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A PROTOCOL FOR THE LOCAL MECHANICAL CHARACTERISATION OF METASTATIC BONE

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Introduction

Osteolytic bone metastases are responsible for long bone fracture leading to restricted mobility or surgery, which severely alter quality of life and have a huge socio-economic impact [1]. Patient-specific finite element (FE) models assessing the strength of tumoral bone segments can help predict bone fracture [2], but their accuracy is hampered by a limited knowledge of metastatic bone mechanical properties. Changing the constitutive law of metastatic and surrounding bone tissues in FE models can have an effect on both the predicted failure load and fracture location [3]. In this context, we proposed an experimental protocol to locally characterize the mechanical properties of metastatic and surrounding bone tissues, with the aim of incorporating them into FE models of metastatic bones.

Materials and methods

Six human bone specimens (femur or rib) containing metastatic and normal tissues were collected post-surgery. The primary cancer was breast (n=2), thyroid, rectal, myeloma or lymphoma. First, mechanical properties of the metastasis (soft tissue) were characterized on fresh frozen samples (Figure 1, left), following a previously published protocol on fresh tumor [4]. Briefly, AFM tests were performed on samples immersed in PBS using a Nanowizard3 AFM (JPK Instruments AG) equipped with an MLCT cantilever (Bruker) and a pyramidal tip. Elastic modulus and elastic fraction, defined as the ratio between equilibrium and instantaneous moduli (0: viscous; 1: elastic), were calculated using Hertz-Sneddon model [5] and standard linear solid model [6], respectively.

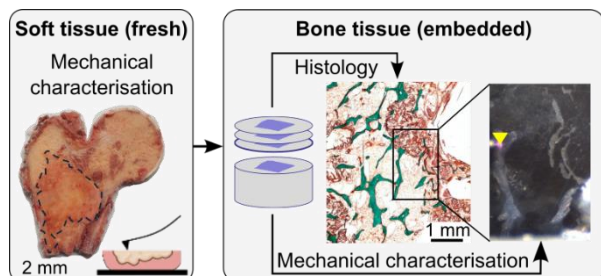


Figure 1: Protocol for the mechanical characterization of metastatic bone from upper femoral extremity. Left: for soft tissue, right: for hard tissue

Second, samples were dehydrated, fixed and embedded, and mechanical properties of bone tissue were characterized (Figure 1, right). Non decalcified

embedded bone samples were sectioned and metastatic, transition, and normal areas were identified from histological sections, using Masson-Goldner's trichrome staining. Force-displacement curves were obtained in each area on the remaining block using a TI950 nanoindenter (Hysitron – Bruker). The elastic modulus was identified using Oliver and Pharr model [7].

Results and discussion

Characterization of soft metastatic tissue revealed a variation in the elastic modulus over two orders of magnitude depending on the specimen (Figure 2). Preliminary tests on bone tissue were performed and results were consistent with the literature [8], with Young's modulus values ranging between 15 and 20 GPa. The remaining specimens will be characterized and a sensitivity study will then be conducted to assess the influence of mechanical properties on the predicted failure load. This work has the potential to improve the accuracy of FE models and quantify uncertainties.

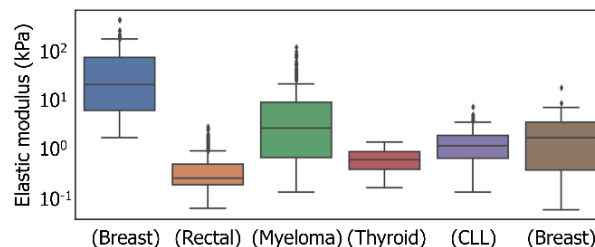


Figure 2: Elastic modulus of each fresh-frozen specimen in the (soft) metastatic area. The type of primary cancer is indicated. CLL: Chronic lymphocytic leukemia.

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