AN *IN VITRO* 3D BONE METASTASIS MODEL BY USING A HUMAN BONE TISSUE CULTURE AND HUMAN SEX-RELATED CANCER CELLS

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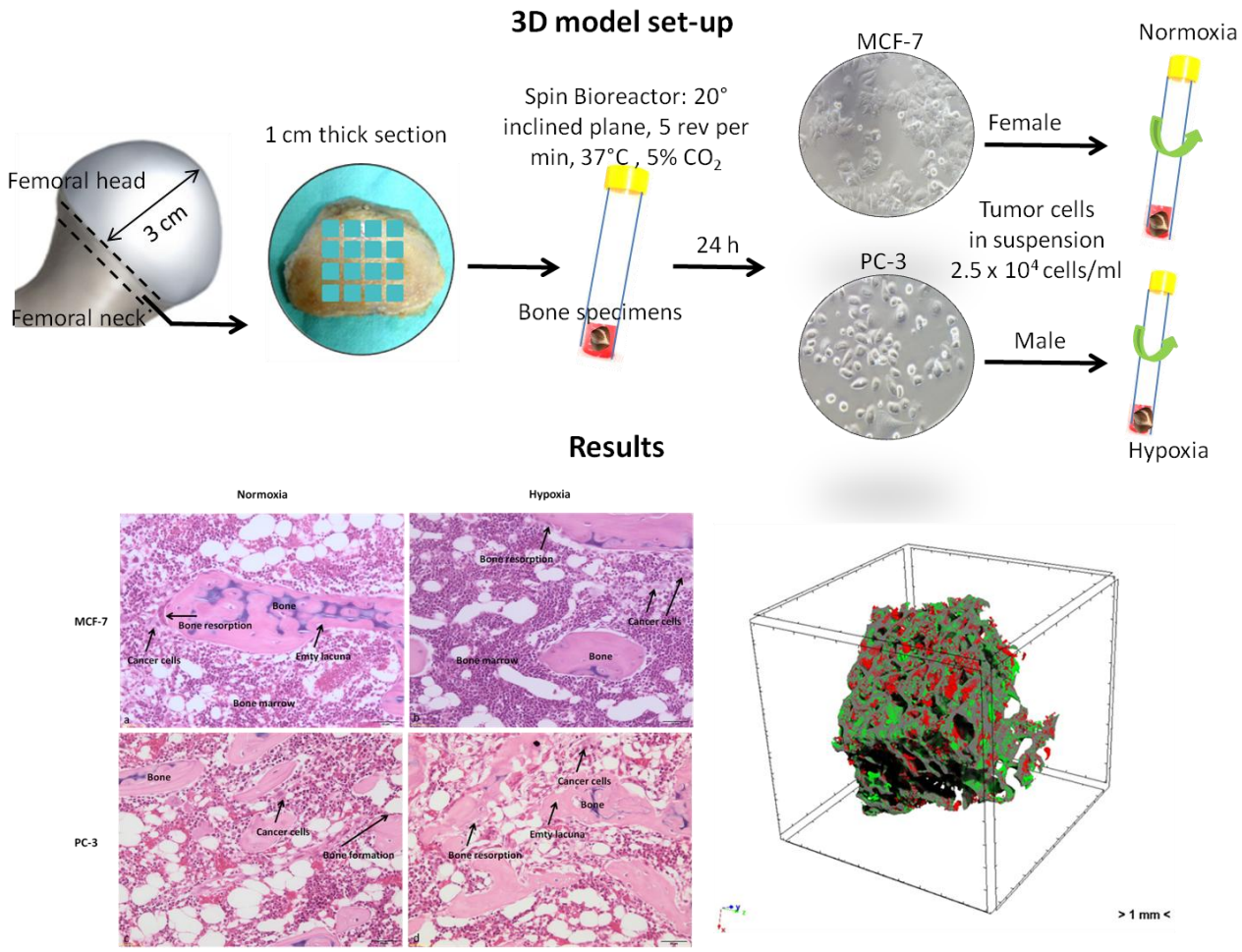
One of the main limitations, when studying cancer-bone metastasis, is the complex nature of the native bone environment and the lack of reliable, simple, inexpensive models that closely mimic the biological processes occurring in patients and allowing the correct translation of results. To enhance the understanding of the mechanisms underlying human bone metastases and in order to find new therapies, we developed an *in vitro* three-dimensional (3D) cancer-bone metastasis model by culturing human breast or prostate cancer cells with human bone tissue isolated from female and male patients, respectively. Bone tissue discarded from total hip replacement surgery was cultured in a rolling apparatus system in a normoxic or hypoxic environment (Figure 1). Gene expression profile, protein levels, histological, immunohistochemical and four-dimensional (4D) micro-CT analyses showed a noticeable specificity of breast and prostate cancer cells for bone colonization and ingrowth, thus highlighting the species-specific and sex-specific osteotropism and the need to widen the current knowledge on cancer-bone metastasis spread in human bone tissues (Figure). Additionally, these model was also used to model differences in tumor growth and colonization between healthy and osteoporotic status. Results of the study support the application of this model in preclinical studies on bone metastases and also follow the 3R principles, the guiding principles, aimed at replacing/reducing/refining (3R) animal use and their suffering for scientific purposes.


3D model set-up
Femoral head
3 cm
Femoral neck
1 cm thick section
Spin Bioreactor: 20° inclined plane, 5 rev per min, 37°C , 5% CO_2
Bone specimens
24 h
MCF-7
PC-3
Female
Male
Tumor cells in suspension 2.5 x 10^4 cells/ml
Normoxia
Hypoxia
Results
Normoxia
Hypoxia
MCF-7
PC-3
Bone
Bone resorption
Cancer cells
Emty lacuna
Bone marrow
Bone formation
> 1 mm <

Figure