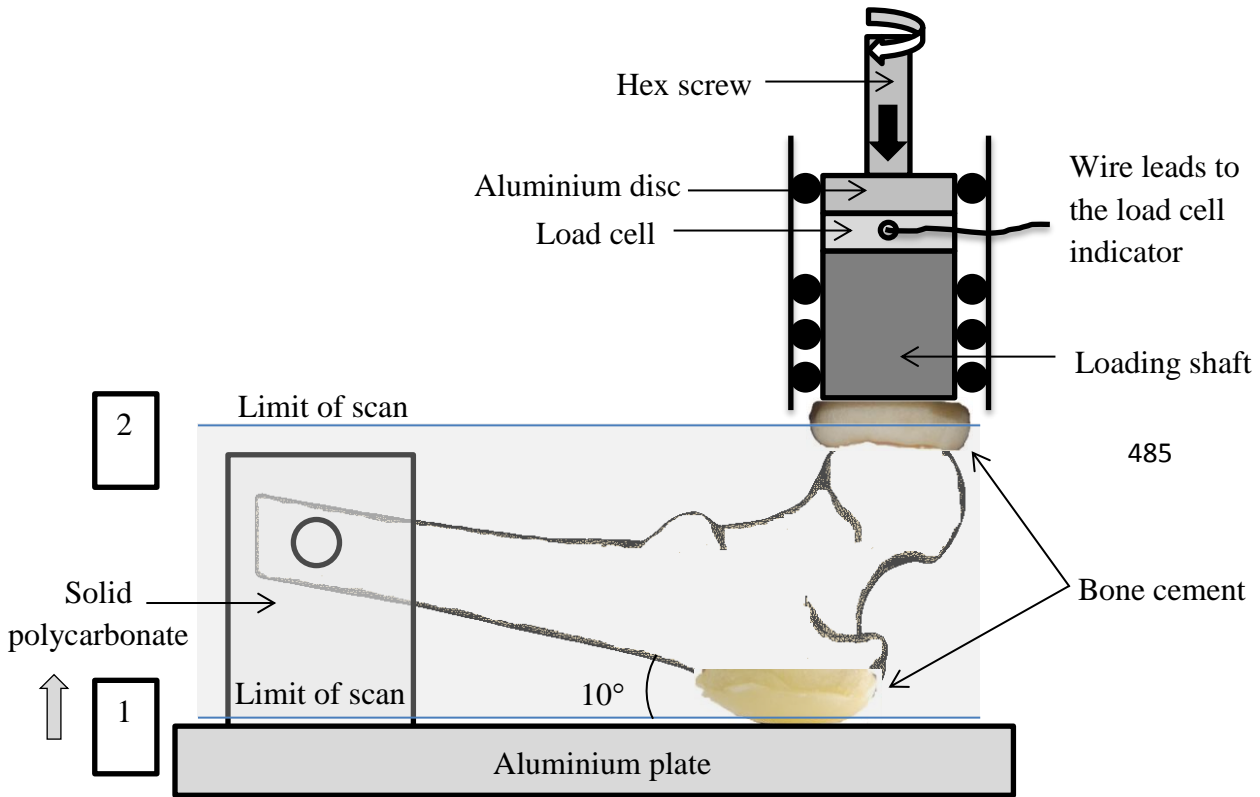
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488 **Figure 1** – Schematic diagram of the mechanical test-setup for Part 2 of the mechanical testing  
 489 which is carried out within a CT scanner. The CT scanning started from position 1 moving to  
 490 position 2. The resulting scan volume contained no metal components and no metal artifacts. For  
 491 Part 1 of the mechanical testing the fixture above was placed within a standard Instron Mechanical  
 492 testing machine and the load introduced via the cross head and load cell of the Instron (replacing  
 493 the load device shown in the upper part of the figure). Also, for part 1 the bottom Aluminium plate  
 494 was replaced by an x-y table.

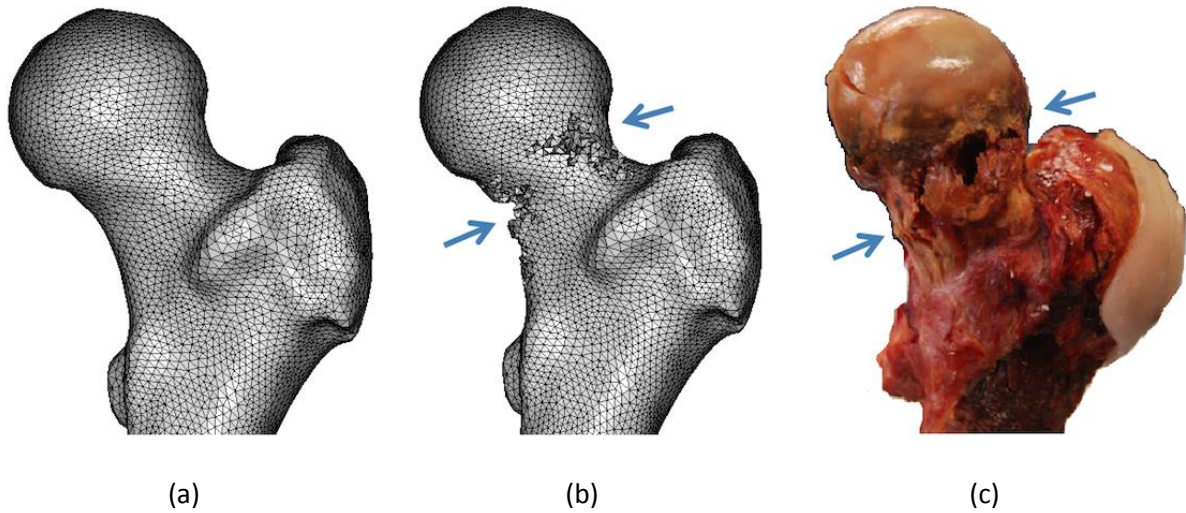
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506 **Figure 2** – (a) FE meshed model before initiation of fracture and (b) the same model with deleted  
507 elements at the point of ultimate fracture load and (c) the actual fractured femur that was simulated  
508 (specimen M2). Both the FE simulation and the experimental test showed a neck type fracture.

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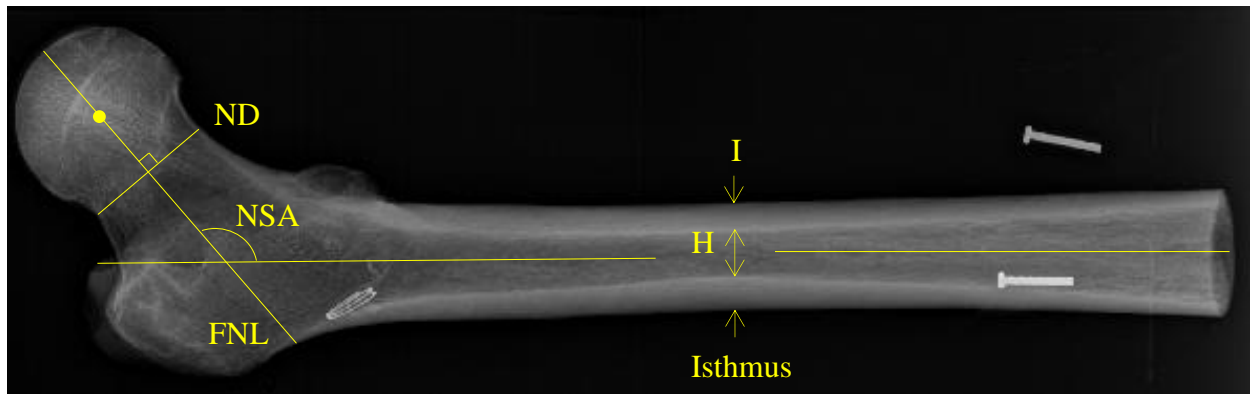
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525 **Figure 3** – Geometrical parameters of the femur. ND = width of femoral neck at its most narrow  
526 point, FNL = femoral neck length, NSA = neck shaft angle measured as angle between the femoral  
527 neck and the femoral shaft axes, and the cortical index (CI) at the femoral isthmus that equals to  
528 the ratio of the femoral diaphyseal diameter (I) minus the intramedullary canal diameter (H) over  
529 the femoral diaphyseal diameter;  $C = (I - H) / I$

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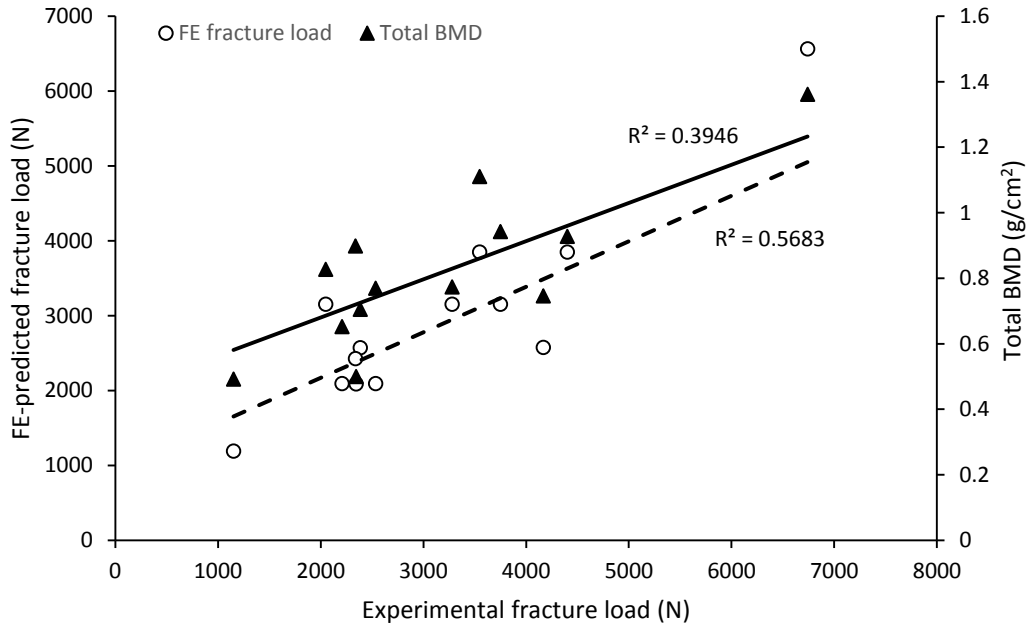
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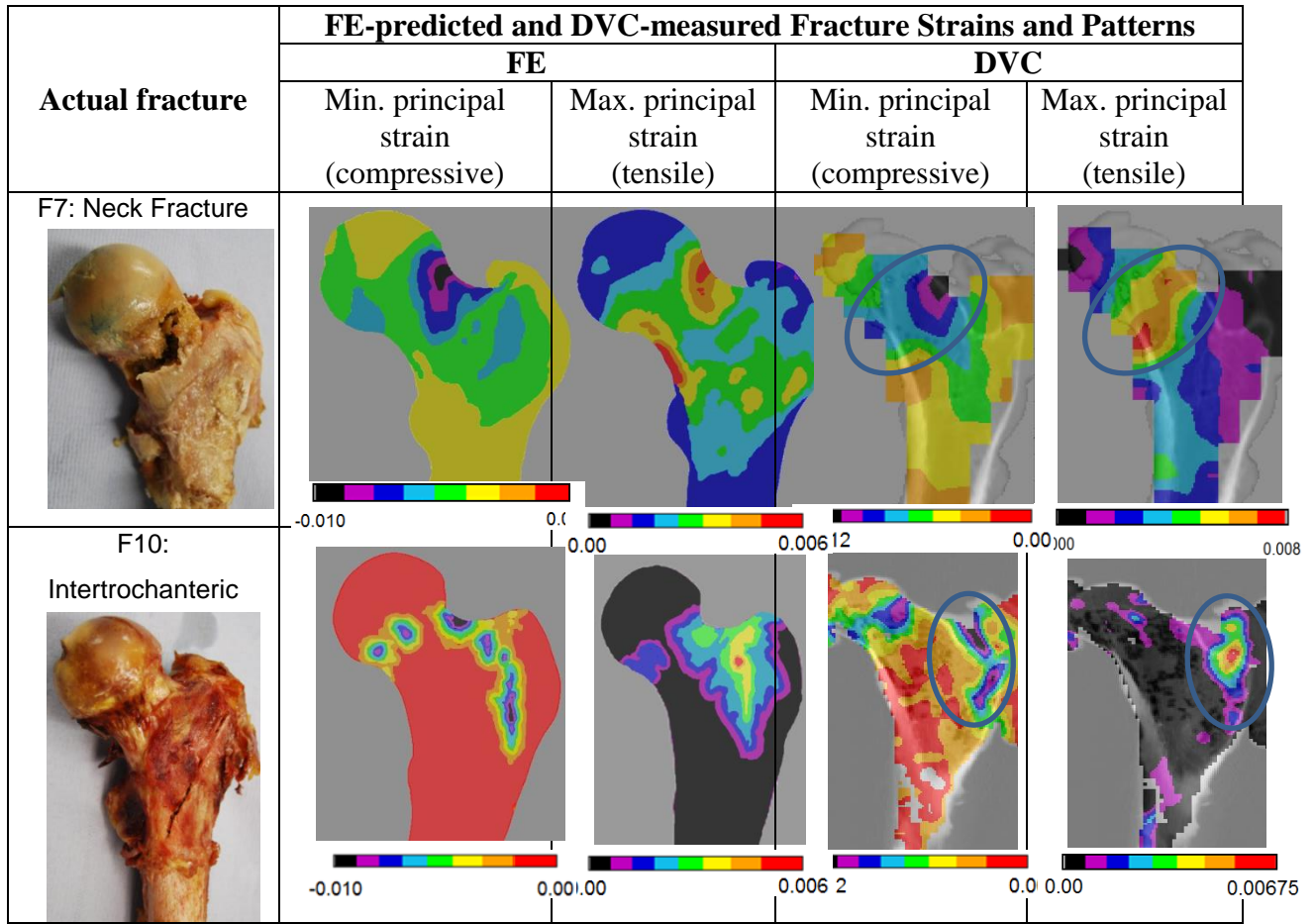
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**Figure 4** - The ability of FE to predict the actual (the experimental) fracture load compared to the ability of DXA-based BMD to predict the actual fracture load. Dashed line relates to FE fracture load data, solid line to BMD data.



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550 **Figure 5** – Comparison of the experimentally observed fractures to the FE-predicted strain and  
 551 fracture patterns as well as to the DVC-measured strains. Top row: Femur F7 exhibiting a femoral  
 552 neck fracture. Bottom row: Femur F10 exhibiting an intertrochanteric fracture. High strain  
 553 concentrations (circled) were apparent in regions where the femoral failure occurred and reflected  
 554 the different fracture modes. Note, the DVC image of femur F10 is shown in an oblique view to  
 555 better demonstrate the strain concentrations.

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557 **Table 1** – Predicted and experimental fracture load and type listed in order of experimental fracture  
 558 load and according to gender.

Specimen	Total BMD (g/cm <sup>2</sup> )	Fracture load (N)		Fracture type Observations in brackets.	
		Experiment	FE	Experiment	FE
F1	0.75	4166	2575	(Subcap oblique/basicervical) Neck	(Basicervical) Intertrochanteric
F2	0.94	3748	3154	(Subcapital) Neck	(Transcervical/basicervical) Neck
F3	0.77	3278	3153	(Basicervical/intertrochanteric) Intertrochanteric	(Basicervical/intertrochanteric) Intertrochanteric
F4	0.77	2534	2094	(Basicervical/intertrochanteric) Intertrochanteric	(Basicervical/transcervical) Intertrochanteric
F5	0.71	2382	2573	(Subcapital) Neck	(Transcervical) Neck
F6	0.50	2342	2091	(Basicervical/intertrochanteric) Intertrochanteric	(Basicervical/intertrochanteric) Intertrochanteric
F7*	0.90	2339*	2425	(Transcervical) Neck	(Subcapital/basicervical) Neck
F8	0.65	2205	2091	(Basicervical) Intertrochanteric	(Cervical/basicervical) Neck
F9	0.83	2049	3153	(Basicervical) Intertrochanteric	(Trochanteric/basicervical) Intertrochanteric
F10*	0.49	1151*	1190	(Intertrochanteric/trochanteric) Intertrochanteric	(Intertrochanteric/trochanteric) Intertrochanteric
M1	1.36	6739	6565	(Intertrochanteric/basicervical) Intertrochanteric	(Basicervical) Intertrochanteric
M2	0.93	4399	3850	(Subcapital/transcervical) Neck	(Cervical) Neck
M3	1.11	3547	3849	(Basicervical/intertrochanteric) Intertrochanteric	(Basicervical) Intertrochanteric
M4	1.00	-	3153	(Subcapital/transcervical) Neck	(Cervical + basicervical) Neck

559 \*the recorded loads prior to failure (specimens used for DVC experiments)

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565 **Table 2** - Summary of the FE-predicted fractures and the observed fractures.

		Experimental	
		Neck	Intertrochanteric
FE	Neck	5	1
	Intertrochanteric	1	7

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**Table 3** – Comparison of specimen characteristics between fracture types.

	Females only					
	Neck fracture (n = 6)	Intertrochanteric fracture (n = 7)	p-value	Neck fracture (n=4)	Intertrochanteric fracture (n=6)	p-value
Female/male	4/2	6/1	0.56	4/0	6/0	n/a
Age (years)	73.8 ± 14.1	64.3 ± 13.6	0.24	76.8 ± 9.0	68.0 ± 10.4	0.21
Exp. Femoral strength (N)	3407 ± 984	2444 ± 797	0.09	3159 ± 938	2260 ± 692	0.12
Height (cm)	168.5 ± 8.4	163 ± 7.5	0.21	163.5 ± 3.1	160.2 ± 4.4	0.23
Weight (kg)	67.5 ± 24.2	74.6 ± 31.8	0.67	72.5 ± 29.6	72.0 ± 34.1	0.98
BMI	24.1 ± 9.6	27.9 ± 11.2	0.53	27.0 ± 10.9	27.7 ± 12.2	0.93
BMD at Neck (g/cm <sup>2</sup> )	0.824 ± 0.092	0.669 ± 0.166	0.08	0.782 ± 0.092	0.624 ± 0.126	0.07
BMD at Wards (g/cm <sup>2</sup> )	0.595 ± 0.064	0.503 ± 0.191	0.27	0.566 ± 0.040	0.445 ± 0.126	0.07
BMD Great Trochanter (g/cm <sup>2</sup> )	0.729 ± 0.167	0.555 ± 0.185	0.11	0.649 ± 0.142	0.493 ± 0.090	0.07
Total BMD (g/cm <sup>2</sup> )	0.870 ± 0.117	0.732 ± 0.213	0.19	0.823 ± 0.115	0.669 ± 0.146	0.12
Isthmus CI	0.59 ± 0.05	0.58 ± 0.07	0.83	0.57 ± 0.05	0.57 ± 0.08	0.90
Neck diameter (cm)	3.2 ± 0.3	3.2 ± 0.3	0.72	3.1 ± 0.2	3.1 ± 0.2	0.96
FNL (cm)	9.9 ± 0.7	9.9 ± 0.7	0.98	9.5 ± 0.3	9.7 ± 0.5	0.51
NSA (°)	127 ± 4.5	125 ± 5.6	0.72	124 ± 3.6	124 ± 3.4	0.80