INTRODUCTION

For many years, pharmaceutical therapies for osteoarthritis (OA) have been focused on the degenerating cartilage. However, there is increasing evidence that bone plays an important role in OA as well. The structural and material properties of the subchondral bone are modified, and bone cysts and osteophytes may develop. The mechanisms behind these bone changes are subject of debate, and a better understanding may help in the development of bone-targeting OA therapies.

There are indications that the changes in bone material properties and bone structure, and cartilage degeneration are interrelated. In different studies, bone matrix stiffness [1], mineralization [2], and bone structure [3] all seemed to change most markedly directly underneath the cartilage. In addition, bone structural changes seemed correlated with the degree of degeneration of the overlying cartilage [3]. Previously, we showed that mechanoregulated bone adaptation probably remains intact in OA [4]. Therefore, we hypothesize that the decrease in matrix mineralization observed in OA is related to the degeneration of the cartilage, and that this decrease in mineralization in turn causes subchondral bone structural changes, through mechanoregulated bone adaptation.

METHODS

Experimental design

We examined 23 tibia plateaus obtained from OA patients after total knee replacement. For each plateau the Kellgren and Lawrence (K&L) score was determined for the medial and lateral side separately, indicating the severity of OA. We classified K&L 0-1 as mild, 2-3 as moderate, and 4 as severe. 49 cylindrical specimens with a diameter of 8 mm were obtained using a diamond-coated drill (mild: n=15, moderate: n=23, severe: n=11). Each specimen was scanned with a microCT scanner (vivaCT 40, Scanco) at a resolution of 21 µm. Subsequently, bone volume fraction (BV/TV) and bone matrix mineralization (Min.BV) were determined for 2 mm thick slices at different depth levels.

Numerical model

We used an established bone adaptation model based on the theory of Huiskes et al. [5] to simulate the effect of changes in bone matrix mineralization on bone structure. In the model, osteocytes respond to the local strain energy density (SED) rate by promoting osteoblastic bone formation, while osteoclasts resorb bone near randomly occurring microcracks (Figure 1). We implemented the model in ABAQUS and used finite element modeling to represent the morphology and material properties of the tissues and to calculate SED values. First, we simulated bone remodeling until a normal bone structure was obtained. Subsequently, to study our hypothesis, we linearly decreased the bone matrix mineralization from -15% at the bone surface to -5% at 3 mm depth, and simulated bone adaptation.
RESULTS

Experiments

Figure 2: Matrix mineralization and bone volume fraction for different severities of OA, at different depth levels. *p<0.05, **p<0.01.

Bone matrix mineralization decreases while bone volume fraction increases with the progression of OA, and these changes are most apparent close to the cartilage (Figure 2).

Figure 3: Bone volume fraction vs. bone matrix mineralization.
Left: all data points. Right: Data averaged per depth level.

Bone matrix mineralization and bone volume fraction were strongly correlated and the difference between OA levels is apparent (Figure 3).

Simulations

The depth-dependent decrease in bone matrix mineralization caused a depth-dependent increase in bone volume fraction (Figure 4), which concurs with the experimental data (Figure 2).

Figure 4: Left: Simulated bone structures (top and middle), and sites of bone formation and resorption after the mineralization decrease (bottom). Right: Bone volume fraction at different depth levels (top and middle), and bone volume fraction change after the decrease in mineralization (bottom).

DISCUSSION

Both bone volume changes and matrix mineralization changes increased with progression of OA, and were most severe directly underneath the cartilage, thereby indicating a relation between the cartilage and subchondral bone changes. We found a strong correlation between bone volume fraction and bone matrix mineralization, which is in concurrence with our hypothesis that the increase in bone volume fraction is caused by decreased mineralization. In addition, our simulations showed that a depth-dependent decrease in bone matrix mineralization could lead to a depth-dependent increase in bone volume fraction through mechanoregulated bone adaptation, in agreement with the experimental data. This supports the hypothesis that observed structural changes in bone during OA can be explained by mechanoregulated bone remodeling.

It should be noted that the increase in bone volume fraction cannot completely be attributed to a decrease in mineralization. Bone volume fraction differences between the mild and severe OA group exceed 50%, while the differences in mineralization are less than 10%. Although Currey showed that the relationship between Young’s modulus and mineralization is approximately cubic [6], it is unlikely that the increase in bone volume fraction can completely be attributed to the decrease in mineralization. Previously, we showed that altered joint mechanics in conditions associated with OA can lead to OA-like bone structural changes via mechanoregulated bone adaption. It is likely that both factors contribute to the bone volume increase. However, altered bone mineralization is the most likely factor to explain the observed depth-dependency.

CONCLUSION

Based on our experimental and simulation results, we conclude that cartilage degeneration and bone matrix mineralization are related in OA, and that the decrease in matrix mineralization contributes to the increase in subchondral bone volume via mechanoregulated bone adaption. Although further research is required to clarify the relationship between cartilage degeneration and bone mineralization in OA, our study may explain the depth-dependency of the bone volume changes and thereby contributes to the understanding of subchondral bone changes in OA.

ACKNOWLEDGEMENTS

We would like to thank dr. P.E. Emans for providing the tibia plateaus and the K&L scores.

REFERENCES

4. Cox, L.G.E. et al., 2010, “Mechanoregulated bone remodeling may explain bone structural changes observed in osteoarthritis”, ASME SBC.