### Impact of Cancer Treatment on Vertebral Bone Strength: A Finite Element Analysis Study

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## **Summary**

Late-stage cancer can spread to bones (bone metastasis), which weakens bone structure. This increases the risk of bone fractures, even under minimal mechanical load. This study used finite element (FE) analysis to assess how cancer treatment affects bone strength. Patients were grouped based on tumor change in size: progression ( $\geq 25\%$  increase), partial response ( $\geq 50\%$  decrease), and stable (< 25% increase/50% decrease). FE predictions of vertebral bone strength indicated that the cancer treatment did not significantly change the bone strength during the treatment period (2.3  $\pm$  1.2 months).

#### Introduction

Immune checkpoint inhibitors (ICI) are commonly used treatments for metastatic disease, but their impact on bone strength remains unclear. Recent studies suggest that ICI treatment could influence the bone microenvironment, potentially altering bone lesions and strength <sup>1</sup>. This study used FE analysis to assess how ICI therapy affects vertebral bone strength in patients with metastatic bone disease, aiming to provide a numerical biomarker for fracture risk.

#### Methods

This study included 104 patients with metastatic non-small cell lung cancer (NSCLC) treated with ICI in Alberta, Canada. Patients were grouped based on bone tumor response to treatment according to the MD Anderson criteria: 51 progression, 17 partial response, and 36 stable, with a mean follow-up of  $2.3 \pm 1.2$  months. FE analysis was used to predict bone strength in the T6 vertebra body segmented from CT scans at baseline and follow-up, after converting attenuation values to bone density using phantom-less calibration procedures <sup>2</sup>. The T6 vertebra was segmented using the TotalSegmentator <sup>3</sup>, and FE models were generated through direct voxel conversion <sup>4</sup>. To estimate vertebral strength, a uniform axial compressive load was applied to the FE model through a virtual layer of bone cement, and strength was defined as the force at 2% deformation <sup>5</sup>. ANCOVA analysis was used to determine the significance of bone strength changes while accounting for the time variation from baseline to follow-up, which ranged from two weeks to 7 months across patients. The confusion matrix was used to assess the alignment between FE predictions of bone strength changes with tumor response.

The ANCOVA analysis revealed that neither the duration of follow-up nor the tumor response significantly influenced strength changes, with a low  $R^2$  of 0.05 and a non-significant overall model (p = 0.19). The confusion matrix showed that 56% of the true stable cases were predicted as stable, while 43% of true partial response cases and 53% of true progression cases were categorized as stable, indicating a bias towards predicting stable bone strength. This indicates that bone strength did not change significantly, regardless of tumor response (Figure 1). This is surprising, as two recent studies showed nearly double incidence of major osteoporotic fractures in the year following ICI initiation  $^1$ .

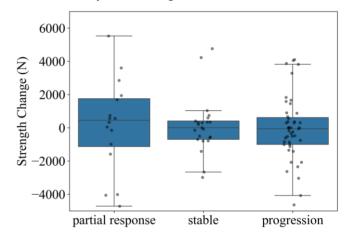


Figure 1: Strength change (N) versus tumor response.

# **Conclusions**

This study found that ICI therapy did not significantly affect vertebral bone strength or strength changes during a mean follow-up of  $2.3 \pm 1.2$  months. However, the long-term implications remain uncertain, highlighting the need for a longer follow-up period.

## References

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### **Results and Discussion**

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