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# Relationship of bone mineral density to progression of knee osteoarthritis

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## Abstract

**Objective—**We sought to evaluate the longitudinal relationship of bone mineral density (BMD) and its change to knee osteoarthritis (OA) progression measured by cartilage outcomes.

**Methods—**We used observational cohort data from the Vitamin D for Knee Osteoarthritis trial. We obtained bilateral femoral neck BMDs as well as knee MRIs in each subject at baseline and subsequently at 12 and 24 months. We measured change in total cartilage volume, tibial and femoral cartilage thickness by manual cartilage segmentation of two sequential knee MRIs in each subject. Multivariable linear regression models were used to examine the associations of baseline BMD and BMD change with the cartilage outcomes, adjusting for baseline age, gender, BMI, malalignment and vitamin D treatment. We validated model fit and assumptions.

**Results—**127 subjects were eligible for analysis. Longitudinal BMD loss was associated with loss of cartilage volume ($\beta$=1.25 per 0.1g/cm$^2$, p=0.02) and tibial cartilage thickness ($\beta$=0.028, p=0.03). BMD loss of a magnitude greater than least significant change (≤ −4.7%) was associated with 1.02% cartilage volume loss per year (p=0.005), 0.014mm femoral cartilage thickness loss (p=0.04) and 0.021mm tibial cartilage thickness loss per year (p=0.009). There were no significant associations between baseline BMD and any of the cartilage outcomes.

**Conclusions—**Longitudinal BMD loss is associated with progressive cartilage loss in knees with OA. Further work to clarify the basis of this relationship could uncover novel therapeutic targets for knee OA.

## Introduction

Changes in bone are closely associated with cartilage damage in osteoarthritis (OA) [1, 2]. Furthermore, the peri-articular bone appears to have an important function in dissipating peri-articular loads. This suggests that systemic bone health may influence the capacity of peri-articular bone to adapt to stresses and stabilize an osteoarthritic joint. If so, interventions for bone health might influence OA progression. However, although bone

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mineral density (BMD) is positively associated with prevalent [3–9] and incident [10–12] OA, its relationship with knee OA progression is less clear [10–12]. Two longitudinal studies suggested that higher baseline BMD is protective of knee OA progression [10, 11] while another failed to find an association [12]. One of these also found a relationship of BMD loss with knee OA progression [10]. However, these studies had limitations including reliance on radiography to classify progression, which is insensitive to change and subject to ceiling effects.

Therefore, using observational cohort data from a knee OA clinical trial, we tested the hypothesis that, in knee OA, low femoral neck BMD (a proxy for systemic bone density) and longitudinal BMD loss, are related to cartilage loss measured using MRI (a measure of OA structural progression).

## Patients and Methods

### Overview

We conducted an observational cohort study using data from the Vitamin D for Knee Osteoarthritis Study, a 2-year, double–blind, placebo-controlled, randomized clinical trial among 146 participants that had null results [13]. The inclusion criteria were age over 45 years and the presence of symptomatic and radiographic (Kellgren-Lawrence (K-L) grade ≥ 2) knee OA in at least one knee, as defined by American College of Rheumatology criteria [14]. We selected one symptomatic knee as the study knee. We followed the study subjects for 2 years and performed annual MRIs of the study knee, and bone density scans of both femoral necks. The study was approved by the Tufts Institutional Review Board.

### Sample Selection

We included all subjects who had at least two MRI scans without motion artifact among the baseline, year 1 and year 2 scans. In cases where all three scans were interpretable, we used the baseline and year 2 images to compute the yearly change in cartilage volume and thickness. For those subjects who withdrew before year 2 scans or for whom one MRI is not interpretable (n=19), we used the scans from the other years (e.g. baseline and year 1) to compute the 1-year change in the outcomes.

### BMD measurement

We obtained BMDs of bilateral femoral necks in each subject at baseline, year 1 and year 2 using a GE Lunar Prodigy Dual-energy X-ray absorptiometry (DXA) Scanner (Madison, WI). Quality assessment was performed prior to the first scan of the day. We calculated the mean neck BMD of each subject by averaging both sides of femoral neck BMDs to estimate systemic BMD in g/cm$^2$. In the case of hip replacement, we included the BMD from the non-replaced side only rather than the average. The precision error for the DXA machine used to obtain BMD in our study was previously published [15]: In this study, mean percentage coefficients of variance (%CVs) in BMD were 1.66% for the femoral neck scans. We defined BMD change per year (g/cm$^2$) as a continuous variable using the following equation: $[(\text{BMD at follow up}) - (\text{BMD at baseline})] * 12/(\text{DXA interval in months})$. We used the similar time points for BMD measurements as those of the MRI scans for each

subject so that the BMD and cartilage were contemporaneous. To create a categorical BMD change variable, we used the least significant change (LSC) as a cutoff to define BMD gain and loss. LSC is a recognized approach to determine meaningful BMD change [16, 17]. LSC is calculated as the BMD change exceeding 2√2times the precision error of a technique [18]. Inserting our CV into the equation, we defined *meaningful gain* as BMD change ≥4.7%, *meaningful loss* as BMD change≤−4.7%, and *no change* as that within ±4.7%.

### Cartilage volume and thickness measurement

We obtained MRIs of the study knees at baseline, year 1 and year 2 follow-up visits using a Siemens Magnetom Avanto 1.5T (Malvern, PA). To calculate cartilage volume, we obtained 3-dimensional sagittal water excitation dual echo steady state (DESS WE) images with slice thickness 1.3 mm. We defined the index compartment (medial or lateral) as that with the most evident damage on X-rays or MRI.

One reader (JYL) performed manual segmentation of tibial and femoral cartilage using a registration process for the paired baseline and follow-up sagittal DESS WE sequences. We used ANALYZE 8.1 ® (Mayo Clinic, Rochester, MN) software to compute the cartilage volumes, and a customized program running in MatLab (The MathWork, Natick, MA) to determine mean cartilage thickness. Intra-tester reliability ICCs for manual segmentation were 0.96 & 0.90 for cross-sectional volume and volume loss, respectively.

We used percent change rather than absolute change to adjust for variability accountable to age, gender and height for cartilage volume. We used the following definitions for cartilage outcomes: Total (tibial and femoral) cartilage volume change per year (%) = 100(%)* {[(total cartilage volume at follow-up) − (total cartilage volume at baseline)]/(total cartilage volume at baseline)}*12/(MRI interval in months); Tibial cartilage thickness change per year(mm) = [(tibial cartilage thickness at follow-up)−(tibial cartilage thickness at baseline)] *12/(MRI interval in months); Femoral cartilage thickness per year(mm) = [(femoral cartilage thickness at follow-up)−(femoral cartilage thickness at baseline)]*12/(MRI interval in months).

### Other variables

We recorded age, gender, BMI, and K-L grade, and vitamin D treatment status at the baseline visit. To define alignment status, we measured the anatomic-axis angle on a standard plain knee posterior–anterior radiograph at baseline, and categorized alignment into three groups similarly as previous studies [19, 20]: varus (<178°), neutral (178°–182°), and valgus (>182°). Bisphosphonate use was a binary variable defined as any bisphosphonate medication use at any time during the trial.

### Statistical analyses

We generated descriptive statistics and plots to examine the data. We performed three sets of linear regression analyses, each with three linear regression models. In each set of models we examined the relationship of BMD and BMD change to each of the cartilage outcomes: percent change in cartilage volume per year, absolute change in tibial and femoral cartilage thickness per year. In the first set, we tested the association between baseline BMD and each

of the cartilage outcomes. We then examined the relationship between continuous BMD change and the cartilage outcomes. Finally, we examined the association between categorized BMD change and the cartilage outcomes. We performed both univariate and multivariable regression. We used multivariable linear regression models to adjust for baseline values of age, gender, body mass index (BMI), alignment status and vitamin D treatment as these are potential confounders in the relationship between BMD and cartilage outcomes. For models examining the relationship between BMD change and knee OA progression, bisphosphonate use was added to the list of potential confounders. We examined Q-Q plots and Cooks D to validate model fit and check assumptions. We also checked the linearity assumption for continuous variables. We compared the baseline characteristics of subjects included in the study with those excluded due to missing data in any of the variables to see if the groups were different. We used R program, version 2.13.1 (2011-07-22) for statistical analyses.

## Results

Total 127 subjects were included in the analyses. The number of subjects included in each model differed according to the availability of dependent variables and covariates. The mean age was 63 years, 41% were male, and mean BMI was 30 $kg/m^2$. The mean baseline BMD was 0.95 $g/cm^2$, and the change of BMD per year was −0.004 $g/cm^2$. 13% of participants had BMD loss beyond the LSC, and only 3% of participants gained BMD above the LSC. The mean follow up period was 22 months (Table 1).

The baseline characteristics of 19 subjects who were excluded due to missing data were compared with subjects included in the study. The excluded subjects were significantly more obese (BMI 34.28±6.76 $kg/m^2$, p=0.003) but otherwise did not differ significantly in terms of age (59.8 ±7.8 years, p=0.17), gender (male 26%, p=0.22), and treatment group assignment (32%, p=0.09). The alignment also did not differ significantly; 10(53%) were varus, 3(16%) were valgus, and 6 (31%) were normal. Baseline K-L grade 2, 3, 4 were 6(32%), 8(42%), 5(26%), respectively.

### Baseline BMD and KOA progression

There was no statistically significant association between baseline BMD and any of the cartilage outcomes in either the univariate or multivariable models (Table 2). We performed a sensitivity analysis removing the most extreme influential points from the models for cartilage volume change and tibial and femoral cartilage thickness and this did not change our results.

### BMD change and KOA progression

There was a significant association of BMD change with cartilage volume change, in both its continuous and categorical forms, and in both the univariate and multivariable models (Table 3). In the multivariable models, a BMD loss of 0.1 $g/cm^2$ was associated with cartilage *volume* loss of 1.25% per year (p=0.02). Subjects who lost BMD beyond the LSC lost an average of 1.02% more cartilage volume per year compared with those without BMD loss (p=0.005). We also found significant relationships of BMD loss with femoral and tibial

cartilage *thickness* change in the multivariable models. BMD loss of 0.1 g/cm$^2$ was associated with tibial cartilage thickness loss of 0.028 mm per year (p=0.03). Subjects who lost BMD beyond the LSC lost an average of 0.021 mm more tibial cartilage thickness per year compared with those without BMD loss (p=0.009).

## Discussion

Our study shows that longitudinal BMD *loss*, measured at a site remote from the knee, is associated with progressive loss of cartilage in knees with OA. This was the first study to examine the relationship between BMD and knee OA progression as measured by cartilage volume and thickness. However, the results are consistent with previous studies that examined this relationship using radiographic outcomes. The Framingham study, for example, also found BMD *loss* to be associated with progression of radiographic joint space narrowing [10].

Our study did not find a significant relationship with BMD *gain*, but only 4 subjects had BMD gain above the LSC. Also, we did not find a relationship of *baseline* BMD with any of our cartilage outcomes. Previous studies have generated inconsistent findings regarding this relationship. The Framingham study was the only longitudinal study that showed a significant relationship with radiographic joint space loss [10], while the Chingford study found a weak association [11], and the MOST study, no association [12]. Our study differed from those in its outcome measures and shorter observation period.

Currently, the biologic mechanism relating BMD loss to cartilage loss in knee OA is conjectural. One mechanistic possibility is that BMD health might provide an environment that supports optimal subchondral bone turnover and remodeling in response to OA stressors, thus favoring joint stabilization [1, 21–23]. Systemic BMD could also be a marker for a range of covariates that mediate or confound the relationship. It is possible that the relationship is mediated biomechanically, for example, by low level of physical activity or by systemic factors such as circulating growth factors or hormones.

If stable BMD mechanistically prevents OA progression, interventions to improve BMD might provide some benefit in regards to OA structural progression. Bisphosphonates, the most commonly used therapeutic agent for osteoporosis, have been investigated as a potential therapeutic agent in OA. A small trial found a non-significant trend towards reduced joint space narrowing as well as symptomatic benefit in the risedronate group [24], but a subsequent larger trial failed to show benefit in structural or symptomatic OA progression [25] although this might be a result of the short follow-up period and the use of insensitive outcomes. Actually, the biochemical measure indicating collagen degradation was reduced in treatment group compared to placebo [25] and a subset analysis of rapid progressors showed benefits of treatment in retaining vertebral trabecular structure [26]. Another study reported reduction in spinal osteophyte progression in those treated with alendronate compared to placebo using a secondary analysis of a trial [27]. It is still unclear if bisphosphonates are beneficial to OA progression, but our finding supports further investigation of therapeutics regarding improving systemic BMD in OA.

Our study has several limitations. Given the number of comparisons made, it is also possible that some of the results represent false positive findings. Although measurement errors in outcome could have occurred, it is likely that they are non-differential with respect to people with baseline BMD or its change, so it would be expected to attenuate measures of association. Reporting percent change for total cartilage volume has been the usual practice given baseline variability, but this measure could generate residual floor or ceiling effects. This is an observational study examining factors associated with knee OA progression among subjects with prevalent radiographic knee OA. In an observational study such as this, restricting the study population to those with prevalent knee OA could generate bias if there are uncontrolled common causes of both knee OA incidence and progression [28, 29] [30]. To address this potential bias, we tried to anticipate and include all available variables that may be common causes of knee OA incidence and progression in multivariable models, such as age, gender, BMI and malalignment. As for all epidemiologic studies, unmeasured confounding remains a potential limitation.

The strengths of our study include the use of more sensitive outcome measures to detect progression. Our cartilage volume and thickness measures are continuous, eliminating problems due to non-linear progression trajectories [30] and potentially enhancing sensitivity to detect progression, and reducing misclassification. Our study should also be generalizable to most individuals with knee OA, since the eligibility criteria for the trial were broad and included the highest radiographic grade (K-L grade 4). We also accounted for measurement error in defining BMD change by computing least significant change (LSC), which was not considered in the prior study [10].

In conclusion, our study suggests that longitudinal BMD *loss* is associated with longitudinal cartilage loss in knees with OA. This relationship could be explained by direct biological interaction between these structures on a biomechanical, autocrine basis or these could be concurrent manifestations of a more systemic process relating to aging. Further work to clarify the basis of this relationship would be informative and potentially lead to novel therapeutic interventions for knee OA progression.

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## References

1. Burr DB. The importance of subchondral bone in the progression of osteoarthritis. J Rheumatol Suppl. 2004; 70:77–80. [PubMed: 15132360]
2. Buckland-Wright C. Subchondral bone changes in hand and knee osteoarthritis detected by radiography. Osteoarthritis Cartilage. 2004; 12(Suppl A):S10–9. [PubMed: 14698636]
3. Foss MV, Byers PD. Bone density, osteoarthrosis of the hip, and fracture of the upper end of the femur. Ann Rheum Dis. 1972; 31(4):259–64. [PubMed: 5045904]

4. Dequeker J. The relationship between osteoporosis and osteoarthritis. Clin Rheum Dis. 1985; 11(2): 271–96. [PubMed: 3899487]
5. Hart DJ, et al. The relationship between osteoarthritis and osteoporosis in the general population: the Chingford Study. Ann Rheum Dis. 1994; 53(3):158–62. [PubMed: 8154931]
6. Cooper C, et al. Osteoarthritis of the hip and osteoporosis of the proximal femur. Ann Rheum Dis. 1991; 50(8):540–2. [PubMed: 1888195]
7. Hannan MT, et al. Bone mineral density and knee osteoarthritis in elderly men and women. The Framingham Study. Arthritis Rheum. 1993; 36(12):1671–80. [PubMed: 8250986]
8. Burger H, et al. Association of radiographically evident osteoarthritis with higher bone mineral density and increased bone loss with age. The Rotterdam Study. Arthritis Rheum. 1996; 39(1):81–6. [PubMed: 8546742]
9. Nevitt MC, et al. Radiographic osteoarthritis of the hip and bone mineral density. The Study of Osteoporotic Fractures Research Group. Arthritis Rheum. 1995; 38(7):907–16. [PubMed: 7612040]
10. Zhang Y, et al. Bone mineral density and risk of incident and progressive radiographic knee osteoarthritis in women: the Framingham Study. J Rheumatol. 2000; 27(4):1032–7. [PubMed: 10782833]
11. Hart DJ, et al. The relationship of bone density and fracture to incident and progressive radiographic osteoarthritis of the knee: the Chingford Study. Arthritis Rheum. 2002; 46(1):92–9. [PubMed: 11817613]
12. Nevitt MC, et al. High systemic bone mineral density increases the risk of incident knee OA and joint space narrowing, but not radiographic progression of existing knee OA: the MOST study. Ann Rheum Dis. 2010; 69(1):163–8. [PubMed: 19147619]
13. McAlindon TE. Clinical Trial of Vitamin D to Reduce Pain and Structural Progression in Knee Osteoarthritis. Arthritis and Rheumatism. 2010; 62(10 Suppl):S294.
14. Altman R. Development of criteria for the classification and reporting of osteoarthritis. Classification of osteoarthritis of the knee. Diagnostic and Therapeutic Criteria Committee of the American Rheumatism Association. Arthritis Rheum. 1986; 29(8):1039–49. [PubMed: 3741515]
15. White J, et al. Precision of single vs bilateral hip bone mineral density scans. J Clin Densitom. 2003; 6(2):159–62. [PubMed: 12794238]
16. Frimeth J, Galiano E, Webster D. Some Physical and Clinical Factors Influencing the Measurement of Precision Error, Least Significant Change, and Bone Mineral Density in Dual-Energy X-Ray Absorptiometry. Journal of Clinical Densitometry. 2010; 13(1):29–35. [PubMed: 19932980]
17. El Maghraoui A, Achemlal L, Bezza A. Monitoring of Dual-Energy X-ray Absorptiometry Measurement in Clinical Practice. Journal of Clinical Densitometry. 2006; 9(3):281–286. [PubMed: 16931345]
18. El Maghraoui A, Roux C. DXA scanning in clinical practice. QJM. 2008; 101(8):605–17. [PubMed: 18334497]
19. Englund M, et al. Meniscal tear in knees without surgery and the development of radiographic osteoarthritis among middle-aged and elderly persons: The multicenter osteoarthritis study. Arthritis & Rheumatism. 2009; 60(3):831–839. [PubMed: 19248082]
20. Neogi T, et al. Subchondral bone attrition may be a reflection of compartment-specific mechanical load: the MOST Study. Annals of the Rheumatic Diseases. 2010; 69(5):841–844. [PubMed: 19762366]
21. Dore D, et al. Subchondral bone and cartilage damage: a prospective study in older adults. Arthritis Rheum. 2010; 62(7):1967–73. [PubMed: 20506256]
22. Dore D, et al. Correlates of subchondral BMD: a cross-sectional study. J Bone Miner Res. 2009; 24(12):2007–15. [PubMed: 19453266]
23. Lo GH, et al. Bone marrow lesions in the knee are associated with increased local bone density. Arthritis Rheum. 2005; 52(9):2814–21. [PubMed: 16145676]
24. Spector TD, et al. Effect of risedronate on joint structure and symptoms of knee osteoarthritis: results of the BRISK randomized, controlled trial [ISRCTN01928173]. Arthritis Res Ther. 2005; 7(3):R625–33. [PubMed: 15899049]

25. Bingham CO 3rd, et al. Risedronate decreases biochemical markers of cartilage degradation but does not decrease symptoms or slow radiographic progression in patients with medial compartment osteoarthritis of the knee: results of the two-year multinational knee osteoarthritis structural arthritis study. Arthritis Rheum. 2006; 54(11):3494–507. [PubMed: 17075851]

26. Buckland-Wright JC, et al. A 2 yr longitudinal radiographic study examining the effect of a bisphosphonate (risedronate) upon subchondral bone loss in osteoarthritic knee patients. Rheumatology (Oxford). 2007; 46(2):257–64. [PubMed: 16837470]

27. Neogi T, et al. The effect of alendronate on progression of spinal osteophytes and disc-space narrowing. Ann Rheum Dis. 2008; 67(10):1427–30. [PubMed: 18276744]

28. Hernan MA, et al. Causal knowledge as a prerequisite for confounding evaluation: an application to birth defects epidemiology. Am J Epidemiol. 2002; 155(2):176–84. [PubMed: 11790682]

29. Dahabreh IJ, Kent DM. Index event bias as an explanation for the paradoxes of recurrence risk research. JAMA. 2011; 305(8):822–3. [PubMed: 21343582]

30. Zhang Y, et al. Methodologic challenges in studying risk factors for progression of knee osteoarthritis. Arthritis Care Res (Hoboken). 2010; 62(11):1527–32. [PubMed: 20617531]

## Table 1

Characteristics of study participants (N=127)

| | **Mean±SD or N(%)** |
|---|---|
| Age, years | 62.74±8.59 |
| Male | 52(41%) |
| Vit D treated | 67(53%) |
| BMI, kg/m$^2$ | 30.12±5.38 |
| Alignment status | |
| Varus | 61(48%) |
| Valgus | 25(20%) |
| Normal | 41(32%) |
| Baseline BMD, g/cm$^2$ | 0.95±0.14 |
| Bisphosphonate use | 14(11%) |
| Radiographic Knee OA grade (K-L grade) | |
| 2 | 67(53%) |
| 3 | 34(27%) |
| 4 | 26(20%) |
| BMD change per year, g/cm$^2$ | −0.004±0.022 |
| Categorized BMD change | |
| BMD gain (more than 4.7%) | 4 (3%) |
| BMD loss (less than −4.7%) | 16 (13%) |
| No change (within ±4.7%) | 104(84%) |
| Cartilage volume change per year, % | −2.14±1.29 |
| Femoral cartilage thickness change per year, mm | −0.034±0.023 |
| Tibial cartilage thickness change per year, mm | −0.029±0.028 |
| Follow up period, months | 22.02 ±4.50 |

SD=standard deviation. All change values were subtracted from follow up to baseline, so that positive values indicate gain and negative values indicate loss. BMI=Body Mass Index, BMD=Bone Mineral Density, OA=osteoarthritis, K-L=Kellgren-Lawrence.

**Table 2**

Relationship between baseline BMD and change in cartilage outcomes

| | Cartilage volume change per year (%) N=126 | | Femoral cartilage thickness change per year (mm) N=121 | | Tibial cartilage thickness change per year (mm) N= 125 | |
|---|---|---|---|---|---|---|
| | **Estimate(SE)** | **p** | **Estimate (SE)** | **p** | **Estimate (SE)** | **p** |
| Baseline BMD | 0.28 (0.85) | 0.73 | 0.004 (0.015) | 0.79 | 0.009 (0.018) | 0.61 |
| Baseline BMD* | 0.33 (0.86) | 0.71 | 0.002 (0.016) | 0.91 | 0.017 (0.019) | 0.39 |

*Adjusted for age, gender, BMI, alignment status, vitamin D treatment.

**Table 3**

Relationship between BMD change and ANNUAL change in cartilage outcomes

| | VOLUME (%) ** | | THICKNESS (mm) | | | |
|---|---|---|---|---|---|---|
| | | | Femoral cartilage** | | Tibial cartilage** | |
| | Estimate(SE) | p | Estimate (SE) | p | Estimate (SE) | p |
| BMD change per year per 0.1g/cm$^2$ † | 1.29 (0.54) | 0.02 | 0.019 (0.009) | 0.04 | 0.021 (0.012) | 0.08 |
| BMD change per year per 0.1g/cm$^2$ †* | 1.25 (0.54) | 0.02 | 0.019 (0.010) | 0.06 | 0.028 (0.012) | 0.03 |
| BMD change* | | 0.02 | | 0.11 | | 0.03 |
| Gain | −0.38 (0.64) | 0.55 | −0.007(0.012) | 0.53 | −0.013(0.029) | 0.37 |
| Loss | −1.02 (0.36) | 0.005 | −0.014 (0.007) | 0.04 | −0.021(0.008) | 0.009 |
| No change | reference | | reference | | reference | |

† A 0.1-unit change is reported because 1unit change in BMD is not clinically possible.

* Adjusted for age, gender, BMI, malalignment status, vitamin D treatment, bisphosphonate use.

** N=124 for volume, 119 for femoral cartilage thickness, 123 for tibial cartilage thickness