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Can we improve the prediction of hip fracture by assessing bone structure using shape and appearance modelling?

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ABSTRACT

Purpose: There is a continuing need to improve the prediction of hip fractures to identify those at highest risk, enabling cost-effective use of preventative therapies.
Methods: The aim of this work was to validate an innovative imaging biomarker for hip fracture by modelling the shape and texture of the proximal femur assessed from dual energy X-ray absorptiometry (DXA) scans. Scans used were acquired at baseline from elderly patients participating in a prospective, placebo-controlled fracture prevention study of the bisphosphonate, clodronate. 182 subjects who subsequently suffered a hip fracture were age, weight and height matched with two controls who did not suffer a fracture during a median 4-year follow-up period. Logistic regression was used to test if variables were good predictors of fracture and adjust for bone mineral density (BMD).
Results: Shape mode 2, reflecting variability in neck-shaft angle, neck width and the size of both trochanters (0.81 (OR), 0.68–0.97 (CI), 0.024 (*P*)), and appearance mode 6, recording grey-level contrast (1.33, 1.11–1.59, 0.002), were significant predictors of hip fracture and remained so after adjustment for BMD (shape mode 2 (0.77, 0.64–0.93, 0.006), appearance mode 6 (1.32, 1.10–1.59, 0.003)). Receiver Operating Curve analysis showed the combination of shape mode 2, appearance mode 6 and BMD was 3% better than any single predictor.
Conclusion: Variables derived from shape and appearance models gave a prediction of fracture comparable to BMD and in combination with BMD gave an improvement in the prediction of hip fracture that could predict an additional 2000 hip fracture cases per year in the UK, potentially saving more than £20 million per year and 10,000 cases in the US.

Introduction and Background

Approximately 340,000 hip fractures occur each year in the United States and, worldwide, the incidence of hip fractures is expected to more than triple from 1.66 million in 1990 to 6.26 million in 2050 [1]. In the European Union, an increase from 414 thousand to 972 thousand cases per annum is expected over the next 50 years [2]. In the UK a recent report from the National Hip Fracture Database, which excludes Scotland [3], has shown immediate management data on 76% of the estimated 70,000 cases occurring annually showing a 30-day mortality rate of approximately 10%. The cost of osteoporotic fractures to the UK economy has been estimated at £1.7 billion, of which more than a third is due to hip fracture [4]. The ability to identify individuals who are at very high risk of hip fracture would allow effective targeting of intervention strategies to substantially reduce the economic burden of fractures.

At present, the gold standard for the diagnosis of osteoporosis is bone mineral density (BMD) measurement by dual energy X-ray absorptiometry (DXA) [5], with each 1 standard deviation (SD) reduction in proximal femur BMD associated with an approximately 2.5–2.8-fold increased risk of fracture. However, BMD constitutes just one factor among many that contribute to the likelihood of an osteoporosis-related hip fracture and increasingly the additional risk factors are being captured using the FRAX risk algorithm [6]. The question remains whether further information on fracture risk can be gained by considering non-BMD information from the DXA scans currently used as the technique of choice to assess BMD. We have developed algorithms for the prediction of hip fracture risk using the shape and "texture" of the hip from traditional radiographic images, using active shape modelling (ASM) [7,8]. Subsequent work in progress has demonstrated that the ASM method can be applied to DXA scans [9–11]. Further, we have now developed an enhanced model of the femur using DXA images by using active appearance modelling (AAM) to capture the pattern of BMD intensities inside the femoral head and neck [12,13]. We found that many of the shape and the appearance modes were largely independent of total hip BMD, age and body mass index, indicating that the models may be useful for identifying a population of osteoporosis

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patients at very high risk of hip fracture. The current work sets out to test this hypothesis in a prospective study of incident hip fractures.

Materials & methods

Study cohort

The data used for this study were baseline hip DXA (Hologic 4500) images taken from an MRC funded investigation into the effect of the bisphosphonate clodronate on fractures in almost 6000 women aged 75 years or older [14]. Full Ethical approval was given for the study by the local ethics review board in 1993. Whilst the principal aim of the study was to examine the efficacy of clodronate, the study was also designed to investigate risk factors for fracture in elderly women, so the study group was designed to be a good representation of UK women of 75 and over. Women were recruited randomly from general practice lists, with no other inclusion criteria (e.g. existing osteoporosis). Exclusion criteria were concurrent treatment for a malignancy, concurrent medication likely to influence skeletal metabolism (other than calcium supplements 500 mg daily), bilateral hip arthroplasties, known malabsorptive states, impaired mental state or concurrent illness that would impede informed consent or compliance with the study, significant impairment of renal or hepatic function (serum creatinine >300 M or alanine aminotransaminase more than twice the upper limit of the reference range, respectively), and serum biochemistry consistent with underlying metabolic bone disease (e.g., osteomalacia) or calcium disorders other than primary hyperparathyroidism. 182 cases of incident hip fractures were documented during a median of 4 years follow-up. Baseline DXA hip images of women who went on to sustain a hip fracture were compared to those of 364 controls, matched for age, height and weight, who remained free of hip fracture during follow-up. Total hip BMD was measured using standard methods and has been reported previously [14].

Active Shape and Appearance Modelling (ASM AND AAM)

ASM and AAM were generated using the active appearance modelling toolkit software (Manchester University, UK) from points placed on each image describing the positions of particular anatomical features and the outline of the pelvis and femur as shown in Fig. 1. The model had 72 points and the template design was derived from previous models developed in our group [15] and optimised to use features clearly and repeatedly visible in the Hologic scans used in this study. The AAM was designed so that it ignored non-bone areas, such as the space between the femoral head and acetabulum, in the analysis.

The modelling process is outlined in a flow diagram (Fig. 2). In order to measure differences in the shape of a set of objects, they must first be aligned as closely as possible. The modelling software uses an affine-type transform (translation, rotation and scaling) to match the outline of the hips, without distorting the proportions. Principal component analysis (PCA) is then applied to produce a number of orthogonal modes that describe the variation of shape or appearance within the dataset. Modes are linear combinations of the original variables (point coordinates). The PCA process calculates the first mode to account for the largest amount of variance within the dataset, the second for the largest amount of variance still remaining and so on. As a result, the useful information in the dataset is contained

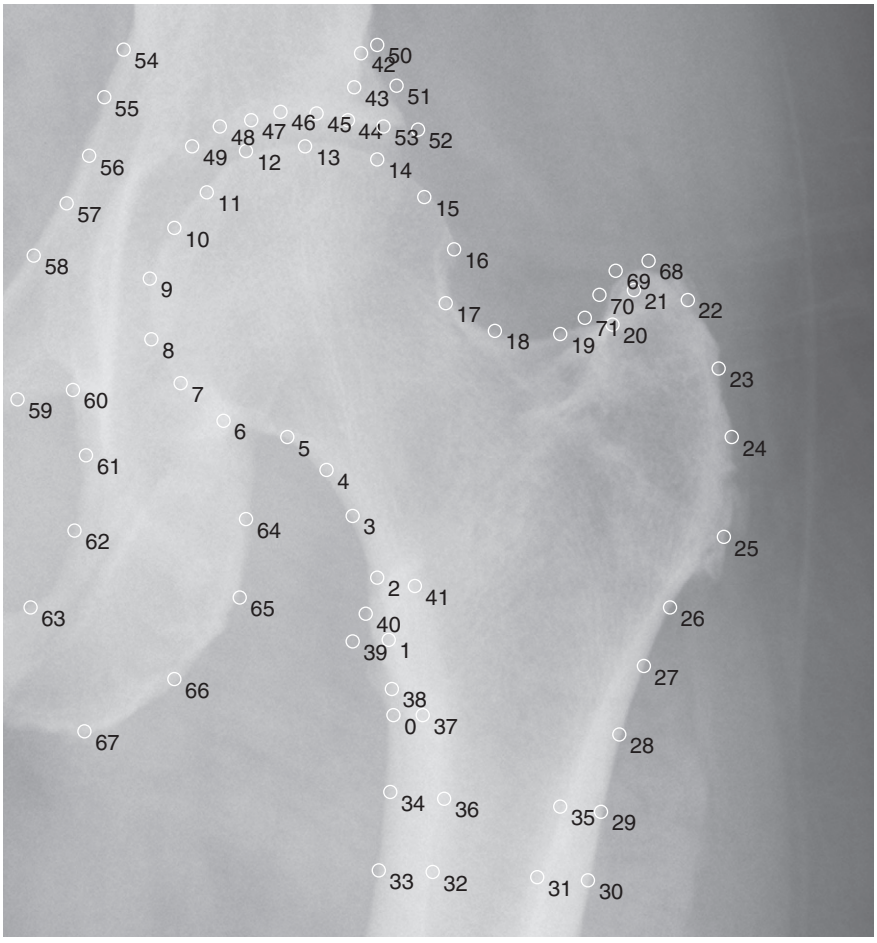

Fig. 1. The point positions for the 72 point model, outlining the femur and parts of the pelvis.