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VISCOELASTIC PROPERTIES OF TUMOUR TISSUE: RELATION WITH STRUCTURE AND COMPOSITION

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Introduction

Mechanical properties of the extracellular matrix (ECM) play a significant role in regulating cancer cell activities [1]. In breast cancer, ECM stiffening promotes tumour progression and metastasis formation, including bone metastasis. In thyroid cancer, an increase or a decrease in the elastic properties was found depending on the histological type [2], suggesting that different cancer cell types likely respond differently depending on their microenvironment. Atomic force microscopy (AFM) has the potential to elucidate the mechanical signature of breast cancerous tissue at the tissue scale [3]. The aim of this study was to characterise the viscoelastic properties of different types of human tumour tissue that frequently metastasize to the bone using AFM and to correlate them with tissue composition.

Material and methods

Human breast (n=6), kidney (n=5), and thyroid (n=4) specimens containing normal and tumour tissue were collected post-surgery. From each specimen, one sample was used for histology (hematoxylin phloxine saffron staining) and one sample was used for AFM testing. Fresh frozen samples were immersed in PBS and AFM tests were performed using a Nanowizard3 AFM (JPK Instruments AG) equipped with an MLCT cantilever (Bruker) and a pyramidal tip. First, tapping mode topography was used to identify a region of interest with minimal slope. Second, 25 force-displacement curves were recorded over the region of interest, following a trapezoidal loading profile. Elastic modulus was identified from the force-indentation curve using the Hertz-Sneddon model [4]. Elastic fraction, defined as the ratio between the equilibrium and instantaneous moduli, was identified from the indentation-time curve using the standard linear solid model [5]. It varies between 0 (viscous) and 1 (elastic).

Results and discussion

The change in the mechanical properties of tumour tissue was highly dependent on the composition and structure of the tissue. Breast tumour samples, which were composed of dense fibrous tissue, displayed an increased elastic modulus compared to their normal counterpart. The elastic properties of kidney tumour samples were differently affected depending on their histological type (Fig 1). Clear cell renal cell carcinomas

(RCC) displayed a high cellular density, which was associated with a decreased elastic modulus (Fig 1A, B). Papillary RCC displayed dense fibrous tissue, which was associated with an increased elastic modulus (Fig 1A, C). One specimen was composed of densely cellular (clear cell RCC) and fibrous (sarcomatoid) regions, resulting in heterogeneous elastic properties (Fig 1A, D). Similarly, the elastic properties of thyroid tumour samples were differently affected depending on their histological type. Moreover, thyroid tumour samples showed a decreased elastic fraction, while no difference was observed for kidney and breast tissue.

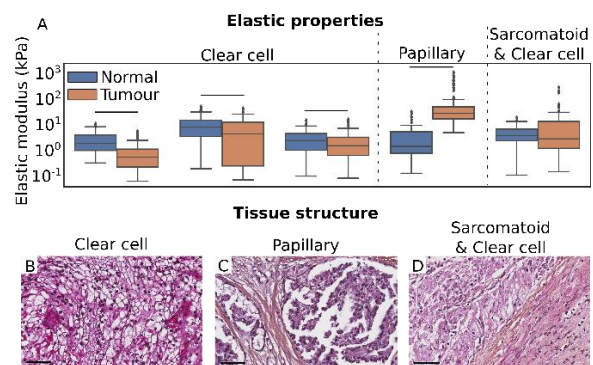


Figure 1: Elastic modulus (A) and histological sections (B, C, D) of kidney tumour specimens of different types. Bars show significant differences between normal and tumour samples ($p < 0.05$). Scale bars: 60 μm .

Results demonstrate that the mechanical properties of tumour tissues are differently affected depending on their type, suggesting a link between the mechanical properties and aggressiveness of the cancer. Future work will assess the relationship between the mechanical properties of tumour tissue and its metastatic potential.

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