PATIENT-SPECIFIC FINITE ELEMENT MODELS DISCRIMINATE BETWEEN PATIENTS WITH AND WITHOUT A PATHOLOGICAL FRACTURE IN METASTATIC BONE DISEASE

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SUMMARY
Current clinical practice lacks an accurate predictor of the femoral fracture risk in patients suffering metastatic bone disease, which results in large numbers of over- and undertreatment. In this in vivo study we assessed whether patient-specific finite element (FE) models were able to discriminate low-risk patients who suffered a pathological femoral fracture from low-risk patients without a femoral fracture. The FE predicted mean femoral strength in the fracture group was significantly lower than in the non-fracture group. Furthermore, we found a good agreement between the predicted and actual failure courses. Thus, we conclude that FE models can improve the discrimination between patients with and without fractures as compared to current clinical methods.

INTRODUCTION
The quality of life of patients suffering metastatic bone disease is severely jeopardized, since metastatic tumours can be very painful and induce a certain risk of pathological fracture. An accurate prediction of this fracture risk is most important as further treatment strategies are based on this prediction. Namely, femoral metastatic lesions which are expected to induce a low fracture risk are conservatively treated for pain with e.g. radiotherapy, whereas lesions with an expected high fracture risk are treated with stabilizing prophylactic surgery. In current clinical practice it is very difficult to distinguish low-risk from high-risk lesions, which leads to large numbers of over- and undertreated patients [1, 2, 3]. However, patient-specific finite element (FE) models have shown to be very promising in the prediction of femoral bone strength in vitro [4, 5, 6]. In this study, we evaluate whether this FE method also is applicable in vivo. More specifically, the aim of this study was to assess whether patient-specific FE models were able to discriminate between low-risk patients who suffered a pathological fracture and low-risk patients who did not fracture their femur.

METHODS
Sixty-two patients with painful bone metastases with a low fracture risk were prospectively followed while being treated for pain with radiation therapy (informed consent was obtained). Quantitative computed tomography (QCT) scans of the femoral regions, with settings as reported previously [6], were retrieved on 3 or 4 predefined points during treatment, depending on the patients’ radiation schedule. From 14 patients, 18 femora with proven malignancy in the proximal femur were selected for FE modelling. Five patients suffered a unilateral pathological fracture during follow-up and two patients suffered a bilateral femoral fracture (fracture group, F). Nine femora that did not fracture served as a control group (non-fracture group, NF). There were no significant differences in body weight, age and radiation schedule at inclusion between the fracture and the non-fracture group.

Patient-specific FE models were generated from the most recent QCT scan series (Figure 1). The CT-images were segmented and subsequently meshed using four-noded tetrahedral elements (mean edge length ~2 mm). Using the calibration data, grey values in the CT scans were converted into calcium equivalent densities and ash densities, respectively. Subsequently, non-linear isotropic material behaviour for the elements in the FE models was adopted [5].

To enable a reproducible orientation for all the FE models, anatomical landmarks were used for rotating and translating to a position representing the single-limb stance-type loading. The proximal half of the femur was modelled, and distal fixation was accomplished by two bundles of high-stiffness springs, only allowing rotation around the dorsoventral axis. The FE models were loaded via a cup (Ø 30 mm, 0.1 mm/inc) until failure. The FE simulations were performed using MSC Marc. The incremental displacement was registered and the total reaction force in the loading direction was calculated. The ultimate bone strength of the femur was defined as the maximal total reaction force. The failure location was defined

Figure 1: The generation of patient-specific FE models.

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by elements that had passed the softening phase in the post-yield material behaviour.

Using independent T-tests, the ultimate strength, the ultimate strength corrected for body weight (BW-corrected ultimate strength), the work and the stiffness were statistically compared between the fracture group and the non-fracture group, with a level of significance at p < 0.05. The predicted fracture locations were compared to the clinical reports that were available.

RESULTS AND DISCUSSION
The FE-predicted mean ultimate strength of the femora in the fracture group was significantly lower than in the non-fracture group. The BW-corrected ultimate strength was most discriminating for this finding; the 95% confidence intervals of the two groups did not overlap (Figure 2A; mean difference 3.66*BW, p < 0.01). In addition, a significant difference was found in the predicted ultimate strength (mean difference 2074 N, p < 0.01) and work (mean difference 6.01 J, p = 0.02). No significant difference in structural stiffness was found (mean difference 0.41 * 10^6 N/m, p = 0.08). In terms of fracture location, we found a good agreement between the predicted failure courses and the fracture locations reported in the fracture group (Figure 3).

![Figure 2](image1.png)

**Figure 2:** Significant differences were found between the fracture group (F) and non-fracture group (NF) in the BW-corrected ultimate strength (A) and work (B), but not in the structural stiffness (C). Error bars show the mean and 95% CI intervals.

These results showed that patient-specific FE models improved the prediction of the femoral fracture risk in patients suffering metastatic bone disease. In a set of femora with an expected low fracture risk, the FE models correctly distinguished between femora with and without a fracture, by only applying a very simple loading condition. In current clinical practice, pathological fracture risk predictions are mainly based on lesion characteristics measured on radiographs or CT scans, and the physicians' experience and intuition. However, it is almost impossible for physicians to take into account other important aspects such as the overall bone strength, the lesion-specific effect on the bone strength and the daily activity pattern of the patient. FE models can allow for these factors, which considerably improves the fracture risk predictions. The results in this study will be validated in the larger patient population to obtain clear thresholds for patient-specific fracture risk predictions.

![Figure 3](image2.png)

**Figure 3:** Schematic overview of clinically reported fracture location (A), failure location predicted by FE model at the moment of failure (B) and just after failure (C).

CONCLUSIONS
We showed a significant improvement in the discrimination between patients with and without fractures as compared to current clinical methods. FE models may therefore be very helpful in the treatment of patients suffering metastatic bone disease.

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REFERENCES