In vitro replication of spontaneous fractures of the proximal human femur

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Abstract

Spontaneous fractures (i.e. caused by sudden loading and muscle contraction, not by trauma) represent a significant percentage of proximal femur fractures. They are particularly relevant as may occur in elderly (osteoporotic) subjects, but also in relation to epiphyseal prostheses. Despite its clinical and legal relevance, this type of fracture has seldom been investigated. Studies concerning spontaneous fractures are based on a variety of loading scenarios. There is no evidence, nor consensus on the most relevant loading scenario. The aim of this work was to develop and validate an experimental method to replicate spontaneous fractures in vitro based on clinically relevant loading. Primary goals were: (i) repeatability and reproducibility, (ii) clinical relevance. A validated numerical model was used to identify the most critical loading scenario that can lead to head–neck fractures, and to determine if it is necessary to include muscle forces when the head–neck region is under investigation. The numerical model indicated that the most relevant loading scenario is when the resultant joint force is applied to the head at 8° from the diaphysis. Furthermore, it was found that it is not essential to include the muscles when investigating head–neck fractures. The experimental setup was consequently designed. The procedure included high-speed filming of the fracture event. Clinically relevant fracture modes were obtained on 10 cadaveric femurs. Failure load should be reported as a fraction of donor’s body-weight to reduce variability. The proposed method can be used to investigate the reason and mechanism of failure of natural and operated proximal femurs.

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1. Introduction

Spontaneous fractures of the hip can be defined as those fractures deriving from physiological or sudden loading, but not from a traumatic event (they may eventually result in secondary trauma, but they are not caused by trauma) (Cotton et al., 1994; Jeffery, 1974; Rockwood et al., 1991; Rüedi and Murphy, 2001). They most frequently occur in elderly (osteoporotic) subjects. Yang et al. (1996) developed two in vitro simulations (later replicated numerically by Gomez-Benito et al., 2005) to determine the biomechanical background for spontaneous hip fractures. They suggested that abnormal muscle contraction of the rotator muscles could induce hip fracture. In addition, bone fractures may occur as a consequence of excessive cyclic loading (Cotton, et al., 1994; Jeffery, 1974; Rockwood et al., 1991; Rüedi and Murphy, 2001). However, cyclic fractures typically occur because of excessive load/activity, and usually do not involve the proximal femur. As the focus of this paper is on fractures of the proximal femur occurring in elderly subjects, cyclic fractures will not be considered hereafter. There are mainly two reasons to investigate the biomechanics of spontaneous fractures of the proximal femoral metaphysis:

(1) A significant fraction (though not the majority) of fractures of the untreated hip in the elderly are not
Associated with a primary traumatic event (Cotton et al., 1994; Rockwood et al., 1991; Rüedi and Murphy, 2001). While the actual estimate of such fraction is difficult (elderly patients are often unable to report whether they fell before or after the fracture), it must account for 10–60% of the hip fractures (Grisso et al., 1991; Michelson et al., 1995; Muckle, 1976). Mayhew et al. (2005) suggested that buckling of the thin cortical shell could be one failure-initiating event if the underlying trabeculae are weakened by osteoporosis.

(2) With the recent return to resurfacing prostheses, concerns exist about risk of neck fractures due to physiological loading (Amstutz et al., 2004; Shimmin and Back, 2005; Shimmin et al., 2005; Siebel et al., 2006). This event is clinically undesirable. It also has serious legal implications (especially in the case of spontaneous fractures).

In most cases, patients cannot recall what motor task was performed at the time of fracture, or report having been stumbling or tripping on an obstacle (Deler et al., 2005; Eckstein et al., 2004; Keyak et al., 1998; Lang et al., 1997; Lochmüller et al., 1998; Mayhew et al., 2005). Traumatic femoral fractures due to impact on the greater trochanter as a consequence of sideways fall have been extensively investigated in vitro (Deler et al., 2005; Eckstein et al., 2004; Keyak et al., 1998; Lang et al., 1997; Lochmüller et al., 1998; Mayhew et al., 2005). Traumatic and spontaneous fractures exhibit different cracking modes and regions (Backman, 1957; Cotton et al., 1994; Eckstein et al., 2004; Keyak, 2000; Keyak et al., 2001a, b; Rockwood et al., 1991).

Several numerical and in vitro studies have been carried out attempting to simulate spontaneous fractures. However, there is no consensus concerning the relevant loading scenario to be simulated. The direction of the force applied on the femoral head ranges between 0° (Lochmüller et al., 1998, 2000, 2002; Lotz et al., 1991), 11° (Link et al., 2003), 20° (Keyak et al., 1998; Keyak, 2000; Lang et al., 1997), 24° (Smith et al., 1992), and 25° (Cody et al., 1999; Delaere et al., 1989) in the frontal plane, or even perpendicular to the shaft (Dalen et al., 1976). In other cases (e.g. Alho et al., 1988; Ota et al., 1999; Patel and Murphy, 2006) the loading direction is not specified (with limitations discussed elsewhere (Cristofolini, 2007)). This lack of agreement concerning the loading scenario undermines comparison between tests, as the direction of the load severely affects the stress distribution (Cristofolini, 1997; Cristofolini and Vicceconti, 1999; Voide et al., 2006), hence failure. Keyak et al. (2001a, b) addressed the issue of the loading direction and tried to assess the relevance of the muscle force on simulated failure (Keyak et al., 2005). Their conclusions were that it should not be necessary to simulate the muscles, and single-leg stance (resultant force at 10° in the frontal plane) and stair-climbing (30° in the sagittal plane) are the most relevant loading conditions. However, their indications cannot be considered conclusive, as they never tested experimentally the single-leg stance loading condition they identified (in all experiments they applied a resultant force at 20° in the frontal plane (Keyak et al., 1998, 2001a, b, 2005)). In addition in the cited work (Keyak et al., 2001a, b), they did not provide any indications on the femoral region subjected to the highest stress–strain levels in the one-leg stance configuration, thus providing no numerical evidence that this configuration may result in clinically relevant neck fractures. Therefore, there is a need for more extensive work based on state-of-the-art FE models, to confirm which is the most relevant loading scenario for replicating in vitro spontaneous neck fractures.

The goals of this work were to:

- develop a rationale and identify the most relevant loading scenario to recreate in vitro spontaneous hip fractures;
- develop the simplest possible testing protocol so as to increase repeatability and reproducibility (including assessment of the need to apply the muscle forces in the in vitro setup);
- validate such protocol by testing a sample of human femurs, and assessing the fractures recreated in vitro, in comparison with those observed in the clinical practice.

2. Materials and methods

2.1. Identification of the most critical loading scenario: FE simulations

A highly detailed finite element (FE) model of a human femur, which was previously validated against experimental measurements (Taddei et al., 2004a, b) was used to complement this study. A relevant donor for the FE study was selected (male, died 51 of intracerebral hemorrhage, free of musculoskeletal disease, smoker, osteoporotic, 175 cm tall, weighing 75 kg). The FE model included a dedicated material mapping strategy to assign suitable material properties to each element (Taddei et al., 2004, 2006a, b). It was used to perform a preliminary sensitivity analysis to address the following two questions:

(1) Does the application of the muscle forces (below the intertrochanteric region) affect the strain distribution in the head–neck region, or is it sufficient to apply the joint load with the right direction and intensity? This question was addressed by simulating inclusion and exclusion of the muscle forces, when the same resultant joint force was simulated under simulated single-leg stance during gait (Bergmann, 2001; Bergmann et al., 2001).

(2) Which is the direction of the hip joint resultant force that can cause the highest risk of failure in the head–neck region with respect to the diaphyseal one, to obtain clinically relevant failure scenario for the proximal femur? In fact, a preliminary study indicated that when unsuitable scenarios are applied, diaphyseal fractures might occur before the head–neck region fails. Once the first question was answered, the second one was addressed by exploring the five most frequent loading scenarios (level walking, stair climbing and...
force components (Fig. 1). A copy of each femoral head was prepared through a system of rails to avoid transmission of horizontal load transfer from the actuator to the head. Muscle forces were not simulated, as the FE models indicated this is not necessary in this situation, when the force lies in the frontal plane at 8\degree from vertical; the cross-rails to eliminate horizontal force components are visible on the top; the two mirrors are visible near the femur (they were oriented so as to reflect the anterior-medial and posterior-medial sides of the femur).

The femoral condyles were potted in a steel box with dental cement meeting the ISO 5833 requirements. The femur was mounted on top of the load cell of the testing machine with the diaphysis at an angle of 8\degree in the frontal plane (as defined by the sensitivity analysis performed with the FE, Section 3.1). Load was applied to the femora head through a system of rails to avoid transmission of horizontal force components (Fig. 1). A copy of each femoral head was prepared with dental cement (covering 1/5 head diameter) to allow uniform load transfer from the actuator to the head. Muscle forces were not simulated, as the FE models indicated this is not necessary in this application (Section 3.1).

Load was applied at a constant displacement rate of 2 mm/s, which resulted in the femurs failing within 0.5–2 s. Load and displacement were recorded by the testing machine (8502, Instron, Canton, MA, USA) at 1000 Hz.

During the destructive test, the event was filmed by means of a high-speed camera (FastCam-X1024PCI, Photron, UK) at 3000–9000 frames/s (actual frame rate depended on the size of the field of vision cropped for each specimen). The camera pointed at the superior-lateral part of the neck. Two mirrors were used to film at the same time the anterior-medial and posterior-medial portions of the neck.

2.3. Assessment of the test protocol

The test protocol above was applied to 10 cadaveric human femurs (Table 1) to confirm if clinically relevant failure modes and fracture load could be obtained. Specimens were chosen from relatively aged donors so as to represent the target population. Suitable fresh-frozen bone specimens were obtained through IIAM (Jessup, PA, USA). They were DEXA-scanned (Excel-Plus, Norland, USA) and CT-scanned (HiSpeed, General Electric, USA) to document bone quality and lack of abnormality or defects. Anatomical dimensions (head diameter and biomechanical length) were measured (Table 1, Ruff and Hayes, 1983).

3. Results

3.1. Most critical loading scenario: FE simulations

In the FE model, the inclusion/exclusion of the abductor muscles affected the strain distribution in the superior aspect of the head–neck region (Fig. 2). However, this effect was quite moderate. Moreover, higher peak tensile strains were found when the muscles were not simulated. Therefore, exclusion of the muscles tends to slightly overestimate the risk of fracture (when the same joint resultant force is applied).

The FE models indicated that, among the directions recorded by Bergmann (2001) and Bergmann et al. (2001), the loading scenario that generates the highest risk of failure of the neck region is the one-leg stance configuration, when the force lies in the frontal plane at 8\degree from the diaphysis (Fig. 3). In fact, while other scenarios have a larger stress below the trochanteric region or in the diaphysis, this is the condition with the highest risk in the neck (i.e. one-leg stance is the loading scenario that, if incrementally scaled, may lead to a fracture in the head–neck region first).

3.2. Results from 10 bone specimens

The test protocol was successfully applied to all specimens, with fractures occurring in the head–neck region (i.e. the region where spontaneous fractures are most likely to occur). In vitro fractures varied from specimen to specimen, and ranged from cervical to inter-trochanteric (Fig. 4). Most of the fractures (80%, Table 1) initiated from the most proximal portion of the neck.

Fig. 1. Experimental setup used to fracture the proximal femurs in vitro. Left: overview of the testing setup where the high-speed camera is visible on the left (directly facing the superior-lateral part of the femur), together with the light source; the bone specimen is under the testing machine on the right. Centre: Intact femur mounted on the material testing machine with the diaphysis at 8\degree from vertical; the cross-rails to eliminate horizontal force components are visible on the top; the two mirrors are visible near the femur (they were oriented so as to reflect the anterior-medial and posterior-medial sides of the femur). Right: detail of the proximal femur, with the mirrors and the copy of the femoral head for applying the load to the femur. The strain gauges bonded on the bone surface were part of a separate study.
## Table 1
Details of the 12 femur specimens investigated

<table>
<thead>
<tr>
<th>Donor’s details</th>
<th>Femur’s data</th>
<th>Failure load</th>
<th>Failure mode</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sex</strong></td>
<td><strong>Age at death</strong></td>
<td><strong>Donor height (cm)</strong></td>
<td><strong>Donor weight (kg)</strong></td>
</tr>
<tr>
<td>Male</td>
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<td>82</td>
</tr>
<tr>
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<tr>
<td>Male</td>
<td>73</td>
<td>175</td>
<td>73</td>
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</tbody>
</table>

In the first four columns, details of the donor are listed. Bone quality is reported in the 6th and 7th column (bone density as % of the young reference population, and of the age-matched population computed based on the Norland DEXA scanner reference population). Biomechanical dimensions (Ruff and Hayes, 1983) are reported in the 8th and 9th columns. Failure load in Newton and as a fraction of the donor’s body weight is reported. The failure mode is reported in the last three columns: based on anatomical location (Rockwood et al., 1991); AO Müller Classification (31-A = extracapsular trochanteric; 31-B = intracapsular neck; 31-C = intracapsular head) (Rüedi and Murphy, 2001); Pauwels’ classification based on fracture direction (I = fracture nearly perpendicular to femoral diaphysis; II = nearly perpendicular to neck axis; III = nearly parallel to femoral diaphysis) (Pauwels, 1935).

Note(1): Failed due to transcervical fracture, but subcapital fracture initiated in parallel;
Note(2): Started from lateral cartilage edge, propagated below lesser trochanter;
Note(3): Started from lateral cartilage edge, bifurcated and propagated along cartilage edge;
Note(4): Started from lateral cartilage edge, propagated along the neck (above lesser trochanter).
Load–displacement curves were highly linear ($R^2 > 0.99$) for most of the loading ramp. Linearity decreased only in the last few hundred Newton, prior to sudden failure. The failure load was $9344 \pm 3140$ N, corresponding to $10.9 \pm 3.0$ body weight (BW) (Table 1). The error affecting the measured failure load was of 2.6% (This includes the intrinsic uncertainty of the testing machine (<0.5%), as well as the errors caused by the transient occurring upon failure).

High-speed movie were successfully obtained for all specimens. They allowed observing the exact time when fracture initiated, and how it propagated across the bone.
4. Discussion and conclusions

Spontaneous fractures of the hip are caused by occasional overloads during daily activities, and are associated with hip resurfacing implants (Cotton et al., 1994; Jeffery, 1974; Rockwood et al., 1991; Rüedi and Murphy, 2001). They are associated with poor bone quality due to age and osteoporosis. In fact, a decrease of bone tissue toughness is associated with age (Wang and Puram, 2004).

Despite some preliminary study (Keyak et al., 2001a, b, 2005), there is no strong indication concerning the most relevant loading scenario for replicating spontaneous neck fractures \textit{in vitro}. The final scope of this paper was to design a knowledge-based test setup to simulate \textit{in vitro} spontaneous fractures of the proximal femur. The three original goals were successfully met:

- Based on a validated FE model, the most critical loading scenario (among the possible motor tasks that a subject typically performs when spontaneous fractures occur) was identified, which should be simulated \textit{in vitro}.
- Based on past experience and on the current FE simulations, the simplest possible testing protocol was designed and implemented. It was demonstrated that it is not necessary to simulate the action of the muscles to investigate fractures in the head–neck region. This enables simplification and better reproducibility both of experimental simulations and of \textit{in vitro} test setups.
- Application of the protocol to 10 femur specimens confirmed its feasibility and reproducibility. Clinically relevant fractures were obtained \textit{in vitro} in all specimens, with failure loads which were compatible with occasional overloads (Bergmann, 2001; Bergmann et al., 2001).

The loading scenario identified as most critical here is compatible with numerical studies (Daniel et al., 2006; Keyak et al., 2001a, b), and is quite similar to the one used by Link et al. (2003) (11° in the frontal plane). Also, this study indicated that it is not necessary to simulate the muscle forces to create a suitable stress state in the head–neck region in accordance with previously published works (Cody et al., 1999; Keyak et al., 2005).

It must be stressed that the scope of this study was to recreate \textit{in vitro} the conditions for spontaneous fractures of the proximal caused by a single sudden loading event (typically in elderly subjects), as opposed to fatigue fractures, which are caused by cyclic loading (usually associated with active subjects, and involving other regions than the proximal femur (Cotton et al., 1994; Jeffery, 1974; Rockwood et al., 1991; Rüedi and Murphy, 2001)). Consistently with most of similar works, the authors recommend simulation of a single-loading ramp, as this seems to best represent the occasional overloading leading to non-traumatic fractures (Grisso et al., 1991; Jeffery, 1974; Michelson et al., 1995; Muckle, 1976; Rockwood et al., 1991). Others (Lochmüller et al., 1998, 2000, 2002) have chosen to apply loading cycles of increasing magnitude.
The most common fracture initiation site was the subcapital region (80% of the specimens). This is the most common type of spontaneous fractures (Cotton et al., 1994; Pauwels, 1935; Rockwood et al., 1991). Indeed, a similar fraction of subcapital fractures was obtained in vitro by others (69%, Cody et al. (1999) and 94%, Keyak et al. (2001a, b)).

The failure loads found here ($9344 \pm 3140$ N) are comparable with the values reported in the literature: Ota et al. (1999) reported a failure load of 8400 N (loading direction not specified); Link et al. (2003) reported a failure load of $8890 \pm 3770$ N (simulated stance); Duchemin et al. (2006) reported a failure load of $9032 \pm 3412$ N (11° in the frontal plane); Smith et al. (1992) reported a range of $9920 \pm 3219$ N (25° in the frontal plane). Such values are found in occasional overloading events such as stumbling or miss-stepping (Bergmann, 2001; Bergmann et al., 2001), which are a suspected cause of spontaneous fractures (Cotton et al., 1994; Rockwood et al., 1991; Rüedi and Murphy, 2001).

The variability of the failure load expressed in N in this study (coefficient of variation, CoV = 34%) is comparable to the values reported in the literature: Lochmüller et al. (2002) and Lochmüller et al. (1998) reported CoV = 27–39%; Duchemin et al. (2006) CoV = 38%; Eckstein et al. (2004) and Link et al. (2003) CoV = 42% (both values are referred to a sample with a wider age range); Cody et al. (1999) CoV = 32%. In fact, a comparison on paired femurs (Eckstein et al., 2004) indicated that the lower bound for repeatability is 15%.

It must be noticed that variability was reduced when the failure load was expressed in terms of fraction of the donor’s BW, rather than in N: the coefficient of variation decreased from 33.6% to 27.5%. This supports the idea of reporting bone strength as a fraction of BW rather than in absolute terms, and is in agreement with the findings of Lochmüller et al. (1998).

It is worth remarking that the strength of the femur measured under this loading scenario is a potential predictor of neck strength when the femur is subjected to a lateral impact (Duchemin et al., 2006; Keyak, 2000; Lochmüller et al., 2002).

There are some limitations of this work that should be discussed. First, the sample size investigated was relatively small. However, the scope of the experimental tests was not to measure the average strength of the femur on a given population, but to provide a validation to the methodology.
Moreover, as no in vivo recording is available for such traumatic events, the FE simulation relied on scaled muscle forces based on stance conditions (Bergmann, 2001; Bergmann et al., 2001), similarly to Keyak et al. (2005).

The test protocol developed and validated herein can thus be applied to investigate spontaneous fractures of the natural femur. It could also be extended to address neck fractures in the presence of epiphyseal prostheses.

Conflict of interest

There is no potential conflict of interest: none of the authors received or will receive direct or indirect benefits from third parties for the performance of this study.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.jbiomech.2007.03.015.

References


