

# Current concept of stress fractures with an additional category of atypical fractures: a perspective review with representative images

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**Abstract:** Stress fractures have traditionally been classified into three categories: fatigue fractures due to overuse of bone with normal elastic resistance; insufficiency fractures due to everyday physiological stress on fragile bone with poor elastic resistance; and pathologic fractures due to bone weakness involving tumors. The concept of atypical fractures has emerged and is considered a type of stress fracture. However, there has been some inconsistency in interpretation when using the traditional classification of stress fractures, and atypical femoral fractures (AFFs) can potentially be classified into subtypes: “typical” AFFs involving bone turnover suppression due to specific drugs (e.g. bisphosphonates) and fragility fractures of the bowed femoral shaft. In this article, the classification of stress fractures is redefined with the addition of atypical fractures as a fourth category, in which biological activity for fracture healing is absent, to promote consistent understanding and interpretation of clinical conditions involving stress fractures.

**Keywords:** atypical fracture, fatigue fracture, fragility fracture, insufficiency fracture, pathologic fracture, stress fracture

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## Introduction

Stress fractures have traditionally been classified into three types: fatigue fractures due to overuse; insufficiency fractures due to bone fragility; and pathologic fractures due to bone weakness involving tumors.<sup>1</sup> Fatigue fractures occur in normal bone that has been overused (e.g. in athletes and military personnel), whereas insufficiency fractures develop in fragile bone that is repeatedly subjected to low levels of stress during everyday physical activity.

In recent years, there has been increasing awareness of the concept of atypical fractures.<sup>2–4</sup> While it is widely known that suppression of bone turnover by specific drugs (e.g. bisphosphonates) increases the risk of atypical femoral fracture (AFF),<sup>5</sup> this type of fracture occurs where there is focal thickening of the lateral cortex and is

considered to be caused by mechanical stress.<sup>6–10</sup> Therefore, atypical fracture can be regarded as a type of stress fracture. However, it has been suggested that AFF can potentially be classified further into bone turnover suppression-related “typical” AFF, which is more common in the subtrochanteric region, and mid-shaft stress fracture of the bowed femoral shaft (SBF).<sup>11,12</sup> Although the pathology of SBF fits with the concept of an insufficiency fracture, bone in patients with AFF is not necessarily fragile or weak.<sup>12–14</sup> In this article, we propose addition of a fourth category in the classification of stress fractures to cover this particular type of fracture.

## Fatigue fractures

Fatigue fractures due to overuse were first described by a Prussian military surgeon in

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**Figure 1.** X-ray image for a 66-year-old woman with a subtrochanteric atypical femoral fracture. She complained of persistent pain in the left thigh and had been taking alendronate for 14 years. The left femur shows significant focal thickening of the lateral cortex with an apparent incomplete fracture line in the subtrochanteric region (arrowhead). The contralateral (right) femur shows a diffusely thickened lateral cortex but no fracture line in the subtrochanteric region (arrows).

1855.<sup>15</sup> The fractures occurred in soldiers who were engaged in long marches and had persistent pain in the feet in the absence of trauma. With the advent of radiography, this type of fatigue fracture was identified as a metatarsal shaft fracture called “march fracture.” Overuse bone injuries in young people (e.g. athletes and military personnel) who engage in vigorous physical activity and are subjected to high levels of stress are now widely recognized.<sup>16–18</sup> A fatigue fracture that develops in any bone with normal elastic resistance and adequate strength is considered a stress fracture. Although the treatment of fatigue fractures is based on removal of excessive and

repeated stress, top athletes require individualized treatment that often includes internal fixation.

### Insufficiency fractures

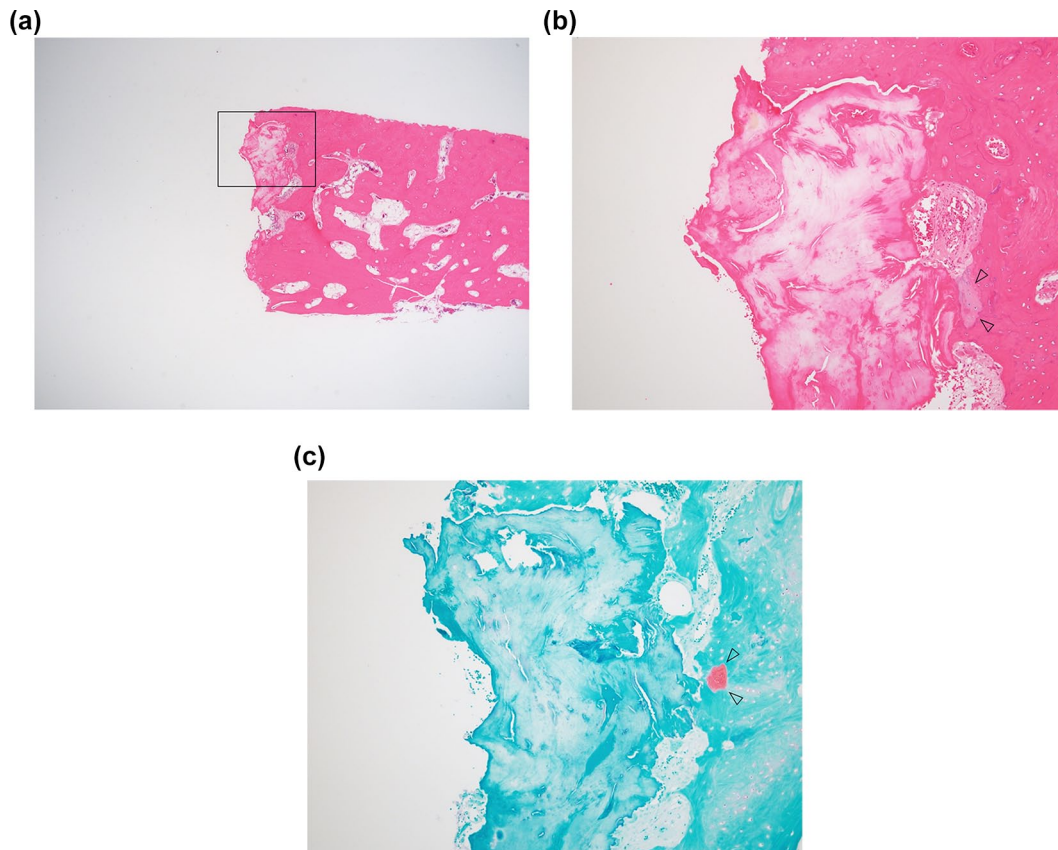
Insufficiency fractures develop in fragile bone with less than normal elastic resistance to mechanical force and may be caused by normal or physiological levels of stress.<sup>1</sup> Insufficiency fracture is an important category of stress fracture that distinguishes stress fractures in abnormal bone except those that are tumor related. Certain diseases (e.g. osteogenesis imperfecta, Paget’s disease of bone, osteomalacia, rickets, hypophosphatasia, osteoporosis, rheumatoid arthritis, hyperthyroidism, osteomyelitis, and poliomyelitis) can reduce the elastic resistance of bone and cause insufficiency fractures.<sup>1,19</sup> Patients who develop this type of fracture tend to be older than those who develop fatigue fractures because of the increasing incidence of underlying disease with advancing age.<sup>1</sup> Treatment of this type of stress fracture ideally includes not only the fracture itself but also the underlying disease in order to improve the elastic resistance and strength of abnormal bone.

### Pathologic fractures

A pathologic fracture is a stress fracture that occurs in bone at the site of a tumor.<sup>1</sup> Tumors associated with this type of stress fracture include benign bone cysts, malignant bone tumors, and bone metastases from various types of cancer.

### Atypical fractures

AFFs are atypical fractures that affect the femoral shaft with or without minor trauma and are reported to be due to suppression of bone turnover by specific drugs (e.g. bisphosphonates, denosumab, glucocorticoids, or proton pump inhibitors).<sup>2–6,20–22</sup> Figure 1 shows a representative X-ray image of subtrochanteric AFF in a 66-year-old woman who had been taking alendronate for 14 years. Healing of these fractures tends to be delayed because of widespread suppression of bone turnover (Figure 2).<sup>4–6,12,23–27</sup> Other factors potentially involved in the pathogenesis of AFF include ethnicity,<sup>4</sup> body mass index,<sup>20</sup> loading stress in daily life,<sup>7–10</sup> femoral morphology,<sup>6–8,11,12,14,28,29</sup> and bone density, quality, and strength.<sup>12–14</sup> Mild mechanical stress during daily activities is undoubtedly involved in the



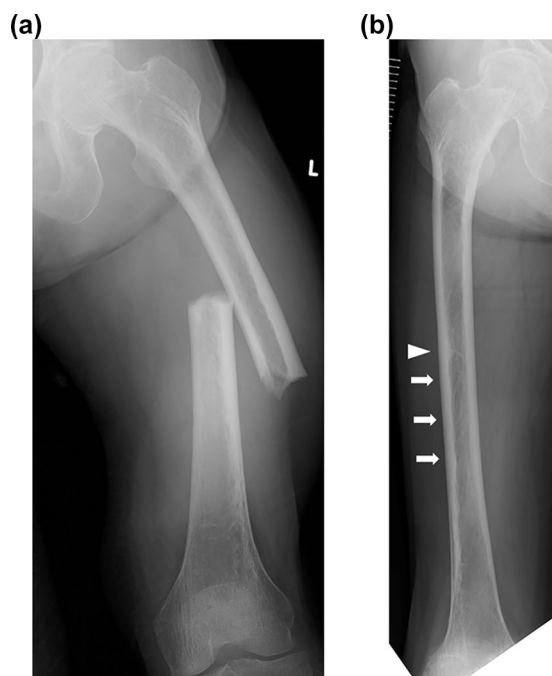
**Figure 2.** Representative histology for an incomplete subtrochanteric atypical femoral fracture (Figure 1) shows suppression of bone remodeling (a, b, hematoxylin-eosin staining; c, safranin O staining). (a) Lower magnification of the bone sample harvested from the cortex on one side of the fracture line during prophylactic internal fixation (20 $\times$ ). The upper side is the surface of the focally thickened lateral cortex and the left side is the fractured surface. (b, c) Higher magnification of the region indicated by a square in Figure 2a (100 $\times$ ). The fractured surface is covered with fragile degenerated bone with no osteoclasts, osteoblasts, or cartilage cells. Endochondral ossification (arrowheads) is found in only a small part of the area adjacent to the degenerated tissue.

onset of AFF.<sup>4,6-10</sup> Mechanical studies using finite-element methods by our research group and Haider *et al.* have demonstrated that the distribution of tensile stress in the femoral shaft as a result of everyday loading stress is affected by femoral morphology (e.g. femoral bowing and the neck-shaft angle).<sup>8,10</sup> Moreover, the location of the AFF is thought to be determined by the distribution of stress, which is influenced by individual differences in bone morphology.<sup>8</sup> Therefore, AFF should be regarded as a type of stress fracture resulting from everyday physiological stress.

### Classification of AFF subtypes

To our knowledge, the first description of a stress fracture of the femoral shaft associated with

bowing deformity dates back to 1975.<sup>30</sup> After encountering an elderly woman with a similar stress fracture of the femur in 1998,<sup>11</sup> well before the first report of an association between suppression of bone turnover and AFF, we focused on this type of stress fracture in elderly Japanese women. This type of fracture was recently defined as an SBF.<sup>7,8,11-13</sup> Figure 3 shows a representative X-ray image of SBF in a 73-year-old woman with no history of exposure to specific drugs (e.g. bisphosphonates, denosumab, glucocorticoids, or proton pump inhibitors). Although all patients with SBF fulfill the case definition of AFF put forward by the American Society for Bone and Mineral Research Task Force in 2014,<sup>6</sup> a number of SBF cases did not have exposure to drugs such as bisphosphonates, and the fracture basically



**Figure 3.** X-ray images for a 73-year-old woman with a mid-shaft stress fracture of the bowed femoral shaft. She had no history of exposure to specific drugs (e.g. bisphosphonates, denosumab, glucocorticoids, or proton pump inhibitors). (a) A displaced fracture of the left femoral shaft (AO/OTA classification, 32A3). The fracture line is transverse with a small medial spike. (b) The contralateral right femur shows bowing deformity in the lateral direction. A slight transverse fracture line (arrowhead) is identified in one of the lateral cortices with slight focal thickening (arrows).

developed in the mid-shaft at the apex of curvature.<sup>11,12</sup> A multifactorial investigation of Japanese patients with AFF showed that mid-shaft AFF tends to develop in elderly women with bowing deformity of the femoral shaft and low bone strength<sup>8,13</sup> but normal biological activity without suppression of bone turnover.<sup>12</sup>

In contrast, biological activity tends to be suppressed due to long-term use of particular drugs in “typical” subtrochanteric AFF,<sup>12</sup> and bone strength in patients with this type of fracture is higher than the average for those of the same age and sex.<sup>13</sup> Based on these site-related characteristics, we have proposed a theoretical classification of AFF subtypes, called Oh’s subtype theory, which can be applied to most patients with AFF, especially in East Asian countries.<sup>12</sup> Although some cases may not be classifiable, most cases of

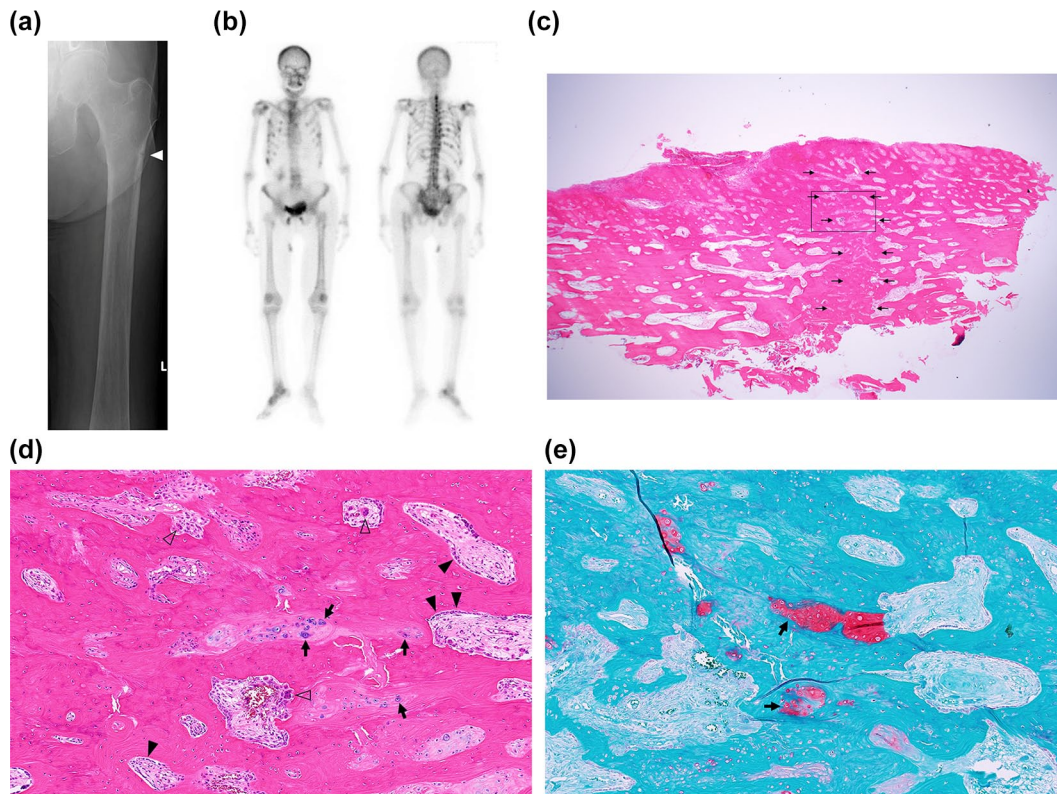
AFF in the East Asian population can be classified as SBF (insufficiency fracture with adequate biological activity that frequently develops in the mid-shaft due to bone fragility and bowing deformity) or “typical” AFF (intractable fracture with inadequate biological activity that often develops in the proximal diaphysis due to long-term pharmacologic suppression of bone turnover).

### New classification of stress fractures

From the perspective of stress fractures, it should be noted that not only SBF (AFF associated with bowing of the femur and bone fragility) but also some femoral diaphysis fractures in fragile bone due to certain diseases (e.g. osteomalacia, rickets, and hypophosphatasia) would essentially be classified as insufficiency fractures, which generally have sufficient biological activity for fracture healing despite fulfilling the current diagnostic criteria for AFF.<sup>6,13</sup> Figure 4 shows representative imaging findings for a 70-year-old woman with an incomplete subtrochanteric AFF who had vitamin D deficiency osteomalacia but adequate biological activity for bone healing. However, there is no bone fragility and no biological activity in cases of “typical” AFF, which frequently develops in the subtrochanteric region.<sup>12–14</sup> Therefore, given the difficulties regarding the establishment of diagnostic criteria and treatment guidelines for AFF with different pathologies, we have suggested a classification of AFF subtypes,<sup>12</sup> and we concurrently redefine the traditional classification of stress fractures. “Atypical fracture” would be included as a fourth subtype of stress fracture in this new classification (Table 1).

Recent studies have raised the possibility of vitamin D deficiency in patients with stress fractures,<sup>31–33</sup> which may also include those with fatigue or insufficiency fractures. Low vitamin D levels would be consistent with underlying bone fragility in patients with insufficiency fractures including SBF (insufficiency fracture in the femoral diaphysis associated with bowing deformity)<sup>12,13</sup> but possibly not in those with “typical” AFFs.

Some reports have described AFFs associated with inherited skeletal dysplasia,<sup>34–37</sup> and there might be quite a few cases of AFFs with various latent inherited diseases (e.g. hypophosphatasia, X-linked hypophosphatemia, pycnodysostosis, and osteopetrosis). If bone fragility associated with inherited skeletal dysplasia triggers the onset



**Figure 4.** An exceptional case of incomplete subtrochanteric atypical femoral fracture in a 70-year old woman. She complained of severe pain in the left thigh. Although she had been taking a proton pump inhibitor for 6 years, she had never been exposed to bisphosphonates. Dual-energy X-ray absorptiometry of the left femoral neck revealed severely decreased bone mineral density of 0.212 g/cm<sup>2</sup>, and blood tests (bone-specific alkaline phosphatase, 156 µg/L; tartrate-resistant acid phosphatase-5b, 1710 mU/dL; phosphorus, 2.2 mg/dL; calcium, 7.4 mg/dL; 25-hydroxyvitamin D, 4.3 ng/mL; fibroblast growth factor 23, 5.9 pg/mL) confirmed the diagnosis of vitamin D deficiency osteomalacia. (a) X-ray image of the left femur shows slight focal thickening of the lateral cortex with an incomplete fracture line in the subtrochanteric region (arrowhead). (b) Bone scintigraphy shows uptake in multiple ribs and vertebral bodies. (c) Lower magnification of the cortical bone sample including the fracture line which was harvested during prophylactic internal fixation (hematoxylin-eosin stain, 12.5×). The surface of the focally thickened lateral cortex is on the upper side and the incomplete fracture site, which is evident on the X-ray image, is located in the center of the sample (small arrows). (d, e) Higher magnification of the region indicated by a square in Figure 4c (100×; d, hematoxylin-eosin stain; e, safranin O stain). Active bone remodeling is demonstrated by abundant infiltration of both osteoclasts (white arrowheads) and osteoblasts (black arrowheads). Interspersed chondrocytes (black arrows) with deposition of cartilage matrix, which is stained red by safranin O, suggest endochondral ossification.

of AFF, it could fall into the category of insufficiency fractures. However, latent diseases may enhance bone turnover suppression by specific drugs (e.g. bisphosphonates) and cause “typical” AFFs, and this remains a subject for future research.

#### Other fractures with atypical fracture characteristics

There have been several reports of periprosthetic or forearm fractures after prolonged treatment

with bone resorption inhibitors that exhibited characteristics of stress/atypical fractures.<sup>38–41</sup> More research is needed to define the diagnostic criteria and treatment for these types of fracture.

#### Conclusion

Stress fractures can currently be divided into four categories: fatigue fractures, insufficiency fractures, atypical fractures, and pathologic fractures. It should be noted that SBF (AFF associated with bowing of the femur and bone fragility) and some

**Table 1.** New classification for stress fractures and characteristics in each category.

Fatigue fracture	Overuse fracture that develops in bone with normal elastic resistance and adequate strength (e.g. in athletes and military personnel)
Insufficiency fracture	Fragility fracture that develops in response to everyday physiological stress in fragile bone with reduced elastic resistance (e.g. osteogenesis imperfecta, Paget's disease of bone, osteomalacia, rickets, hypophosphatasia, osteoporosis, rheumatoid arthritis, hyperthyroidism, osteomyelitis, and poliomyelitis) but that generally has sufficient biological activity for fracture healing
Atypical fracture	Intractable iatrogenic fracture that usually develops in the femoral diaphysis with or without minor trauma as a result of reduced bone remodeling to physiological stress due to bone turnover suppression associated with long-term administration of specific drugs (e.g. bisphosphonates, denosumab, glucocorticoids, and proton pump inhibitors) and that fundamentally lacks biological activity for fracture healing
Pathologic fracture	Pathologic fracture that develops in weakened bone involving a tumor (e.g. a benign or malignant bone tumor and bone metastasis)

Not only stress fractures of the bowed femur associated with bone fragility in the elderly<sup>7,8,11–13</sup> but also some femoral diaphysis fractures in fragile bone due to certain diseases (e.g. osteomalacia: Figure 4) would essentially be classified as an insufficiency fracture, which generally has sufficient biological activity for fracture healing, despite fulfilling the current diagnostic criteria<sup>6</sup> for atypical femoral fracture.

femoral diaphysis fractures in fragile bone due to certain diseases (e.g. osteomalacia) would essentially be classified as insufficiency fractures despite fulfilling the current diagnostic criteria for AFF.

#### Author contributions

YO: conceptualization; data curation; funding acquisition; investigation; methodology; project administration; validation; visualization; writing—original draft; writing—review and editing. KY: conceptualization; data curation; investigation; validation; visualization; writing—original draft; writing—review and editing. TY: conceptualization; methodology; writing—review and editing. MK: conceptualization; resources; supervision; writing—review and editing. AO: conceptualization; methodology; project administration; resources; supervision; and writing—review and editing.

#### Conflict of interest statement

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#### Ethical approval

This work was approved by the Tokyo Medical and Dental University Faculty of Medicine IRB (approval ID: M2000-2229). All procedures involving human participants were performed in accordance with the ethical standards of the relevant institutional and/or national research committees and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. All patients included in this article provided informed consent for their data to be published. The data were fully anonymized, thereby protecting the patients' privacy and dignity.

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**References**

- Pentecost RL, Murray RA and Brindley HH. Fatigue, insufficiency, and pathologic fractures. *JAMA* 1964; 187: 1001–1004.
- Shane E, Burr D, Ebeling PR, *et al.* Atypical subtrochanteric and diaphyseal femoral fractures: report of a task force of the American Society for Bone and Mineral Research. *J Bone Miner Res* 2010; 25: 2267–2294.
- Schilcher J, Michaëlsson K and Aspenberg P. Bisphosphonate use and atypical fractures of the femoral shaft. *N Engl J Med* 2011; 364: 1728–1737.
- Bogdan Y. Atypical femur fractures. In: Tornetta III P, Ricci WM, Court-Brown CM, *et al.* (eds) *Rockwood and Green's fractures in adults*. 9th ed. Alphen aan den Rijn: Wolters Kluwer, 2019, pp. 2341–2355.
- Odvina CV, Zerwekh JE, Rao DS, *et al.* Severely suppressed bone turnover: a potential complication of alendronate therapy. *J Clin Endocrinol Metab* 2005; 90: 1294–1301.
- Shane E, Burr D, Abrahamsen B, *et al.* Atypical subtrochanteric and diaphyseal femoral fractures: second report of a task force of the American Society for Bone and Mineral Research. *J Bone Miner Res* 2014; 29: 1–23.
- Oh Y, Wakabayashi Y, Kurosa Y, *et al.* Potential pathogenic mechanism for stress fractures of the bowed femoral shaft in the elderly: mechanical analysis by the CT-based finite element method. *Injury* 2014; 45: 1764–1771.
- Oh Y, Fujita K, Wakabayashi Y, *et al.* Location of atypical femoral fracture can be determined by tensile stress distribution influenced by femoral bowing and neck-shaft angle: a CT-based nonlinear finite element analysis model for the assessment of femoral shaft loading stress. *Injury* 2017; 48: 2736–2743.
- Martelli S, Pivonka P and Ebeling PR. Femoral shaft strains during daily activities: implications for atypical femoral fractures. *Clin Biomech* 2014; 29: 869–876.
- Haider IT, Schneider P, Michalski A, *et al.* Influence of geometry on proximal femoral shaft strains: implications for atypical femoral fracture. *Bone* 2018; 110: 295–303.
- Oh Y, Wakabayashi Y, Kurosa Y, *et al.* Stress fracture of the bowed femoral shaft is another cause of atypical femoral fracture in elderly Japanese: a case series. *J Orthop Sci* 2014; 19: 579–586.
- Oh Y, Yamamoto K, Hashimoto J, *et al.* Biological activity is not suppressed in mid-shaft stress fracture of the bowed femoral shaft unlike in “typical” atypical subtrochanteric femoral fracture: a proposed theory of atypical femoral fracture subtypes. *Bone* 2020; 137: 115453.
- Tano A, Oh Y, Fukushima K, *et al.* Potential bone fragility of mid-shaft atypical femoral fracture: biomechanical analysis by a CT-based nonlinear finite element method. *Injury* 2019; 50: 1876–1882.
- Kim JW, Kim JJ, Byun YS, *et al.* Factors affecting fracture location in atypical femoral fractures: a cross-sectional study with 147 patients. *Injury* 2017; 48: 1570–1574.
- Breithaupt M. Zur pathologie des menschlichen fusses. *Med Zeitung* 1855; 24, 36, 37: 169–177, 169–171, 175–177.
- Milgrom C, Giladi M, Stein M, *et al.* Stress fractures in military recruits. A prospective study showing an unusually high incidence. *J Bone Joint Surg Br* 1985; 67: 732–735.
- Bolin D, Kemper A and Broinson PG. Current concepts in the evaluation and management of stress fractures. *Curr Sports Med Rep* 2005; 4: 295–300.
- Steele CE, Cochran G, Renninger C, *et al.* Femoral neck stress fractures: MRI risk factors for progression. *J Bone Joint Surg Am* 2018; 100: 1496–1502.
- Devas MB. Stress fractures of the femoral neck. *J Bone Joint Surg Br* 1965; 47: 728–738.
- Mahjoub Z, Jean S, Leclerc JT, *et al.* Incidence and characteristics of atypical femoral fractures: clinical and geometrical data. *J Bone Miner Res* 2016; 31: 767–776.
- Thompson RN, Armstrong CL and Heyburn G. Bilateral atypical femoral fractures in a patient prescribed denosumab—a case report. *Bone* 2014; 61: 44–47.
- Kaku T, Oh Y, Sato S, *et al.* Incidence of atypical femoral fractures in the treatment of bone metastasis: an alert report. *J Bone Oncol* 2020; 23: 100301.
- Elniel AR and Giannoudis PV. Atypical fractures and molecular environment: what do we know? *Injury* 2018; 49: 1953–1958.

24. Prasarn ML, Ahn J, Helfet DL, *et al.* Bisphosphonate-associated femur fractures have high complication rates with operative fixation. *Clin Orthop Relat Res* 2012; 470: 2295–2301.
25. Teo BJ, Koh JS, Goh SK, *et al.* Post-operative outcomes of atypical femoral subtrochanteric fracture in patients on bisphosphonate therapy. *Bone Joint J* 2014; 96-B: 658–664.
26. Schilcher J. High revision rate but good healing capacity of atypical femoral fractures. A comparison with common shaft fractures. *Injury* 2015; 46: 2468–2473.
27. Koh A, Guerado E and Giannoudis PV. Atypical femoral fractures related to bisphosphonate treatment: issues and controversies related to their surgical management. *Bone Joint J* 2017; 99-B: 295–302.
28. Sasaki S, Miyakoshi N, Hongo M, *et al.* Low-energy diaphyseal femoral fractures associated with bisphosphonate use and severe curved femur: a case series. *J Bone Miner Metab* 2012; 30: 561–567.
29. Hagen JE, Miller AN, Ott SM, *et al.* Association of atypical femoral fractures with bisphosphonate use by patients with varus hip geometry. *J Bone Joint Surg Am* 2014; 96: 1905–1909.
30. Devas M. Stress fractures of the femur. In: Devas M (ed.) *Stress fractures*. Edinburgh: Churchill Livingstone, 1975, pp. 107–129.
31. Ruohola JP, Laaksi I, Ylikomi T, *et al.* Association between serum 25(OH)D concentrations and bone stress fractures in Finnish young men. *J Bone Miner Res* 2006; 21: 1483–1488.
32. Lappe J, Cullen D, Haynatzki G, *et al.* Calcium and vitamin D supplementation decreases incidence of stress fractures in female navy recruits. *J Bone Miner Res* 2008; 23: 741–749.
33. Miller TL and Best TM. Taking a holistic approach to managing difficult stress fractures. *J Orthop Surg Res* 2016; 11: 98.
34. Whyte MP. Atypical femoral fractures, bisphosphonates, and adult hypophosphatasia. *J Bone Miner Res* 2009; 24: 1132–1134.
35. Sutton RA, Mumm S, Coburn SP, *et al.* “Atypical femoral fractures” during bisphosphonate exposure in adult hypophosphatasia. *J Bone Miner Res* 2012; 27: 987–994.
36. Genest F and Seefried L. Subtrochanteric and diaphyseal femoral fractures in hypophosphatasia—not atypical at all. *Osteoporos Int* 2018; 29: 1815–1825.
37. Nguyen HH, van de Laarschot DM, Verkerk AJMH, *et al.* Genetic risk factors for atypical femoral fractures (AFFs): a systematic review. *JBMR Plus* 2018; 2: 1–11.
38. Leclerc JT, Michou L, Vaillancourt F, *et al.* Prevalence and characteristics of atypical periprosthetic femoral fractures. *J Bone Miner Res* 2019; 34: 83–92.
39. MacKenzie SA, Ng RT, Snowden G, *et al.* Periprosthetic atypical femoral fractures exist and are associated with duration of bisphosphonate therapy. *Bone Joint J* 2019; 101: 1285–1291.
40. Tan SH, Saseendar S, Tan BH, *et al.* Ulnar fractures with bisphosphonate therapy: a systematic review of published case reports. *Osteoporos Int* 2015; 26: 421–429.
41. Niikura T, Lee SY, Sakai Y, *et al.* Rare non-traumatic periprosthetic femoral fracture with features of an atypical femoral fracture: a case report. *J Med Case Rep* 2015; 9: 103.