MicroCT analysis revealed niche-specific localization of osteolytic versus osteoblastic lesions in PCSD1, a new patient-derived xenograft model of bone metastatic prostate cancer.

We established PCSD1, a new metastasis prostate cancer xenograft model in mice. Mixed osteolytic and osteoblastic bone lesions formed. MicroCT analysis was used to evaluate microstructural changes.

Anna Kulidjian*[8], Tomonori Yamaguchi[8] , Christina N. Wu [3,4] , Michelle Muldong [3, 5, 6], Takeshi Hirata[1,2], Seung Chol Park [2,3], Omer Raheem[5,6], Koichi Masuda[8], Christina A.M. Jamieson[3,5,6]

1 Department of Urology, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences
2 Department of Urology, Wonkwang University School of Medicine and Hospital, Iksan, South Korea
3 Moores Cancer Center, University of California, San Diego
4 Dept of Medicine, University of California, San Diego
5 Departments of Urology, University of California, San Diego
6 Department of Surgery, University of California, San Diego
7 Department of Radiation Oncology, University of California, Los Angeles
8 Department of Orthopaedic Surgery, School of Medicine, University of California, San Diego

*Presenting author

Introduction and objective: Prostate cancer bone metastasis occurs in 50-90% of men with advanced disease for which there is no cure. Bone metastasis leads to debilitating fractures, severe bone pain, therapy resistance and rapid decline. There are few pre-clinical models to understand the interaction between the bone microenvironment and prostate cancer. We established PCSD1, a new bone metastasis prostate cancer xenograft model in mice. Cells isolated from a surgical prostate cancer bone metastasis patient specimen were injected directly into the endosteal space of the femurs of immunodeficient mice. Tumor growth resulted in mixed osteolytic and osteoblastic bone lesions which closely resembled the lesions in the patient. In this study microCT analysis was used to evaluate microstructural changes in this patient-derived xenograft bone metastatic model of prostate cancer.
Material and Methods: PCSD1 cells or the Control sample consisting of Matrigel plus media alone were injected into the right femurs of *Rag2*$^{-/-}$□*c*$^{-/-}$ male mice. MicroCT scanning was performed on mouse femurs at 8-10 weeks post-injection. Femurs with injection holes in the condyle that were detectable in microCT scans were selected for microstructural analysis (PCSD1 group, n=13, Control group, n=8).
Results: The injected femurs of both the PCSD1 and Control mice were significantly shorter compared to their un-injected contra-lateral femurs, however, the PCSD1-injected femurs had additional, substantial changes compared to the Control mice as seen in both 2D and 3D microCT images. First, the bone volume (BV) and the ratio of bone volume (BV) to total volume (BV/TV) were both significantly decreased at the proximal and distal ends of the femurs only in the PCSD1 group ($p<0.01$ respectively). Conversely, BV in the cortical bone along the central length of the bone shaft was significantly increased in the PCSD1 group ($p<0.05$). Second, the diameter of the bone

shaft of the right femur increased significantly only in the PCSD1 group compared to Control ($p<0.01$). Third, an abnormal bone enlargement was observed at the third trochanter to the lateral side only in the PCSD1 group. Interestingly, changes in trabecular bone in the PCSD1 group could be sub-divided into either osteolytic or osteoblastic in nature, however, as a whole the differences in trabecular bone were not significant between the PCSD1 group and the Control group.

Conclusion: PCSD1-induced bone lesions were osteolytic at the distal and proximal ends of the femur and osteoblastic in the cortical bone of the femur shaft. The changes in trabecular bone were either osteoblastic or osteolytic which may be a transitional region. Thus, we detected and quantified bone region-specific effects of PCSD1 xenograft tumor cell growth in the femur. We are currently determining the effects of therapies on regional bone lesion formation in the PCSD1 model to determine if there are differential effects on osteolytic versus osteoblastic lesions and if specific bone regions may preferentially support therapy resistance.