THE STUDY OF VISCOELASTIC RESPONSE IN TUMOR-METASTASIZED BONE USING DMA

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INTRODUCTION

Skeletal metastasis is prevalent in many malignancies, such as breast, prostate, thyroid, renal and lung cancers. In fact, bone metastases will be developed in more than 70% of patients with advanced breast and prostate cancer, in 30%-40% of patients with lung cancer [1], and cancer cells can promote osteolytic and cause destructive bone lesions. To quantify this change in bone, Bone Mineral Density (BMD) is typically used to measure bone quality and for diagnoses to be made. Previous research showed that BMD decreased by 10% in the tumor-induced bone [2]. However, it is believed that BMD alone is not sufficient to predict fracture risk [3]. For example, research conducted by Segal et al (2007) shows that, using current BMD standard, about one-third of elderly hip fracture patients might not have been diagnosed as being at risk [4]. Besides BMD, viscoelasticity is another parameter that can potentially measure bone quality. This study endeavours to investigate the possible trends in viscoelastic changes with the onset of bone metastasis, and aims to establish viscoelastic damping as a novel predictor of fracture risk.

METHODS

W256 malignant breast cancer cells were injected directly into the left distal tibia of female Sprague Dawley rats, while a sham operation was performed on the right tibia. 30 days were allowed for tumor proliferation and growth in the rat tibia. After that, the bones were harvested and machined to a small specimen with desirable size, 0.6×1.2×5mm (thickness×width×length), using BUEHLER IsoMet 1000 Precision Sectioning Saw. Viscoelastic damping of the bone specimen was obtained using the Dynamic Mechanical Analyzer (Figure 1) at room temperature (23ºC) and wet environment, and specimen was subjected to a single cantilever oscillating stress. Frequency scanning test was carried out over the range of 0.01 to 70Hz, 25 testing points per decade in log scale.

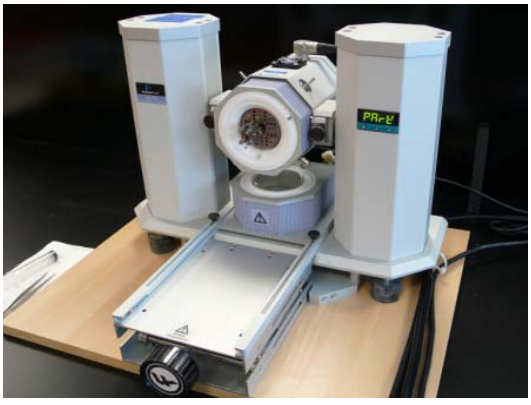
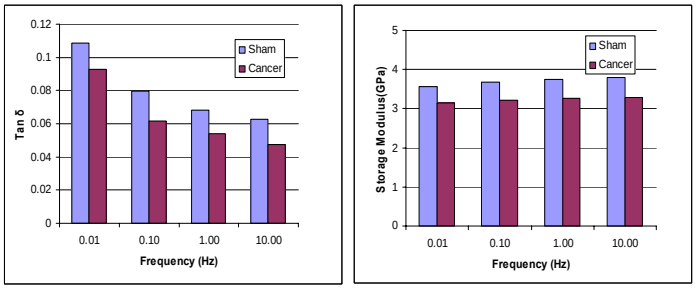


Figure 1: The Dynamic Mechanical Analyzer: PerkinElmer DMA 8000

RESULTS AND DISCUSSION

Compared to sham-operated controls, the slope of loss tangent (tan δ) was greatly increased by 62% at low frequencies (0.001 – 0.1Hz), by 28% at mid frequencies (0.01 – 30Hz) and 34% at high frequencies (30 – 70Hz) in the tumor-induced bone. On the whole frequency range, the slope of loss tangent (tan δ) was 28% higher in the tumour injected bone ($p<0.05$). In addition, tan δ of tumor-induced tibia was decreased by 23%. 32%, 29%, 32% compared to the sham-operated controls at 0.01Hz, 0.1Hz, 1Hz, and 10Hz respectively (Figure 2(a)). Young's modulus was also decreased by 12% compared to the sham-operated controls at 0.01Hz and by 13% compared to the sham-operated controls at 0.1Hz, 1Hz and 10Hz (Figure 2(b)).



(a) (b)

Figure 2: Comparison of (a) Loss tangent and (b) Storage Modulus between sham-operated and cancer-injected bones at 0.01Hz, 0.1Hz, 1Hz, and 10Hz

CONCLUSIONS

Results showed that viscoelastic response of tumor-implanted bones is significantly lower as compared to that of sham-operated bones which indicates viscoelastic property might be able to quantify bone quality, as well as to predict pathological fractures. Based on these preliminary results, we investigated the correlation between fracture risk and the viscoelastic response in a metastasized bone.

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