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Raju, V. orcid.org/0000-0002-0746-4516 and Koorata, P.K. orcid.org/0000-0001-9141-8741 (2023) Computational assessment on the impact of collagen fiber orientation in cartilages on healthy and arthritic knee kinetics/kinematics. *Medical Engineering & Physics*, 117. 103997. ISSN 1350-4533

<https://doi.org/10.1016/j.medengphy.2023.103997>

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1 **Computational assessment on the impact of collagen fiber orientation in**
2 **cartilages on healthy and arthritic knee kinetics/kinematics**

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23 Abstract: 339 words

24 Main Text: 5732 words

25 **Abstract**

26 *Background:*

27 The inhomogeneous distribution of collagen fiber in cartilage can substantially influence the
28 knee kinematics. This becomes vital for understanding the mechanical response of soft
29 tissues, and cartilage deterioration including osteoarthritis (OA). Though the conventional
30 computational models consider geometrical heterogeneity along with fiber reinforcements in
31 the cartilage model as material heterogeneity, the influence of fiber orientation on knee
32 kinetics and kinematics is not fully explored. This work examines how the collagen fiber
33 orientation in the cartilage affects the healthy (intact knee) and arthritic knee response over
34 multiple gait activities like running and walking.

35 *Methods:*

36 A 3D finite element knee joint model is used to compute the articular cartilage response
37 during the gait cycle. A fiber-reinforced porous hyper elastic (FRPHE) material is used to
38 model the soft tissue. A split-line pattern is used to implement the fiber orientation in femoral
39 and tibial cartilage. Four distinct intact cartilage models and three OA models are simulated
40 to assess the impact of the orientation of collagen fibers in a depth wise direction. The
41 cartilage models with fibers oriented in parallel, perpendicular, and inclined to the articular
42 surface are investigated for multiple knee kinematics and kinetics.

43 *Findings:*

44 The comparison of models with fiber orientation parallel to articulating surface for walking
45 and running gait has the highest elastic stress and fluid pressure compared with inclined and
46 perpendicular fiber-oriented models. Also, the maximum contact pressure is observed to be
47 higher in the case of intact models during the walking cycle than for OA models. In contrast,
48 the maximum contact pressure is higher during running in OA models than in intact models.
49 Additionally, parallel-oriented models produce higher maximum stresses and fluid pressure
50 for walking and running gait than proximal-distal-oriented models. Interestingly, during the

51 walking cycle, the maximum contact pressure with intact models is approximately three times
52 higher than on OA models. In contrast, the OA models exhibit higher contact pressure during
53 the running cycle.

54 *Interpretation:*

55 Overall, the study indicates that collagen orientation is crucial for tissue responsiveness. This
56 investigation provides insights into the development of tailored implants.

57 **Keywords:** Collagen fiber orientation; Fiber reinforced biphasic model; Gait cycle; Knee
58 articular cartilage; Osteoarthritis;

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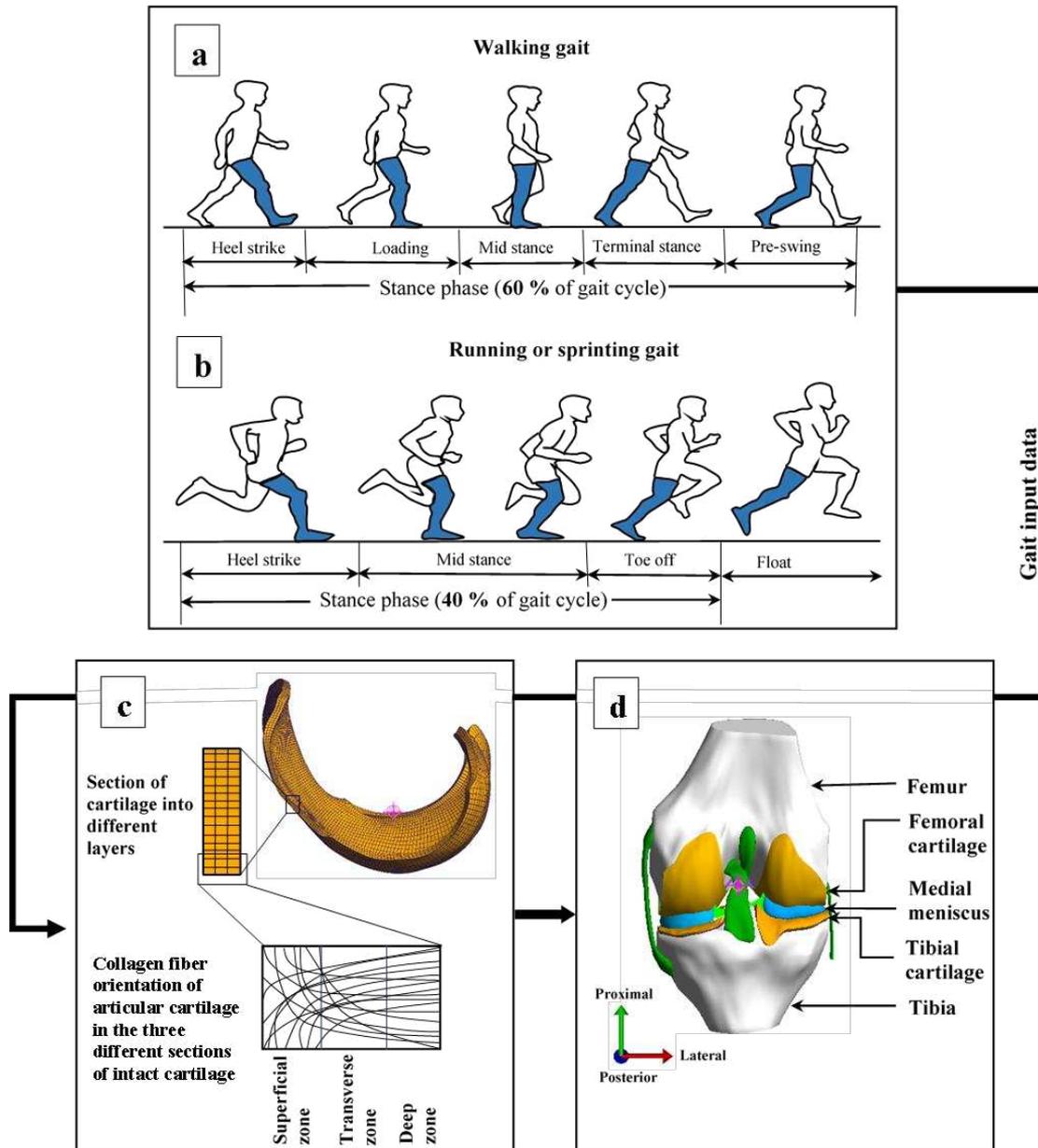
76

77 **1. Introduction**

78 Daily physical activities like walking, jogging, and running lead to significant compressive
79 loads on the knee cartilage, causing knee osteoarthritis (OA), especially in older people [1–4].
80 The articular cartilage constituents such as collagen fibers, proteoglycan matrix, and
81 interstitial fluid collectively withstand body weight (BW) during activities like walking,
82 running, stair climbing, and kneeling. The load on the knee joint is different for each of these
83 activities 1BW, 1.5BW, 2BW, and 4BW, respectively [5–7]. The collagen network of
84 articular cartilage protects chondrocytes, withstands high tensile force, and protects cartilage
85 from rupture. This network attaches the cartilage to the subchondral bone and provides
86 attachment for proteoglycans [8]. In the loading and unloading stages, the osmotic pressure
87 increases in the articular cartilage, significantly increasing the interstitial fluid pressure. The
88 body force is distributed throughout the cartilage during the loading stage and increases the
89 shearing force on the articulating surface. Hence collagen fibers are subjected to complex
90 loading conditions due to the interstitial fluid pressure and shearing force [9–11]. OA leads to
91 degradation in cartilage structure in terms of fibrillation and proteoglycan depletion,
92 hindering the mechanical characteristics of the cartilage [12–15]. To better understand
93 cartilage degradation associated with OA, it would be convenient to characterize the collagen
94 fiber orientations and their responses in a complex loading environment under different gait
95 activities.

96 The collagen fibers in cartilage provide mechanical rigidity, which helps to maintain the solid
97 matrix's structure. Also, the fibers are distributed heterogeneously throughout the cartilage,
98 with their structure similar to an arcade-like design from the articulating surface to the
99 subchondral bone [16,17]. The fibrils are oriented parallel to the articular surface in the
100 superficial zone. However, they become more randomly oriented in the transitional zone and
101 turn perpendicular to the bone-cartilage interface in the deep zone to firmly anchor the tissue

102 to the subchondral bone [18–20]. The fiber orientation in the respective zones is represented
 103 with split-line patterns is the most widespread technique used in the literature [21–23].



104
 105 **Fig. 1.** Schematic of workflow: (a) the stance phase of the walking gait cycle; (b) the stance
 106 phase of the running gait cycle; (c) sagittal view of femoral cartilage with the orientation of
 107 collagen fibers in a depth-wise direction; (d) finite element model of the knee joint where the
 108 gait input data and various collagen fiber orientation models are applied.

109 The fiber network is known to be organized differently in healthy and arthritic cartilage. The
110 collagen fiber orientation significantly influences the tissue response and the contact
111 mechanism for OA cartilage [7,24]. In addition, it is reported that the tissue response is
112 highly sensitive to fiber reorientation and loading direction [25]. Fiber reorientation is the
113 major mechanism when loading perpendicular to collagen fiber orientation; however, when
114 loading parallel to the fiber direction, a reduction in collagen fibers crimp and fiber
115 reorientation occurs [26]. Hence it is necessary to understand the behavior of cartilage
116 response with respect to the collagen fiber orientation. Even though literature is available on
117 the tissue responses for arthritic cartilage cases, the relation between collagen fiber
118 orientation/loading direction and tissue response is not adequately studied [3,27–29].

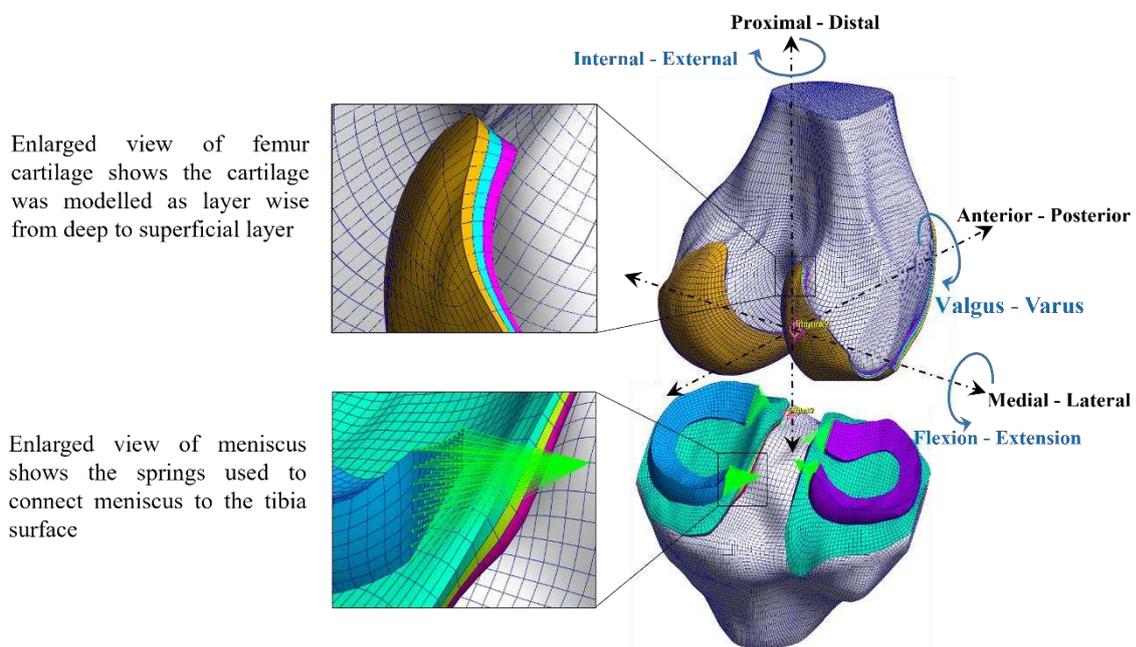
119 It is reported that depth-dependent fiber-oriented cartilage models can accurately estimate the
120 realistic contact stress and fluid pressure in the knee joint [30]. However, the knee responses
121 from daily activities such as walking and running by considering the depth-dependent
122 cartilage characteristics are missing in the literature. In addition, the biphasic hyperelastic
123 material models (neo-Hookean) available in commercial software do not capture the critical
124 tissue response, such as the distribution of interstitial fluid pressure and shear stress [31].
125 However, results from the current fiber network model show an increase in the interstitial
126 fluid pressure on the contact surface and could capture it during knee loading.

127 Also, the orientation of collagen fibers is crucial to the mechanical responses of connective
128 tissue and load-bearing tissue because it serves as the tissue's structural foundation [32]. The
129 study of the mechanics of collagen fiber orientation advances the understanding of the
130 mechanism of tissue formation from scratch. However, there is currently a lack of knowledge
131 regarding the mechanism behind fiber orientation. Also, the literature results suggest that
132 collagen orientation plays a critical role in soft tissue response during load transmission of the
133 knee joint [26]. Hence, the present study's objective is to investigate how collagen fiber

134 orientation affects the mechanical response of the cartilage during the gait cycle. Moreover,
 135 the walking and running knee responses are calculated for the parallel and perpendicular
 136 loading conditions with respect to the collagen fiber alignment. We hypothesise that the
 137 vertical collagen fiber-oriented network plays a significant role in supporting and protecting
 138 articular cartilage. Damage to this network would affect the mechanics of the joint and
 139 increase the tissue's susceptibility to OA. Multiple oriented cartilage models are created and
 140 analysed for various gait cycles. The results help researchers to develop better assistance
 141 devices for arthritis patients for subject-specific activities like walking and running.
 142 Additionally, this research contributes to developing subject-specific composite knee implant
 143 material with depth-dependent features by implanting fibers in particular orientations
 144 following the activity requirements.

145 **2. Methods**

146 *2.1 Finite Element Model*



147
 148 **Fig. 2.** The schematic diagram of the finite element model shows that the gait input data
 149 (forces and rotations) are applied on all 6 degrees of freedom of the knee joint through the
 150 three mutually perpendicular axes.

151 A case study is performed based on open-knee geometry [33], simulating the walking and
152 running cycle to study the influence of collagen fiber orientation in multiple gait activities.
153 The tibiofemoral joint is segmented from a female subject (70 years, 77 kg) into femur, tibia,
154 collateral ligaments (MCL and LCL), cruciate ligaments (ACL and PCL), menisci (lateral
155 and medial), and cartilage (femoral and tibial) as given in Figure 1. The finite element model
156 of the knee joint is imported in FEBio Studio 1.2.0 (University of Utah and Columbia
157 University) an open-source finite element analysis software and static analysis is performed
158 [34].

159 The soft tissues and bone are discretized into 56,433 hexahedral elements and 25,220 shell
160 elements. The soft tissues such as cartilage, ligaments and meniscus are meshed with
161 hexahedral brick elements (HEX8), and the bones such as tibia and femur are meshed with
162 shell elements (QUAD4). A mesh convergence test is carried out to ensure that the solution
163 shouldn't change when the mesh is refined. Multiple iterations are performed on the model
164 from element length 0.5 to 2 mm in 0.5 mm increments. The optimum element length
165 calculated for generating the same contact pressure on the surface is approximately 1 mm.
166 Also, the software's mesh inspector is used to refine the model and ensure no stress or strain
167 singularities. The current study, however, assumes each layer's mesh size is the same for
168 numerical convergence purposes. The cartilage is divided into three layers in the direction of
169 cartilage thickness, from the superficial layer to the deep layer shown in Figure 2. The
170 Meniscal attachment to the tibia is modelled using a set of linear springs with a total spring
171 constant of 350 N/mm at each meniscal horn. Eighty-eight linear springs are attached to the
172 tibial plateau at each horn attachment. The spring constants of each spring are calculated
173 using Eq. (1), where k is the stiffness of each spring, E is the elastic modulus of the meniscal
174 horn, A is the total horn face area, and N is the number of nodes on that face [35–38].

175
$$k = \frac{EA}{NL} \quad (1)$$

176 The 3D geometry used for the present investigation is segmented from a 70-year-old subject,
177 the cartilage and other soft tissues are intact, and no evidence of arthritis is reported in the
178 source [33]. Also, there might be a difference in the thickness of cartilage and ligaments of
179 the current geometry due to pathological conditions compared with younger subjects. This
180 may cause a slight variation in mechanical response compared to the actual response. This is
181 a significant limitation of subject-specific finite element model studies like this. Researchers
182 also developed an instrument to evaluate the methodological quality for subject-specific finite
183 element studies dedicated to orthopaedics. This can make it easier to assess the quality in the
184 systematic reviews of finite element models [39].

185 *2.2 Gait input data*

186 The gait input data (forces and rotation) are applied to the knee joint through the three
187 mutually perpendicular axes shown in Figure 2. In this work, the gait data are taken from the
188 literature and imported into the model for simulation [40–44]. Six different but simultaneous
189 movements occur between the femur and tibia during the walking and running gait cycle. It is
190 divided into three rotations (extension–flexion, internal-external, and varus-valgus) and three
191 force components (anterior-posterior, medial-lateral, and proximal-distal) [45].

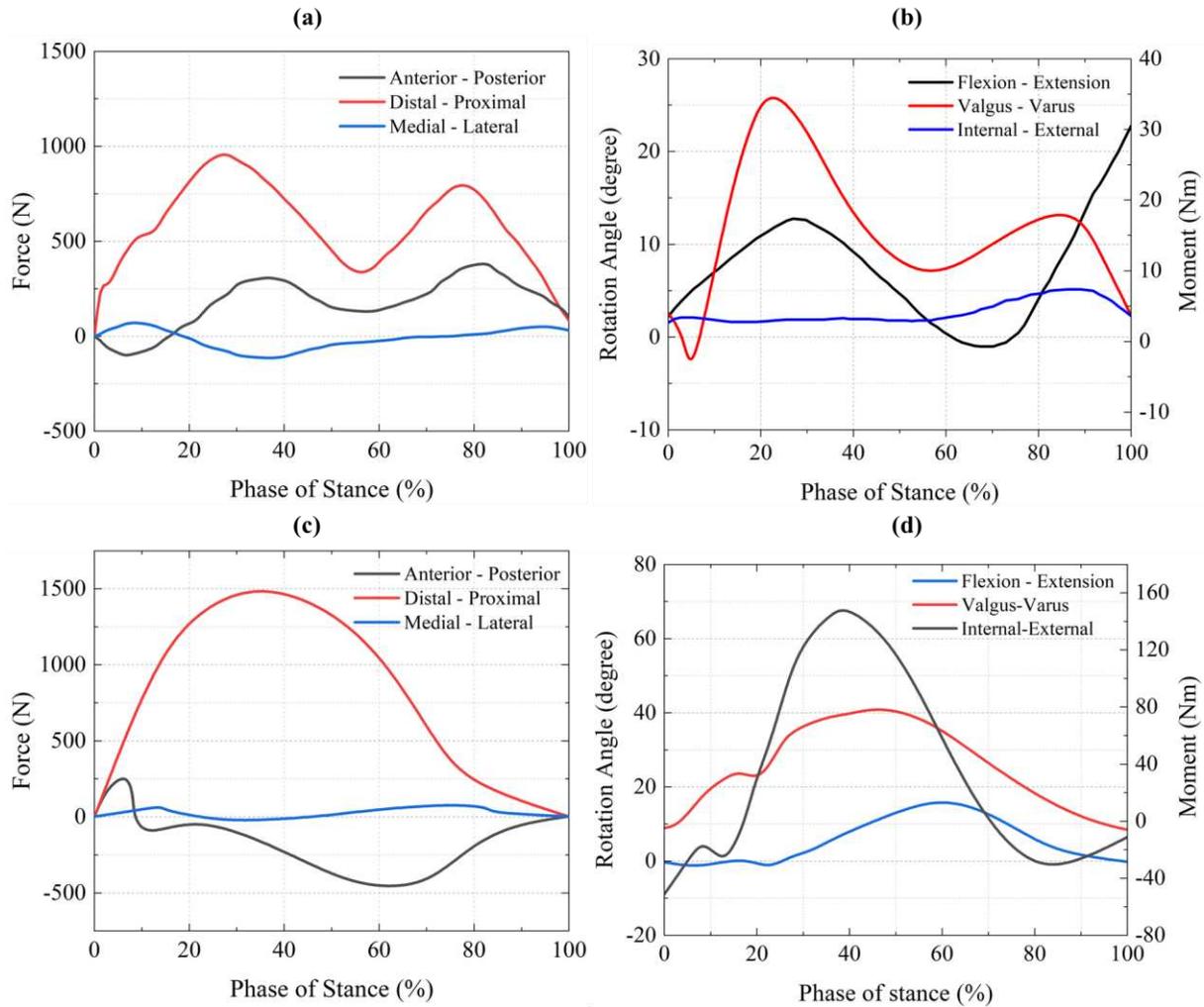
192 The walking kinetic and kinematic data are obtained from a subject (28 years old male, 82
193 kg) who walked on a 10 m track at an average speed (of 1.7 m/s) [28]. The typical human
194 walking speed is between 1.2 m/s and 1.4 m/s, but the present study uses data from the
195 literature that the subject's average walking speed is 1.7 m/s. The running data were obtained
196 from a subject (22 years old male, 76 kg average) running at 4.07 m/s in a 30 m walkway
197 [46]. The authors of both studies used 3D motion capture and anatomical marker systems to

198 track walking and running data and converted them into knee kinetics and kinematics data
199 with commercial software.

200 The walking gait data are adapted from a young, healthy subject, whereas the structure of the
201 knee tissues developed from a pathological, aged subject. Also, the gait pattern of younger
202 adults varies from that of older subjects, even with good health conditions, due to differences
203 in knee extension and shorter stride length [47,48]. In the present work, the gait data are
204 taken from young individuals with longer stride lengths (1.7 m/s), even though the height of
205 an individual also changes the gait pattern [49]. Hence such pre-clinical work without the
206 study of in vivo models is another limitation of the work. In addition, the weight of the knee
207 model and the applied load measured from the human subject are different. Nevertheless, this
208 weight mismatch will not affect the results significantly since the tissue response mainly
209 depends on the gait input data and the cartilage material model. Since the same geometry is
210 used in all subject cases, the study focuses primarily on the tissue response to various
211 activities. Parametric modelling technology can be used to overcome the mismatching
212 between applied load and knee joint weight. This technique can quickly build models to
213 overcome weight mismatching limitations [50]. This can be considered in future research
214 with orthopaedic modelling limitations.

215 *2.3 Contact and boundary conditions*

216 In the model, the tibia is constrained in all degrees of freedom, whereas the femur is
217 subjected to rotation for the gait input data. Also, translational forces are applied to the femur.
218 The interaction between cartilage-cartilage and cartilage-meniscus is set to be frictionless.
219 The meniscus is connected to the tibial surface with elastic springs to mimic the anterior and
220 posterior horn attachment.



221

222 **Fig. 3.** Input gait data for the analysis: (a) the components of forces (N) act on the knee joint
 223 in all three degrees of freedom during the stance phase of the walking gait cycle; (b) the
 224 rotation angle (degrees) in the sagittal plane (flexion-extension), frontal plane (valgus-varus
 225 or abduction-adduction) and transverse plane (internal-external) respectively during the
 226 stance phase of walking cycle [28]; (c) the forces as acting on the knee joint during the
 227 running gait (d) the rotation in all three plains of the joint during running gait [46].

228 At the initial simulation stage, the cartilage and meniscus are made to make light contact to
 229 achieve the initial convergence. A displacement-controlled input is applied to the femur to
 230 achieve convergence for attaining the initial contact. Also, the contact between ligament-
 231 ligament and ligament-cartilage is chosen as frictionless. Following the initial conditions,

232 forces and rotations applied during the stance phase of the gait cycle through a cylindrical
 233 joint in the analysis. The tibia is fixed in space for the entire analysis time. The femur is
 234 prescribed the corresponding gait input data in all three linear and rotational directions for a
 235 time frame of 0–1.5s for the walking cycle. Similarly, the corresponding force and rotation
 236 data are applied to the femur for a time frame of 0–1s for the running cycle. The forces
 237 (proximal-distal, anterior-posterior, and medial-lateral) and rotations (flexion-extension,
 238 valgus-varus and internal-external) during the stance phase of the gait cycle for walking and
 239 running applied to the model are given in Figure 3.

240 *2.4 Material models*

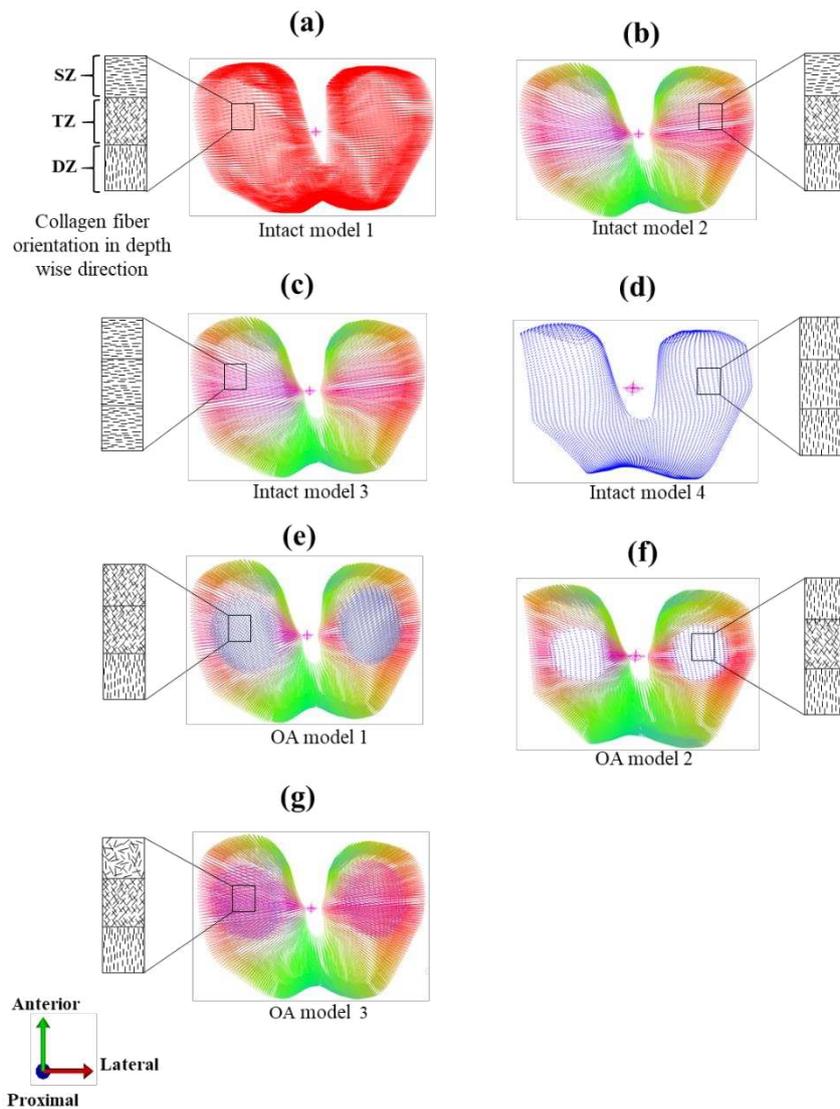
241 The soft tissue is divided into fibrillar (collagen fibers) and non-fibrillar (proteoglycan matrix
 242 and interstitial fluid) components [17]. To simplify the model, the inhomogeneous
 243 compressive modulus of the matrix is neglected [51,52]. A fiber-reinforced porous
 244 hyperelastic (FRPHE) model is used for implementing the biphasic articular cartilage tissue
 245 (femoral and tibial cartilage). The collagen fibers are embedded in the ground matrix since
 246 fibers can only withstand tension and cannot sustain on their own. A fiber with exponential
 247 power-law provided by Eq. (2) is utilised to model the collagen fibers. A neo-Hookean
 248 compressible hyperelastic material model given by Eq. (4) is employed to model the
 249 proteoglycan ground matrix. The strain-dependent permeability nature of tissue is
 250 implemented based on the Holmes-Mow model given by Eq. (5) [53–62].

251 The fiber strain energy density function is given by,

$$252 \quad \psi = \frac{\xi}{\alpha\beta} \left(\exp \left[\alpha (I_n - 1)^\beta \right] - 1 \right) \quad (2)$$

$$253 \quad N = \sin \varphi \cos \theta e_1 + \sin \varphi \sin \theta e_2 + \cos \varphi e_3 \quad (3)$$

254 Where $I_n = \lambda_n^2 = N.C.N$, λ_n = the fiber stretch, N = the fiber orientation represented by θ and
 255 φ [deg] given by Eq. (3), ξ = representing a measure of the fiber modulus [MPa], α =
 256 coefficient of exponential argument, β = power of exponential argument (fiber nonlinearity),
 257 θ, φ = spherical angle for fiber orientation [deg].



258

259 **Fig. 4.** Different femoral cartilage models based on distinct collagen fiber orientation are
 260 represented using the split-line pattern. (a-d) shows the intact cartilage model, and (e-g)
 261 represents osteoarthritic models. The fiber orientation in the depth-wise direction is shown in
 262 the boxes.

263 The proteoglycan matrix strain energy density function (Mooney-Rivlin) is given by:

264
$$\psi = C_1(I_1 - 3) + C_2(I_2 - 3) + \frac{1}{D}(\ln J)^2 \quad (4)$$

265 where C_1, C_2, D are hyperelastic material constants, when $C_2 = 0$ the model reduces to neo-
 266 Hookean constitutive model, I_1, I_2 are the first and second invariants corresponding to the left
 267 Cauchy-Green deformation tensor, J is Jacobian of the deformation given by $\det(F)$, and F
 268 is the deformation gradient. $D = 2/K$ and $C_1 = \mu/2$ where K is the bulk modulus and μ is
 269 the shear modulus. The strain-dependent permeability of soft tissue is described using the
 270 Holmes-Mow constitutive equation given in Eq. (5) and Eq. (6) [59,62,63].

271
$$K_s = k(J)I \quad (5)$$

272
$$k(J) = k_0 \left(\frac{J - \varphi_0}{1 - \varphi_0} \right)^{\alpha_1} e^{\frac{1}{2}M(J^2 - 1)} \quad (6)$$

273 Where $k(J)$ is a strain-dependent component, k_0 is isotropic hydraulic permeability, M is an
 274 exponential strain-dependent co-efficient and α_1 is a power-law exponent. The
 275 inhomogeneity in the solid phase of the tissue is modelled by varying the volume fraction
 276 along the thickness direction. The solid volume fraction φ_0 is given in Eq. (7), where z varies
 277 from 0 to 1 from cartilage surface to subchondral bone [64].

278
$$\varphi_0 = 1 - (.8 - .15z) \quad (7)$$

279 Seven different femoral and tibial cartilage models are created to investigate the influence of
 280 collagen fiber orientation in the superficial zone and depth direction for an intact and arthritic
 281 knee. The femoral cartilage models created are shown in Figure 4. The first four models
 282 represent the intact knee, and the rest three the arthritic knee cases. The collagen fiber

283 orientation is defined using split-line patterns, and the direction of the fibers is controlled
 284 using the model. The split-line patterns are obtained from the literature [21,23,30,65–67].
 285 **Table 1.** Material constants for FRPHE intact and arthritic cartilage models (intact model-1
 286 and OA model-1).

Material Constants	Intact knee			Arthritic knee			Source			
	Deep zone	Middle zone	Superficial zone	Deep zone	Middle zone	Superficial zone				
Collagen fiber: (Fiber exponential power uncoupled)	ξ (MPa)	9.19	4.595	4.595	9.19	4.595	2.297	2.297	4.595	[30,56]
	α	0	0	0	0	0	0	0	0	
	β	2	2	2	2	2	2	2	2	
	Θ (deg)	0	0	0	0	0	0	0	0	
	φ (deg)	0	45	-45	90	0	45	-45	90	
Proteoglycan matrix: (compressible hyperplastic neo-Hookean)	μ (MPa)	1.82	1.82	1.82	0.91	0.91	0.91	0.91	0.91	[55]
	K (MPa)	1860	1860	1860	930	930	930	930	930	
Interstitial fluid: Permeability (Perm-Holmes-Mow)	K_0 (mm ⁴ /Ns)	.00174	.00174	.00174	.00174	.00174	.00174	.00174	.00174	[59,63]
	M	7.1	7.1	7.1	7.1	7.1	7.1	7.1	7.1	
	α	2	2	2	2	2	2	2	2	
Density	ρ_s (tonnes/mm ³)	1×10^{-9}	[52]							
	ρ_r (tonnes/mm ³)	1.5×10^{-9}								
Volume fraction	φ_0	0.2	0.275	0.35	0.2	0.275	0.275	0.35	0.35	

287

- 288 i) In intact model-1, the split lines are aligned in the medial-lateral direction in the
289 femur and tibial cartilage. The split-line representation is shown in Figure 4(a). The
290 model-1 mimics the arcade-like collagen structure.
- 291 ii) In intact model-2, the split lines are aligned in the plane of the articulating surface,
292 and the direction is pointed outward from the centre according to the geometry
293 illustrated in Figure 4(b). Also, the orientation along the depth-wise path mimics an
294 arcade-like structure.
- 295 iii) In intact model-3, the split line pattern is aligned similar to model-2; It is the same for
296 all three zones, as shown in Figure 4(c).
- 297 iv) In the intact model-4, the split-line pattern is aligned along the proximal-distal
298 direction, as shown in Figure 4(d), and it is the same for all zones.

299 The arthritic zone where fibrillation occurs for the osteoarthritic cartilage model is selected.
300 The split-line pattern orientation is assigned to obtain the influence of collagen orientation in
301 the OA knee. Three different OA models are used to investigate the impact of collagen fiber
302 orientation.

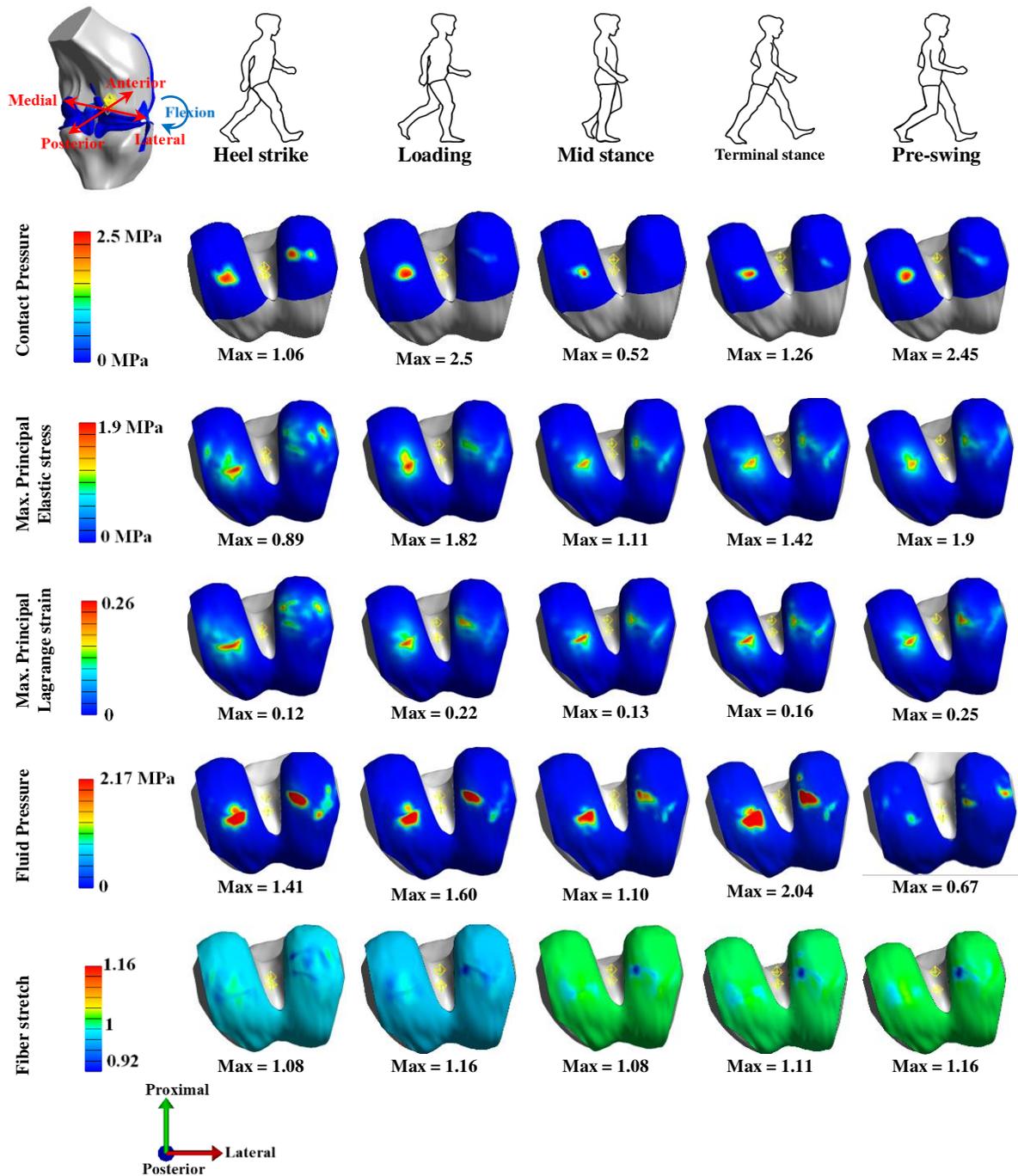
- 303 v) The split-line pattern is aligned such that it is equally inclined to the medial-lateral
304 and proximal-distal axis in OA model-1. Also, the alignment is restricted inside the
305 arthritic zone, as shown in Figure 4(e).
- 306 vi) The split-line pattern is aligned in the proximal-distal direction, as shown in Figure
307 4(f) in OA model-2.
- 308 vii) The OA model-3 represents the random split-line orientation of collagen fibers, as
309 shown in Figure 4(g).

310 The properties of the FRPHE cartilage material are implemented into the model according to
311 Table1. Even though some of the proteoglycan matrix parameters are chosen as constant
312 throughout the depth of the tissue, the depth-dependent heterogeneity is applied based on the

313 matrix's strain-dependent permeability characteristics, which are represented using Equations
314 4-6. Also, the depth-dependent attributes of the solid material (proteoglycan matrix) and fluid
315 (interstitial fluid), such as density, are chosen as the same throughout the depth to simplify
316 the model. The collagen fibers are assumed to be oriented perpendicular or inclined to the
317 articular surface of the cartilage for severe OA conditions compared with the intact case. This
318 orientation affects the tissue response, and it is believed that these multiple-oriented collagen
319 models may predict the actual tissue response due to the change in direction. These fiber
320 orientation changes are named fibrillation, reported in the literature [23,68].

321 The menisci, collateral, and cruciate ligaments are modelled as transversely isotropic
322 poroelastic, and the constants are chosen from the literature [69–72]. Another limitation of
323 this study is that even though the meniscus and ligaments are made of fiber-reinforced
324 poroviscoelastic material, they were represented using transversely isotropic poroelastic
325 material. However, this simplification of the model aids in resolving the analysis's
326 convergence problem when impact-loading scenarios like running and walking are present. In
327 the current investigation, the transversely isotropic viscous menisci tissue and fiber-
328 reinforced viscous cartilage interchange fluid may impact the cartilage's interstitial fluid
329 pressure. This change in interstitial fluid pressure can affect the cartilage's stress, strain, and
330 contact pressure distribution due to the dissipated mechanical energy during the cyclic
331 compression on the meniscus. Meanwhile, the alteration brought on by the results from other
332 tissue types is disregarded, which is another limitation of the work. The present study focuses
333 on the mechanical response of fiber-reinforced cartilage tissue rather than other tissues.
334 Additionally, the literature implies that transversely isotropic material can be an alternative to
335 fiber-reinforced material in predicting tissue responses [72–74].

336 **3. Results**

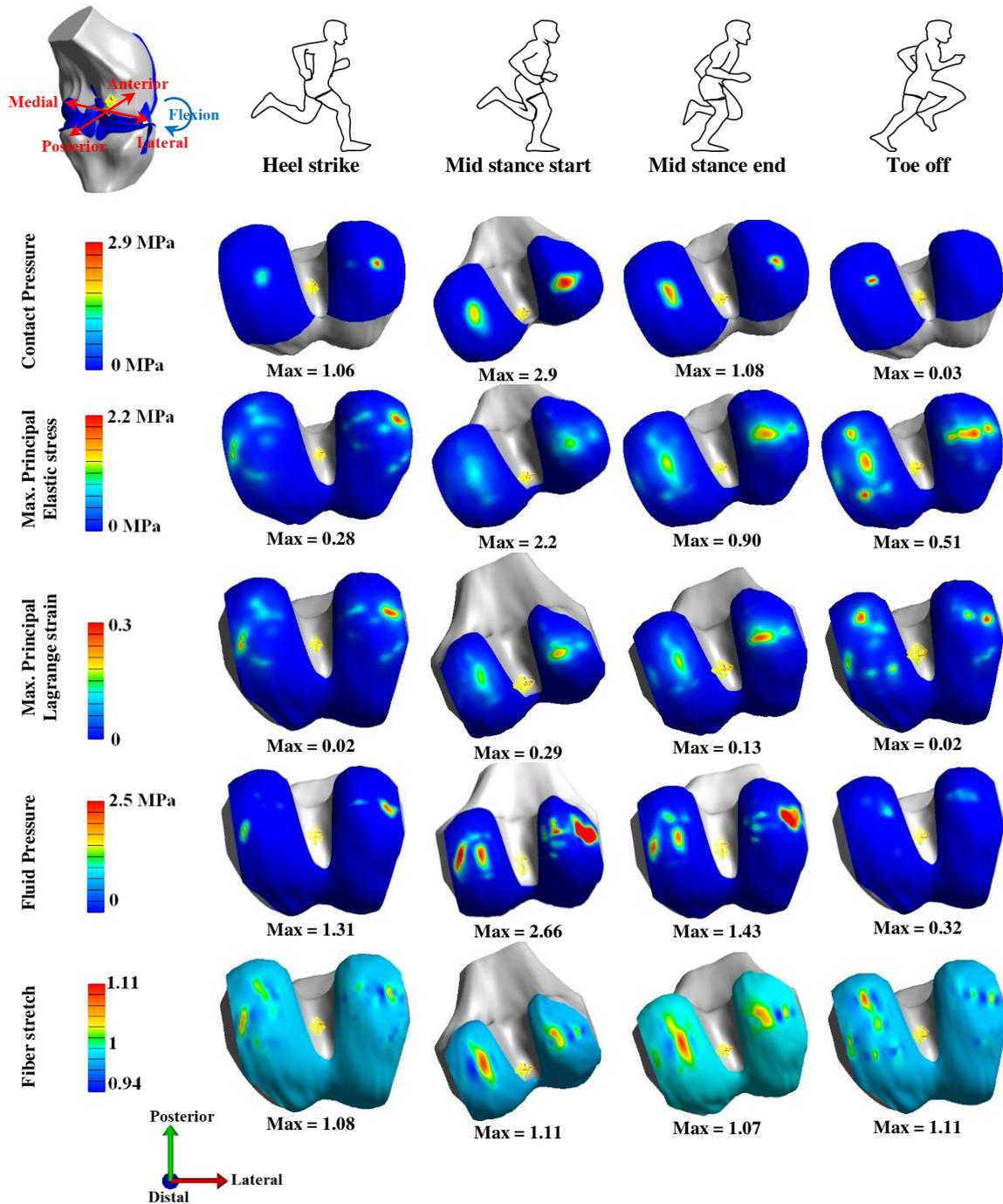


337
 338 **Fig. 5.** Contours of mechanical responses of femoral cartilage on the surface of intact model-
 339 1 during the stance phase of walking (60% gait cycle).

340 Figure 5 shows the contours of different mechanical responses of the femoral articular
 341 cartilage during the stance phase of the walking gait cycle. It displays the variation in various
 342 mechanical responses, such as contact pressure, principal elastic stress, Lagrange strain, fluid

343 pressure, and fiber stretch of the biphasic cartilage. Throughout the cycle, it is seen that the
344 contact pressure generated on the articulating surface varies, and maximum contact pressure
345 of 2.5 MPa is observed at the end of the heel strike on the lateral side. According to published
346 research, osteoarthritis is most prone to develop on the articulating surface where the
347 maximum contact pressure is generated [75].

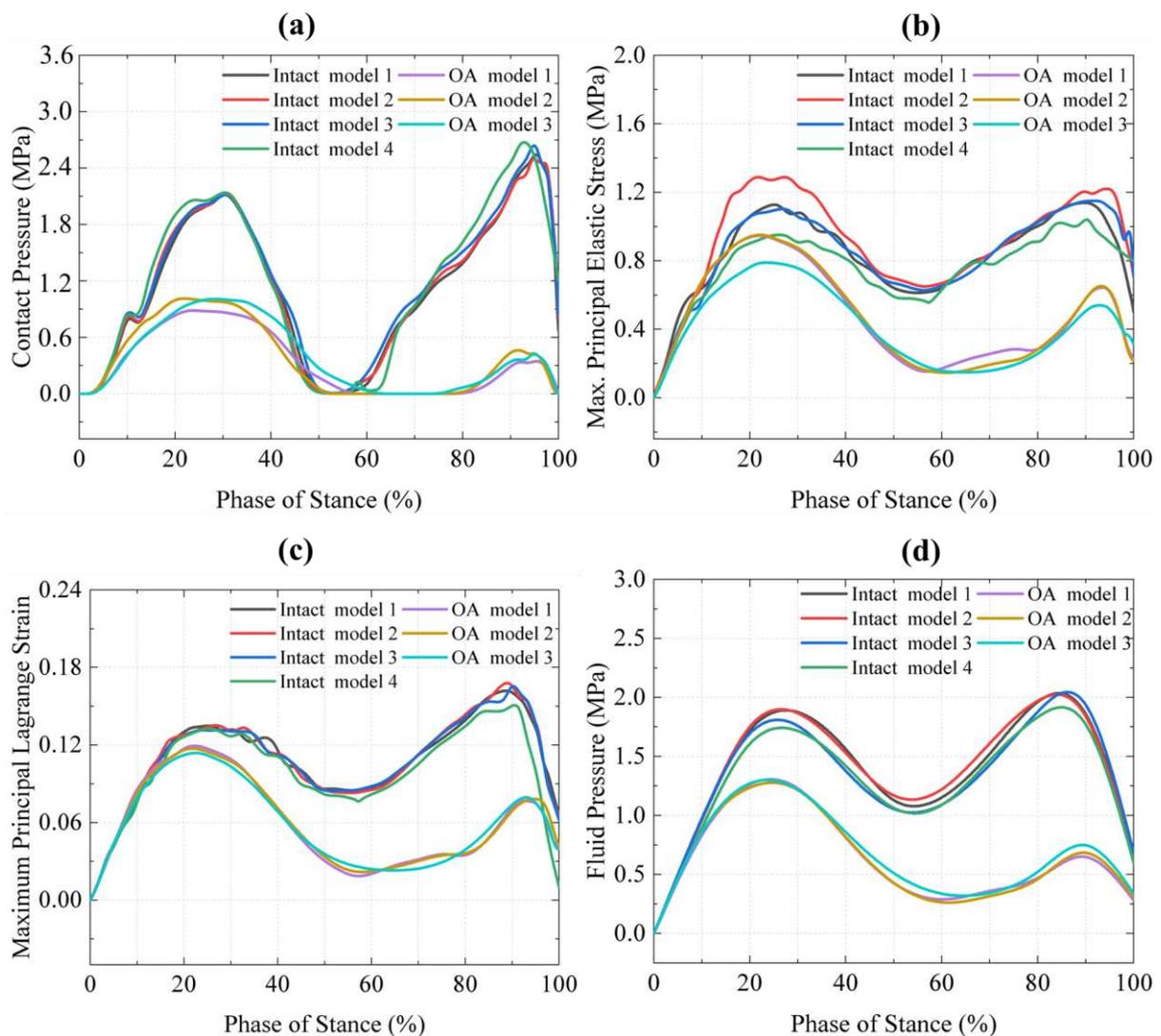
348 Figure 6 depicts the contours of various mechanical responses throughout the running gait
349 cycle. However, this also shows a similar trend in the contact pressure, as the maximum value
350 of 2.9 MPa is observed at the end of the heel strike. The maximum contact pressure on the
351 articulating surface of the cartilage during walking and running cases is 2.5 MPa and 2.9
352 MPa. On the walking cycle, the maximum values are at 30% and 90% of the stance phase,
353 whereas on the running cycle, the maximum value is obtained at 40%. Figures 1(a) and 1(b)
354 shows the loading and the terminal stance of the gait cycle are the stances where the highest
355 percentage of body weight acts on the knee joint during walking. In a gait cycle, these stances
356 are situated at roughly the 30% and 90% positions of the stance phase. Thus, there is a chance
357 that the area will experience the maximum mechanical responses. Similarly, during a running
358 cycle, the maximum body weight that can bear on the knee joint is at mid-stance during the
359 stance phase. Also, the trend of tissue responses for both cases is entirely different during the
360 gait. The mismatch in trends between mechanical responses between loading and terminal
361 stances may be due to the percentage of body weight acting on the knee joint during the
362 respective stances. Also, the mismatch in the mechanical responses between walking and
363 running gait may be due to the variation in the magnitude of body weight acting on the knee
364 joint for walking and running. The maximum elastic stress and Lagrange strains are
365 concentrated in the lateral-medial epicondyle area of the femoral cartilage during walking
366 gait; however, during the running gait, these maximum values are observed in the posterior
367 side of the knee cartilage.



368
 369 **Fig. 6.** Contours of mechanical responses of femoral cartilage on the surface of intact model-
 370 1 during the stance phase of running (40% gait cycle).

371 Further, maximum principal stress of 1.82 MPa is produced throughout the walking cycle,
 372 which is more than the fluid pressure of 1.60 MPa that is produced during the loading stance
 373 (first peak in the loading curve). However, the principal stress produced at the terminal
 374 stance, 1.42 MPa, is less than the fluid pressure, 2.04 MPa (second peak in the loading

375 curve). A fluid pressure of 2.66 MPa is produced during the running cycle at the mid-stance
 376 start (the maximum peak in the loading curve), which is more than the maximum primary
 377 stress of 2.20 MPa produced. The medial side of the femoral cartilage experiences the
 378 maximum stresses and strains during the whole stance period of the walking gait. In contrast,
 379 the lateral compartment of the cartilage has the maximum responses during the running gait.
 380 The collagen fiber stretch also changes during the stance phase, with most variation seen in
 381 the running rather than walking cycle.



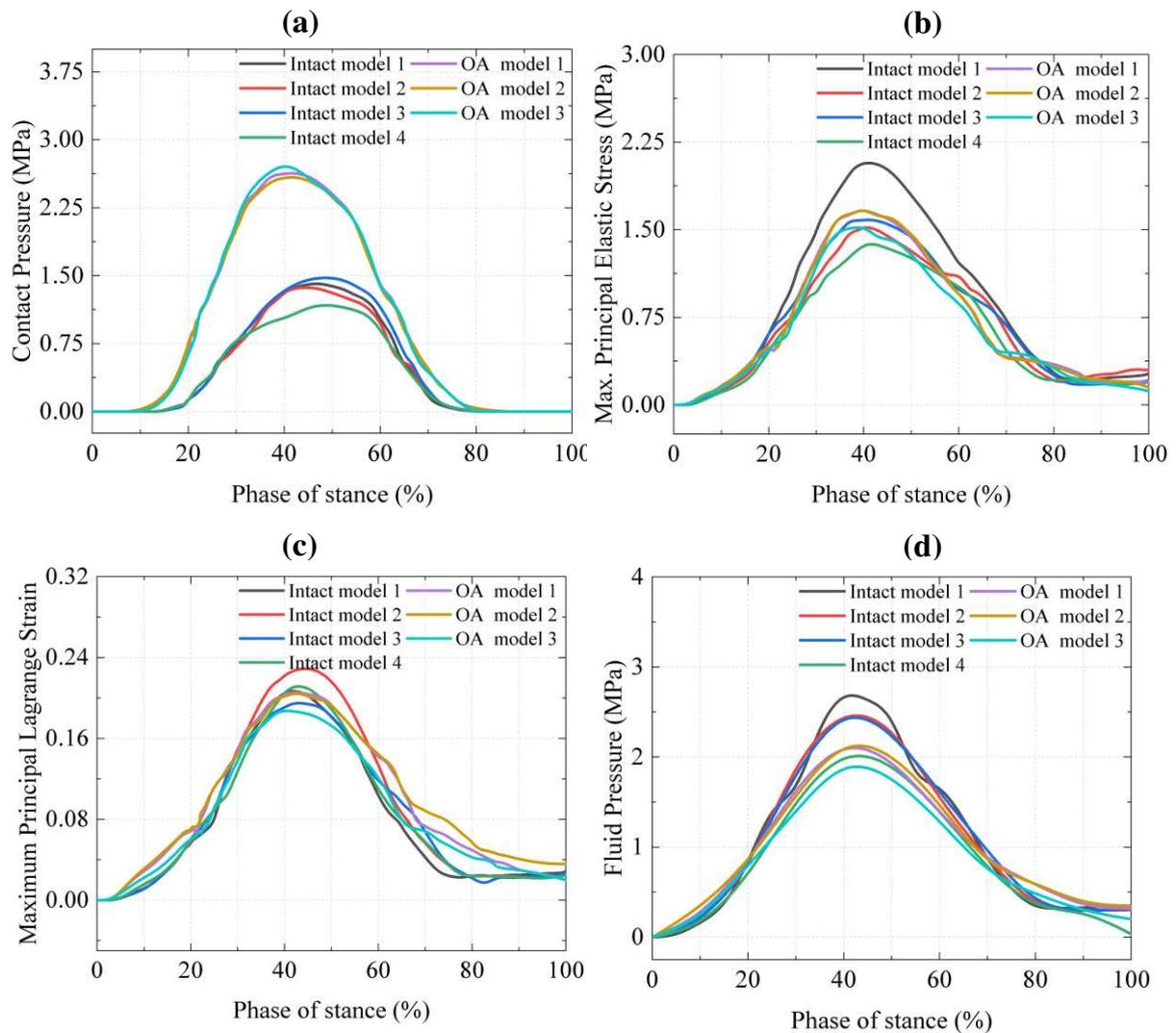
382
 383 **Fig. 7.** The comparison of mechanical characteristics of cartilage for different models during
 384 the stance phase of walking gait: (a) the contact pressure generated on the articulating

385 surface; (b) maximum principal elastic stress produced on the articular zone; (c) maximum
386 principal Lagrange strain; (d) maximum fluid pressure generated in the biphasic cartilage.

387 Figure 7 shows the variation in mechanical responses for different collagen fiber-oriented
388 models during the stance phase of the gait cycle. All intact and arthritic models show similar
389 trends in contact pressure, maximum principal elastic stress, maximum principal Lagrange
390 strain, and fluid pressure. The maximum contact pressure generated on OA cartilage is higher
391 than the intact cartilage model during the running cycle. However, the intact model observes
392 elevated contact pressure during the walking cycle. The study indicates that running degrades
393 cartilage morphology as peak contact stresses rise. Also, it is well known that OA can cause
394 the cartilage's surface layer to deteriorate. Hence, the contact pressure produced by the OA
395 model, where collagen fibers orientated normally to the articulating surface at the cartilage-
396 cartilage interface, can be greater than in the intact model, where collagen fibers are parallel
397 to the articulating surface at the cartilage-cartilage interface.

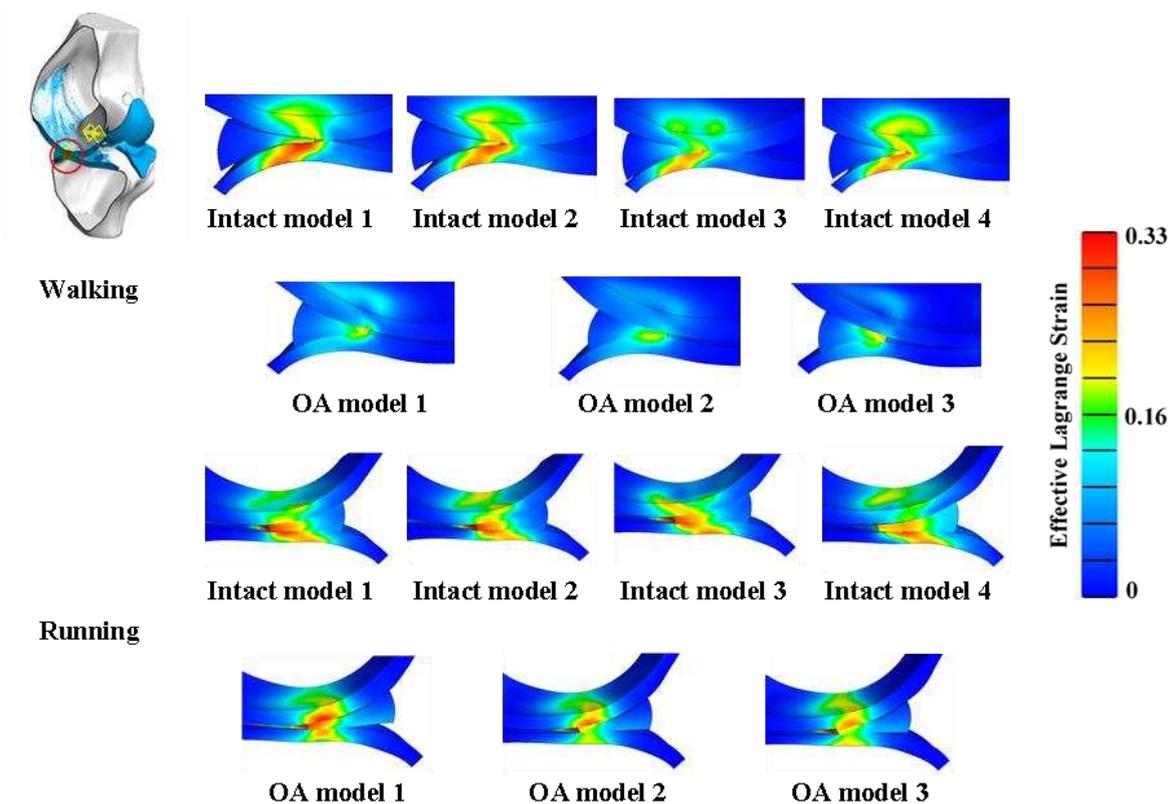
398 The intact model aligned with the proximal-distal direction has a higher contact pressure than
399 the other models shown in Figure 7(a). Also, there is a 200% difference in the contact
400 pressure for intact and OA models, and contact pressure reaches zero during the mid-stance
401 (40-60% of the stance phase) for both models. In the walking gait, two contact pressure peaks
402 are observed (during the 30% and 90% stance phases, respectively). During the first peak,
403 contact pressure for intact models is two times higher than for OA models, and during the
404 second peak, it is five times higher. Figure 7(b) shows higher principal stress for the intact
405 parallel split-line model and lower principal stress for the random split-line oriented OA
406 model during walking gait. According to previous experimental research, Green-Lagrange
407 strain is a crucial indication of cell damage compared to other results such as contact
408 pressure, principal stress, and fluid pressure [76,77]. Figure 7(c) shows that the maximum
409 principal Lagrange strain has higher values for intact models than OA models. One can

410 observe that the difference in strain between these two sets of models significantly increases
 411 from 20% to 90% of the phase of stance. Figure 7(d) shows maximal interstitial fluid pressure
 412 in soft tissue. As expected, intact models give rise to higher fluid pressure than OA models.
 413 Among intact models, models 1 and 2 (parallel-oriented collagen fiber models) show elevated
 414 responses.



415
 416 **Fig. 8.** The comparison of mechanical characteristics of cartilage for different models during
 417 the stance phase of running gait: (a) the contact pressure generated on the articulating surface;
 418 (b) maximum principal elastic stress produced on the articular zone; (c) maximum principal
 419 Lagrange strain; (d) maximum fluid pressure generated in the biphasic cartilage.

420 Figure 8 illustrates the mechanical responses of various models throughout the running gait.
 421 Even though the mechanical responses for both the walking and running cycles are
 422 comparable to the gait input data, it is interesting to note that the contact pressure created
 423 during the running cycle is more significant for the OA model than the intact model (Figure
 424 8(a)). Also, the maximum contact pressure generated is higher for the randomly oriented OA
 425 model (OA model 3) and the minimum for the perpendicularly oriented intact model (Intact
 426 model 4). Further, it can be observed that the contact pressure for walking gait (Figure 7(a))
 427 is strikingly high for intact models than for OA models, which is not the case for running
 428 gait.



429 **Fig. 9.** The effective Lagrange strain in the sagittal plane sectional view of the articulating
 430 region (femur cartilage-meniscus-tibial cartilage interface) of the knee joint at the maximum
 431 loading position during the stance phase of walking and running gait.
 432

433 Figure 8(b) shows elastic stress distribution, where the parallel split-line model (Intact model
 434 1) exhibits the highest elastic stress, whereas the proximal-distal aligned model exhibits

435 lower elastic stress. The Lagrange strain is plotted in Figure 8(c). One can observe that the
436 strain distribution trend is almost similar for all the simulated cases. This response differs
437 greatly from the walking gait scenario (Figure 7(c)). Like the Lagrange strain, interstitial
438 fluid pressure in Figure 8(d) also shows a similar trend. However, a closer observation
439 indicates an increase of $\sim 40\%$ in fluid pressure in the case of intact models with parallel-
440 oriented intact models experiencing higher fluid pressure than perpendicular or inclined ones.
441 Figure 9 shows the effective Lagrange strain in the femoral-tibial cartilage and meniscus
442 contact region for walking and running cases. During the walking cycle, the tibial cartilage
443 exhibits a higher strain in the case of intact models, while only the meniscus has a higher
444 strain in OA models. Conversely, during the running cycle, the meniscus shows a higher
445 strain in the case of intact models, and the femoral cartilage exhibits a higher strain in the case
446 of OA models. In addition, it can be observed that the inclined intact model-3 shows lower
447 tibial cartilage strain than the parallel-oriented models during the walking case and during the
448 running cycle, the perpendicularly oriented intact model-4 exhibits lower tibial cartilage
449 strain. Further, during the running cycle, the maximum strain is detected in the tibial
450 cartilage-meniscus interface for intact models, whereas the maximum strain is observed in the
451 femoral cartilage-meniscus interface for OA models.

452 **4. Discussion**

453 A subject-specific knee geometry with six degrees of knee kinetics and kinematics data
454 concerning walking and running gait is utilised for the present knee investigation. An FRPHE
455 cartilage model with control on collagen fiber orientation and osteoarthritic characteristics are
456 used for the analysis. Also, different fiber-oriented cartilage models are created for intact and
457 osteoarthritic cases. The model determines contact pressure in the articulating area, principal
458 stress, Lagrange strain, interstitial fluid pressure, and cartilage fiber stretch, all of which are
459 essential factors in the evaluation of cartilage degradation [13,73,78–80]. The findings imply

460 that the collagen fibril orientations, as revealed by split lines, play a significant role in
461 regulating cartilage strains and stresses.

462 The experimental investigation by [81] predicted larger contact pressures during the heel
463 strike on the medial compartment compared to those on the lateral compartment, which is
464 consistent with our model. Our model yielded contact pressures of 2 and 3 MPa at the lateral
465 and medial compartments, respectively, at 50% of the stance phase (1500 N). These values
466 are also in the same range as those found in past computational studies (1-5 MPa with loads
467 between 1000 and 1800 N) [75,82–87].

468 In the gait input data for knee kinetics and kinematics, forces and rotations corresponding to
469 particular activities are applied to the FE knee model [88–92]. One limitation of the approach
470 is that it uses a small displacement and rotation in the initial step to bring the model into
471 contact with the cartilages and meniscus to achieve initial convergence. Moment-driven and
472 rotation-driven are the two methods used to input flexion-extension, valgus-varus, and
473 internal-external rotations to the knee model [93,94]. However, the present study uses a
474 rotation-driven method to implement knee rotations, as shown in Figures 3(b) and 3(d). Also,
475 it is unclear whether the FE model should be driven by a moment or a rotation because both
476 methods predict identical measures in the literature [75].

477 The peak mechanical response magnitudes of the intact models are substantially more
478 extensive than the OA model during walking gait, as shown in Figure 7; while running, peak
479 magnitudes are observed for OA cases. Regarding the contact pressure produced, OA models
480 have higher values than the intact model during running. The research shows that running
481 worsens cartilage structure as the peak contact stresses increase. Additionally, it's generally
482 understood that OA can worsen the cartilage's outer layer. As a result, the contact pressure
483 created by the OA model, in which collagen fibers are typically oriented to the articulating
484 surface at the cartilage-cartilage interface, may be greater than in the intact model. Studies

485 have revealed a strong correlation between the development and initiation of OA over a long
486 period, and contact pressure rises on articular cartilage [95,96].

487 Our findings of cartilage mechanics while walking and running align with overall trends from
488 earlier computational studies and indirect experimental assessments [97]. The maximum
489 Lagrange strain that we anticipate will occur during the first peak tibiofemoral load during
490 walking (0.22) agrees with the 20% strain measured in the literature [98]. The magnitudes of
491 our anticipated strains also closely matched those in [99], where the authors used a
492 continuum-based finite element model of the knee to apply joint loads estimated from inverse
493 dynamics at four instances of the gait cycle. Our findings concur with earlier simulation
494 studies, suggesting that loads and collagen fiber orientation likely go together. According to
495 these findings, stress increases when collagen fibers are randomly oriented, and superficial
496 cartilage strain decreases along the split line directions parallel to the articular surface during
497 the walking cycle [100,101]. This conclusion is supported by experimental data showing that
498 cartilage's tensile strength is highest when evaluating the split liner pattern perpendicular to
499 the collagen fiber direction [102,103].

500 However, during the running gait, the highest value for Lagrange strain is generated in the
501 intact model-2 with split-line patterns parallel to the articulating surface, as shown in Figure
502 8(c), and it indicated the higher risk of OA, as excessive strain contributes to OA [21,28,104].
503 The maximum fiber stretch is obtained in the deep zone during running gait, whereas a lesser
504 fiber stretch is received in the superficial layer, as illustrated in Figure 5. It may be caused by
505 impact loading in the joint during running; however, the maximum fiber stretch in the
506 superficial zone during walking can be seen in Figure 4. Hence, the fiber stretch values help
507 to predict the gait data [105]. The maximum elastic stresses during walking and running cycle
508 are obtained for models with split-line patterns parallel to the articulating surface for intact
509 models, as shown in Figures 7(b) and 8(b). The study demonstrates that the direction of the

510 cartilage's collagen fibres affects the maximum stress generated and, therefore, is associated
511 with osteoarthritis.

512 **5. Conclusions**

513 The study presents a novel method to control collagen fiber orientation for FRPHE cartilage
514 models for knee joint analysis. This study suggests that during the walking cycle, the
515 maximum contact pressure is observed to be greater in intact models than in OA models;
516 however, during running, the maximum value is more remarkable in OA models than in
517 intact models. Also, the maximum stresses and fluid pressure are obtained for parallel-
518 oriented models than proximal-distal oriented models for both walking and running gait.
519 However, the maximum principal Lagrange strain predicts a similar trend for both intact and
520 OA models throughout the running stance phase; the parallel-oriented models exhibit a higher
521 value than perpendicular and inclined ones. These results will aid researchers in developing
522 improved assistive devices for arthritis patients who engage in subject-specific activities such
523 as walking and running.

524 **Conflicts of Interest**

525 The authors declare that they have no known competing financial interests or personal
526 relationships that could have appeared to influence the work reported in this paper.

527 **Funding**

528 DST-INSPIRE Faculty Award (File No.: DST/INSPIRE/04/2016/000735), Govt. of India

529 **Ethical Approval**

530 Not required

531 **Acknowledgements**

532 The authors gratefully acknowledge the financial support of the DST-INSPIRE Faculty
533 Award, Govt. of India, in executing the computational part of this work.

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