Introduction: Age-related fractures, specifically those which involve the hip, are an increasing public health care concern. Current treatment and prevention strategies are based on systemic pharmacologic therapies designed to inhibit bone loss. Although osteoporosis is a systemic disease, fractures are local events that occur when the load applied to a bone is greater than the bone’s strength. It may be that a therapy which induces bone formation locally and therefore increases bone strength in regions of bone that are weak, may decrease the overall fracture risk. Previous studies in ovariectomized rats induced local bone formation with recombinant human bone morphogenetic protein-2 (rhBMP-2) compared to untreated, ovariectomized control animals (Li et al, JBMR, 12:S130, 1997).

The goal of this study is to use computational modeling to determine the feasibility of reducing hip fracture risk by inducing local bone changes in the human proximal femur. To achieve this goal, we examined the effect of local control animals (Li et al, JBMR, 12:S130, 1997) morphogenetic protein-2 (rhBMP-2) compared to untreated, ovariectomized treated with a single intraosseous injection of recombinant human bone density of the proximal tibia was 30-70% greater in ovariectomized rats compared to untreated, ovariectomized control animals (Li et al, JBMR, 12:S130, 1997).

The parameters that were varied included the magnitude of the local density increase on the failure load of the proximal femur. To achieve this goal, we examined the effect of local and global bone density increases on the failure load of the proximal femur. The parameters that were varied included the magnitude of the local density increase, the volume of the augmented region, and the number of regions.

Methods: A 66 year old female proximal femur was obtained from the Harvard Anatomical Gifts program and scanned using dual-energy x-ray absorptiometry to determine the level of osteopenia (femoral BMD t-score < -2.5). The femur was imaged on a peripheral QCT scanner (XCT3000, Stratec Medizintechnik GmbH, Phoerheim, GER) with a resolution of 0.2 mm per pixel edge and a 2 mm slice separation. Using custom, semi-automated techniques, a finite element (FE) model was generated from the geometry extracted from the CT scans. The model consisted of 3168 20-noded isoparametric quadratic elements. This number of elements was determined using a convergence test. The material properties of each element were determined from the local density in the region of the element based on the CT data (Ashman et al, J Biomech. 22:895, Snyder & Schneider, JOR8:422).

Six different models of the proximal femur were generated (Figure 1), including (1) baseline model, (2) model with one small region at the superolateral transcervical region of the femoral neck with a density increase of 25% relative to the baseline condition, (3) same as (2) with the relative density increase of 40%, (4) same as (2), except the volume of the region was 5 times greater, (5) model with three small regions at the superolateral transcervical, subcervical, and inferomedial subcapital region of the femoral neck with 25% relative density increases, and (6) a model in which density of every element was increased by 5% relative to its baseline value. This last model (#6) was designed to simulate the possible skeletal response to a systemic anti-resorptive treatment, such as alendronate (Liberman et al, NEJM, 333(22): 1437, 1995). For the ‘small’ regions, all finite elements whose centroid was located within a 9 mm diameter x 10mm length cylindrical region were augmented. In the ‘large’ region, all elements whose centroid was within a cylinder of 20 mm diameter x 20 mm length were augmented.

Boundary conditions representing a fall with impact on the lateral greater trochanter (Courtney et al., JBJS, 77-A:387,1995) were applied to all six models. A user defined subroutine that interfaces with ABAQUS (HKS, Pawtucket RI) FE software was used to calculate the isoparametric body load based on the maximum principal strain failure criterion. This criterion has previously been validated on specimens of trabecular bone in multiple loading modes (Oden et al. ORS 1998, 110). In the algorithm, a load or displacement was applied to the model. The stresses and strains for the prescribed boundary conditions were calculated. Each element integration point was checked for yielding based on the chosen failure-theory and if failed, the modulus was reduced. The load or displacement was then raised and the process repeated until global failure. The peak of the load deflection curve signified the ultimate or failure load.

Results: The predicted failure load for the intact bone was 2218N. The change in the average density in the femoral neck and trochanteric regions, similar to what might be reflected in a standard DXA evaluation, ranged from 0.23% for the single, small region (model 1) to 5% for the model (6) simulating the response to systemic therapy (Table 1). The predicted failure load increased from 5.4% for the model #6 (systemic therapy simulation) to nearly 15% for the model (#4) with a large region (~5 cm) of increased density (Table 1). All of the models with local density increases had predicted failure loads that were similar to or greater than that predicted for the model with a global density increase of 5%, despite the fact that the average density change was less than half that of the model with a global density increase.

Discussion: These findings suggest that it is possible to strengthen the bone against fracture in a fall by increasing the density of a small region of the proximal femur. By increasing the size of the local region of increased density, the predicted failure load increased even further. In this one FE model, however, there was no additional benefit to increasing density in several regions in the femoral neck. In conclusion, the increase in failure load from a local increase (25%) in density in a small region was comparable to the benefit of a lower (5%) but global density augmentation. Thus, an anabolic agent or growth factor that could be locally delivered and could stimulate rapid bone formation, may be an alternative or adjunct to traditional anti-resorptive osteoporosis treatments.

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