

# Relationship of magnetic resonance measures of bone quality with bone mineral density in corticosteroid treated boys with Duchenne muscular dystrophy

Kunnath Ravindranunni R<sup>1</sup>, Cho K<sup>2</sup>, Rosen A<sup>2</sup>, Kumar SD<sup>2</sup>, Hurreh MM<sup>2</sup>, Bernier AV<sup>1</sup>, Tuna IS<sup>1</sup>, Vandeborne K<sup>1</sup>, Walter GA<sup>1</sup>, Rajapakse CS<sup>2</sup>, Willcocks RJ<sup>1</sup>  
<sup>1</sup>University of Florida; <sup>2</sup>University of Pennsylvania

## INTRODUCTION

- Duchenne muscular dystrophy (DMD) is a progressive neuromuscular disorder<sup>1</sup>.
- Osteoporosis occurs in DMD due to corticosteroid use<sup>2</sup>, decreased bone loading<sup>3</sup> and multiple other factors results in fractures<sup>4</sup>, and leads to increased morbidity and mortality<sup>5</sup>.
- Dual-energy X-ray absorptiometry bone mineral density (DXA-BMD) is the gold standard for bone health assessment<sup>6</sup> in adult osteoporosis, however, it is an insufficient predictor of fracture risk in DMD<sup>7</sup>.
- Magnetic resonance (MR) imaging can assess bone quality through bone marrow fat fraction (BMFF) and cortical/trabecular microstructure<sup>8,9</sup>.
- These measures are correlated with age and corticosteroid use in DMD.

## PURPOSE

- To investigate the relationship between MR-based bone quality metrics including BMFF and cortical and trabecular microarchitectural measures and BMD in corticosteroid-treated boys with DMD.

## METHODS

### SUBJECTS

Groups	Number of subjects (n)	Age in years (Mean ± SD)	Corticosteroid exposure duration in years
DMD	14	12.7 ± 3.2	8.0 ± 3.2

\* Any difference in (n) in individual graph is because invalid data points were excluded from analysis

- In this cross-sectional observational study, a 3-Tesla whole body MRI scanner (Siemens Prisma/Philips Achieva) was used for MR imaging.
- BMFF was measured from L4 vertebral body and distal femur using MRS and Dixon method respectively.
- High resolution gradient echo images were obtained of the distal femur and then analyzed to extract trabecular and cortical bone characteristics.
- Trabecular microarchitectural measures were analyzed from bone volume fraction map derived from the MR images
- Using the MR images, a micro-level finite element analysis (FEA) models were developed to estimate distal femur stiffness.
- DXA-BMD was taken from clinical scan reports provided by participants.

## CONCLUSION

- MR measures of bone quality are significantly associated with DXA-BMD in boys with DMD.
- MRI may offer additional information on specific bone characteristics that are negatively affected by DMD and corticosteroid use.

## ACKNOWLEDGEMENTS

- We thank all participants
- A portion of this work was performed in the McKnight Brain Institute at the National High Magnetic Field Laboratory's Advanced Magnetic Resonance Imaging and Spectroscopy (AMRIS) Facility, which is supported by National Science Foundation Cooperative Agreement **DMR-2128556** and **DMR-1644779** and the State of Florida.
- Funding: US Department of Defense (**W81XWH-21-1-0566**, PI: Willcocks).

## REFERENCES

- Ward LM et al. 2018 Oct;142 (Suppl 2):S34-S42.
- Bushby, K., et al. Lancet Neurol, 2010, 9(1): p. 77-93.
- Söderpalm, A.-C., et al. Acta Paediatrica, 2012, 101(4): p. 424-432.
- Ward LM et al. 2019 Feb;26(1):39-48. doi: 10.1097/MED.0000000000000456.
- Kanis, J. A., *Diagnosis of osteoporosis and assessment of fracture risk*. Lancet, 2002, 359(9321): p. 1929-36.
- Patsch, J.M., et al., *Noninvasive imaging of bone microarchitecture*. Ann N Y Acad Sci, 2011, 1240: p. 77-87.
- Bray, T. J et al., Br J Radiol, 91(1089), 20170344. <https://doi.org/10.1259/bjr.20170344>
- Alic, L. et al., Muscle Nerve, 64(1), 8-22. <https://doi.org/10.1002/mus.27133>
- Rajapakse, C. S. et al., Radiology, 276(2), 526-535. <https://doi.org/10.1148/radiol.15141850>
- Cordes, C. *Frontiers in endocrinology*, 7, 74. <https://doi.org/10.3389/fendo.2016.00074>
- Gatti, D., *Osteoporosis Int* 6, 355-360 (1996). <https://doi.org/10.1007/BF01623008>
- Currey JD, Brear K, Zioupos P. *J Biomech* 1996; 29: 257-60.

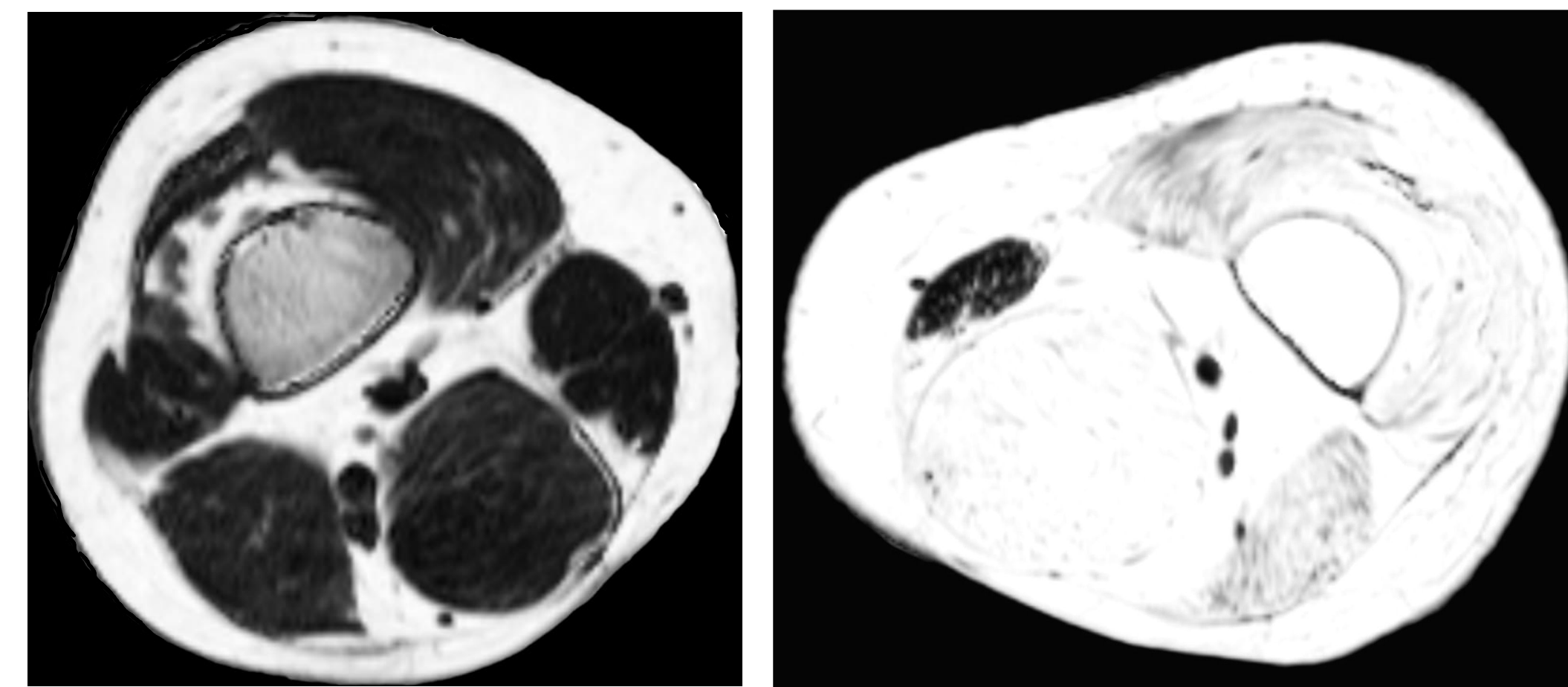


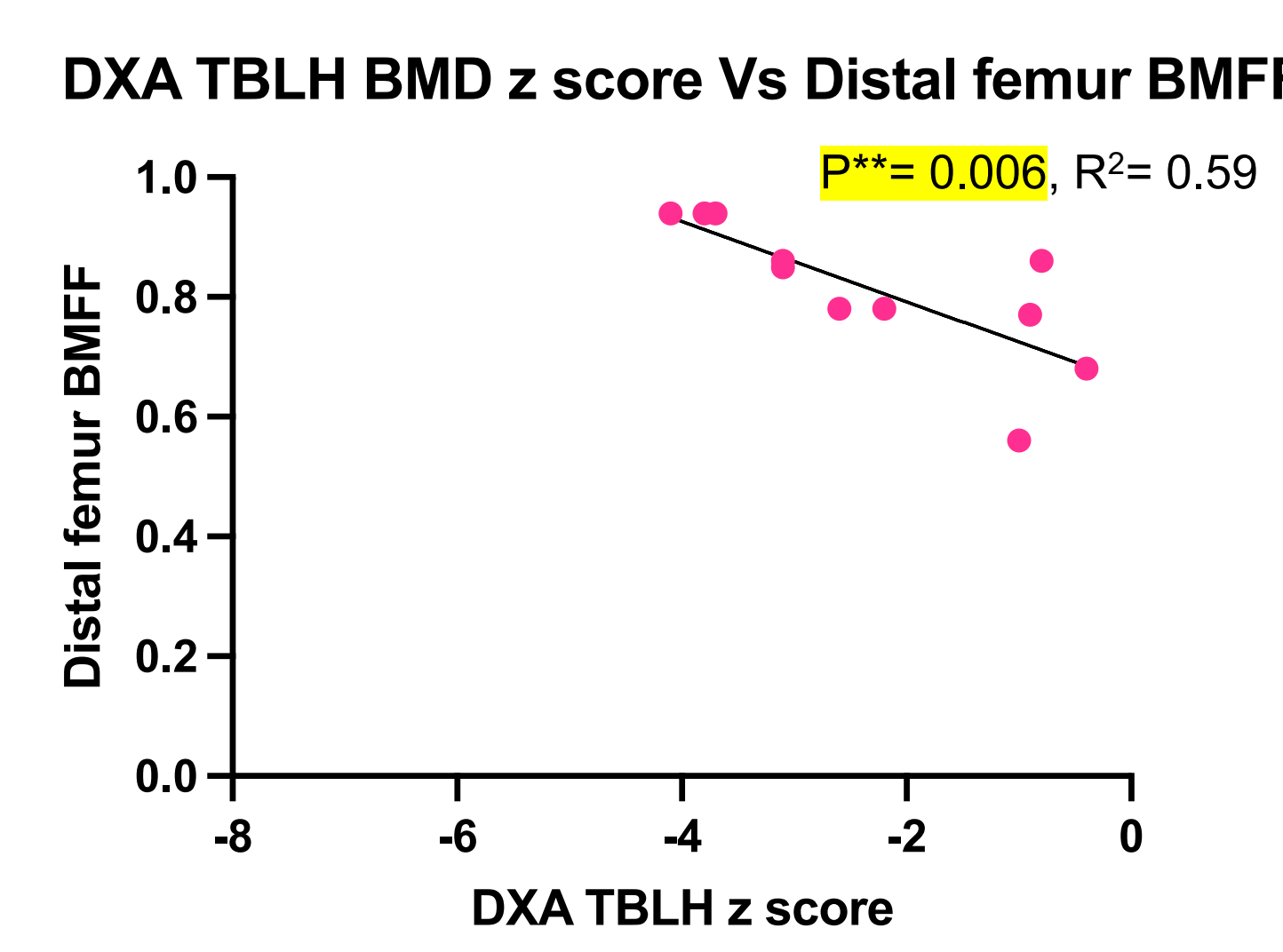
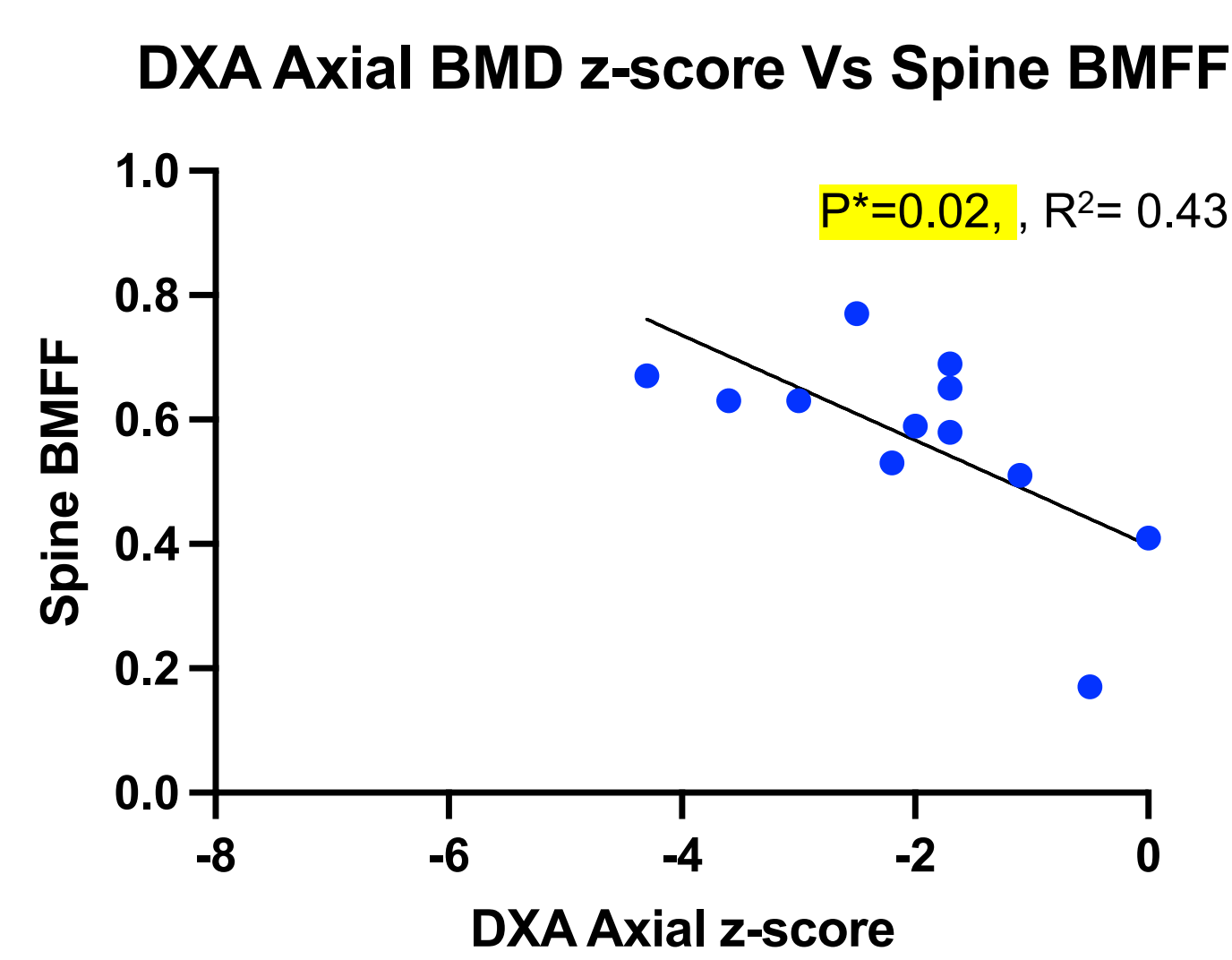
Fig1. Visual comparison of MRI images of 8 years old boy with DMD (on the left image) and 17.5 years old boy with DMD (on the right)

BMD z-score Range	Interpretation
+1 to +2	Bone density measure higher than that of peers with similar age, sex, and body size.
0	Bone density measure consistent with the average of peers with similar age, sex, and body size.
-1	Bone density measure slightly lower than that of peers with similar age, sex, and body size.
-2	Bone density measure moderately lower than that of peers with similar age, sex, and body size.
-2.5 or lower	Significantly low bone density; may indicate secondary osteoporosis.

Definition of osteoporosis in pediatrics: BMD z-score ≤ -2 + vertebral fracture or clinically significant fracture

## RESULTS

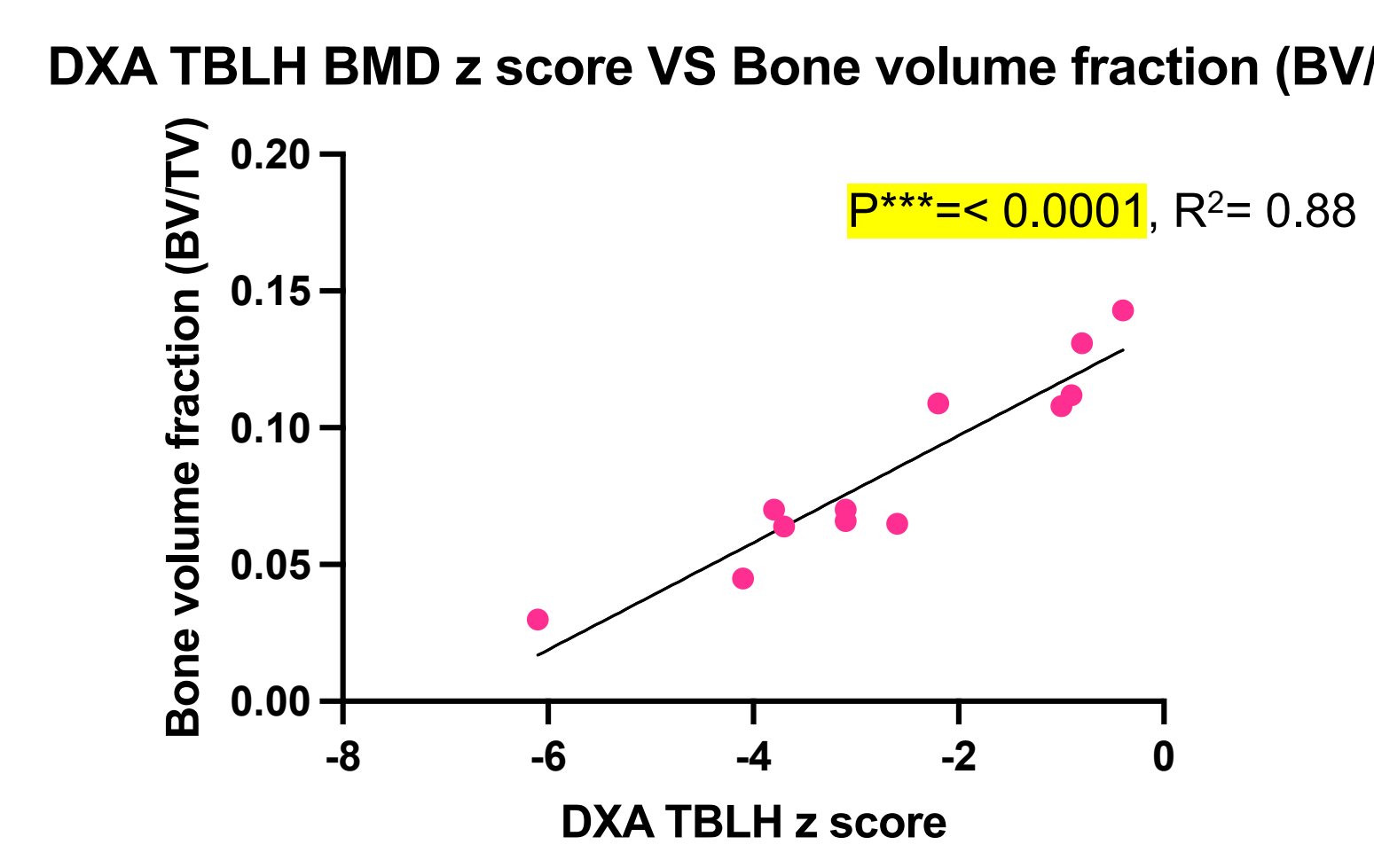
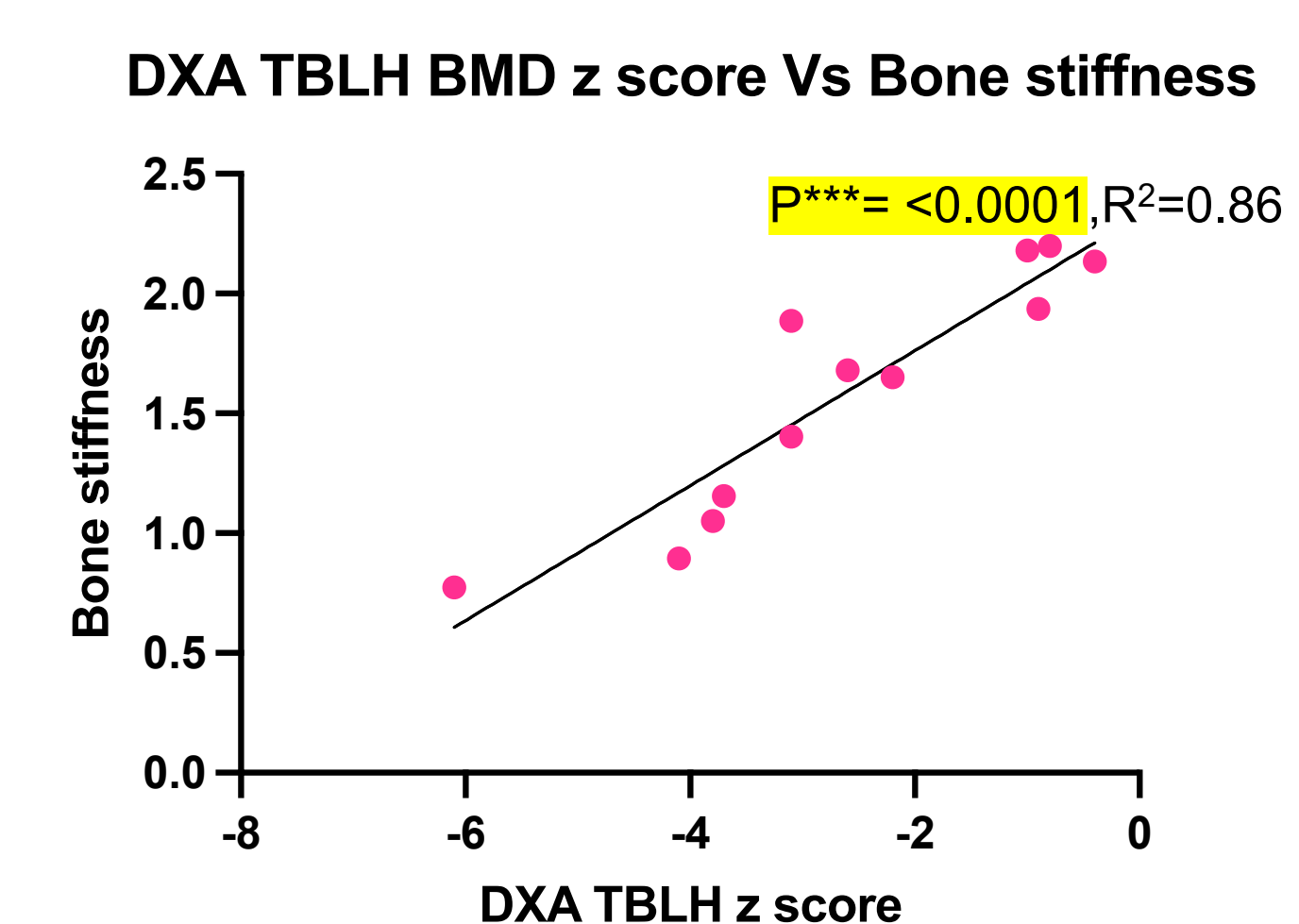
### Correlation of DXA BMD z-score with BMFF



Higher bone mineral density z-scores are significantly associated with lower bone marrow fat fraction.

Increased bone marrow fat fraction is associated with osteoporosis in multiple populations<sup>10</sup>.

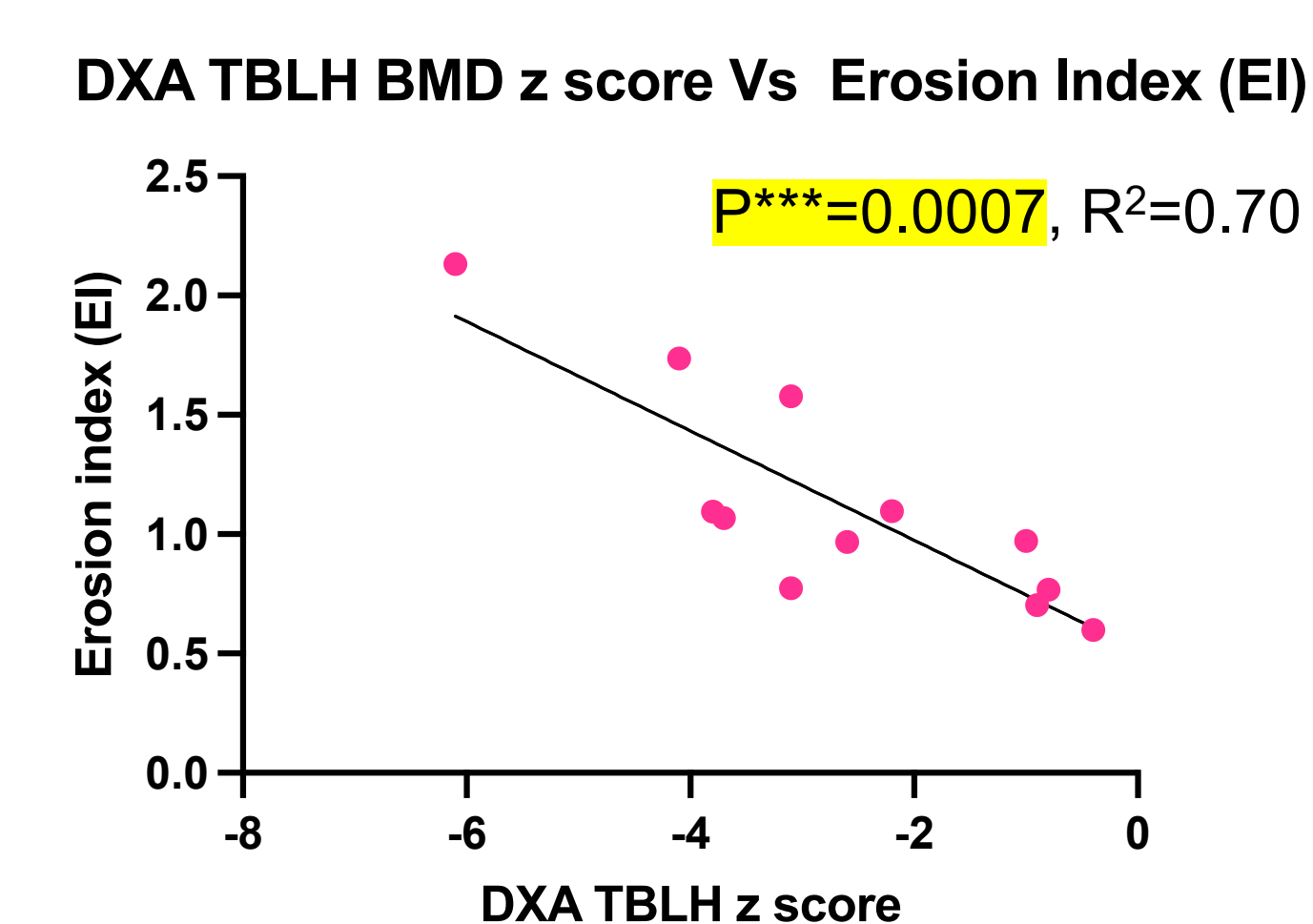
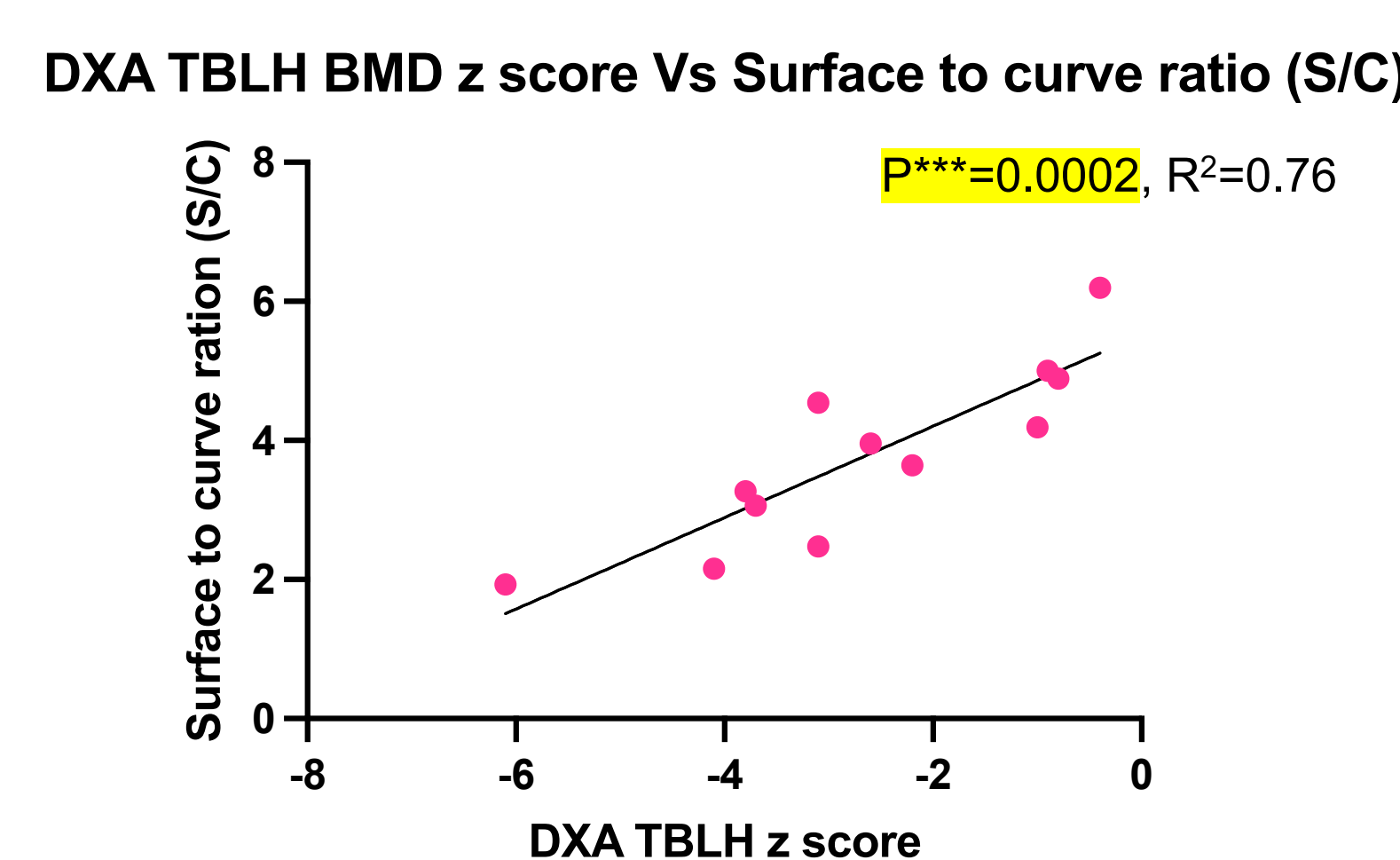
### Correlation of DXA BMD z-score with Bone Stiffness and Bone volume fraction



Both bone stiffness (estimated by finite element analysis) and trabecular bone volume fraction, which measures how much of the trabecular bone region is bone tissue, were strongly associated with bone mineral density z-score.

BV/TV= Bone volume/total volume

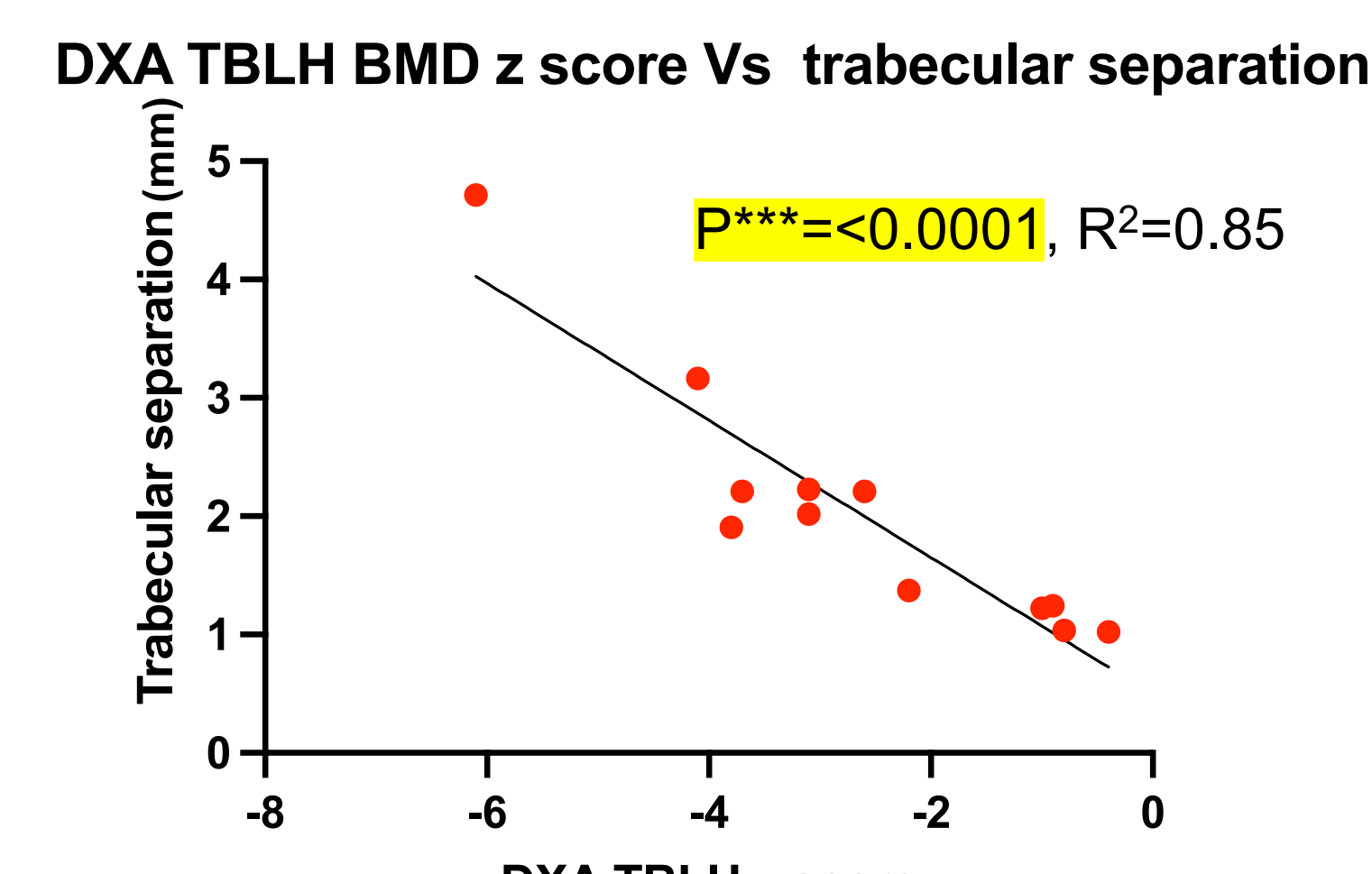
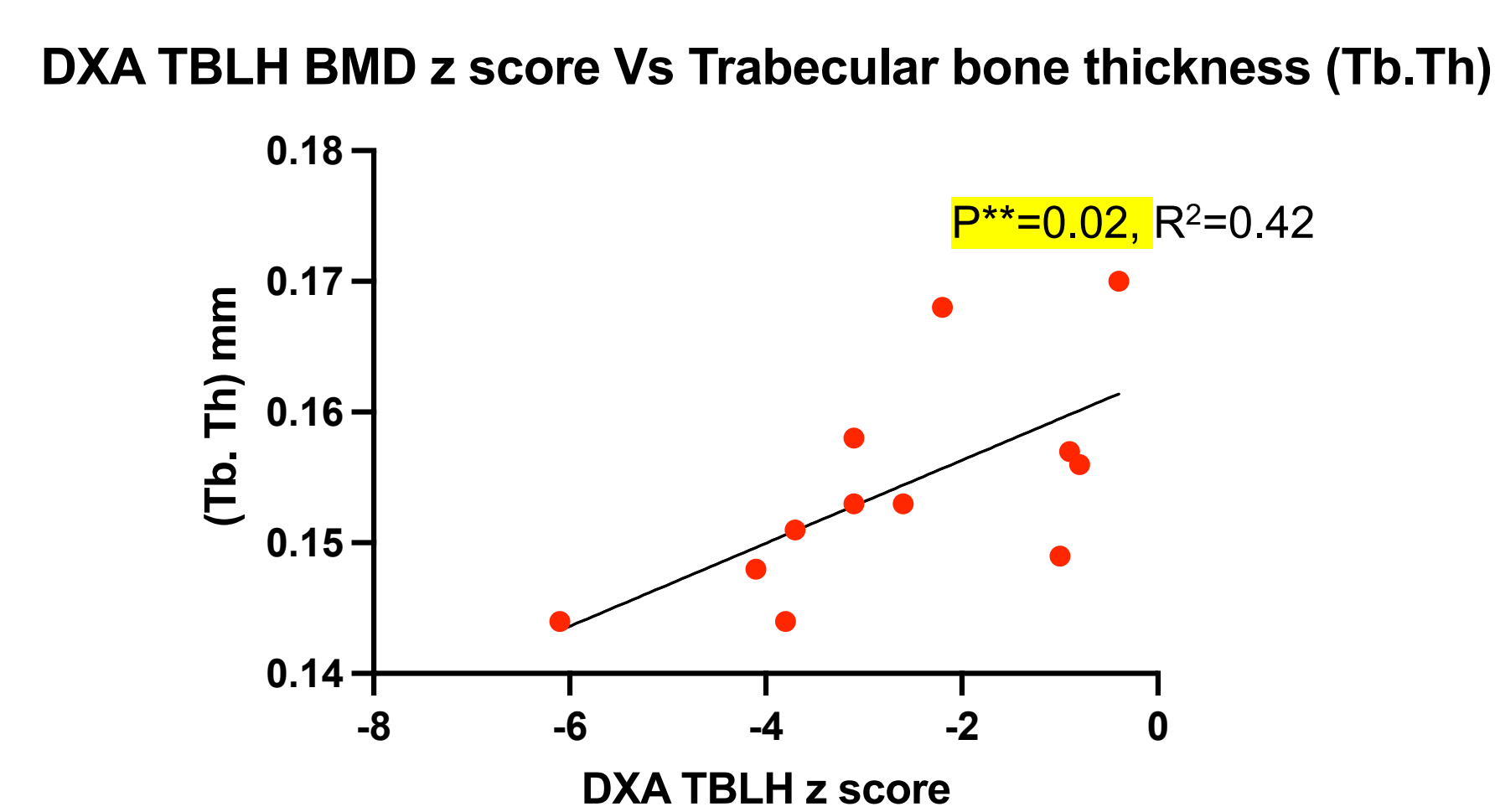
### Correlation of DXA BMD z-score with Surface to Curve ratio (S/C) and Erosion index (EI)



Erosion of trabecular bone results in the conversion of plate-like trabecular structures to rod-like structures.

This process is captured in the surface-to-curve ratio and the erosion index, both of which are associated with BMD z-score.

### Correlation of DXA BMD z-score with Trabecular thickness and Trabecular separation

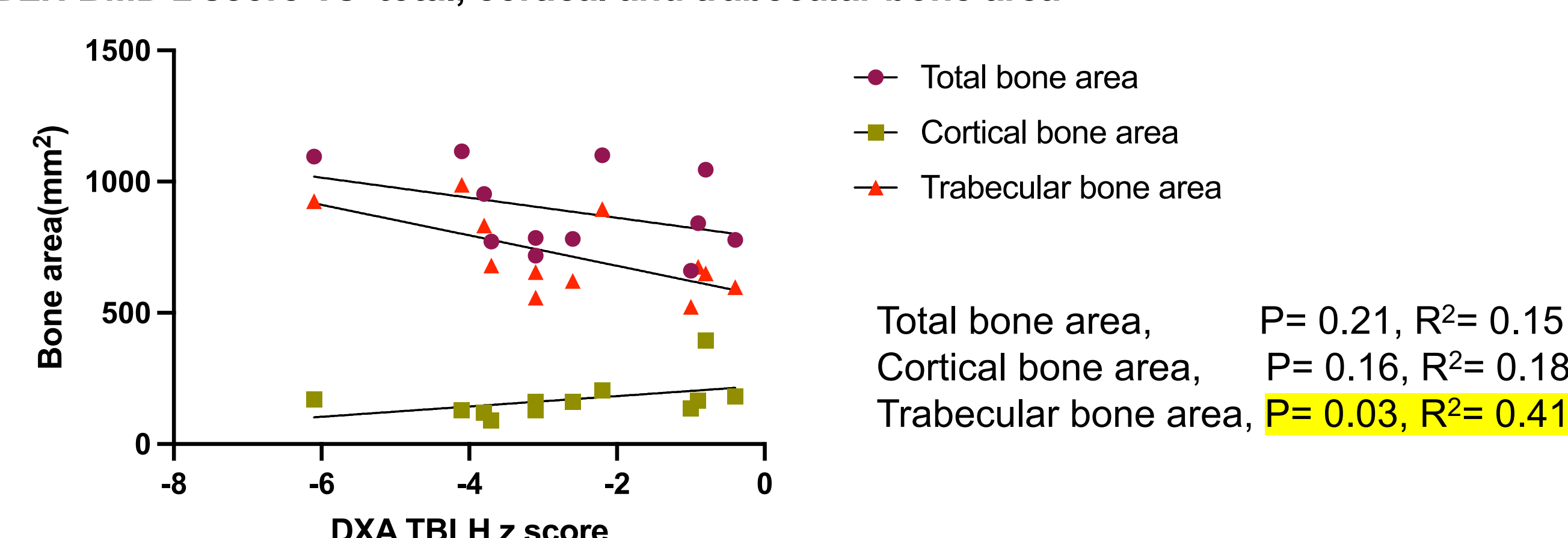


Trabecular separation and thickness are inversely related, with both parameters contribute to bone strength and overall bone density.

Both trabecular thickness and separation are significantly correlated with BMD z-score.

### Correlation of DXA BMD z-score with Bone area

DXA TBLH BMD z score Vs total, cortical and trabecular bone area



The significant relationship between trabecular bone area and bone mineral density aligns with the finding that trabecular bone density decreases with age, but its overall area increases, leading to a higher proportion of trabecular bone over total bone. This suggests that age-related bone adaptations predominantly affect trabecular bone structure rather than total or cortical bone area, reinforcing its relevance in bone turnover and fracture risk assessment<sup>11</sup>.

With age, cortical thickness and cortical bone area increases and it is related to increased bone density in cortical area<sup>12</sup>.