

1 **Simulated tibiofemoral joint reaction**
2 **forces for three previously studied gait**
3 **modifications in healthy controls**

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53 **ABSTRACT**

54 *Gait modifications, such as lateral trunk lean (LTL), medial knee thrust (MKT) and toe-in gait (TIG), are*
55 *frequently investigated interventions used to slow the progression of knee osteoarthritis. The Lerner knee*
56 *model was developed to estimate the tibiofemoral joint reaction forces (JRF) in the medial and lateral*
57 *compartments during gait. These models may be useful for estimating the effects on the JRF in the knee as*
58 *a result of gait modifications. We hypothesized that all gait modifications would decrease the JRF*
59 *compared to normal gait. Twenty healthy individuals volunteered for this study (26.7 ± 4.7 years, $1.75 \pm$*
60 *0.1 m, 73.4 ± 12.4 kg). Ten trials were collected for normal gait as well as for the three gait modifications:*
61 *LTL, MKT, and TIG. The data was used to estimate the JRF in the first and second peaks for the medial and*
62 *lateral compartments of the knee via OpenSim using the Lerner knee model. No significant difference from*
63 *baseline was found for the first peak in the medial compartment. There was a decrease in JRF in the*
64 *medial compartment during the loading phase of gait for TIG (6.6%) and LTL (4.9%) and an increasing JRF*
65 *for MKT (2.6%) but none were statistically significant. A significant increase from baseline was found for*
66 *TIG (5.8%) in the medial second peak. We found a large variation in individual responses to gait*
67 *interventions which may help explain the lack of statistically significant results. Possible factors influencing*
68 *these wide range of responses to gait modifications include static alignment and the impacts of variation*
69 *in muscle coordination strategies used, by participants, to implement gait modifications.*

70 **Keywords:** *Gait modification, knee osteoarthritis, joint reaction forces, OpenSim*

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71 **INTRODUCTION**

72 Osteoarthritis (OA) of the knee is a major cause of disability and affects more
73 than 19% of the adult population over the age of 45 in the United States [1, 2]. Excessive
74 joint reaction forces (JRF) have been implicated in the development and progression of
75 knee OA [3, 4]. Gait modifications are a promising non-invasive intervention used to
76 reduce JRFs in the knee as evidence suggests that they may slow the progression of the
77 disease [5-7]. A number of gait modifications have been identified that may help reduce
78 the JRF in the medial compartment of the knee. Three common modifications
79 investigated include lateral trunk lean (LTL) [6-14], medial knee thrust (MKT) [7-9, 11,
80 15-19], and toe-in gait (TIG) [7-9, 11, 17, 20]. A systematic review of gait interventions
81 [7] found that when paired with real-time biofeedback (RTB), the three interventions
82 chosen for this study show the greatest potential to reduce the knee adduction moment
83 (KAM) in patients with knee OA. Real-time biofeedback can help improve the adoption
84 of gait interventions and allow for the magnitude of modifications to be tailored to
85 subject specific responses.

86 Many studies investigating gait modifications rely on surrogate measures, such
87 as KAM and the knee flexion moment (KFM), to assess knee loads [17, 21-29]. In studies
88 investigating knee OA it has been demonstrated that there is an association between
89 KAM is and disease progression [30-33] while the contribution of KFM is less clear. One
90 study found that both KAM and KFM equally contributed to estimates of total knee joint
91 moments but that as the disease progressed KAM influenced increased while KFM
92 influence decreased [30]. While some studies have found a connection between KFM

93 and knee OA, especially in the first peak [20, 32], others have failed to show a strong
94 connection [31, 34].

95 The LTL modification has been shown to reduce KAM when the trunk angle is
96 modified by a sufficient amount [6, 9, 35, 36] but it has also been reported that the
97 modification may lead to discomfort in the spine and ipsilateral knee and hip joints [6].
98 The MKT modification with real-time visual feedback has also been shown to reduce
99 KAM in healthy subjects [9, 15, 36, 37]. A subject specific simulation study on a patient
100 with grade 2 medial knee OA suggested that MKT could reduce both the first and second
101 knee adduction torque peaks [16]. After gait retraining the patient was able to closely
102 reproduce the knee adduction torque reductions, calculated by the simulation study,
103 while walking in a laboratory setting [16]. The TIG modification using RTB has been
104 shown to also reduce peak KAM in some studies [17, 35], however, other research has
105 not demonstrated a significant decrease in KAM when using TIG with visual RTB [9, 38].
106 A study in healthy controls using TIG without RTB showed a statistically significant
107 reduction in first peak KAM but found no reduction in JRF as estimated by a
108 musculoskeletal model [39]. While some studies have found that KAM may provide a
109 reasonable indicator for the JRF at the first peak of stance, the relationship between
110 KAM and the joint contact force is not as strong for the second peak of stance [20, 34].
111 Additionally, research in children and adolescent's has indicated that KAM may not be a
112 good predictor of knee joint contact force independent of leg alignment [40].

113 With the advancement in computing power computational models are becoming
114 a common approach to directly estimate JRFs in the knee during gait [41-48]. While it is

115 impractical to measure JRFs in-vivo [49], computational models are capable of
116 estimating internal forces during functional movements (i.e. walking, running, crouch
117 gait) [45, 46, 50-54]. OpenSim is an open-source software application for modeling,
118 simulating, and analyzing movement [47]. It provides a flexible and robust tool that can
119 be used by researchers to simulate how altered movement patterns can affect internal
120 joint loading [41-47, 55-64]. Lerner et al. (2015) developed an OpenSim model (Lerner
121 model) that allows for the direct estimation of the medial and lateral JRF in the knee.

122 Previous research has identified muscle forces as a major determinant of
123 simulated compressive tibiofemoral contact forces thus variations in muscle activity
124 greatly influence the accuracy of knee JRF predictions [50, 65]. The weighted static
125 optimization objective function minimizes the sum of squared muscle activations while
126 incorporating individual muscle weighting values as described in detail in previous
127 research [52]. A common finding in past studies was that a weighted static optimization
128 approach provides improved results over the default OpenSim static optimization (SO)
129 [44, 45, 52, 66] by allowing researchers to reduce the force output in muscles that are
130 causing increased error in JRF estimates. Many of these studies use in vivo data from
131 instrumented knee implants to determine the weights for the objective function by
132 minimizing the difference between the experimental and in vivo data [44, 45]. This is an
133 infeasible approach to take when trying to estimate the effects of gait interventions in
134 healthy or pathological subjects where no in vivo data is available. In order to
135 implement the Lerner model an alternative approach to using in vivo data is needed for
136 determining appropriate weights for muscles that exhibit larger than expected

137 activations and forces as calculated by *SO*. Ensuring a proper weight for the model is
138 important to reduce the overestimation of JRF in the model.

139 The purpose of this study was to examine the effect of three commonly studied
140 gait interventions using RTB on the simulated JRF in a cohort of healthy participants. We
141 hypothesized that all three interventions would reduce the first peak joint reaction force
142 compared to baseline values. A second purpose of the study was to evaluate a visual
143 inspection method for identifying muscles and weights for the weighted *SO* approach.

144 **METHODS**

145 **Participants**

146 Twenty healthy individuals were recruited from the university community to
147 participate in the study. Their dominant limb was determined by identifying their
148 preferred leg in a kicking task [67]. Eligibility criteria included no reported knee, hip, or
149 back pain that required treatment within the prior six months and no previous lower
150 limb or back surgery. Exclusion criteria included any cognitive impairment that would
151 impact motor learning and existing neurological or musculoskeletal impairments that
152 would affect gait. All participants provided written informed consent prior to
153 participation and the study was approved by the George Mason University Institution
154 Review Board. Participant demographics are presented in Table 1.

155 **Instrumentation**

156 Prior to data collection, retroreflective markers were attached to the lower
157 extremities and trunk (53 markers) as shown below in Fig. 1. One cluster was located on
158 the lower back and four clusters were placed bilaterally on the thigh and shank

159 segments. Twelve tracking markers were placed on various anatomical locations and ten
160 markers were placed on the feet. Ten calibration markers were used for static and
161 dynamic calibration trials. For the static calibration trial participants stood motionless on
162 a single force plate with their feet parallel to the anterior–posterior axis of the
163 laboratory. Visual3D software (C-Motion, Germantown MD, USA) used data from the
164 static trial to generate a kinematic model for each participant which included the trunk,
165 pelvis, thigh, shank, and foot segments. For the dynamic calibration trial participants
166 complete three clockwise rotations of the pelvis [68]. The data from the dynamic
167 calibration was used to estimate hip joint center for the model. Calibration markers
168 were removed before data collection. During data collection marker trajectories were
169 tracked using eight high-speed motion analysis cameras (Vicon, Oxford, England)
170 sampling at 200 Hz. Ground reaction force (GRF) was collected using four floor
171 embedded force plates sampling at 1000 Hz (Bertec, Columbus, OH). The force plates
172 were aligned in a single 2.4 m long row.

173 **Data Collection**

174 *Baseline trials*

175 Participants walked at a self-selected speed along a 6-meter laboratory walkway.
176 Timing gates (Brower Timing Systems, Draper, UT, USA) were positioned at the start and
177 end of four in-line force plates (2.4 meters long) and were used to measure the average
178 walking speed per trial. For a trial to be valid, one full contact with a force plate by the
179 dominant limb was required. Participants completed 10 valid baseline trials.

180 *Gait modification trials*

181 Gait modification parameters were individualized for each participant using their
182 mean and standard deviation (*sd*) from baseline trials. Ranges for each gait modification
183 were created so that gait parameters fell within a range of 1–3 *sd* greater (TIG and LTL)
184 or lesser (MKT) than baseline for the first five trials and 3–5 *sd* greater or lesser than
185 baseline for the second five trials. The 1–3 *sd* range was considered a small modification
186 while the 3–5 *sd* range was considered a large modification. In total six target ranges
187 were calculated for each participant: small and large LTL, small and large MKT, and small
188 and large TIG.

189 Standardized verbal instructions, as described in previous research [69], were
190 provided before implementing each modification. Participants were allowed to
191 complete as many practice trials as desired to become comfortable with each
192 modification and additional verbal feedback was provided during practice trials as
193 needed. Gait modification trials were completed in a fixed order: LTL, MKT, and TIG.
194 Successful trials required at least one clean foot strike on the force plate, with the
195 dominant limb, and an average gait speed $\pm 5\%$ relative to baseline average speed.
196 Unsuccessful trials were not counted towards the 10 required for each modification.

197 For each of the 3 gait modification strategies studied, participants performed ten
198 trials using RTB. The visual feedback was delivered using Visual3D via a line graph
199 projected on a wall in front of the lab walkway as shown in Fig. 2. The graph indicated
200 the angle of the current gait modification parameter during the stance phase of gait and
201 was updated during each step of the dominant limb. A range representing the lower and
202 upper limits of the gait modification parameter (1–3 or 3–5 *sd*) was displayed on the

203 graph (i.e. the green band in Fig. 2). Participants modified their gait according to
204 provided cues so that the line representing the gait parameter fell within the calculated
205 range. If during a trial a participant fell outside the provided range, they were instructed
206 to adjust their gait on the subsequent trial.

207 *Musculoskeletal Simulation of Walking*

208 Recorded data were first imported to Visual3D (C-Motion, Germantown MD,
209 USA) for pre-processing as described in previous research [9]. OpenSim compatible
210 format files were then exported from Visual3D. Prior to export, Visual3D runs inverse
211 kinematics on the data and provides kinematic and kinetic .mot files for each trial. The
212 exported files were used to create three dimensional simulations for the stance phase of
213 gait using OpenSim 3.2. To simulate the muscle forces required to reproduce the
214 measured kinematics and kinetics *SO* was run on the data using OpenSim 3.2. Prior to
215 *SO*, the gait2392 model was scaled to each subject's height and weight. In addition to
216 the default *SO* cost function for minimizing the sum of the muscle activations squared
217 [47] each trial was also iteratively run through a weighted *SO* function based on
218 previously described methods [44, 45, 52]. OpenSim 3.2 was used for this process
219 because the weighted *SO* plug-in was built to be compatible with this version of the
220 software and has not yet been updated to work with the latest version of OpenSim [70].

221 In order to identify muscles and corresponding weights the results of *SO* were
222 visually inspected to identify any muscles identified in previous research that
223 contributed to increase knee load estimates (e.g. quadriceps's, hamstrings, calves) and
224 that had a force that was 2 to 3 times greater than estimated forces from other lower

225 extremity muscle groups. A weight of 2 was initially applied to that muscle group and a
226 weighted *SO* was re-run and the results visually inspected to determine the effect of the
227 weight on the muscle force outputs. The weight was increased until the weighted *SO*
228 output for the identified muscle fell within a comparable range to the other lower
229 extremity muscles.

230 If there were multiple muscles with extreme force estimates, then muscles were
231 weighted and evaluated in a set order for all gait intervention trials. The order was to
232 apply a weight to the gastrocnemius (GAS) muscles followed by weights applied to the
233 GAS and the vastus lateralis (GAS-VL) muscle, then to the GAS, VL, and vastus
234 intermedius/vastus medialis (GAS-VI-VL-VM) muscles, and finally to the GAS, VL, VI, VM,
235 and the rectus femoris (GAS-VI-VL-VM-RF) muscles. The muscle weight values started at
236 two and were systematically adjusted until the muscle force output values from the
237 weighted *SO* did not show any large spikes in the *SO* output.

238 After the default *SO* and the weighted *SO* was completed, the knee JRFs for the
239 medial and lateral compartment were computed using the OpenSim JointReaction
240 analyses on the scaled Lerner model using OpenSim 3.3 which is capable of resolving the
241 JRFs in the knee into medial and lateral components [44].

242 **Statistical Analysis**

243 Descriptive statistics were reported while a within-group repeated measures
244 analysis of variance (RM ANOVA) was used to compare JRF of participants' dominant
245 limb across the four different gait conditions. A RM ANOVA was used with both the
246 medial and lateral JRF for the first and second peaks during the stance phase of gait.

247 Prior to running the RM ANOVA, data was checked for outliers and normality. Next,
248 Mauchly's test of sphericity was assessed. If the data failed the assumption of sphericity,
249 a Greenhouse-Geisser correction was used. If results were significant for the RM ANOVA
250 pairwise comparisons were calculated. Statistical analyses were performed using the
251 ggstatsplot [71] package in R version 4.1.0 (R Foundation, Vienna, Austria,
252 <https://www.R-project.org>) with an alpha level set at 0.05 *a priori*.

253 **RESULTS**

254 Mean JRF by gait conditions for the first and second peaks in both the medial
255 and lateral knee compartment are shown below in Table 2. Post hoc analysis of the data
256 indicated that the averages for JRF in both the small and large conditions did not differ
257 significantly from each other, therefore, the results were combined into a single average
258 across the three interventions for statistical analysis. Therefore, the statistical analysis
259 consisted of 10 trials each for the baseline, LTL, MKT, and TIG.. Previous analysis
260 indicated that subjects had a difficult time getting the modification to accurately fall
261 within the prescribed bandwidth but were generally able to meet the lower bound of
262 the prescribed modification [9].

263 The main effects of the RM ANOVA for the vertical JRFs are presented in Fig. 3
264 through 66. For the first peak JRF in the medial compartment there was no significant
265 difference between conditions ($F(1.7, 32.3)=1.70, p=.20$). For the second peak in the
266 medial compartment there was a statistically significant difference between conditions
267 ($F(1.8, 34.4)=4.71, p=0.02$). Pairwise comparisons indicated that the TIG condition had a
268 smaller JRF compared to baseline ($p=0.04$).

269 For the first peak JRF in the lateral compartment there was a statistically
270 significant difference between conditions ($F(1.8, 34.7)=10.56, p=0.0004$). Pairwise
271 comparisons indicated an increased JRF for MKT compared to baseline ($p=0.01$). For the
272 second peak in the lateral compartment there was a statistically significant difference
273 between conditions ($F(3.0, 57.0)=3.81, p=0.01$). However, pairwise comparisons
274 indicated no significant difference between any condition and baseline.

275 Mean JRF (normalized by body weight) during the stance phase of gait is shown
276 for the four gait conditions in both the medial and lateral compartments in Fig. 7.

277 **DISCUSSION**

278 This study compared the effects of three gait modifications on the simulated
279 JRFs in the medial compartments of the knee in healthy participants. The primary
280 purpose was to determine if LTL, MKT, and TIG reduced the JRFs in the medial
281 compartment of the knee in healthy individuals. Our hypothesis was not supported by
282 the data, which showed no statistically significant difference between baseline and any
283 of the gait interventions in the medial compartment during the loading phase (e.g. first
284 peak) of gait.

285 For individuals at risk for, or diagnosed with, medial compartment knee *OA*,
286 reducing the JRF in the first peak is generally thought to be of high importance and gait
287 interventions are commonly found to reduce either KAM or JRF in the first peak. While
288 there was decreasing JRF in our study, the results were not statistically significant. The
289 LTL modification has been shown to reduce KAM in healthy and pathological
290 populations [9, 12, 72, 73]. One study did find that a healthy participant, when given

291 verbal queues, could increase their JRF by using LTL type modification [74]. While this is
292 counter to what would be expected we had a similar finding in our unpublished study
293 that used data from a participant with an instrumented knee implant performing LTL.

294 In contrast to the LTL, the MKT modification showed an increasing JRF but it was
295 also not significant. The MKT has been shown to decrease both KAM and JRF in previous
296 studies [9, 15, 16, 75, 76]. One issue related to MKT is that of the three studied gait
297 modifications we found MKT was the most difficult for participants to adopt, and
298 therefore, the lack of results in our study could be due to inconsistent implementation
299 of the MKT intervention [9]. If some participants were not able to correctly implement
300 MKT it could have led to spurious data that obscured the results of the entire group.

301 Overall, our results for MKT contradict previous research [72, 76, 77] with one possible
302 explanation being that the outcome of gait interventions can be subject-specific [9, 78]
303 and may be influenced by parameters such as anatomical alignment [79, 80], body mass
304 index [81, 82], and individual gait biomechanics [78]. From a modeling perspective
305 calculated JRF values are influenced by muscle activation and force estimates [74] so
306 increased muscle activity, used by the model to match participant kinematics, during
307 stance phase in MKT may influence the magnitude of the JRF in the first peak.

308 During TIG participants exhibited decreasing JRF but the results were also not
309 statistically significant. Previous research on KAM in TIG has been inconclusive [78, 83-
310 86] so these results were not unsurprising. However, a recent study that used
311 musculoskeletal modeling with TIG found no change in JRF even with a decrease in KAM
312 so our results are consistent with their findings [39].

313 While the second peak in the medial compartment may be less important for
314 subjects with knee OA [20, 34], our data indicated a statistically significant difference
315 between conditions for the propulsion phase of gait in the medial compartment ($p=.02$).
316 The post-hoc pairwise comparisons indicated that TIG in the second peak produced a
317 greater JRF than baseline ($p=.04$). Previous research on TIG has found inconclusive
318 results on the effect of TIG on KAM so this isn't necessarily unexpected [11]. As shown in
319 previous research the Lerner knee model may overestimate the JRF in the second peak
320 of the medial compartment in normal gait [44] and unpublished data from our lab found
321 larger error in the second peak when using MKT or LTL gait. While the weighted *SO* can
322 reduce the error greatly [44, 87] the errors can still be 20% or larger, as compared to the
323 less than 10% error in the medial compartment for MKT and LTL gait.

324 One of the main goals of these gait interventions is to reduce the JRF in the
325 medial compartment, however, a consequence may be that the load is transferred to
326 another compartment. While our data did not find statistically significant reductions in
327 JRFs in the medial compartment, there was a statistically significant difference from
328 baseline in the lateral compartment for both the first ($p=.004$) and second ($p=.01$) peaks.
329 Post hoc tests indicated that the JRF during MKT increased from baseline ($p=.01$) in the
330 first peak but did not increase from baseline in the second peak. One factor to consider
331 for this data is that in an unpublished validation study with the model it was found to
332 overestimate JRF in the lateral compartment to a greater extent than in the first peak of
333 the medial compartment, especially when applied to MKT and LTL interventions.

334 Therefore, the results in the lateral compartment may be skewed due to limitations of
335 the model.

336 Data from previous research [87] suggests that this modeling approach can
337 provide robust results for simulated JRFs in the medial compartment during the loading
338 phase. Therefore, one possible explanation for lack of results is the intervention does
339 not have a large effect on JRFs in the knee during the first peak. Another possibility is
340 that there could be a large variation in individual responses to gait interventions that
341 are averaged out in the aggregated data. Fig. 8 shows a summary of the responses to
342 each intervention as a percentage increase or decrease from their baseline JRF values by
343 study participant. Three participants had large (i.e. >30%) reductions in their baseline
344 values while five had large increases. In addition, some individuals showed an increase
345 from baseline for some gait modifications but a decrease for others. Previous research
346 has reported a similar finding when evaluating KAM in all three modifications [9]. There
347 has also been research that showed individual variation in the response to toe-in gait
348 [78] and toe-out gait [85]. It is possible that no single variable contributes to an
349 individual's response but that it is a combination of several variables. For example, a
350 participant's response may be affected by the level of strength in their leg muscles
351 interacting with static knee alignment, BMI, and/or other variables.

352 While research has demonstrated that gait modifications with RTB may help
353 reduce the JRF in the medial compartment of the knee one limitation to this approach is
354 that the majority of feedback is focused on joint kinematics, such as joint angles. Muscle
355 contraction across a joint also contributes to JRF and recent research has shown that

356 providing RTB of muscle activation patterns allows individuals to alter their JRF by
357 changing the activation patterns of their muscles during gait [88]. This recent study
358 found that participants were able to reduce knee JRF, during late stance, in a normal
359 walking gait by 12% (± 12) by shifting their muscle activation patterns from the
360 gastrocnemius to the soleus muscle. It is possible that in gait modification studies
361 participants are using different muscle coordination strategies to meet the RTB targets
362 during modification. For example, someone trying to use MKT may unintentionally
363 increase their knee JRF as a result of the particular muscle contraction strategies they
364 use to meet the kinematics of the movement pattern. In addition to factors like static
365 alignment these differences in movement coordination strategies may be contributing
366 to the results shown in Fig 8 and offer a possible additional consideration for why some
367 participants show decreasing JRF while others show increasing JRF. An alternative
368 approach that may be worth investigating is providing RTB of both kinematic and muscle
369 activation patterns, to subjects performing gait modifications, in order to gain a better
370 understanding of each element's relative contribution to JRF.

371 There are several limitations to this study. First, while the results of the visual
372 inspection method for identifying muscles and corresponding weights for the weighted
373 *SO* was successful, it lacked objective metrics for decision criteria. An improved
374 approach to the process would be to take a statistical measure, such as the mean of all
375 lower extremity muscles forces, during the second half of stance, and for any muscle
376 with an excessive force estimate increase the weight until the muscle force estimate is
377 within 1 or 2 standard deviations of that median value. However, more work should be

378 done to further evaluate this process for identifying muscle weighting and identifying
379 the optimal appropriate range could be developed experimentally. Another limitation to
380 this analysis was a lack of imaging data for participants. This did not allow us to
381 accurately determine static knee alignment and contact locations and reduced the
382 benefit of the Lerner model. The Lerner model has modifiable parameters which lets
383 you adjust the knee alignment in the frontal plane as well as the contact locations
384 between the tibia and femur. While we did attempt to estimate the values from
385 Visual3D, the estimate of knee alignment calculation from the software differs from the
386 approach described by Lerner et al [44, 89] in their validation study and we were not
387 confident enough in the values to use them for this study. Lastly, it is also possible that
388 the sample size may not have been large enough to provide the power to detect
389 differences in our data.

390 **CONCLUSION**

391 This study did not find the hypothesized decrease in simulated JRF in the medial
392 compartment of the knee for TIG, LTL, and MKT. Lack of results may be as a result of
393 individual variation in response to gait modifications. Factors involved in this variation
394 may include static alignment of the lower extremity or muscle coordination patterns
395 used to meet gait modification targets. It is possible that gait interventions cannot be
396 uniformly applied to all participants with the expectation that they will all respond with
397 reductions in JRF. Individual factors may lead some participants to have decreased JRF
398 as a result of a modification while others may experience increased JRF. It is also
399 possible that there may be variation within an individual in how they respond to

400 different gait modifications with some leading to reduced JRF and others increasing JRF.
401 Future work should be done to develop a greater understanding of how different factors
402 contribute to individual responses in JRFs as a result of gait modification.

403

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408 National Institutes of Health.

409 **NOMENCLATURE**

BMI	Body mass index
<i>F</i>	Female
GAS	Gastrocnemius
GAS-VL	Gastrocnemius and vastus lateralis
GAS-VI-VL-VM	Gastrocnemius, vastus intermedius vastus lateralis, and vastus medialis
GAS-VI-VL-VM-RF	Gastrocnemius, vastus intermedius vastus lateralis, vastus medialis, and rectus femoris
JRF	Joint reaction force
KAM	Knee adduction moment
KFM	Knee flexion moment

kg	Kilogram
<i>L</i>	Left
LTL	Lateral trunk lean
<i>M</i>	Male
<i>m</i>	Meter
MKT	Medial knee thrust
<i>N</i>	Number
OA	Osteoarthritis
<i>R</i>	Right
RM ANOVA	Repeated measures analysis of variance
<i>sd</i>	Standard deviation
<i>SO</i>	Static optimization
TIG	Toe-in gait

411 REFERENCES

- 412 [1] Cross M., Smith E., Hoy D., Nolte S., Ackerman I., Fransen M., Bridgett L.,
 413 Williams S., Guillemin F., Hill C. L., Laslett L. L., Jones G., Cicuttini F., Osborne
 414 R., Vos T., Buchbinder R., Woolf A., March L., 2014, "The global burden of hip and
 415 knee osteoarthritis: estimates from the global burden of disease 2010 study," *Ann*
 416 *Rheum Dis*, 73(7): 1323-30. <https://doi.org/10.1136/annrheumdis-2013-204763>
- 417 [2] Lawrence R. C., Felson D. T., Helmick C. G., Arnold L. M., Choi H., Deyo R. A.,
 418 Gabriel S., Hirsch R., Hochberg M. C., Hunder G. G., Jordan J. M., Katz J. N.,
 419 Kremers H. M., Wolfe F., National Arthritis Data W., 2008, "Estimates of the
 420 prevalence of arthritis and other rheumatic conditions in the United States. Part II,"
 421 *Arthritis Rheum*, 58(1): 26-35. <https://doi.org/10.1002/art.23176>
- 422 [3] Ratzlaff C. R., Koehoorn M., Cibere J., Kopec J. A., 2012, "Is lifelong knee joint
 423 force from work, home, and sport related to knee osteoarthritis?," *Int J Rheumatol*,
 424 2012: 584193. <https://doi.org/10.1155/2012/584193>
- 425 [4] Sharma L., Hurwitz D. E., Thonar E. J., Sum J. A., Lenz M. E., Dunlop D. D.,
 426 Schnitzer T. J., Kirwan-Mellis G., Andriacchi T. P., 1998, "Knee adduction moment,
 427 serum hyaluronan level, and disease severity in medial tibiofemoral osteoarthritis,"
 428 *Arthritis Rheum*, 41(7): 1233-40. [https://doi.org/10.1002/1529-0131\(199807\)41:7<1233::AID-ART14>3.0.CO;2-L](https://doi.org/10.1002/1529-0131(199807)41:7<1233::AID-ART14>3.0.CO;2-L)
- 430 [5] Ferrigno C., Stoller I. S., Shakoor N., Thorp L. E., Wimmer M. A., 2016, "The
 431 feasibility of using augmented auditory feedback from a pressure detecting insole to
 432 reduce the knee adduction moment: A proof of concept study," *J Biomech Eng*,
 433 138(2): 021014. <https://doi.org/10.1115/1.4032123>
- 434 [6] Hunt M. A., Simic M., Hinman R. S., Bennell K. L., Wrigley T. V., 2011,
 435 "Feasibility of a gait retraining strategy for reducing knee joint loading: increased
 436 trunk lean guided by real-time biofeedback," *J Biomech*, 44(5): 943-47.
 437 <https://doi.org/10.1016/j.jbiomech.2010.11.027>
- 438 [7] Eddo O., Lindsey B., Caswell S. V., Cortes N., 2017, "Current evidence of gait
 439 modification with real-time biofeedback to alter kinetic, temporospatial, and
 440 function-related outcomes: A review," *International Journal of Kinesiology & Sports*
 441 *Science*, 5(3): 21-35. <https://doi.org/10.7575/aiac.ijkss.v.5n.3p.35>
- 442 [8] Fregly B. J., 2012, "Gait modification to treat knee osteoarthritis," *HSS J*, 8(1): 45-
 443 48. <https://doi.org/10.1007/s11420-011-9229-9>
- 444 [9] Lindsey B., Eddo O., Caswell S. V., Prebble M., Cortes N., 2020, "Reductions in
 445 peak knee abduction moment in three previously studied gait modification
 446 strategies," *Knee*, 27(1): 102-10. <https://doi.org/10.1016/j.knee.2019.09.017>
- 447 [10] Miller R. H., Esterson A. Y., Shim J. K., 2015, "Joint contact forces when
 448 minimizing the external knee adduction moment by gait modification: A computer
 449 simulation study," *Knee*, 22(6): 481-89. <https://doi.org/10.1016/j.knee.2015.06.014>
- 450 [11] Simic M., Hinman R. S., Wrigley T. V., Bennell K. L., Hunt M. A., 2011, "Gait
 451 modification strategies for altering medial knee joint load: a systematic review,"
 452 *Arthritis Care Res (Hoboken)*, 63(3): 405-26. <https://doi.org/10.1002/acr.20380>
- 453 [12] Simic M., Hunt M. A., Bennell K. L., Hinman R. S., Wrigley T. V., 2012, "Trunk
 454 lean gait modification and knee joint load in people with medial knee osteoarthritis:
 455 the effect of varying trunk lean angles," *Arthritis Care Res (Hoboken)*, 64(10): 1545-
 456 53. <https://doi.org/10.1002/acr.21724>

- 457 [13] Hunt M. A., Birmingham T. B., Bryant D., Jones I., Giffin J. R., Jenkyn T. R.,
458 Vandervoort A. A., 2008, "Lateral trunk lean explains variation in dynamic knee
459 joint load in patients with medial compartment knee osteoarthritis," *Osteoarthritis*
460 *Cartilage*, 16(5): 591-99. <https://doi.org/10.1016/j.joca.2007.10.017>
- 461 [14] Mundermann A., Asay J. L., Mundermann L., Andriacchi T. P., 2008, "Implications
462 of increased medio-lateral trunk sway for ambulatory mechanics," *J Biomech*, 41(1):
463 165-70. <https://doi.org/10.1016/j.jbiomech.2007.07.001>
- 464 [15] Ferrigno C., Wimmer M. A., Trombley R. M., Lundberg H. J., Shakoor N., Thorp L.
465 E., 2016, "A reduction in the knee adduction moment with medial thrust gait is
466 associated with a medial shift in center of plantar pressure," *Med Eng Phys*, 38(7):
467 615-21. <https://doi.org/10.1016/j.medengphy.2016.03.008>
- 468 [16] Fregly B. J., Reinbolt J. A., Rooney K. L., Mitchell K. H., Chmielewski T. L., 2007,
469 "Design of patient-specific gait modifications for knee osteoarthritis rehabilitation,"
470 *IEEE Trans Biomed Eng*, 54(9): 1687-95.
471 <https://doi.org/10.1109/TBME.2007.907637>
- 472 [17] Jackson B., Gordon K. E., Chang A. H., 2018, "Immediate and short-term effects of
473 real-time knee adduction moment feedback on the peak and cumulative knee load
474 during walking," *J Orthop Res*, 36(1): 397-404. <https://doi.org/10.1002/jor.23659>
- 475 [18] Kinney A. L., Besier T. F., Silder A., Delp S. L., D'Lima D. D., Fregly B. J., 2013,
476 "Changes in in vivo knee contact forces through gait modification," *J Orthop Res*,
477 31(3): 434-40. <https://doi.org/10.1002/jor.22240>
- 478 [19] Walter J. P., D'Lima D. D., Colwell C. W., Jr., Fregly B. J., 2010, "Decreased knee
479 adduction moment does not guarantee decreased medial contact force during gait," *J*
480 *Orthop Res*, 28(10): 1348-54. <https://doi.org/10.1002/jor.21142>
- 481 [20] Richards R. E., Andersen M. S., Harlaar J., van den Noort J. C., 2018, "Relationship
482 between knee joint contact forces and external knee joint moments in patients with
483 medial knee osteoarthritis: effects of gait modifications," *Osteoarthritis Cartilage*,
484 26(9): 1203-14. <https://doi.org/10.1016/j.joca.2018.04.011>
- 485 [21] Tan H. H., Mentiplay B., Quek J. J., Tham A. C. W., Lim L. Z. X., Clark R. A.,
486 Woon E. L., Yeh T. T., Tan C. I. C., Pua Y. H., 2020, "Test-retest reliability and
487 variability of knee adduction moment peak, impulse and loading rate during
488 walking," *Gait Posture*, 80: 113-16. <https://doi.org/10.1016/j.gaitpost.2020.05.029>
- 489 [22] Wang S., Chan K. H. C., Lam R. H. M., Yuen D. N. S., Fan C. K. M., Chu T. T. C.,
490 Baur H., Cheung R. T. H., 2019, "Effects of foot progression angle adjustment on
491 external knee adduction moment and knee adduction angular impulse during stair
492 ascent and descent," *Hum Mov Sci*, 64: 213-20.
493 <https://doi.org/10.1016/j.humov.2019.02.004>
- 494 [23] Tomoya T., Mutsuaki E., Takuma I., Yuta T., Masayoshi K., 2019, "A mathematical
495 modelling study investigating the influence of knee joint flexion angle and extension
496 moment on patellofemoral joint reaction force and stress," *Knee*, 26(6): 1323-29.
497 <https://doi.org/10.1016/j.knee.2019.10.010>
- 498 [24] Nie Y., Wang H., Xu B., Zhou Z., Shen B., Pei F., 2019, "The relationship between
499 knee adduction moment and knee osteoarthritis symptoms according to static
500 alignment and pelvic drop," *Biomed Res Int*, 2019: 7603249.
501 <https://doi.org/10.1155/2019/7603249>

- 502 [25] Konrath J. M., Karatsidis A., Schepers H. M., Bellusci G., de Zee M., Andersen M.
503 S., 2019, "Estimation of the knee adduction moment and joint contact force during
504 daily living activities using inertial motion capture," *Sensors (Basel)*, 19(7): 1681.
505 <https://doi.org/10.3390/s19071681>
- 506 [26] Luc-Harkey B. A., Franz J. R., Blackburn J. T., Padua D. A., Hackney A. C.,
507 Pietrosimone B., 2018, "Real-time biofeedback can increase and decrease vertical
508 ground reaction force, knee flexion excursion, and knee extension moment during
509 walking in individuals with anterior cruciate ligament reconstruction," *J Biomech*,
510 76: 94-102. <https://doi.org/10.1016/j.jbiomech.2018.05.043>
- 511 [27] Telfer S., Lange M. J., Sudduth A. S. M., 2017, "Factors influencing knee adduction
512 moment measurement: A systematic review and meta-regression analysis," *Gait
513 Posture*, 58: 333-39. <https://doi.org/10.1016/j.gaitpost.2017.08.025>
- 514 [28] Teng H. L., MacLeod T. D., Link T. M., Majumdar S., Souza R. B., 2015, "Higher
515 knee flexion moment during the second half of the stance phase of gait is associated
516 with the progression of osteoarthritis of the patellofemoral joint on magnetic
517 resonance imaging," *J Orthop Sports Phys Ther*, 45(9): 656-64.
518 <https://doi.org/10.2519/jospt.2015.5859>
- 519 [29] Creaby M. W., 2015, "It's not all about the knee adduction moment: the role of the
520 knee flexion moment in medial knee joint loading," *Osteoarthritis Cartilage*, 23(7):
521 1038-40. <https://doi.org/10.1016/j.joca.2015.03.032>
- 522 [30] Asay J. L., Erhart-Hledik J. C., Andriacchi T. P., 2018, "Changes in the total knee
523 joint moment in patients with medial compartment knee osteoarthritis over 5 years,"
524 *J Orthop Res*, 36(9): 2373-79. <https://doi.org/10.1002/jor.23908>
- 525 [31] Chang A. H., Moisio K. C., Chmiel J. S., Eckstein F., Guermazi A., Prasad P. V.,
526 Zhang Y., Almagor O., Belisle L., Hayes K., Sharma L., 2015, "External knee
527 adduction and flexion moments during gait and medial tibiofemoral disease
528 progression in knee osteoarthritis," *Osteoarthritis Cartilage*, 23(7): 1099-106.
529 <https://doi.org/10.1016/j.joca.2015.02.005>
- 530 [32] Chehab E. F., Favre J., Erhart-Hledik J. C., Andriacchi T. P., 2014, "Baseline knee
531 adduction and flexion moments during walking are both associated with 5 year
532 cartilage changes in patients with medial knee osteoarthritis," *Osteoarthritis
533 Cartilage*, 22(11): 1833-39. <https://doi.org/10.1016/j.joca.2014.08.009>
- 534 [33] Erhart-Hledik J. C., Chehab E. F., Asay J. L., Favre J., Chu C. R., Andriacchi T. P.,
535 2021, "Longitudinal changes in tibial and femoral cartilage thickness are associated
536 with baseline ambulatory kinetics and cartilage oligomeric matrix protein (COMP)
537 measures in an asymptomatic aging population," *Osteoarthritis Cartilage*, 29(5): 687-
538 96. <https://doi.org/10.1016/j.joca.2021.02.006>
- 539 [34] Holder J., Trinler U., Meurer A., Stief F., 2020, "A systematic review of the
540 associations between inverse dynamics and musculoskeletal modeling to investigate
541 joint loading in a clinical environment," *Front Bioeng Biotechnol*, 8: 603907.
542 <https://doi.org/10.3389/fbioe.2020.603907>
- 543 [35] Shull P. B., Lurie K. L., Cutkosky M. R., Besier T. F., 2011, "Training multi-
544 parameter gaits to reduce the knee adduction moment with data-driven models and
545 haptic feedback," *J Biomech*, 44(8): 1605-09.
546 <https://doi.org/10.1016/j.jbiomech.2011.03.016>

- 547 [36] Simic M., Hinman R. S., Wrigley T. V., Bennell K. L., Hunt M. A., 2011, "Gait
548 modification strategies for altering medial knee joint load: a systematic review,"
549 *Arthritis Care Res (Hoboken)*, 63(3): 405-26. <https://doi.org/10.1002/acr.20380>
- 550 [37] Barrios J. A., Crossley K. M., Davis I. S., 2010, "Gait retraining to reduce the knee
551 adduction moment through real-time visual feedback of dynamic knee alignment," *J*
552 *Biomech*, 43(11): 2208-13. <https://doi.org/10.1016/j.jbiomech.2010.03.040>
- 553 [38] Richards R., van den Noort J. C., van der Esch M., Booij M. J., Harlaar J., 2018,
554 "Gait retraining using real-time feedback in patients with medial knee osteoarthritis:
555 Feasibility and effects of a six-week gait training program," *Knee*, 25(5): 814-24.
556 <https://doi.org/10.1016/j.knee.2018.05.014>
- 557 [39] Cui W., Wang C., Chen W., Guo Y., Jia Y., Du W., Wang C., 2019, "Effects of Toe-
558 Out and Toe-In Gaits on Lower-Extremity Kinematics, Dynamics, and
559 Electromyography," *Applied Sciences*, 9(23): 5245.
- 560 [40] Holder J., Drongelen S., Meurer A., Stief F. Statistical comparison of contact forces
561 and moments in the knee joint during walking in participants with and without
562 valgus malalignment. *ESMAC: Gait & Posture*, 2020:155-56.
- 563 [41] Eskinazi I., Fregly B. J., 2016, "An open-source toolbox for surrogate modeling of
564 joint contact mechanics," *IEEE Trans Biomed Eng*, 63(2): 269-77.
565 <https://doi.org/10.1109/TBME.2015.2455510>
- 566 [42] Xu H., Bloswick D., Merryweather A., 2015, "An improved OpenSim gait model
567 with multiple degrees of freedom knee joint and knee ligaments," *Comput Methods*
568 *Biomech Biomed Engin*, 18(11): 1217-24.
569 <https://doi.org/10.1080/10255842.2014.889689>
- 570 [43] Martelli S., Valente G., Viceconti M., Taddei F., 2015, "Sensitivity of a subject-
571 specific musculoskeletal model to the uncertainties on the joint axes location,"
572 *Comput Methods Biomech Biomed Engin*, 18(14): 1555-63.
573 <https://doi.org/10.1080/10255842.2014.930134>
- 574 [44] Lerner Z. F., DeMers M. S., Delp S. L., Browning R. C., 2015, "How tibiofemoral
575 alignment and contact locations affect predictions of medial and lateral tibiofemoral
576 contact forces," *J Biomech*, 48(4): 644-50.
577 <https://doi.org/10.1016/j.jbiomech.2014.12.049>
- 578 [45] Knarr B. A., Higginson J. S., 2015, "Practical approach to subject-specific
579 estimation of knee joint contact force," *J Biomech*, 48(11): 2897-902.
580 <https://doi.org/10.1016/j.jbiomech.2015.04.020>
- 581 [46] Gerus P., Sartori M., Besier T. F., Fregly B. J., Delp S. L., Banks S. A., Pandy M.
582 G., D'Lima D. D., Lloyd D. G., 2013, "Subject-specific knee joint geometry
583 improves predictions of medial tibiofemoral contact forces," *J Biomech*, 46(16):
584 2778-86. <https://doi.org/10.1016/j.jbiomech.2013.09.005>
- 585 [47] Delp S. L., Anderson F. C., Arnold A. S., Loan P., Habib A., John C. T.,
586 Guendelman E., Thelen D. G., 2007, "OpenSim: open-source software to create and
587 analyze dynamic simulations of movement," *IEEE Trans Biomed Eng*, 54(11): 1940-
588 50. <https://doi.org/10.1109/TBME.2007.901024>
- 589 [48] Otten E., 2003, "Inverse and forward dynamics: models of multi-body systems,"
590 *Philos Trans R Soc Lond B Biol Sci*, 358(1437): 1493-500.
591 <https://doi.org/10.1098/rstb.2003.1354>

- 592 [49] Hart D. A., Martin C. R., Scott M., Shrive N. G., 2021, "The instrumented sheep
593 knee to elucidate insights into osteoarthritis development and progression: A
594 sensitive and reproducible platform for integrated research efforts," *Clin Biomech*
595 (Bristol, Avon), 87: 105404. <https://doi.org/10.1016/j.clinbiomech.2021.105404>
596 [50] Demers M. S., Pal S., Delp S. L., 2014, "Changes in tibiofemoral forces due to
597 variations in muscle activity during walking," *J Orthop Res*, 32(6): 769-76.
598 <https://doi.org/10.1002/jor.22601>
599 [51] Lerner Z. F., Haight D. J., DeMers M. S., Board W. J., Browning R. C., 2014, "The
600 effects of walking speed on tibiofemoral loading estimated via musculoskeletal
601 modeling," *J Appl Biomech*, 30(2): 197-205. <https://doi.org/10.1123/jab.2012-0206>
602 [52] Steele K. M., Demers M. S., Schwartz M. H., Delp S. L., 2012, "Compressive
603 tibiofemoral force during crouch gait," *Gait Posture*, 35(4): 556-60.
604 <https://doi.org/10.1016/j.gaitpost.2011.11.023>
605 [53] Seth A., Sherman M., Reinbolt J. A., Delp S. L., 2011, "OpenSim: a musculoskeletal
606 modeling and simulation framework for in silico investigations and exchange,"
607 *Procedia IUTAM*, 2: 212-32. <https://doi.org/10.1016/j.piutam.2011.04.021>
608 [54] Gu W., Pandy M. G., 2020, "Direct validation of human knee-joint contact
609 mechanics derived from subject-specific finite-element models of the tibiofemoral
610 and patellofemoral joints," *J Biomech Eng*, 142(7): 071001.
611 <https://doi.org/10.1115/1.4045594>
612 [55] Meireles S., De Groote F., Reeves N. D., Verschuere S., Maganaris C., Luyten F.,
613 Jonkers I., 2016, "Knee contact forces are not altered in early knee osteoarthritis,"
614 *Gait Posture*, 45: 115-20. <https://doi.org/10.1016/j.gaitpost.2016.01.016>
615 [56] Haight D. J., Lerner Z. F., Board W. J., Browning R. C., 2014, "A comparison of
616 slow, uphill and fast, level walking on lower extremity biomechanics and
617 tibiofemoral joint loading in obese and nonobese adults," *J Orthop Res*, 32(2): 324-
618 30. <https://doi.org/10.1002/jor.22497>
619 [57] Richards C., Higginson J. S., 2010, "Knee contact force in subjects with symmetrical
620 OA grades: differences between OA severities," *J Biomech*, 43(13): 2595-600.
621 <https://doi.org/10.1016/j.jbiomech.2010.05.006>
622 [58] Winby C. R., Lloyd D. G., Besier T. F., Kirk T. B., 2009, "Muscle and external load
623 contribution to knee joint contact loads during normal gait," *J Biomech*, 42(14):
624 2294-300. <https://doi.org/10.1016/j.jbiomech.2009.06.019>
625 [59] Uicker J. J., Sheth, P. N. *Matrix methods in the design analysis of multibody systems*.
626 Charlottesville, VA: University of Virginia, 2007.
627 [60] Shelburne K. B., Torry M. R., Pandy M. G., 2006, "Contributions of muscles,
628 ligaments, and the ground-reaction force to tibiofemoral joint loading during normal
629 gait," *J Orthop Res*, 24(10): 1983-90. <https://doi.org/10.1002/jor.20255>
630 [61] Taylor W. R., Heller M. O., Bergmann G., Duda G. N., 2004, "Tibio-femoral
631 loading during human gait and stair climbing," *J Orthop Res*, 22(3): 625-32.
632 <https://doi.org/10.1016/j.orthres.2003.09.003>
633 [62] Hurwitz D. E., Sumner D. R., Andriacchi T. P., Sugar D. A., 1998, "Dynamic knee
634 loads during gait predict proximal tibial bone distribution," *J Biomech*, 31(5): 423-
635 30. [https://doi.org/10.1016/S0021-9290\(98\)00028-1](https://doi.org/10.1016/S0021-9290(98)00028-1)

- 636 [63] Schipplein O. D., Andriacchi T. P., 1991, "Interaction between active and passive
637 knee stabilizers during level walking," *J Orthop Res*, 9(1): 113-19.
638 <https://doi.org/10.1002/jor.1100090114>
- 639 [64] Morrison J. B., 1970, "The mechanics of the knee joint in relation to normal
640 walking," *Journal of Biomechanics*, 3(1): 51-61. [https://doi.org/10.1016/0021-9290\(70\)90050-3](https://doi.org/10.1016/0021-9290(70)90050-3)
641
- 642 [65] Herzog W., Longino D., Clark A., 2003, "The role of muscles in joint adaptation and
643 degeneration," *Langenbecks Arch Surg*, 388(5): 305-15.
644 <https://doi.org/10.1007/s00423-003-0402-6>
- 645 [66] Knarr B. A., Higginson J. S., Zeni J. A., 2016, "Change in knee contact force with
646 simulated change in body weight," *Comput Methods Biomech Biomed Engin*, 19(3):
647 320-23. <https://doi.org/10.1080/10255842.2015.1018193>
- 648 [67] Cortes N., Quammen D., Lucci S., Greska E., Onate J., 2012, "A functional agility
649 short-term fatigue protocol changes lower extremity mechanics," *J Sports Sci*, 30(8):
650 797-805. <https://doi.org/10.1080/02640414.2012.671528>
- 651 [68] Schwartz M. H., Rozumalski A., 2005, "A new method for estimating joint
652 parameters from motion data," *J Biomech*, 38(1): 107-16.
653 <https://doi.org/10.1016/j.jbiomech.2004.03.009>
- 654 [69] Eddo O. O., Lindsey B. W., Caswell S. V., Prebble M., Cortes N., 2019,
655 "Unintended Changes in Contralateral Limb as a Result of Acute Gait Modification,"
656 *J Appl Biomech*, 36(1): 13-19. <https://doi.org/10.1123/jab.2019-0031>
- 657 [70] Steele K. M., Tresch M. C., Perreault E. J., 2015, "Consequences of biomechanically
658 constrained tasks in the design and interpretation of synergy analyses," *J*
659 *Neurophysiol*, 113(7): 2102-13. <https://doi.org/10.1152/jn.00769.2013>
- 660 [71] Patil I., 2021, "Visualizations with statistical details: The 'ggstatsplot' approach.,"
661 *Journal of Open Source Software*, 6(61): 3167. <https://doi.org/10.21105/joss.03167>
- 662 [72] Gerbrands T. A., Pisters M. F., Theeven P. J. R., Verschueren S., Vanwanseele B.,
663 2017, "Lateral trunk lean and medializing the knee as gait strategies for knee
664 osteoarthritis," *Gait Posture*, 51: 247-53.
665 <https://doi.org/10.1016/j.gaitpost.2016.11.014>
- 666 [73] Tokuda K., Anan M., Takahashi M., Sawada T., Tanimoto K., Kito N., Shinkoda K.,
667 2018, "Biomechanical mechanism of lateral trunk lean gait for knee osteoarthritis
668 patients," *J Biomech*, 66: 10-17. <https://doi.org/10.1016/j.jbiomech.2017.10.016>
- 669 [74] Pizzolato C., Reggiani M., Saxby D. J., Ceseracciu E., Modenese L., Lloyd D. G.,
670 2017, "Biofeedback for gait retraining based on real-time estimation of tibiofemoral
671 joint contact forces," *IEEE Trans Neural Syst Rehabil Eng*, 25(9): 1612-21.
672 <https://doi.org/10.1109/TNSRE.2017.2683488>
- 673 [75] Schache A. G., Fregly B. J., Crossley K. M., Hinman R. S., Pandy M. G., 2008, "The
674 effect of gait modification on the external knee adduction moment is reference frame
675 dependent," *Clin Biomech (Bristol, Avon)*, 23(5): 601-08.
676 <https://doi.org/10.1016/j.clinbiomech.2007.12.008>
- 677 [76] Fregly B. J., D'Lima D. D., Colwell C. W., Jr., 2009, "Effective gait patterns for
678 offloading the medial compartment of the knee," *J Orthop Res*, 27(8): 1016-21.
679 <https://doi.org/10.1002/jor.20843>
- 680 [77] Meyer A. J., D'Lima D. D., Besier T. F., Lloyd D. G., Colwell C. W., Jr., Fregly B.
681 J., 2013, "Are external knee load and EMG measures accurate indicators of internal

- 682 knee contact forces during gait?," *J Orthop Res*, 31(6): 921-29.
683 <https://doi.org/10.1002/jor.22304>
- 684 [78] Uhlich S. D., Silder A., Beaupre G. S., Shull P. B., Delp S. L., 2018, "Subject-
685 specific toe-in or toe-out gait modifications reduce the larger knee adduction
686 moment peak more than a non-personalized approach," *J Biomech*, 66: 103-10.
687 <https://doi.org/10.1016/j.jbiomech.2017.11.003>
- 688 [79] Hoch M. C., Weinhandl J. T., 2017, "Effect of valgus knee alignment on gait
689 biomechanics in healthy women," *J Electromyogr Kinesiol*, 35: 17-23.
690 <https://doi.org/10.1016/j.jelekin.2017.05.003>
- 691 [80] Clement J., Toliopoulos P., Hagemester N., Desmeules F., Fuentes A., Vendittoli P.
692 A., 2018, "Healthy 3D knee kinematics during gait: Differences between women and
693 men, and correlation with x-ray alignment," *Gait Posture*, 64: 198-204.
694 <https://doi.org/10.1016/j.gaitpost.2018.06.024>
- 695 [81] Sharma L., Lou C., Cahue S., Dunlop D. D., 2000, "The mechanism of the effect of
696 obesity in knee osteoarthritis: the mediating role of malalignment," *Arthritis Rheum*,
697 43(3): 568-75. [https://doi.org/10.1002/1529-0131\(200003\)43:3<568::AID-](https://doi.org/10.1002/1529-0131(200003)43:3<568::AID-)
698 [ANR13>3.0.CO;2-E](https://doi.org/10.1002/1529-0131(200003)43:3<568::AID-ANR13>3.0.CO;2-E)
- 699 [82] Silva F. R., Muniz A. M. d. S., Cerqueira L. S., Nadal J., 2018, "Biomechanical
700 alterations of gait on overweight subjects," *Research on biomedical engineering*,
701 34(4): 291-98. <https://doi.org/10.1590/2446-4740.180017>
- 702 [83] Lynn S. K., Kajaks T., Costigan P. A., 2008, "The effect of internal and external foot
703 rotation on the adduction moment and lateral-medial shear force at the knee during
704 gait," *J Sci Med Sport*, 11(5): 444-51. <https://doi.org/10.1016/j.jsams.2007.03.004>
- 705 [84] Bechard D. J., Birmingham T. B., Zecevic A. A., Jones I. C., Giffin J. R., Jenkyn T.
706 R., 2012, "Toe-out, lateral trunk lean, and pelvic obliquity during prolonged walking
707 in patients with medial compartment knee osteoarthritis and healthy controls,"
708 *Arthritis Care Res (Hoboken)*, 64(4): 525-32. <https://doi.org/10.1002/acr.21584>
- 709 [85] Hunt M. A., Takacs J., 2014, "Effects of a 10-week toe-out gait modification
710 intervention in people with medial knee osteoarthritis: a pilot, feasibility study,"
711 *Osteoarthritis Cartilage*, 22(7): 904-11. <https://doi.org/10.1016/j.joca.2014.04.007>
- 712 [86] Charlton J. M., Hatfield G. L., Guenette J. A., Hunt M. A., 2018, "Toe-in and toe-out
713 walking require different lower limb neuromuscular patterns in people with knee
714 osteoarthritis," *J Biomech*, 76: 112-18.
715 <https://doi.org/10.1016/j.jbiomech.2018.05.041>
- 716 [87] Prebble M., Wei Q., Eddo O., Lindsey B., Caswell S. V., Cortes N., 2019,
717 "Preliminary analysis: The effects of gait interventions on knee joint contact forces
718 in healthy adults," *Medicine & Science in Sports & Exercise*, 51(6S): 703.
719 <https://doi.org/10.1249/01.mss.0000562592.89136.7b>
- 720 [88] Uhlich S. D., Jackson R. W., Seth A., Kolesar J. A., Delp S. L., 2022, "Muscle
721 coordination retraining inspired by musculoskeletal simulations reduces knee contact
722 force," *Sci Rep*, 12(1): 9842. <https://doi.org/10.1038/s41598-022-13386-9>
- 723 [89] Tsushima H., Morris M. E., McGinley J., 2003, "Test-retest reliability and inter-
724 tester reliability of kinematic data from a three-dimensional gait analysis system," *J*
725 *Jpn Phys Ther Assoc*, 6(1): 9-17. <https://doi.org/10.1298/jjpta.6.9>
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Figure Captions List

- Fig. 1 Marker placement for data collection. Individual tracking markers (22 markers) were attached to the manubrium, 7th cervical vertebrae, right scapula, 10th thoracic vertebrae, and bilaterally to the posterior and lateral calcaneus, 5th distal metatarsal, 1st proximal metatarsal, 2nd metatarsophalangeal joint, tibial tuberosity, lateral iliac spine, posterior superior iliac spine, and acromion. Three tracking markers were arranged to form a triangular cluster and were attached to the lumbar region. Four tracking clusters (18 markers) were placed on the lateral aspect of the thigh and shank. Ten calibration markers were attached bilaterally to the lateral and medial malleoli, lateral and medial knee joint lines, and greater trochanters[9]
- Fig. 2 Example of visual feedback graph provided to participants that was projected onto the laboratory wall during each trial
- Fig. 3 Repeated measures ANOVA for the mean joint reaction force (N) in the 1st peak in the medial compartment for baseline, lateral trunk lean, medial knee thrust, and toe-in gait
- Fig. 4 Repeated measures ANOVA for the mean joint reaction force (N) in the 2nd peak in the medial compartment for baseline, lateral trunk lean, medial knee thrust, and toe-in gait

- Fig. 5 Repeated measures ANOVA for the mean joint reaction force (N) in the 1st peak in the lateral compartment for baseline, lateral trunk lean, medial knee thrust, and toe-in gait
- Fig. 6 Repeated measures ANOVA for the mean joint reaction force (N) in the 2nd peak in the lateral compartment for baseline, lateral trunk lean, medial knee thrust, and toe-in gait
- Fig. 7 Mean joint reaction force (normalized by body weight) in the medial and lateral knee compartments for baseline, lateral trunk lean, medial knee thrust, and toe-in gait
- Fig. 8 Percentage reduction in joint reaction force from baseline values, by individual participant, for toe-in gait, lateral trunk lean, and medial knee thrust

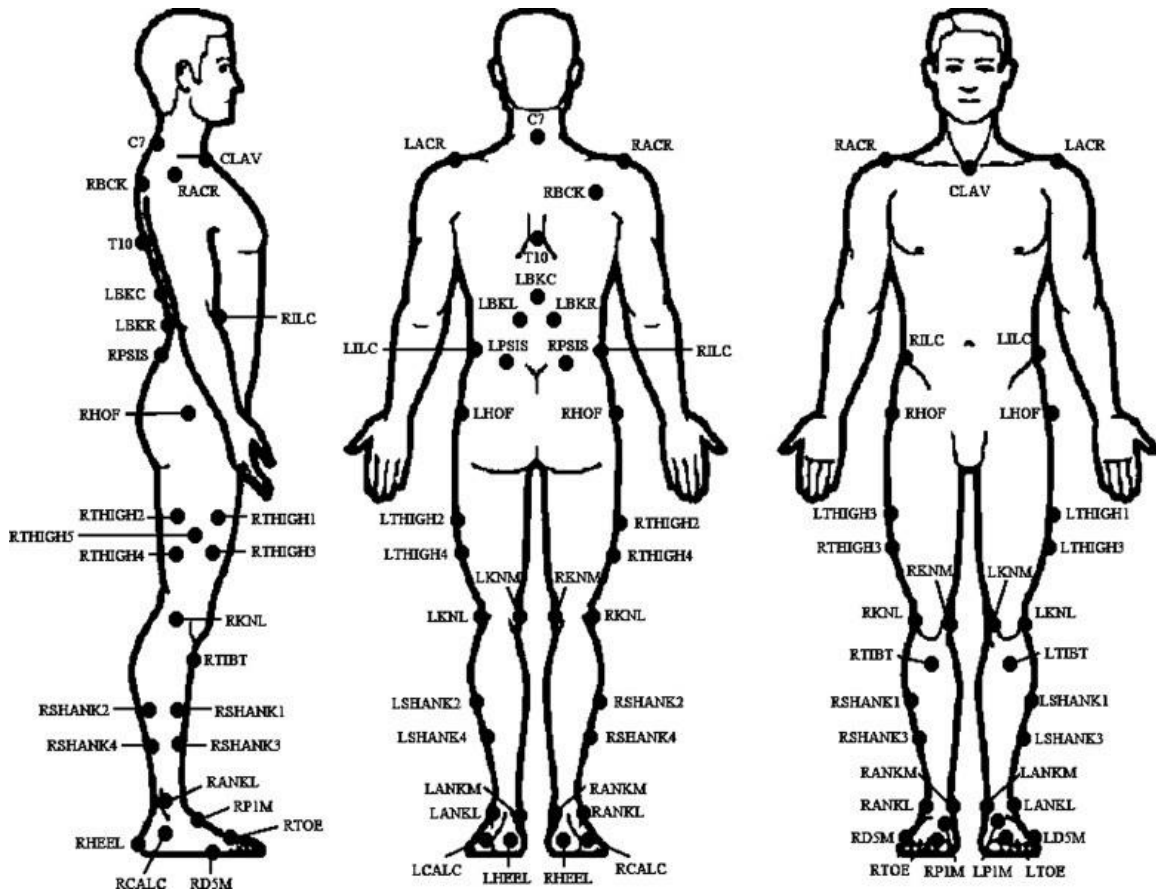
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Table Caption List

Table 1 Participant characteristics

Table 2 Peak mean ($\pm sd$) joint reaction forces during gait for baseline, lateral trunk lean, medial knee thrust, and toe-in gait for the first and second peak in the medial compartment and the first and second peak in the lateral compartment

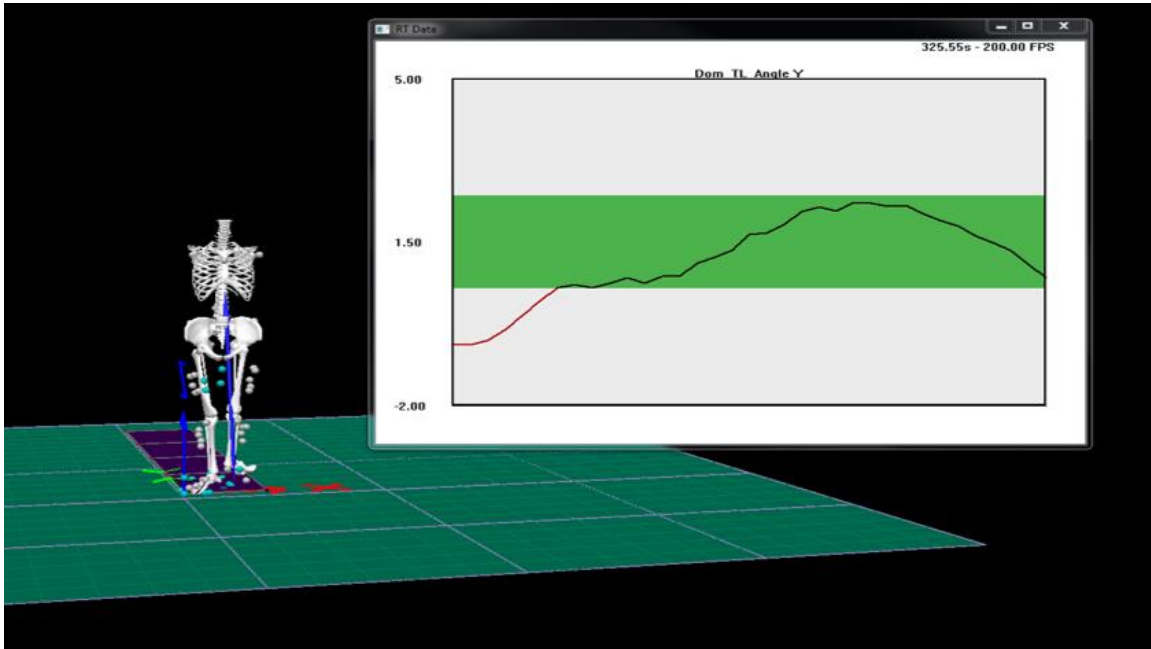
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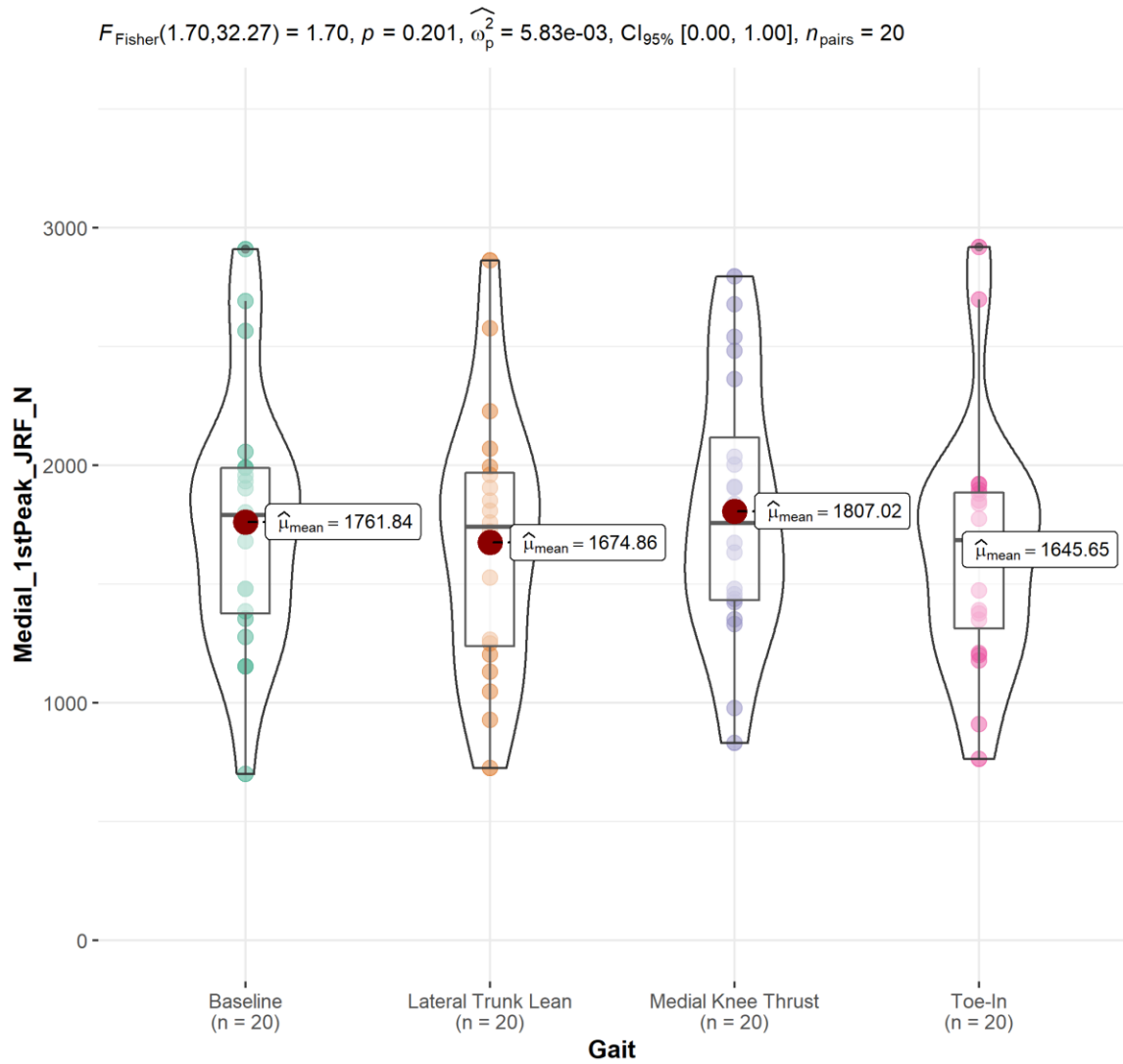
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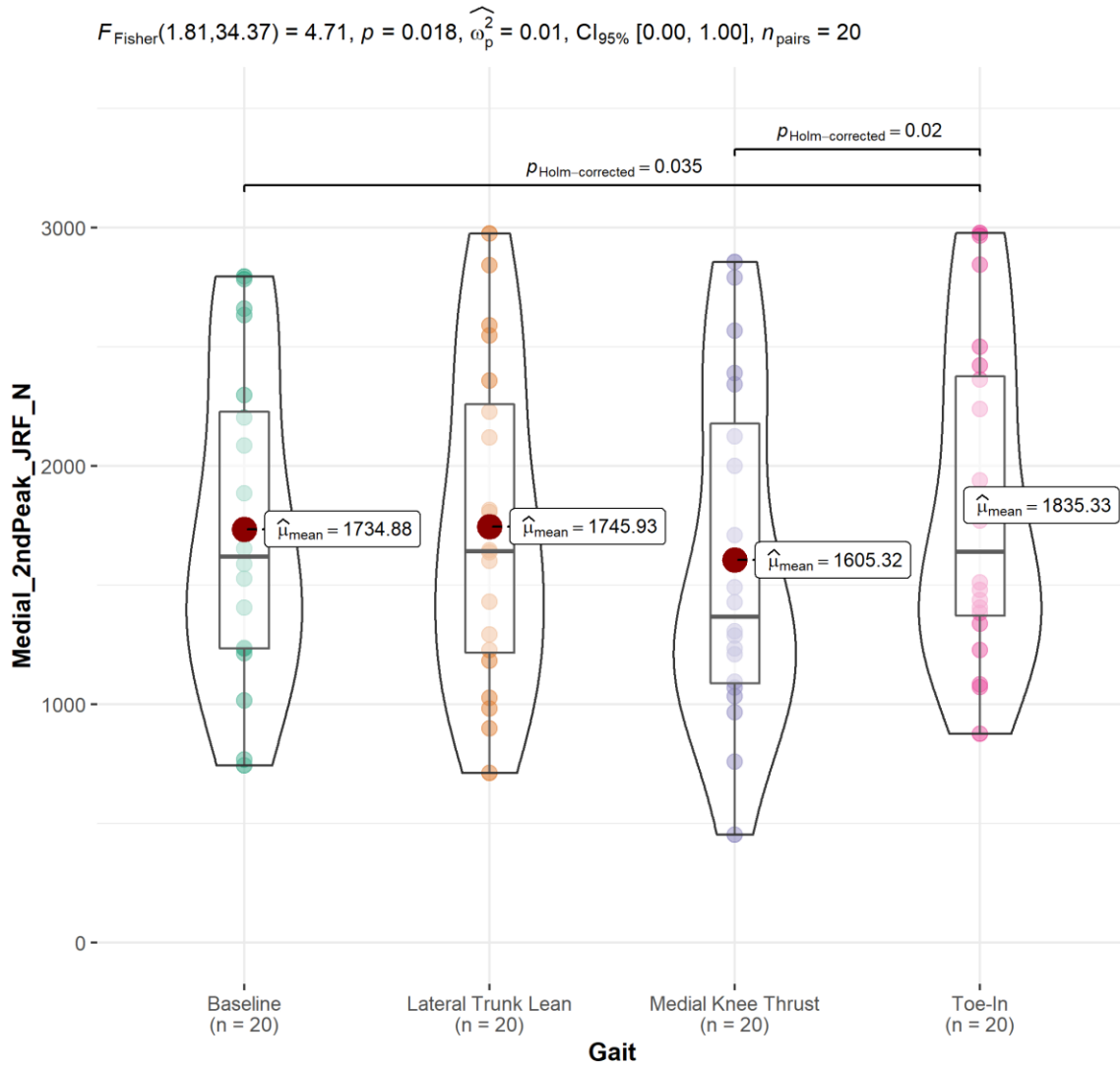
Fig. 2 Example of visual feedback graph provided to participants that was projected onto the laboratory wall during each trial



Pairwise test: **Student's t-test**; Comparisons shown: **only significant**

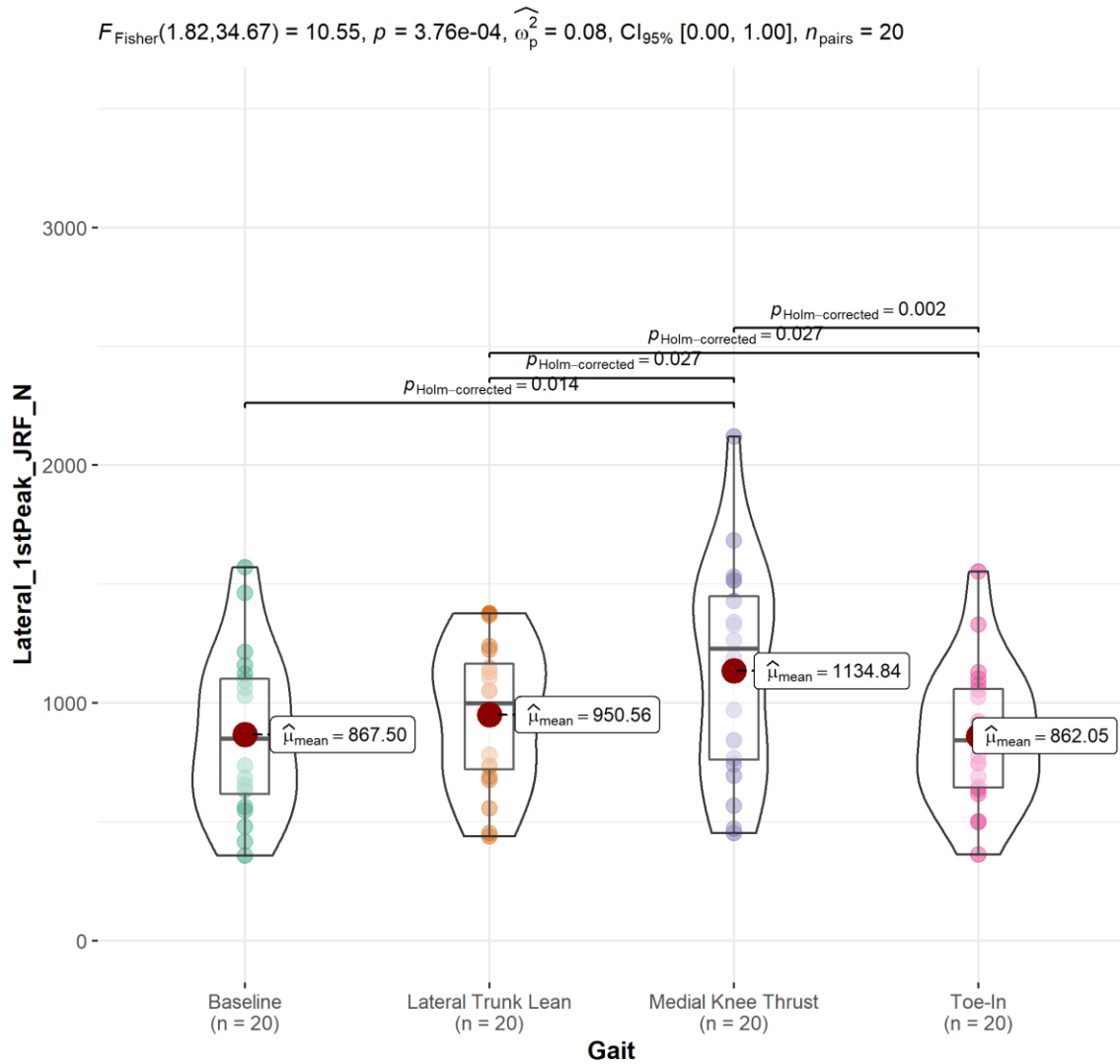
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Fig. 3 Repeated measures ANOVA for the mean joint reaction force (N) in the 1st peak in the medial compartment for baseline, lateral trunk lean, medial knee thrust, and toe-in gait



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Fig. 4 Repeated measures ANOVA for the mean joint reaction force (N) in the 2nd peak in the medial compartment for baseline, lateral trunk lean, medial knee thrust, and toe-in gait



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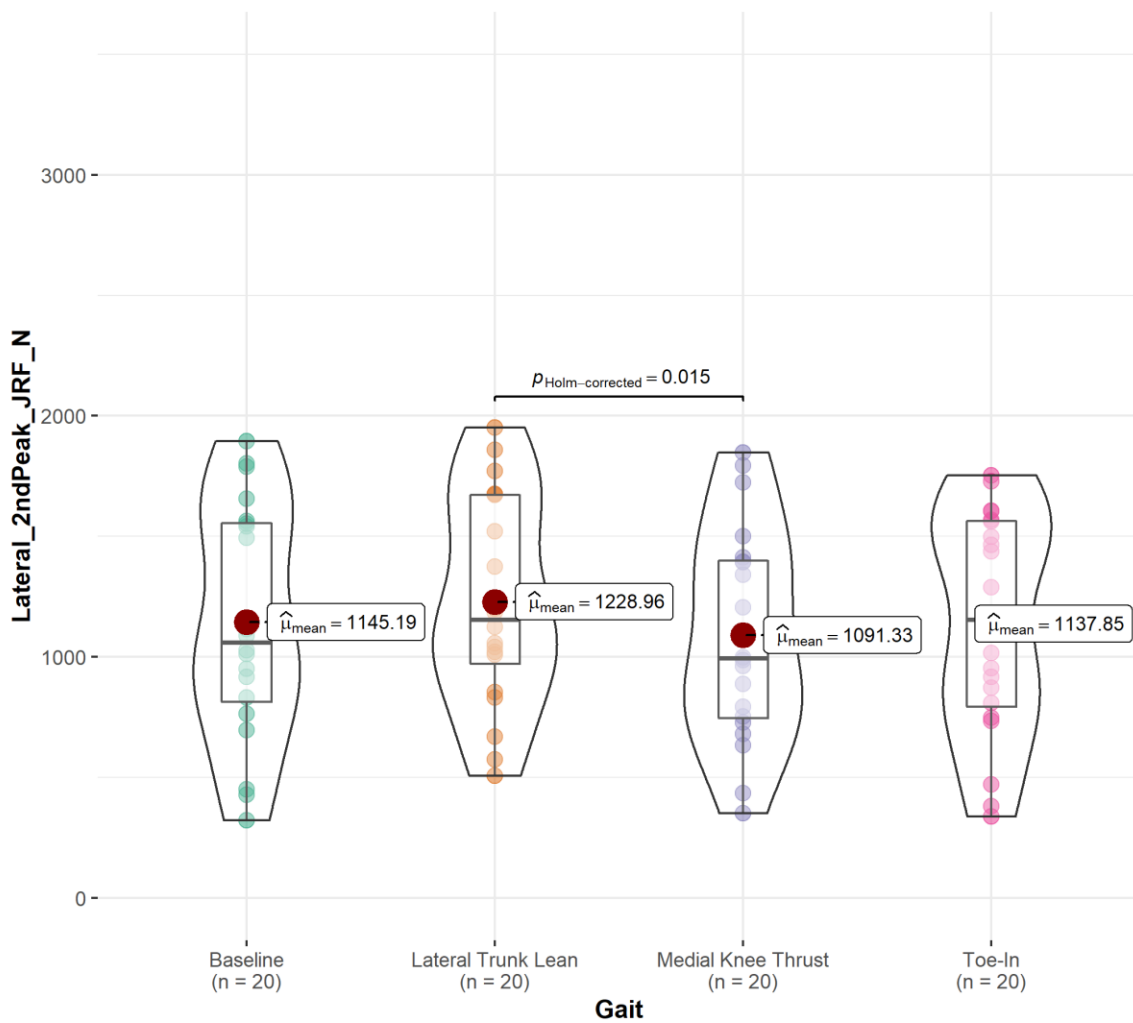
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Fig. 5 Repeated measures ANOVA for the mean joint reaction force (N) in the 1st peak in the lateral compartment for baseline, lateral trunk lean, medial knee thrust, and toe-in gait

Pairwise test: **Student's t-test**; Comparisons shown: **only significant**

$$F_{\text{Fisher}}(2.45, 46.54) = 3.81, p = 0.022, \hat{\omega}_p^2 = 8.51\text{e-}03, \text{CI}_{95\%} [0.00, 1.00], n_{\text{pairs}} = 20$$

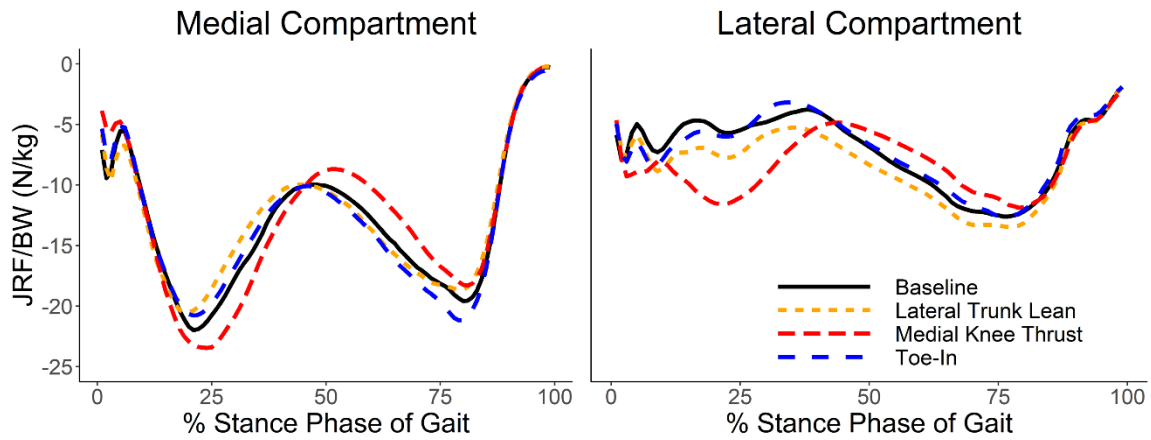


Pairwise test: **Student's t-test**; Comparisons shown: **only significant**

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Fig. 6 Repeated measures ANOVA for the mean joint reaction force (N) in the 2nd peak in the lateral compartment for baseline, lateral trunk lean, medial knee thrust, and toe-in gait

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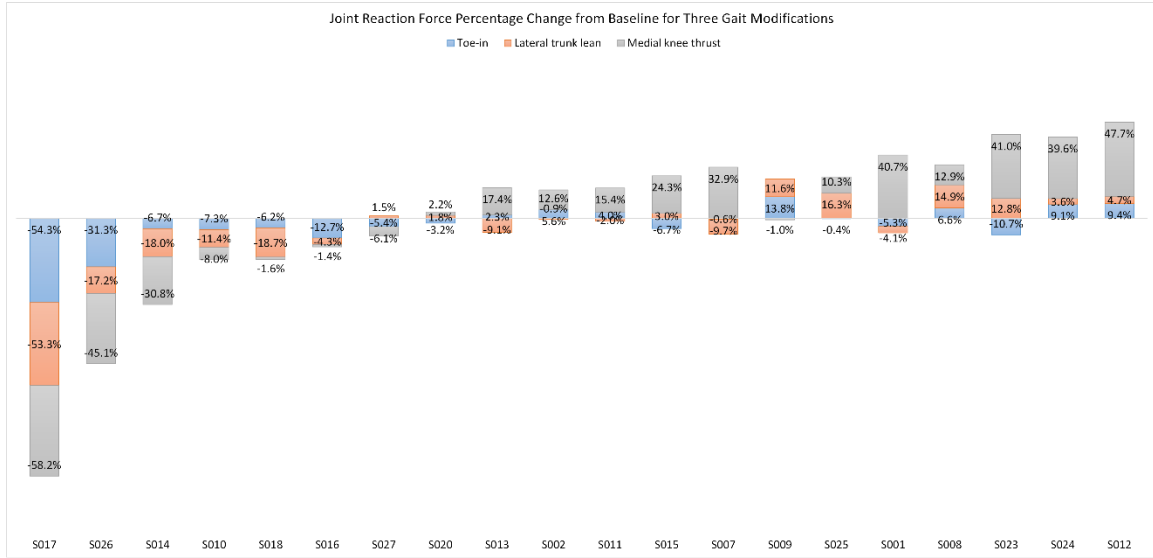
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Fig. 7 Mean joint reaction force (normalized by body weight) in the medial and lateral knee compartments for baseline, lateral trunk lean, medial knee thrust, and toe-in gait



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Fig. 8 Percentage reduction in joint reaction force from baseline values, by individual participant, for toe-in gait, lateral trunk lean, and medial knee thrust

778 **Table 1 Participant characteristics**
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Characteristics	Mean (<i>sd</i>)
<i>N</i>	20
Gender (<i>M/F</i>)	12/8
Dominant Limb (<i>R/L</i>)	18/2
Age (years)	26.7 (4.7)
Height (<i>m</i>)	1.75 (0.1)
Mass (<i>kg</i>)	73.4 (12.4)
BMI	23.9 (3.0)

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781 **Table 2 Peak mean ($\pm sd$) joint reaction forces during gait for baseline, lateral trunk**
 782 **lean, medial knee thrust, and toe-in gait for the first and second peak in the medial**
 783 **compartment and the first and second peak in the lateral compartment**
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	Med_1stPeak_FY Mean ($\pm sd$)	Med_2ndPeak_FY Mean ($\pm sd$)	Lat_1stPeak_FY Mean ($\pm sd$)	Lat_2ndPeak_FY Mean ($\pm sd$)
Baseline	1761.84 (± 166.40)	1734.88 (± 170.65)	867.50 (± 122.46)	1145.19 (± 88.48)
LTL	1674.86 (± 185.31)	1745.93 (± 228.67)	950.56 (± 164.65)	1228.96 (± 143.37)
MKT	1807.02 (± 249.57)	1605.32 (± 245.75)	1134.84 (± 183.07)	1091.33 (± 161.62)
TIG	1645.65 (± 159.61)	1835.33 (± 182.29)	862.05 (± 107.33)	1137.85 (± 100.73)

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