EFFECT OF TUMOUR-INDUCED OSTEOLYSIS AND EFFICACY OF ANTI-RESORPTIVE AND CHEMOTHERAPEUTIC TREATMENTS IN METASTATIC BONE DISEASE

[1]X. Chen, [2]L.S. Fong, [3]X. Yang, [4]P. Maruthappan, [5]Y.S. Chung, [6]H.J. Oh, [7]T. Lee
[1-4,7]Division of Bioengineering, National University of Singapore, Singapore
[5]Department of Endocrinology & Metabolism, Ajou University, Korea
[6]Cheil General Hospital & Women's Healthcare Center, Korea
[7]Taeyong Lee; email: bielt@nus.edu.sg, web: www.bioeng.nus.edu.sg/biomechanics/

INTRODUCTION

Skeletal metastases are the most common complication of malignancies such as breast and prostate cancers [1]. In tumour-induced osteolysis, bone resorption is increased by the neoplastic activation of osteoclasts which results in rapid bone loss, change in the architectural integrity and ultimately, the load-bearing capacity of the affected bone. Fracture risk is increased by this deterioration in bone structure. The purpose of this pilot study is to assess the efficacy of anti-resorptive (Ibandronate) and chemotherapeutic (Paclitaxel) drug treatments in preserving skeletal integrity in terms of structural and biomechanical parameters, using an experimental model of tumour-induced osteolysis.

METHODS

Forty two 8-10 week old male Sprague Dawley rats were randomly divided into four experimental groups – control (Sham), tumour-only (Tumor), Ibandronate-treated (IB), and Paclitaxel-treated (PAC), of which only animals in the control group were not inoculated with tumour cells. To simulate bone metastasis, approximately 2.5×10^6 osteolytic Walker 256 (W256) cells were surgically injected into the right femoral medullary cavity via the intercondylar notch to induce tumour growth. Animals in the tumour-only group received no drug treatment while those in the IB and PAC groups received Ibandronate and Paclitaxel drug administrations respectively post-surgery. Serum DPD (deoxypyridinoline) concentration was monitored via regular blood collection to observe the progress of bone resorption. Three animals from each group were euthanized every 10 days (maximum of 30 days). After euthanasia, both femora were harvested, cleaned of soft tissue and stored at -20ºC. [3]The femora were thawed to room temperature (25 ºC) prior to micro-CT scanning at a resolution of 35 µm to obtain bone volume.

RESULTS AND DISCUSSION

Some abnormality in the medullary cavity of the femur, suspected to be localized tumor growth, was observed in the micro-CT images of the animals with implanted tumor cells (Fig. 1a). In contrast, the medullary cavities of the femora from the control group appeared clear (Fig. 1b).

(a)

(b)

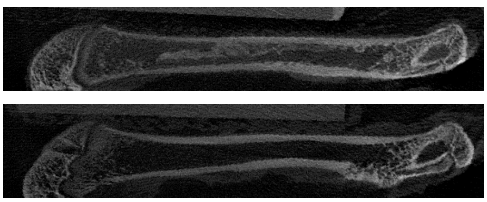

Figure 1: 35 µm/pixel resolution micro-CT sagittal images of (a) an operated femur with tumor cells inoculated (b) an operated femur without tumor cells inoculated

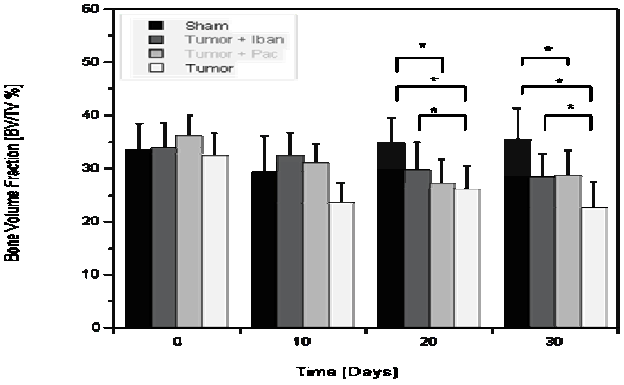

Figure 2: Bone Volume Fraction (BV/TV %) results of Sham, Tumor, Ibandronate-treated and Paclitaxel-treated groups, where * indicates significant difference between groups, $p < 0.05$. One-way ANOVA analysis for each time period was carried out, with Bonferroni adjustments used for each pair-wise comparison.

It could be observed that significant reduction in the bone volume fraction due to presence of tumour occurred after 20 days. (Figure 2) Ibandronate treatment had an effect of increasing bone volume fraction significantly as compared to the tumor-only group due to its anti-resorptive effect. However, the effect is systemic as resorption activities in the intact left femur are suppressed as well. Paclitaxel treatment also increased bone volume fraction over the tumor-only group, though compared to the sham-group there remained a significant difference. Nonetheless, it could be seen that Paclitaxel treatment has the effect of improving bone quality in tumour-induced osteolytic rat model.

CONCLUSIONS

Tumor induced-osteolysis caused significant bone loss after 20 days, as observed from the micro-CT results. Both Ibandronate and Paclitaxel treatment have been successfully shown to have the effect of improving bone quality in the tumour–induced osteolytic rat model.

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