Multiscale In-slico examination of the biomechanics of cartilage under gender-driven composition

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INTRODUCTION: Knee joint cartilage injuries and subsequent slowly progressive degenerative diseases are leading sources of long-term disability [1]. They have a higher occurrence and are more often generalized in women than men, specifically after meniscal or ligament injuries or after age 50 [2]. The reason for this gender bias alteration is currently unknown, and very little explanation has been linked to the difference in cartilage composition between gender without any further study on its effect on the mechanical response. We argue that a clear understanding of the relationship between the gender-driven cartilage composition and its effect on the mechanical response of the cartilage may elucidate the mechanical underpinnings associated with the observed high prevalence of women's cartilage alteration. Thus, in this study, we seek to develop a multi-structure model of cartilage, incorporating the cell distributions with their microenvironment, to investigate the mechanical effect of the difference in the gender-driven cartilage composition.

METHODS: This study developed a multi-structure model for the articular cartilage (Fig. 1a), including anatomical cell distributions and their micro-environment (collagen II, VI, IX, pericellular and extracellular matrix). The model was built based on a pyramidical tiling technique, starting from cellular and non-cellular units differentiating by including the chondrocytes, pericellular, and minor collagen structures (VI, IX). This cellular and non-cellular unit generated a periodic unit respecting the depth-dependent characteristic of the cartilage microstructures. Finally, by tiling the periodic units, an axisymmetric model was constructed with dimensions that resemble those of the articular cartilage samples (plug) used in the reported unconfined testing paradigm [3]. A poro-hyperelastic swelling material model was used for the cartilage matrices, while a nonlinear elastic model was used for collagenous structures [4]. The cartilage model has been simulated under an unconfined test [3] with varied material parameters mimicking the cartilage gender composition differences [5]. This latter was implemented on the female model by decreasing the collagen IX volume fraction and the deep proteoglycan concentration by a ratio of 1:1.81 and 1:3, respectively [5].

RESULTS: The simulation of the multi-structure model shows that cartilage reaction force varied substantially between gender (Fig.1b). With the female model, this reaction force decreased by 0.8 N (from 2.2N in the male model to 1.4 N in the female model) in the peak loading instance and by an average of 29% within the dynamic phase of loading. At the steady state, the equilibrium moduli decreased substantially by almost 36% compared with the male one. In addition, supported cell forces (average of 38 %) and cell volume changes (average of 26%) decreased with the female model over the superficial and random layers of the cartilage. Furthermore, a random selection of the cartilage cell and its microenvironments from the three different layers of the articular cartilage shows a clear alteration in the stress distribution between gender (Fig.1, c, d). These stresses decrease in the top layers and increase in the bottom ones.

DISCUSSION: The developed composite model of the articular cartilage has successfully described the experimentally observed temporal response characteristics in an unconfined testing configuration within the male model [3], which is considered in this scenario as a reference model (considered experiments conducted on male samples). The inclusion of the female materials properties' alteration within the reference model substantially changes the aggregate response of the article cartilage, where less resisting loading capability has been computed. This macro reaction was associated with a clear alteration of the micro-mechanics of the chondrocyte and its microenvironments. As a result, much less circumferential forces were supported by the cells as well as the pericellular and territorial matrices. This micro load lower resisting capacity, which was located mainly in the upper region of the cartilage depth, may be explained by the great alteration of the proteoglycan concentration in the deep layer of the cartilage. This proteoglycan alteration led to a flaccid cartilage structure that favored less micro-volume changes and hence less structural forces resistance.

SIGNIFICANCE: The results demonstrate the ability of the current construct to capture the mechanical intricate mediated by the cartilage sex-driven composition, which could explain the sex-related difference in the prevalence of cartilage injuries and diseases.

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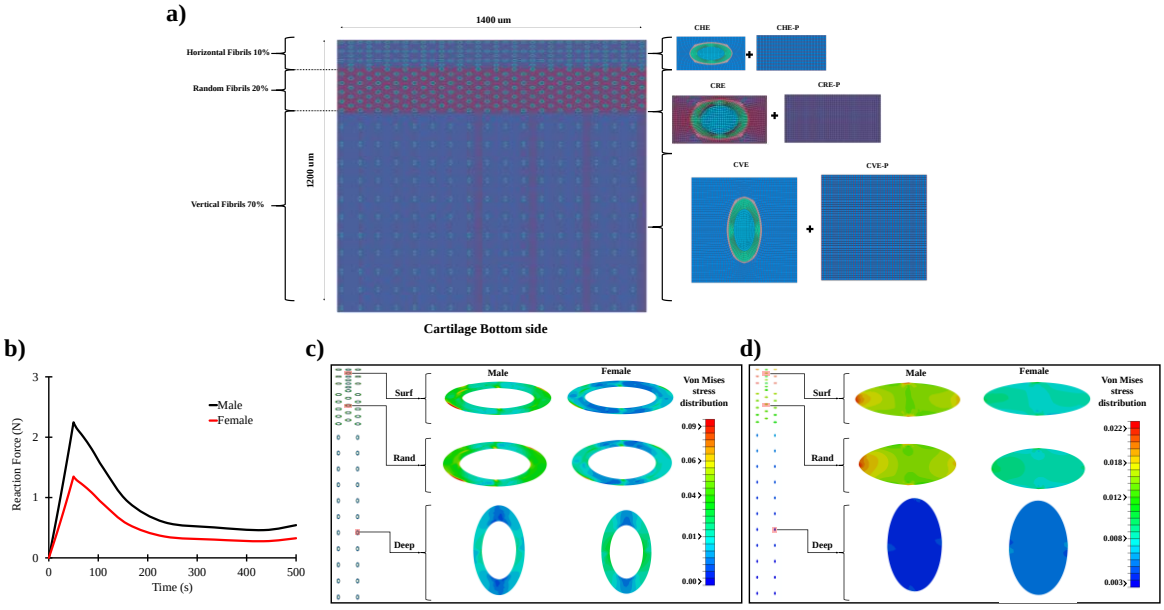

Fig. 1: a) Articular cartilage multi-structure model. (b) Reaction force computed from unconfined compression test. (c) pericellular matrix and (d) cellular stress distribution.