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DIGITAL FUNCTIONAL IMAGING AT MICROSCALE: OSTEOSARCOMA MICROENVIRONMENT AND TREATMENT RESISTANCE

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1. Introduction

Osteosarcoma (OST) is a malignant primary bone tumor that mainly affects children and young adults. It is characterized by the anarchic production of bone by tumor cells. The high genomic complexity of OST has not allowed the identification of recurrent therapeutic molecular targets or specific treatment resistance biomarkers. This genomic complexity leads to an intra tumoral and inter individual heterogeneity [1] which can be explored at different scales: metabolomic, molecular, tissue or macroscopic scales. OST components are moreover subject structural and fluid mechanical effects adding supplementary complexity in the understanding tumor microenvironment.

Using porous media theory, we developed a new digital functional imaging technique to explore mechanical and transport properties of tissue from histological and immunohistological human data. We found correlations between elastic properties, convective properties and cell distribution into the microenvironment depending upon treatment response and we highlighted the impact on neo-formed bone microarchitecture.

2. Materials and Methods

We propose a consistent upscaling method to characterize the mechanical properties of tumoral microenvironment which is a strongly heterogeneous porous medium. The core is a sequential grid-block approach [2] after applying dedicated image segmentations. The methodology is adapted to large size binarized images (50000px*50000px) extracted from histological and immunohistological slices obtained in clinical routines. Interstitial fluid flow and elastic models are explored. Piecewise constant equivalent parameters such as tissular permeabilities and stiffness coefficients are determined with reliability.

3. Results

On a cohort of 4 patients, it was found that chemotherapy was more efficient in lacy-like neo-formed bone regions compared to trabecular-like neo-formed bone regions with areas of good response matching with a decreasing number of residual cells and a decreasing local tissue permeability and stiffness (fig 1).

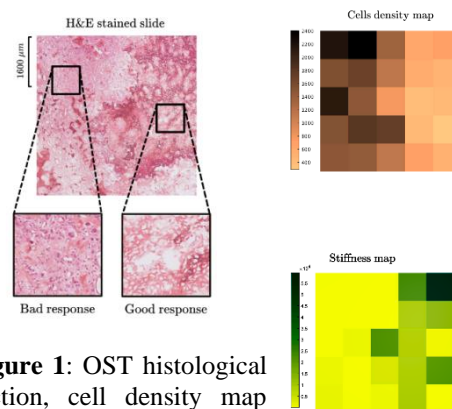


Figure 1: OST histological section, cell density map (bad response to treatment corresponds to high cell density) and stiffness map.

4. Discussion and Conclusions

We have developed an innovative approach based on heterogeneous porous media theory and based on data from clinical setting to explore tumoral microenvironment properties. This new *in silico* functional imaging technique, is generic and could be adapted for different physics and other cancers.

5. References

1. Gomez-Brouchet et al, Cancers 2021.
2. Durlafsky. Water Res. Research, 1991.

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