DISTRIBUTION OF S, Ca, Fe AND Zn IN HUMAN OSTEOSARCOMA TISSUE DETERMINED WITH SYNCHROTRON AND LABORATORY M-XRF ANALYSIS

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Osteosarcoma is the most common primary bone malignancy, typically occurring during the adolescent growth spurt, but there is a second, smaller peak in the elderly. It is characterized by the production of tumour osteoid and immature bone matrix by malignant cells. With today's combination of chemotherapy and surgery long-term survival rates of more than 70% have been reported. However, very little is still known about the etiology of the tumour. In order to further improve treatment and to develop new treatment strategies it is pivotal to get more insight into the fundamental biology of the disease.

In recent years, dramatic changes in minor and trace elements were found in various different cancer types - e.g. breast cancer, prostatic carcinoma. These metals bind to proteins - so called metalloproteins - that perform different biological and physiological functions. However, very little is known about trace element levels and accumulations in osteosarcoma.

Nine bone samples of human osteosarcomas are obtained following surgical resection at the Dept. of Orthopaedics, Medical University of Vienna, Vienna, Austria. Four samples were histologically identified as high-grade (G3) osteoblastic osteosarcomas, three as chondroblastic sarcomas and two samples were anablastic osteosarcoma. The samples contained tumour tissue as well as adjacent normal healthy bone tissue as an internal control. The study was approved by the ethics committee at the Medical University. The uncalcified samples were examined by quantitative backscattered electron imaging using a pixel resolution of 1 µm. Grey-level images were generated to differentiate between healthy bone tissue and the mineralized and non-mineralized tumour tissue. Areas of interest were analyzed with Synchrotron Radiation induced confocal micro x-ray fluorescence analysis (SR µ-XRF) to determine the distribution of Ca, Sr, Zn, Fe in tumour tissue and healthy bone. Measurements were performed at the FLUO beamline at ANKA using a beam size of 15x12 µm² and a depth resolution of 20 µm for Au-La, with primary excitation energy of 17 keV. In addition measurements using the confocal low power µ-XRF setup, equipped with a vacuum chamber to enable the detection of light elements, at the Atominstitut of the Vienna University of Technology, have been done in the same regions of interest, using beam size of 50x50x50 µm³ determined for Cu-Kα. Our synchrotron measurements revealed significant differences between healthy bone and calcified cancerous tissue. A positive correlation of Fe and Zn and an accumulation of these elements in calcified cancerous tissue could be observed. Increased Fe levels were found in both tumour types, but the degree of Fe accumulation was much higher in the chondroblastic tumour tissue. The Ca levels of cancerous matrix were slightly different compared to the levels in healthy bone, depending on the type of bone cancer. Despite the lower resolution the laboratory analysis showed similar results, with additional information on the distribution of the light elements S and P. In case of chondroblastic sarcomas increase S levels have been found in the non mineralized cancerous matrix. These finding may lead to new insights into basic tumour biology of osteosarcomas.