

# Altered vertebral biomechanical properties in prostate cancer patients following androgen deprivation therapy

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**INTRODUCTION:** Androgen deprivation therapy (ADT) is the standard of care for advanced prostate cancer (PC). Studies have shown a significant decrease in bone density by 1.5-4.0% annually following ADT, which exceeds normal annual bone loss for healthy aging males [1]. Dual energy x-ray absorptiometry (DXA) is the 'gold standard' clinical method for measuring BMD and determining fracture risk. As a 2D projected measurement, DXA cannot provide information on the 3D shape and the large regional variation in vertebral geometries and the distribution of BMD throughout the bone volume which are known to influence bone strength [2]. Therefore, to fully capture bone strength in prostate cancer patients, a 3D quantitative evaluation of the bone biomechanics is necessary.

**METHODS:** Dataset obtained from ANTELOPE clinical trial included PC patients receiving ADT (n=25) and matched controls (n=25). Densitometric properties were obtained from the DXA scans: areal BMD (aBMD), and QCT scans: trabecular volumetric BMD (tvBMD) and integral volumetric BMD (ivBMD) which is a measure of both the cortical and trabecular compartments. 3D finite element (FE) models of the T12 vertebra were reconstructed from QCT scans performed at baseline and 12 months. Bone was modelled in ANSYS as heterogenous, isotropic, and elastic-plastic, with material properties based on the patient-specific densitometry calibration and phenomenological relationships. FE analysis simulated failure by compression (1.9% strain) to analyse the structural: stiffness and ultimate load, and mechanical properties: normalised stiffness and ultimate strength.

**RESULTS:** ADT reduces both densitometric and mechanical properties in men with PC (Figure 1). On average, between the baseline and 12-month visits, the patients receiving ADT displayed a significant reduction in aBMD (aBMD: -4% p<0.01) whilst the aBMD in the control group had increased (+2.3% p<0.01). tvBMD and ivBMD at 12 months had a larger decrease than aBMD for the patients who received ADT (tvBMD: -17% p<0.01 and ivBMD: -11% p<0.01) whilst the control group showed no significant change. At 12 months, the FE analysis resulted in an even larger decrease in mechanical properties for the patients receiving ADT than both aBMD and ivBMD but similar to tvBMD (stiffness: -14% p<0.01, failure load: -16% p<0.01, normalised stiffness: -14% p<0.01, ultimate strength: -16% p<0.01), compared to the control group.

A moderate but significant correlation was found between the percentage change in aBMD and the percentage change in ultimate strength for the pooled data (r = 0.44-0.46 p<0.01), while a moderate insignificant correlation was found in the treated and control groups. Strong correlations between the percentage change in tvBMD or ivBMD and the percentage change in ultimate strength were found (r = 0.78-0.93 p<0.001, r = 0.88-0.96 p<0.001) (Figure 2).

**DISCUSSION:** This study observed a significant decrease in aBMD following ADT after 12 months, at 4%. Similar, but amplified trends were observed in the treated group for trabecular vBMD and integral vBMD, reducing by 17% and 11% respectively over 12 months. FE has been shown to predict larger changes than those seen in aBMD from DXA in osteoporotic patients [3], [4]. This could be explained by accounting for BMD distribution in 3D which has been indicative of strength gains and cortical thickness which has also proven to be important when predicting fracture risk.

The weak correlation between aBMD and mechanical properties may be due to the overestimation of aBMD by central DXA due to anatomical features and the inclusion of posterior spinous processes and the inability to provide information on 3D shape, large regional variation in vertebral geometries and the distribution of BMD throughout the bone. The highest correlation between densitometric and predicted mechanical properties was observed when using ivBMD. This can be explained considering that the ivBMD is calculated across the whole vertebral body and provides information from trabecular and cortical bone compartments, both of which contribute to the vertebral body compressive strength.

The material properties of bone were modelled as isotropic, neglecting the anisotropic nature of bone. Nonetheless, the intrinsic anisotropy of the trabecular bone was modelled by using relatively small element size (1mm) and the assignment of heterogeneous material properties in function of the local BMD. Incorporating other loading conditions such as torsion and bending could improve the analysis. However, it is well known that compression is the most significant loading condition for most fracture modes and therefore is most used within the field of FE vertebral mechanics.

**SIGNIFICANCE/CLINICAL RELEVANCE:** ADT treatment for 12 months in a cohort of PC patients reduces both bone mineral density and mechanical properties. The predictive ability of aBMD is low in comparison to tvBMD and ivBMD, suggesting the determination of the vBMD might be of higher value when assessing patients bone strength in clinical practice.

## REFERENCES:

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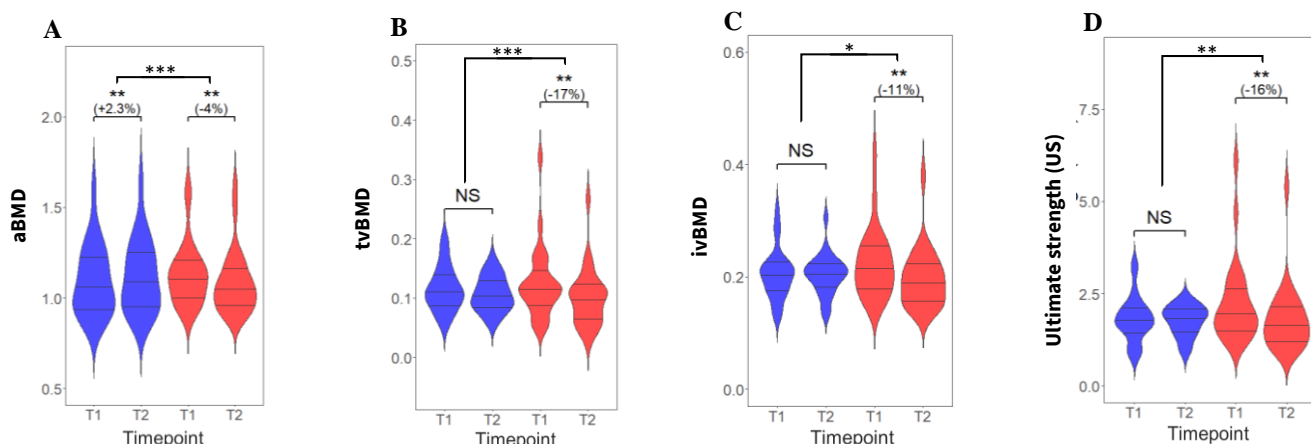


Figure 1. Violin plots of both cohorts and both time points are shown for (A) aBMD, (B) trabecular vBMD, (C) integral vBMD, and (D) ultimate strength. \*p<0.05, \*\*p<0.01, \*\*\*p<0.001. Abbreviations: T1 – baseline, T2 – 12 months

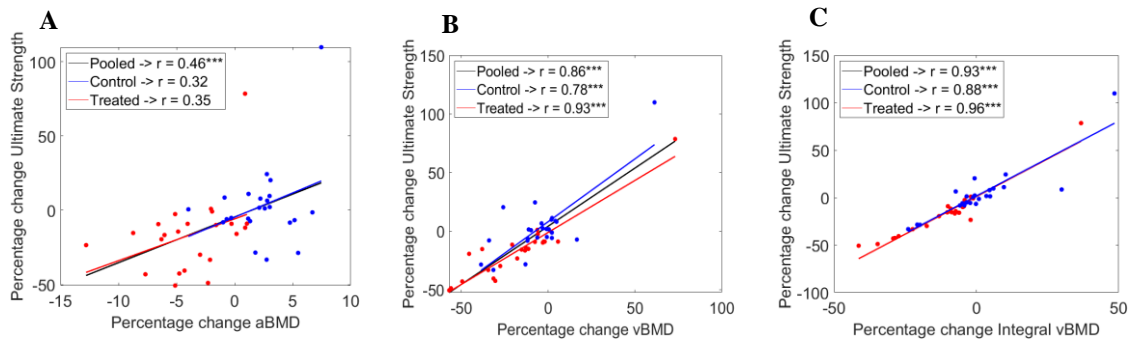


Figure 2. Linear regression analysis for percentage change ultimate strength vs (A) percentage change aBMD, (B) percentage change trabecular vBMD and (C) percentage change integral vBMD. \*\* $p < 0.01$ , \*\*\* $p < 0.001$ .