Microfluidic-assisted 3D biofabrication of a human breast-to-bone (B2B) metastasis model for cancer cell invasion studies

Lucia Iafrate[1,2], Biagio Palmisano[3], B., Silvia Franco[4], Roberta Angelini[4], Mara Riminucci [3], Franco Marinozzi[1], Giancarlo Ruocco[2], Fabiano Bini[1], Gianluca Cidonio[1,2,5].

[1] Department of Mechanical and Aerospace Engineering (DIMA), University of Rome "La Sapienza", 00184 Rome, Italy
[2] Center for Life Nano- & Neuro-Science (CLN2S), Italian Institute of Technology (IIT), Rome, 00161 Rome, Italy
[3] Department of Molecular Medicine, Sapienza University of Rome, 00161 Rome, Italy
[4] Dipartment of Pysics, Sapienza University of Rome, 00185 Rome, Italy
[5] Bone and Joint Research Group, Centre for Human Development, Stem Cells and Regeneration, Institute of Developmental Sciences, University of Southampton, Southampton SO16 6YD, United Kingdom

BACKGROUND

Understanding metastatic homing in breast cancer

Breast cancer frequently metastasizes to bone, driving poor prognosis and secondary dissemination.

Challenges in bone metastasis modelling
Current models fail to recapitulate the complexity of the bone metastatic niche. Physiologically relevant systems are needed to study homing and enable therapeutic development.

AIM OF THE PROJECT
To develop a physiologically relevant 3D breast-to-bone (B2B) model using microfluidic-assisted bioprinting to recapitulate metastatic homing in a bone-like microenvironment. The model integrates HBMSCs and breast cancer cells to enable real-time investigation of invasion, tumour-bone interactions, and EGF-mediated colonization, providing a platform which is able to support pre-clinical evaluation of targeted therapies.

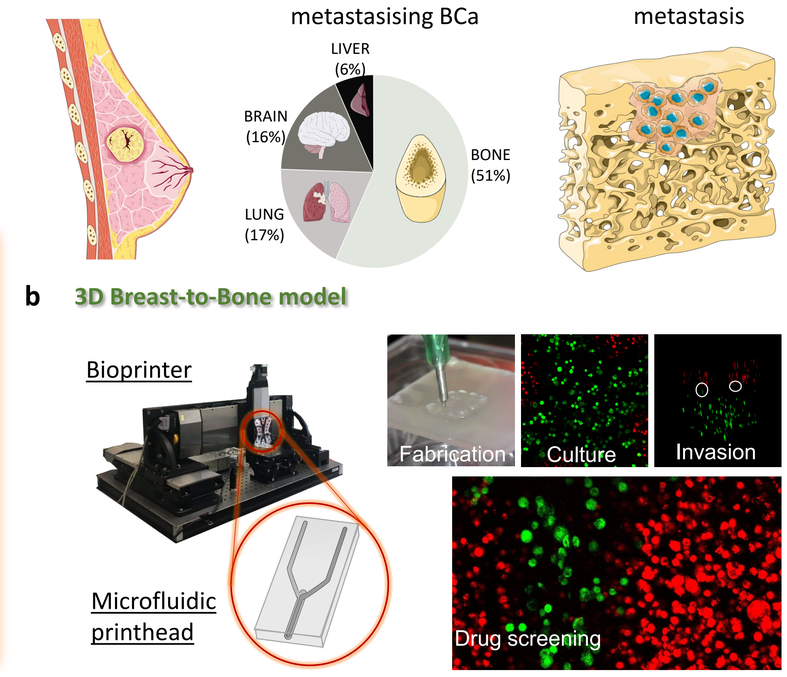
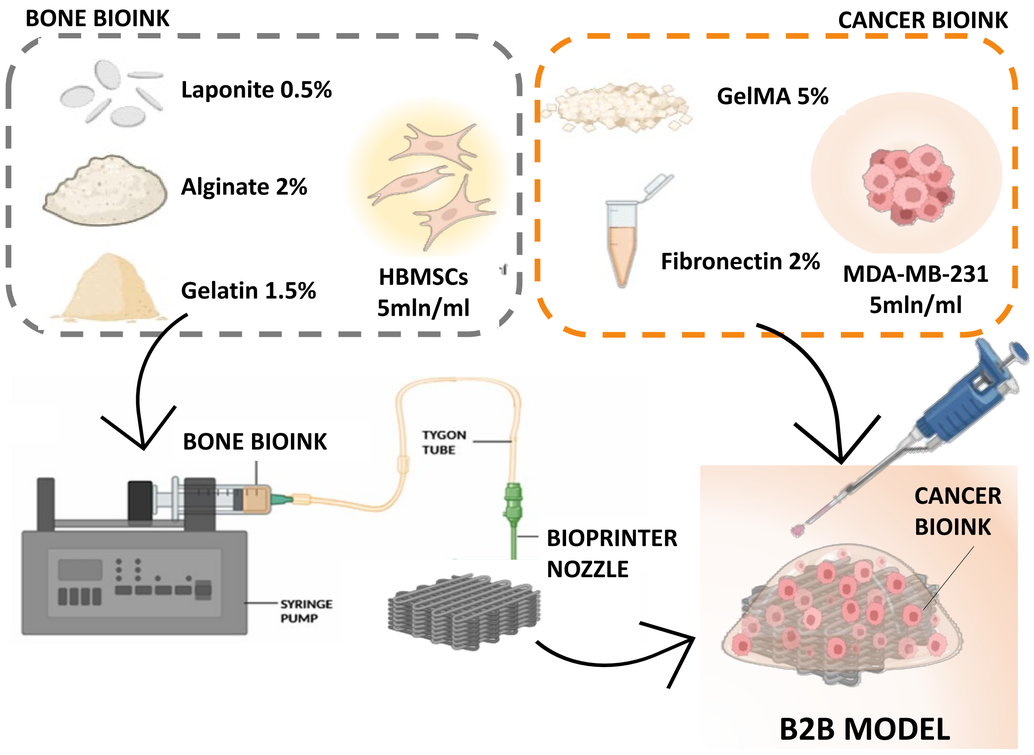


Figure 1. (a) Clinical problem: the musculoskeletal system is a major site of BCa metastasis. **(b) 3D Breast-to-Bone model**: B2B 3D bioprinted model recapitulates key stages of dissemination and colonization in a bone-like microenvironment.

MATERIALS & METHODS

3D MICROFLUIDIC BIOPRINTING OF B2B MODEL



Lattice-like pattern (6 × 6 mm, 3 mm in height)
Crosslink: CaCl2 0.33M + Ru (10mM)+ SPS (20mM) + Visible light

RESULTS & DISCUSSION

Detailed structure of B2B model.

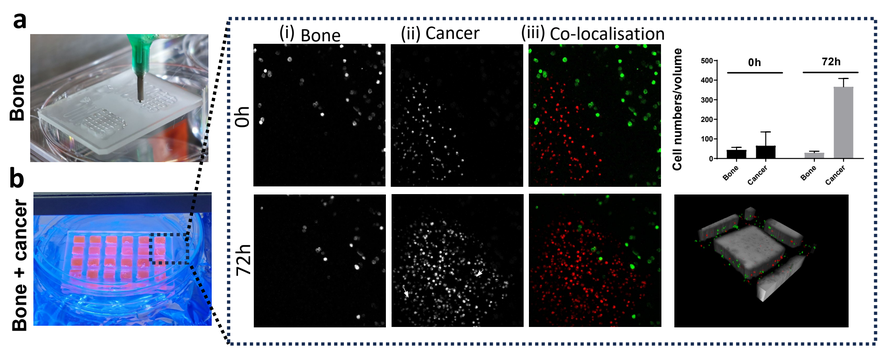


Figure 3. (a) Bone bioprinted compartment is localising HBMSCs within the lattice construct **(b)** B2B model: (**b-i-ii-iii)** Breast cancer compartment can hold BCa cells in place, facilitating proliferation and migration in bone compartment over time. Scale bar: 200 μm

Breast cancer invade skeletal tissue using EGF-residing in bone

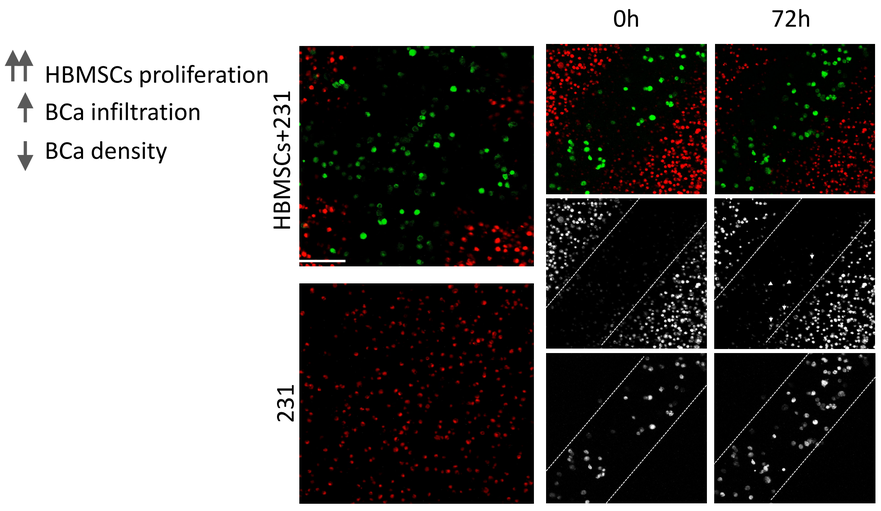


Figure 4. MDA-MB-231 cells showed an infiltration into HBMSC- and EGF-laden scaffolds, indicating a directional migration and infiltration into the bone compartment. **3D matrix embedding promotes active tumour-bone interactions and more physiologically relevant invasion.**
Scale bar: 100 μm.

Breast cancer proliferate inducing bone contraction

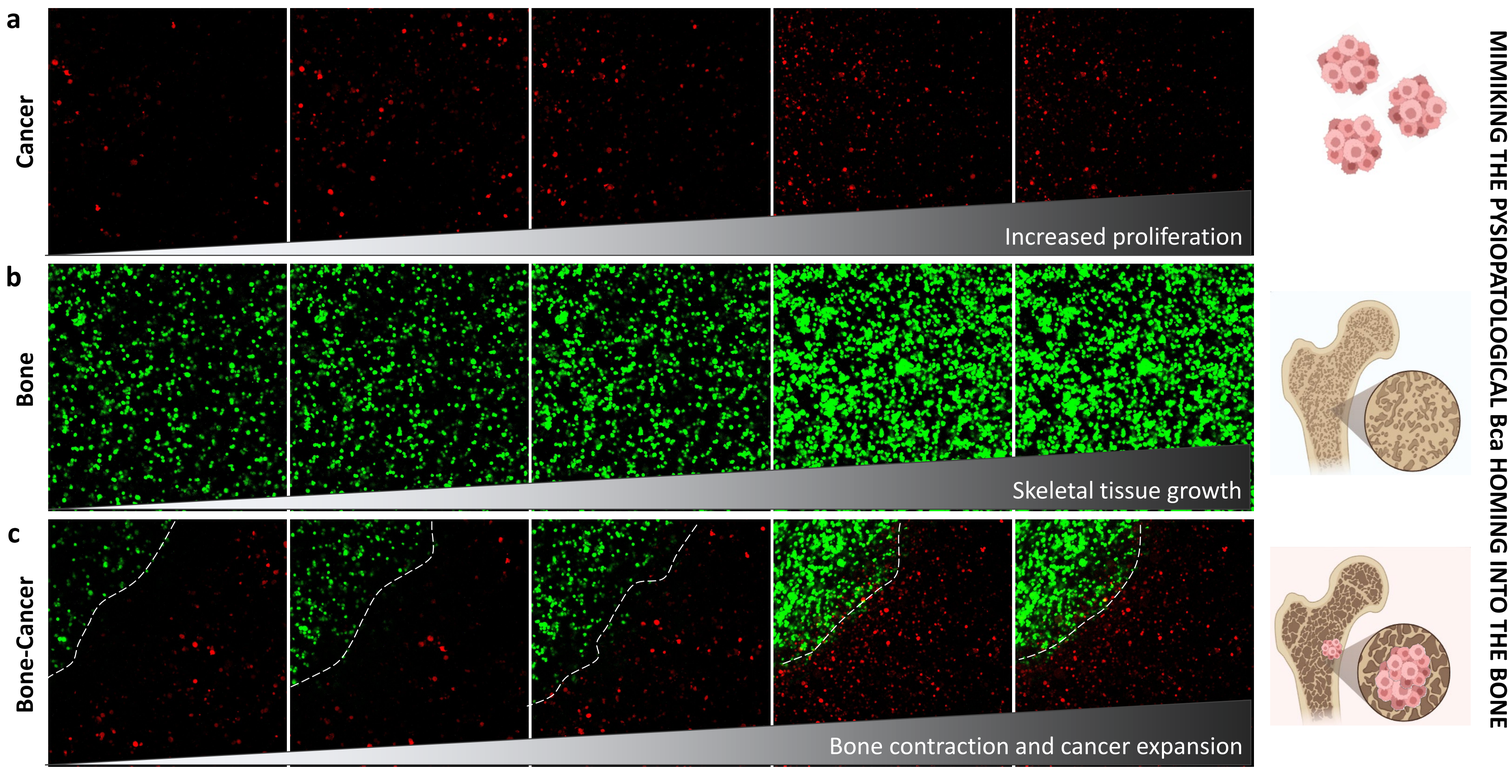


Figure 5. (a) Increased breast cancer cell proliferation (red) in B2B cancer compartment. **(b)** Progressive bone tissue growth over time (green) in cancer-free scaffolds mimiking the physiological proliferation of bone compartment. **(c)** Time-course imaging illustrating increased breast cancer cell proliferation (red), concomitant bone tissue growth (green), and progressive bone contraction, leading to tumor expansion at the bone-cancer interface and mimicking human bone metastasis development

Long-term B2B model guide cancer maturation and full bone infiltration and damage

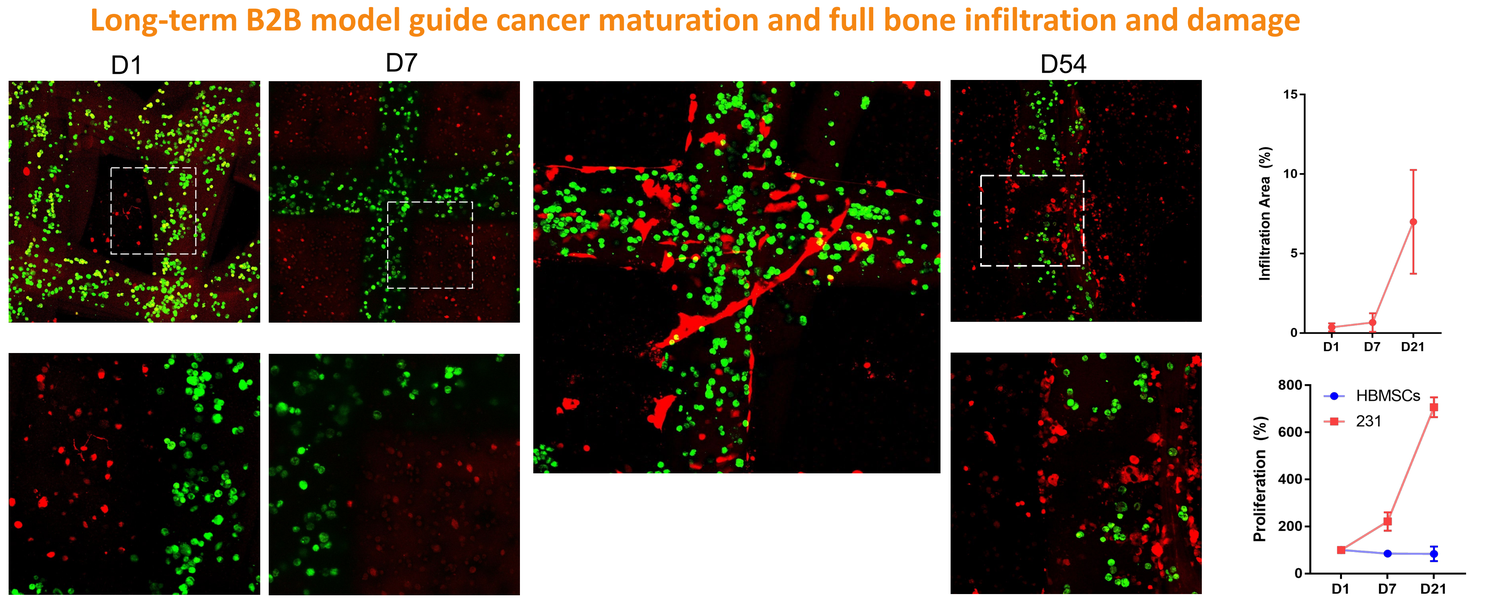


Figure 6. (a) Long-term culture validates the robustness of the model. Over nearly two months, progressive cancer maturation is observed, with evident cancer cell homing **(b)**, increased proliferation **(c)**, and extensive ECM degradation. These processes are accompanied by sustained and dynamic interaction with the bone microenvironment, ultimately leading to full tissue infiltration and structural damage, thereby recapitulating key features of human bone metastasis.

CONCLUSION

We developed a physiologically relevant 3D breast-to-bone (B2B) model that recapitulates key aspects of cancer cell invasion and colonization within a bone-like microenvironment. EGF drives directional homing and tumour–bone interactions, while EGFR inhibition (Lapatinib) effectively blocks invasion and preserves the stromal compartment. This platform provides mechanistic insight into early metastatic events and represents a valuable tool for pre-clinical evaluation of targeted therapies.

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lucia.iafrate@uniroma1.it