INTRODUCTION
Bisphosphonate treatments result in a substantial reduction in the incidence of clinical osteoporotic fractures, an effect that is not explained by the concomitant increase in BMD [1]. Because of this, there is much current clinical interest in bone quality. By definition, bone quality represents a change in strength of the bone after accounting for changes in bone density. For trabecular bone, this should be manifested by a change in the strength-density relation, and/or, a change in the ratio of strength to density. We are aware of no biomechanical studies that have shown conclusively the effects of any type of bisphosphonate treatment on the strength-density characteristics for trabecular bone, nor how such characteristics are altered by any treatment-induced changes in microarchitecture. Such biomechanical changes may also be sensitive to the loading mode, e.g. compression vs. torsion, since there is evidence from aging studies that microarchitecture changes may be accentuated in non-habitual loading directions.

Thus, our objective was to determine the effect of any microarchitectural changes induced by risdonate treatment on the strength-volume fraction characteristics for trabecular bone, comparing responses for compression vs. torsional loading. This study is unique in its focus on microarchitecture-related strength characteristics and its response comparison for two different loading modes.

METHODS
Twenty female beagle dogs, aged 1–2 years, were randomly assigned to control and treated groups. The control group (n=10 animals) was treated daily with oral saline, the treated group (n=10 animals) was treated daily with oral risdonate (0.5mg/kg/day) for a period of 1 year [2]. The ducks were then sacrificed. The T-10 vertebral bodies obtained from the harvested ducks were scanned with micro-CT at 18 [m resolution (Scanco 80, Basserdorf, Switzerland). Two cylindrical cores (diameter=3.5mm, height=6mm) were virtually removed from each scan such that the basivertebrae foramen and the cortex were avoided. Because the mean trabecular spacing of this type of bone is about 0.4 mm [3], the continuum assumption for the small specimens still held [4].

The same tissue-level elastic properties a Young’s modulus of 18.5 GPa and Poisson’s ratio of 0.3 — and yield strength properties tensile and compressive yield strain values of 0.33% and 0.81%, respectively — were assigned to the control and treated groups in order to eliminate any possible effect of variations in tissue material properties. Using custom code running on multiple processors on an IBM supercomputer [5], two fully nonlinear finite element analyses — including material and geometric non-linearities — were performed on each model (n=40 total) using compressive and torsional apparent loading to failure. Bone volume fraction, apparent level strength (0.2% offset yield stress) and the bone strength:volume fraction ratio were calculated for both loading modes and statistically compared accounting for the replicates.

RESULTS
As expected, the treated group had a higher bone volume fraction and strength as compared to the control group, but percent changes in strength were much higher than in volume fraction (Table 1). Even so, the strength-volume fraction relationship was not statistically different between the control and treated groups (Figure 1) for either compression (p=0.17) or torsion (p=0.09). The strength:volume fraction ratio for torsion was higher for the treated group (p=0.005), while there was no significant difference in this parameter (p=0.19) for compression. The strength:volume fraction ratio depended (p<0.05) on volume fraction except for the treated group loaded in compression (Figure 2).

DISCUSSION
For the purposes of this study, we have defined a change in bone quality as a fundamental change in the strength-volume fraction characteristics. Statistically, there were no detectable changes in the strength-volume fraction relation with risdonate treatment for either compressive or torsional loading. But there was a non-significant trend, particularly for compression, for the bone to have slightly lower strength than expected from the control behavior, as evidenced by the slight shift in strength values to the right of the control strength-volume fraction relation. Why this trend would exist, and be more pronounced for compressive loading, is not clear at this juncture. As the bone increases in volume fraction, the ratio of strength to volume fraction increases, naturally and with treatment. But since there were no appreciable changes in the strength-volume fraction relation with treatment, there do not appear to any “quality” effects associated with the microarchitecture that are independent of bone density. The main caveats of this study were the use of a non-bone loss animal model, and a maximum spatial resolution of 18 microns. We conclude that if these trends also exist in human bone, it is unlikely that changes in microarchitecture — at a scale of 18 microns or above — can explain why anti-resorptive treatments are so effective clinically despite the modest clinical increases in BMD.

Table 1: Comparison of control and treated groups (Mean ± SD).

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>Treated</th>
<th>% Change</th>
<th>p value</th>
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<tbody>
<tr>
<td>Volume fraction, VF</td>
<td>0.20 ± 0.03</td>
<td>0.24 ± 0.01</td>
<td>20.0</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Compression: yield stress (MPa)</td>
<td>8.0 ± 2.5</td>
<td>10.7 ± 1.6</td>
<td>33.7</td>
<td>0.007</td>
</tr>
<tr>
<td>Torsion: yield stress (MPa)</td>
<td>40.2 ± 8.6</td>
<td>44.1 ± 5.7</td>
<td>9.7</td>
<td>0.19</td>
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Figure 1: Yield strength-volume fraction relationship for the control and treatment groups in compression (Left) and torsion (Right).

Figure 2: Variation of Yield strength/Volume fraction metric with volume fraction in compression (Left) and torsion (Right).

REFERENCES

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ACKNOWLEDGEMENTS
Proctor & Gamble, NIH AR47838, NPACE-UCB 266.