Clinical CT-Based Finite Element Simulation of Spatial Bone Damage Accumulation Strongly Predicts Osteolytic and Osteosclerotic Human Vertebrae Strength and Stiffness.

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INTRODUCTION: The infiltration of metastatic bone lesions affecting the spinal column degrades the vertebral bone quality and architecture, causing a high patient risk of pathological vertebral fractures (PVF). Establishing the patient's PVF risk and, critically, the location of failure within the pathologic vertebra remains an unmet clinical need for managing patients with metastatic spine disease. This study developed a novel damage-based computational framework for modeling the effect of metastatic bone lesions on spatial damage accumulation patterns in human pathologic vertebrae. Our objective was to test the FE-framework prediction of the strength and stiffness of human pathologic vertebrae containing osteolytic and osteosclerotic bone lesions from CT imaging.

METHODS: 11 thoracic and lumbar vertebrae from donors with cancer (prostate, breast, lung, and kidney), radiographically showing osteolytic and osteosclerotic bone metastases, were CT imaged (0.31m^3 voxel size, µCT100, Scanco, Switzerland) and mechanically tested to failure in axial compression. In order to model the spatially heterogeneous vertebral bone response, we implemented a constitutive bone model proposed by Johnson et al. [1], which captures the viscoelastic and viscoplastic behavior of vertebral bone. The framework constitutive model was extended to 1) account for the nonlinear relationships between trabecular bone material property and volume density (BV/TV) [2] and 2) incorporate a continuum damage accumulation model to capture the resulting softening of the spatial bone structure [3]. To calibrate the material model parameters, we used an iterative procedure in which we solved the boundary value problem of a selected model using trial values for the material parameters until the predicted load-displacement matches that of the experiment. The simulation results fully describe the temporal evolution of the vertebra's stresses, strains, and damage fields. The mechanical tests were simulated using the developed framework to evaluate the metastasis's effect on the evolution of spatial damage in the vertebral bodies and to compute vertebral strength and stiffness.

RESULTS SECTION: The osteosclerotic vertebrae simulated strength, a mean and standard deviation of 7.44 (3.35) kN, and stiffness [20.60 (9.03) kN/mm] was significantly higher than the osteolytic vertebrae's simulated strength [2.49 (1.24) kN, p=0.0204] and stiffness, [8.61 (3.75) kN/mm, p=0.0405]. Regression analysis showed the damage-based model strongly predicted the measured vertebral strength (R^2=0.95, p<0.0001) and stiffness (R^2=0.78, p=0.0003), independent of lesion type, Fig 1. The FE model predicted bone damage in lytic vertebrae to progress in a spatially diffused manner throughout the body in response to increased loading, resulting in extensive damage to the bone network, Fig 2.[A]. By contrast, in the osteosclerotic vertebrae, damage accumulation was largely confined to regions of low bone volume to tissue volume that interspersed the osteosclerotic regions of high BV/TV, Fig 2.B. For both lesion types, vertebral failure was predicted when the cancellous bone damage evolved to the vertebral cortexes.

DISCUSSION: Using a newly developed computational damage-based model, we demonstrate that metastasis type differentially affects the evolution of spatial damage and that this damage pattern strongly predicts vertebral strength and stiffness across lesion types. The strong association between damage accumulation and vertebral strength and stiffness permitted us to localize the points of initial failure and the subsequent fracture patterns. Our model offers a pathway for developing image-based diagnostics to predict the risk and location of impending failure within the vertebral body. Current work is focused on experimentally validating the model's damage prediction for pathologic human spines under functional loads computed from patient-specific musculoskeletal models.

SIGNIFICANCE/CLINICAL RELEVANCE: Spine metastases produce severe pain and vertebral fracture risk. Predicting bone expected fracture location and spinal instability are critical for guiding therapy to reduce the risk of severe complications and neural compression and remains an unmet clinical need.

REFERENCES: 1) Johnson, et al, *Acta Biomaterialia*. 2010: 4073-80. 2) Zysset, P, J Biomech, 2003. **36**(10): 1469-85. 3.Dall'Ara, E., et al., *Bone*. 2013, p. 27-38.

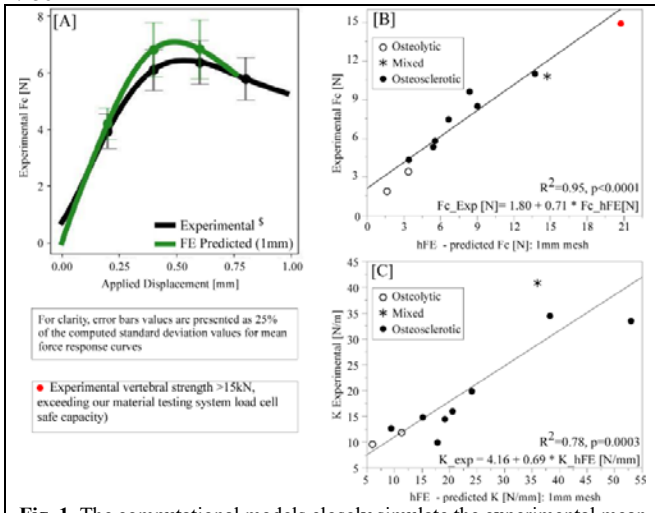

Fig. 1. The computational models closely simulate the experimental mean load displacement across all vertebrae [A], strongly predicting the measured vertebral strength [B] and stiffness [C].

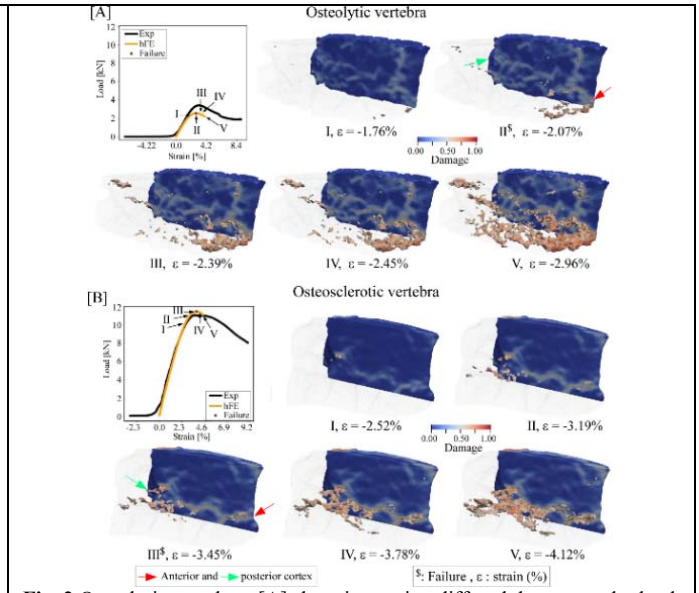

Fig. 2 Osteolytic vertebrae [A] show increasing diffused damage under load. In osteosclerotic vertebra [B], Fig 2.A, the damage bypasses the sclerotic bone progressing via the low-density regions. Vertebral failure occurs when bone damage evolved to the vertebral cortexes (marked by color arrows, Fig 2).