Large 3D maps of bone tissues at single-cell resolution

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Breast and prostate cancer are amongst the most common and deadly forms of cancer namely due to the formation of metastasis, which is the leading cause of death in both cancer types. In particular, bone tissue is a preferential site for metastasis formation, with 70% of metastatic breast and prostate cancers developing bone metastases. Their important death rates are mainly due to the lack of understanding of the bone metastasis formation process, which prevented the scientific community from finding effective treatments limiting the spread of the disease. Two main models have historically been used to study bone metastasis development - *in vitro* 2D cultures of cancer cells and *in vivo* animal models - but none of them succeeded at faithfully recapitulating the human bone microenvironment, which is thought to play a crucial role in the process. There is therefore a real need for better biomimetic models that would give new insights on the formation of bone metastasis, eventually leading to the development of drugs specifically targeting this process. In recent years, tissue engineered models appeared as promising alternatives to conventional models, although they still require important improvements to be considered as truly recapitulating tumor features *in vitro*. The work developed here thus aimed at ultimately deriving new ways of improving bone tissue engineered models for the study of breast and prostate cancer metastasis by comparing their 3D tissular and cellular contents with the ones of human bone tissues harboring metastasis. Through the use of CODA on seven tissue engineered bone samples infused with either prostate or breast cancer cells, this report presents the first ever in-depth characterization of tissue engineered models at the millimeter scale and with single-cell resolution. Indeed, CODA allowed for the creation of fully annotated 3D digital reconstructions of the different samples, which were then used to perform quantification of cellular and tissular contents. It has led to preliminary results that need to be confirmed by further investigations before being compared with quantitative results obtained on *in situ* bone metastasis of breast and prostate cancer.

Keywords: Prostate Cancer, Breast Cancer, Bone metastasis, Tissue Engineering, Convolutional Neural Networks, Biomedical Image Registration, Cell Detection

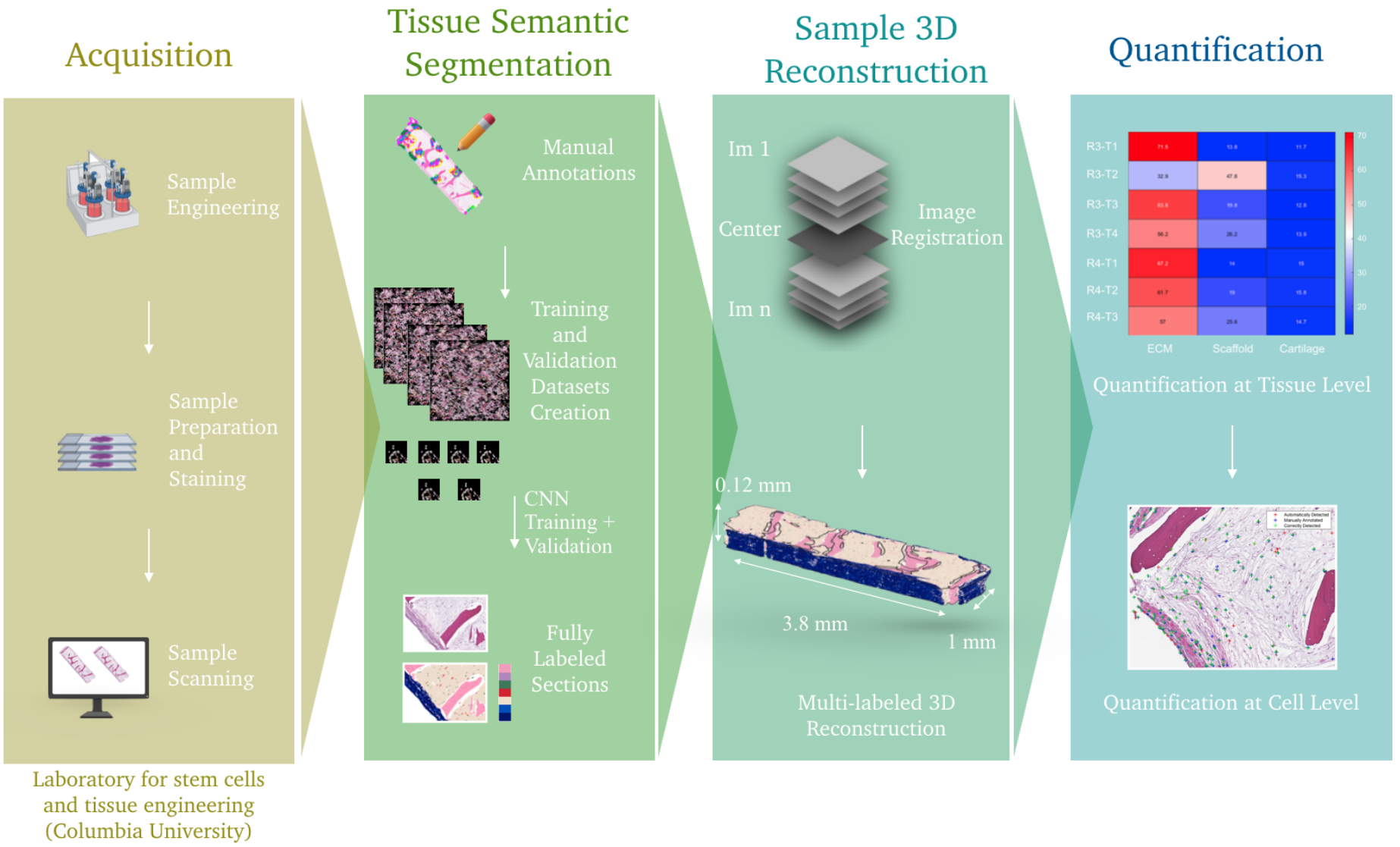


Figure 1: CODA workflow adapted to tissue engineered bone samples.

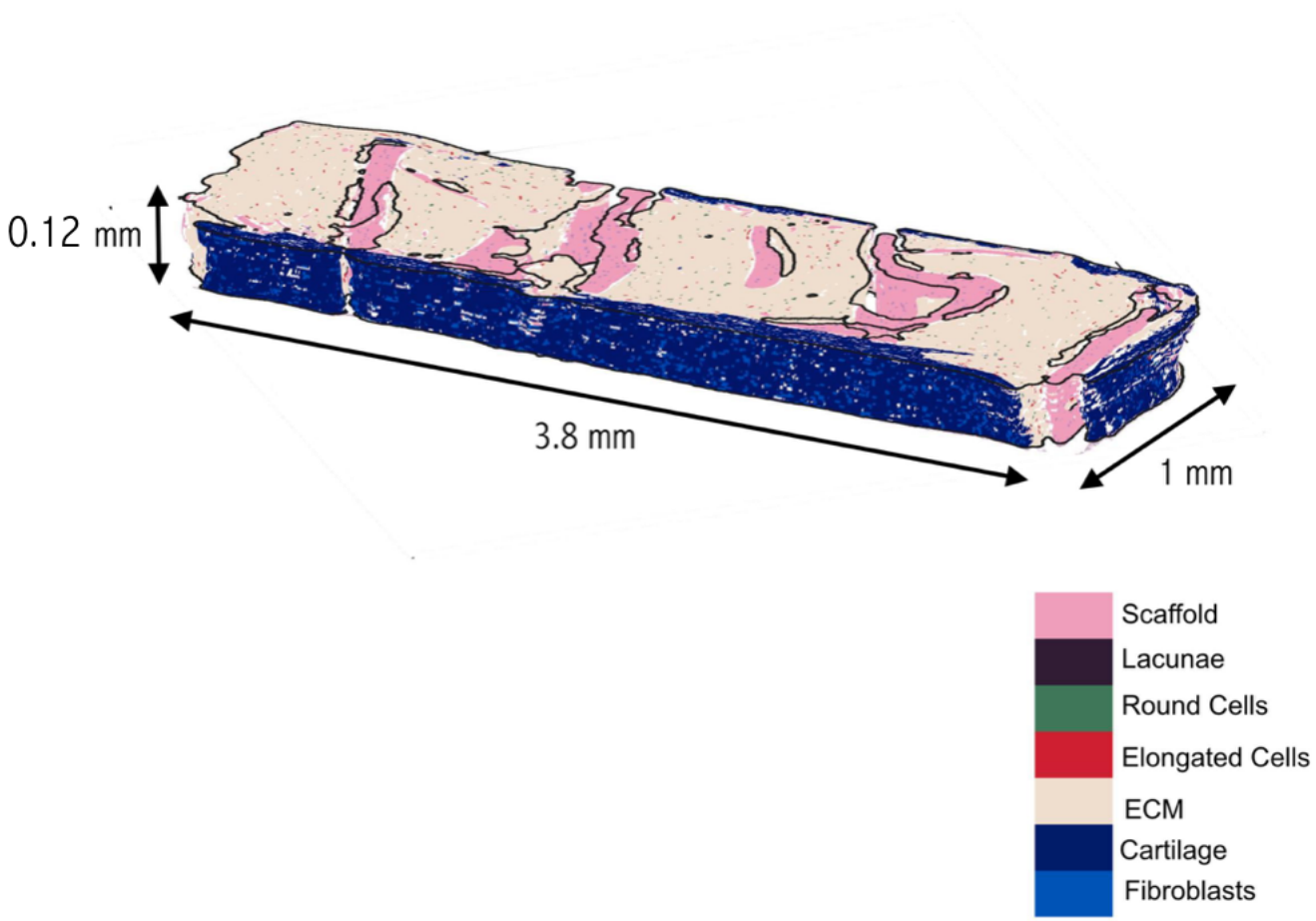
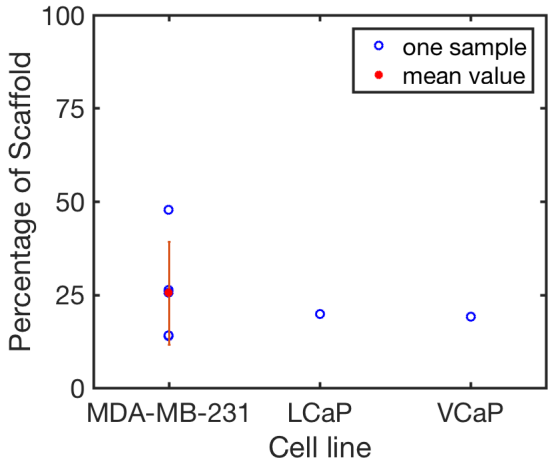
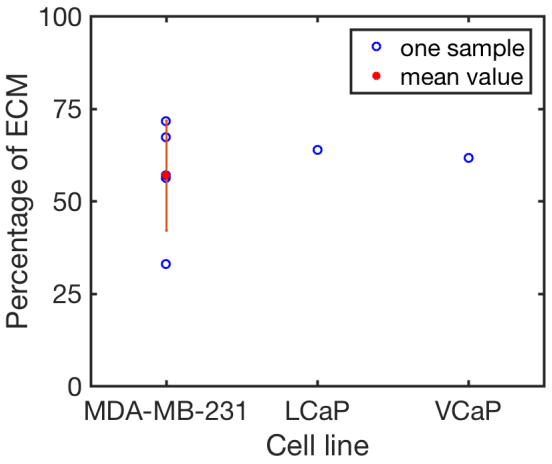


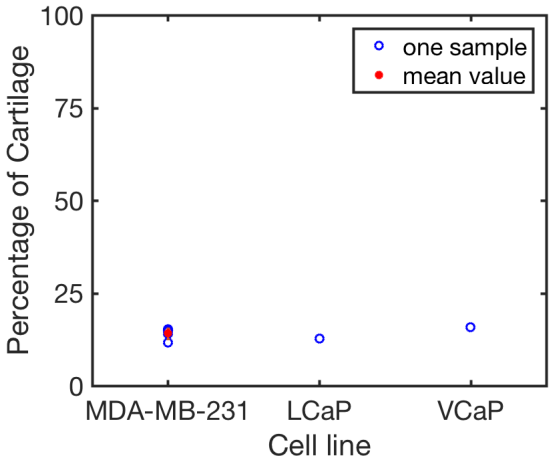
Figure 2: Fully labeled digital reconstruction of sample R3-T1.



(a) Percentage of scaffold inside samples in function of cancer cell line.

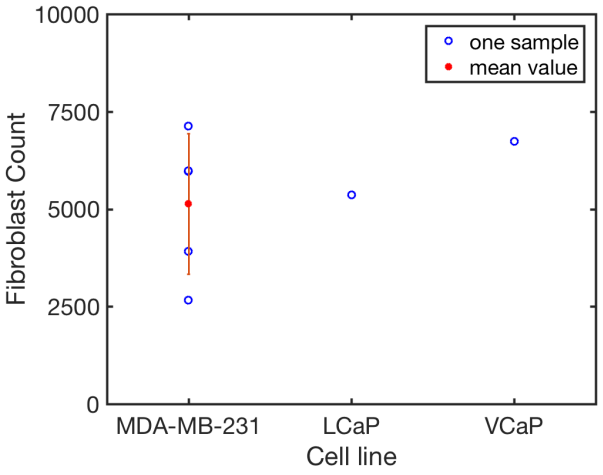


(b) Percentage of ECM inside samples in function of the cancer cell line.

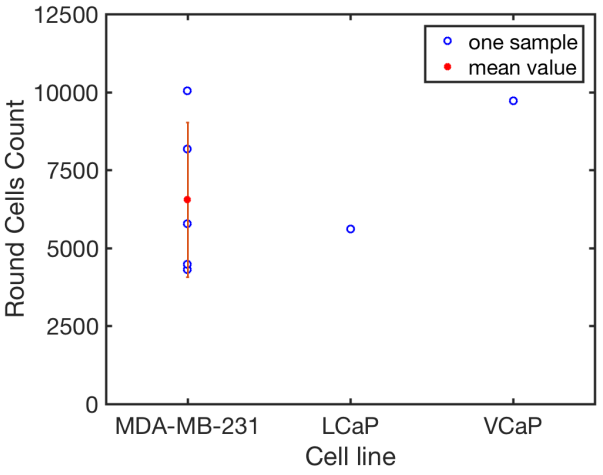


(c) Percentage of cartilage in function of the cancer cell line.

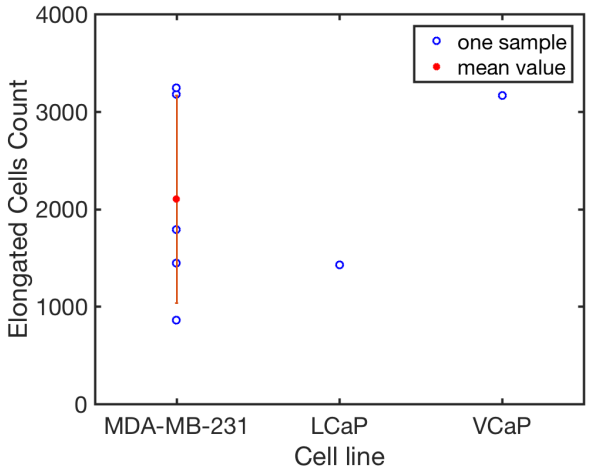
Figure 3: Percentage of tissue inside the samples in function of the cancer cell line.



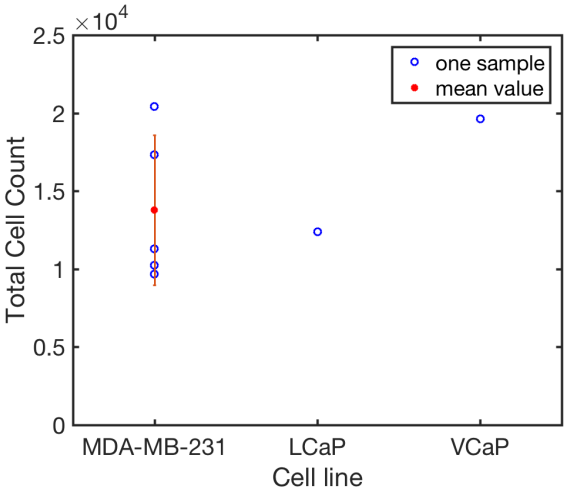
(a) Fibroblast count in each sample in function of the cancer cell line used in the sample.



(b) Round cells count in each sample in function of the cancer cell line used in the sample.



(c) Elongated cells count in each sample in function of the cancer cell line used in the sample.



(d) Total cell count in each sample in function of the cancer cell line used in the sample.

Figure 4: Cell counts in each sample in function of the cancer cell line used in the sample.