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1 **PERSONALISED 3D KNEE COMPLIANCE FROM CLINICALLY VIABLE**

2 **KNEE LAXITY MEASUREMENTS: A PROOF OF CONCEPT EX VIVO**

3 **EXPERIMENT**

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32 **Keywords:** Knee stiffness; compliance matrix; laxity; clinical tests, ligament injury.

33

34 **Abstract**

35 Personalised information of knee mechanics is increasingly used for guiding knee
36 reconstruction surgery. We explored use of uniaxial knee laxity tests mimicking Lachman
37 and Pivot-shift tests for quantifying 3D knee compliance in healthy and injured knees. Two
38 healthy knee specimens (males, 60 and 88 years of age) were tested. Six-degree-of-freedom
39 tibiofemoral displacements were applied to each specimen at 5 intermediate angles between
40 0° and 90° knee flexion. The force response was recorded. Six-degree-of-freedom and
41 uniaxial tests were repeated after sequential resection of the anterior cruciate, posterior
42 cruciate and lateral collateral ligament. 3D knee compliance (C_{6DOF}) was calculated using
43 the six-degrees-of-freedom measurements for both the healthy and ligament-deficient knees
44 and validated using a leave-one-out cross-validation. 3D knee compliance (C_{CT}) was also
45 calculated using uniaxial measurements for Lachman and Pivot-shift tests both conjointly and
46 separately. C_{6DOF} and C_{CT} matrices were compared component-by-component and using
47 principal axes decomposition. Bland-Altman plots, median and 40th-60th percentile range
48 were used as measurements of bias and dispersion. The error on tibiofemoral displacements
49 predicted using C_{6DOF} was < 9.6 % for every loading direction and after release of each
50 ligament. Overall, there was good agreement between C_{6DOF} and C_{CT} components for both
51 the component-by-component and principal component comparison. The dispersion of
52 principal components (compliance coefficients, positions and pitches) based on both uniaxial
53 tests was lower than that based on single uniaxial tests. Uniaxial tests may provide
54 personalised information of 3D knee compliance.

55

56 1 Introduction

57 Knee reconstruction surgery postoperative outcome is determined by a variety of
58 surgery variables and their interaction specific to each patient [1]. As such, personalised
59 models of knee mechanics are increasingly used for pre- and post-surgical assessment of knee
60 function and for guiding the intra-operative decision-making in knee replacement and
61 ligament reconstruction surgery [2]. For example, personalized models based on the healthy
62 knee can be used to restore loading patterns in passive restraints in the contra-lateral injured
63 knee whereas personalized models of the injured knee may inform the decision process for
64 proper management of knee injuries. However, generating personalised models is complex as
65 it requires combining information of subject's anatomy from medical images [3,4], knee
66 motion and material properties [5] or performing complex six-degree-of-freedom (6DOF)
67 tests for determining 3D knee compliance [6,7]. In this study, we explore the use of two
68 different uniaxial knee laxity tests for determining the 3D knee compliance in healthy and
69 injured knees.

70 Personalised knee models can provide the contribution to knee function of each knee
71 structure. For example, ex vivo knee laxity measurements have been used to calibrate
72 ligament stiffness in models of native [8] and artificial knees [9]. Some authors combined
73 personalised knee anatomy from Magnetic Resonance Images and ex vivo knee laxity
74 measurements [3,4] while others modelled knee mechanics of knee specimens using both
75 imaging and complex in vitro experiments [2,5]. In a previous study by Lamberto et al. [6]
76 we have developed a protocol for measuring ex vivo the 3D knee compliance matrix of the
77 tibiofemoral joint and demonstrated the feasibility of embedding 3D knee compliance in
78 models of human motion for studying knee mechanics in vivo [7]. However, determination of

79 3D knee compliance requires complex experimental protocols that are impractical in the
80 clinic [6].

81 Arthrometers are clinically viable solutions for providing objective measurements of
82 knee laxity along a single direction of movement [1,10,11]. For example, the integrity of the
83 anterior cruciate ligament (ACL) can be assessed using measurements of tibiofemoral motion
84 while applying an anterior tibial force of 134 N at 20° – 30° knee flexion (Lachman test,
85 [12]). The Pivot-shift test provides both information of ACL integrity and general knee
86 stability by applying to the knee a medial force while the knee is kept 30° – 40° flexed and
87 20° internally rotated [13]. Establishing a relationship between clinical knee laxity tests (e.g.,
88 Lachman and Pivot-shift) and 3D knee compliance requires to first establish the relationship
89 between the two uniaxial measurements and the 3D knee compliance matrix and then to
90 assess the tools that could be used to obtain the measurements required when in the clinics.
91 Here, we tackled the first step and hypothesised that in vitro measurements of knee
92 compliance obtained using simple uniaxial tests mimicking Lachman and Pivot-shift tests can
93 be used to determine, conjointly or in isolation, the 3D knee compliance in healthy and
94 injured knees.

95 The aim of this study was to calculate and compare 3D knee compliance using full
96 6DOF and uniaxial experiments mimicking Lachman and Pivot-Shift tests in healthy and
97 ligament-deficient knees. We developed a protocol for measuring 3D knee compliance using
98 the hexapod robot by Ding et al. [14]. 3D knee compliance matrices based on full 6DOF
99 experiments were calculated, validated using leave-one-out cross validation, and compared to
100 corresponding matrices based on uniaxial experiments using bias and dispersion indicators.

101 **Materials and Methods**

102 Experimental procedure

103 Two fresh-frozen right knees from two male donors (age at death: 60 and 88; body
104 weight: 91 kg for both donors; height: 178 and 183 cm) were obtained from a body donation
105 program (Science Care, Phoenix, USA). Ethics clearance was obtained from the institutional
106 Ethics Committee at Flinders University. Ligaments, cartilage and menisci were found intact
107 on MRI inspection [15] and surgical inspection.

108 Specimens were thawed 24 hours at room temperature. Tibia, fibula and femur were
109 cut at mid shaft and soft tissues removed 15 cm above and below the femoral epicondyles.
110 Tibiofemoral joint coordinate system was defined according to the work of Grood and Suntay
111 [16], assuming coincident tibial and femoral coordinate systems at full knee extension. The
112 tibia was cemented in an aluminium cup by aligning the tibial plateau to the cup's base. Tibia
113 and fibula were rigidly fixed using a cortical screw. The femur was fixed to the specimen
114 holder using a transfix pin through the femoral diaphysis and four cortical screws.

115 The femur's specimen holder was mounted on the hexapod robot (Figure 1) through a
116 screw mechanism. The vertical distance between the bottom and top plate, the knee centre
117 (midpoint between medial and lateral femoral epicondyles) and the x-, y- and z- offset were
118 used for mounting the knee specimen, ensuring alignment of knee and hexapod robot
119 coordinate systems. Two different reference configurations were defined using an auxiliary
120 device (Figure 2) for testing the specimens over 90° knee flexion despite the relatively small
121 range of motion of the hexapod robot (approximately $\pm 25^\circ$). Firstly, the knee specimen
122 flexed at 15° was fixed on the hexapod device, ensuring the knee sagittal plane and trans-
123 epicondylar axis were aligned to the device planes and tested at 0°, 15°, 30° knee flexion
124 angle. Secondly, the knee was flexed at 75° was similarly fixed to the hexapod device and
125 tested at 60° and 90° knee flexion angle (Figure 2).

126 The force response to controlled tibiofemoral displacement and rotation (position-
127 control) about each of the six axes was measured. The neutral tibiofemoral position at each
128 knee flexion angle was determined by defining the knee flexion path offering minimal
129 resistance using a hybrid control algorithm built-in the hexapod control system [14]. Positive
130 and negative displacements and rotations were applied from the neutral tibiofemoral position
131 at 0.33 mm/s and 0.33°/s, respectively. Axial translations were run at 0.10 mm/s. The
132 displacement direction was reversed when knee stiffness, displacement and load exceeded,
133 respectively, 20% increase from linear force response, ± 10 mm medial and anterior
134 displacement, ± 5 mm proximal displacement, $\pm 10^\circ$ rotation, 200 N and 20 Nm.

135 The force-control tests mimicked the uniaxial Lachman [17] and Pivot-Shift tests [13]
136 using an adaptive velocity-based load control algorithm [18]. An anterior tibial force of ± 100
137 N was used for mimicking the Lachman test. A ± 10 Nm moment about the abduction and
138 internal rotation axis was applied to mimic the Pivot-Shift test.

139 Position-control (6DOF) and uniaxial force-control experiments were repeated after
140 sequential resection of anterior cruciate, posterior cruciate and lateral collateral ligaments by
141 a single experienced orthopaedic surgeon. Anterior and posterior cruciate ligaments were
142 released through an anterior incision and patella tendon split (Figure 1c) while the final
143 release of the lateral collateral ligament was completed through a lateral incision. Each
144 incision was sutured after resection. The force threshold causing the displacement direction to
145 reverse for the 6DOF tests was reduced by 10% – 20% after each resection.

146 The compliance matrix

147 The compliance matrix C_{6DOF} was determined using position-control measurements
148 and an earlier work [6]. Displacement and load matrices were:

$$[\Delta X] = [X - X_0] = [X_{medial}^{+/-} X_{anterior}^{+/-} X_{axial}^{+/-} X_{adduction}^{+/-} X_{internal}^{+/-}] \quad (1)$$

$$[\Delta F] = [F - F_0] = [F_{medial}^{+/-} F_{anterior}^{+/-} F_{axial}^{+/-} F_{adduction}^{+/-} F_{internal}^{+/-}] \quad (2)$$

149 where X_0 and F_0 represent the generalised displacement and force vector for each test; $X_i^{+/-}$
 150 contains linear and angular displacements in the joint coordinate systems; $F_i^{+/-}$ contains the
 151 forces and moments. The coefficient of determination was calculated for studying the
 152 linearity of the force-displacement relationship. The compliance matrix was calculated
 153 (Matlab, The MathWorks, USA) by minimizing the difference between measured and
 154 predicted displacements. The objective function $J(C)$ was formulated as:

$$155 \quad J(C) = \|[C_{6DOF}][\Delta F] - [\Delta X]\|_{mm} + w \cdot \|[C_{6DOF}][\Delta F] - [\Delta X]\|_{rad} \quad (3)$$

156 where the first term represents the norm of the error on translational components and the
 157 second term represents the norm of error on rotational components. The weight w was used
 158 for evenly weight translational and rotational errors and assumed equal to the femoral inter-
 159 epicondyles distance. The compliance matrix C_{ct} was similarly calculated using the Lachman
 160 and Pivot-shift tests conjointly and separately. C_{ct} and C_{6DOF} matrices were also
 161 decomposed using principal axis decomposition, thus providing an equivalent system of two
 162 orthogonal sets of three torsional and three screw springs defined by compliance coefficients,
 163 position, pitches and directions [19].

164 The model accuracy was quantified using a leave-one-out cross-validation. Datasets
 165 of ΔX and ΔF were randomly divided in five groups, four for training and one for validation.
 166 Components in the original C_{ct} and C_{6DOF} matrices were grouped into translational, rotational
 167 and coupled movements components. Components in the decomposed matrices were grouped
 168 into compliance coefficients, directions, positions and pitches.

169 Tibiofemoral translations and rotations were predicted using C_{6DOF} matrices. The
170 error was calculated as the difference between predicted ($D_{predicted}$) and measured
171 tibiofemoral displacement ($D_{measured}$). The root mean square error was calculated and
172 normalized by the displacement range:

$$173 \quad NRMSE = \frac{RMSE(D_{predicted}-D_{measured})}{D_{max}-D_{min}} * 100 \quad (4)$$

174 The NRMSE's mean and standard deviation were calculated for each specimen and test.

175 Bland-Altman plots, median and 40th – 60th percentile range were used as measures of bias
176 and dispersion for comparing C_{ct} and C_{6DOF} matrices.

177 **2 Results**

178 The coefficient of determination calculated from the recorded force and displacement
179 was systematically above 0.9. The tibiofemoral displacement error committed by matrix
180 C_{6DOF} was below 9.6% for each specimen, ligaments' integrity and loading direction. The
181 normalised error was $NRMSE = 9.6\% \pm 1.9\%$ for translations and $NRMSE = 6.1\% \pm 0.7\%$
182 for rotations in one specimen and $NRMSE = 8.4\% \pm 1.6\%$ (translations) and $NRMSE = 6.7\%$
183 $\pm 1.1\%$ (rotations) for the other.

184 The compliance matrix C_{ct} and C_{6DOF} showed a good component-by-component
185 agreement both in the knee joint space and after principal component decomposition (Figure
186 3 – 4). In the knee joint space, similar bias and dispersion were found using both uniaxial
187 tests and the Lachman-like test only. The bias was below 0.00473 ± 0.00062 mm\N for
188 translations, 0.00347 ± 0.00099 N⁻¹ for rotations and 0.00010 ± 0.00005 N⁻¹ × mm⁻¹ for
189 coupled movements. Using the Pivot-shift tests only, bias and dispersion were higher,
190 particularly for translation; the bias (0.01763 mm\N) was more than three times higher than

191 that calculated using both uniaxial tests while dispersion ($-0.00523 \text{ mm}\backslash\text{N}$) was more than
192 eight times higher than the dispersion calculated using both uniaxial tests. Principal
193 components showed comparable bias and dispersion using Lachman- and Pivot-shift-like
194 tests separately, showing a moderately lower dispersion of the compliance coefficients,
195 positions and pitches but not of directions in the Pivot-Shift test only matrix. A general
196 further reduction of bias and dispersion of compliance coefficients, positions and pitches but,
197 again, not for directions, was observed using both uniaxial tests (Figure 4 and Table 2).

198 **Discussion**

199 We proposed a novel protocol for 6DOF testing of human knees, calculating 3D knee
200 compliance matrices using 6DOF experiments and simpler uniaxial tests mimicking Lachman
201 and Pivot-Shift tests. We found that combined uniaxial tests mimicking Lachman and Pivot-
202 shift tests can best provide information of compliance coefficients, position and pitches along
203 the principal axes of the 3D tibiofemoral compliance matrix, showing higher dispersion of
204 their directions. Therefore, 3D knee compliance can be obtained from a reduced number of
205 accurate uniaxial measurements of knee laxity.

206 The compliance matrix C_{6DOF} , calculated using full 6DOF experiments, predicted
207 tibiofemoral displacements and rotations within 9.6% error for both specimens in intact and
208 ligament-deficient conditions (three ligaments completely resected). Similar results were
209 obtained during earlier work [6] using a serial manipulator, as opposed to the parallel
210 hexapod robot used in the present study, hence providing confidence on the robustness of the
211 method developed here and expanding its validity to multi ligament-deficient knees. There
212 was a good component-by-component agreement between 3D knee compliance based on
213 6DOF and uniaxial experiments (Figure 3 – 4) showing a moderate bias for each studied
214 component. Principal axes decomposition showed lower dispersion of compliance

215 coefficients, position and pitches, but not directions, when using both uniaxial tests conjointly
216 over that provided by each uniaxial test separately. Therefore, uniaxial tests mimicking
217 Lachman and Pivot-shift tests can provide information of 3D knee compliance. Principal axes
218 decomposition appears to better capture the increased level of information provided by both
219 uniaxial tests over the representation of 3D knee compliance in the knee joint space.

220 This study has limitations. Firstly, the present study shows that uniaxial tests
221 mimicking Lachman and Pivot-shift tests can be used to determine salient features of the 3D
222 knee compliance in healthy and ligament-deficient knees. Further research is required to
223 determine whether clinically available technologies (e.g., arthrometers) can provide enough
224 information for determining 3D knee compliance and ultimately guiding the clinical
225 management of knee ligament injuries. Secondly, the generality of the present conclusion is
226 limited by only two specimens used, likely resulting in a narrower range of knee compliances
227 than that in human knees. Describing knee compliance in the broader population was outside
228 the purely methodological scope of the present study. Thirdly, the sequential ligament
229 resection performed in the present study may not represent the complex and variable range of
230 possible knee injuries. Here, we showed that the procedure developed is robust to a range of
231 knee health conditions, from intact to ligament-deficient knees. Fourthly, the contribution to
232 3D tibiofemoral stiffness of the anterior incision and re-suture was not quantified
233 independently from that of ligament resection. However, ligament are the major soft-tissue
234 constraints of tibiofemoral motion and changes of knee stiffness due to the anterior incision
235 and its subsequent suture are likely smaller than changes of knee stiffness due to each
236 ligament resection.

237 In conclusion, we developed a method for determining 3D knee compliance in healthy
238 and ligament deficient knees using uniaxial tests mimicking common Lachman and Pivot-

239 shift tests. This may support the development of clinically-viable procedures for the analysis
240 of knee mechanics in specific patients.

241 **Conflicts of Interest:**

242 None.

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245 Research Council (DP180103146; FT180100338); and the UK EPSRC (MultiSim project,
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247 **Ethical Approval:**

248 Ethics clearance was obtained from the institutional Ethics Committee at Flinders
249 University (SBREC 6832).

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315

316

317 **TABLES**
 318

| Components | | Units | Both tests ($\times 10^4$) | Lachman test ($\times 10^4$) | Pivot-shift ($\times 10^4$) |
|-------------------|--|------------------------------------|--|--|---|
| Translation | | mm\N | 47.3 (-6.2) | 36.7 (2.2) | 176.3 (-52.3) |
| Rotation | | N ⁻¹ | 34.7 (9.9) | 13.7 (-2.8) | 24.8 (-23.2) |
| Coupling | | N ⁻¹ × mm ⁻¹ | 0.6 (-0.3) | 1.0 (-0.5) | 1.8 (1) |

319 Table 1 – Bias (median) and dispersion (40th - 60th percentile range) of the component-by-
 320 component comparison of C_{CT} and C_{6DOF}. Translational, rotational and coupled components are
 321 grouped together. Dispersion is reported in brackets.

322

| Components | | Units | Both tests ($\times 10^4$) | Lachman test ($\times 10^4$) | Pivot-shift ($\times 10^4$) |
|-------------------------|-------------------|-----------------|--|--|---|
| Compliance coefficients | Screw springs | mm\N | 11.5 (-0.2) | 19.8 (-7.7) | 22.6 (-0.4) |
| | Torsional springs | N ⁻¹ | 74.1 (14.6) | 43.5 (23.3) | 217.7 (9.4) |
| Directions | Screw springs | | 2035.9 (1117.8) | 1359.3 (47.4) | 2395.9 (-543.8) |
| | Torsional springs | | 2319 (-1204.9) | 835.7 (40.4) | 1513.1 (-31.3) |
| Positions | | mm | 69.8 (-2.2) | 131.0 (12.9) | 168.4 (24.4) |
| Pitches | | mm | 76.8 (10.5) | 91.2 (-22) | 269.1 (88.9) |

323 Table 2 – Bias (median) and dispersion (40th - 60th percentile range) of C_{CT}'s principal
 324 components. Dispersion is reported in brackets.

325

326 **FIGURE CAPTIONS**

327 Figure 1 – From the left-hand side: (a) frontal view of the hexapod robot and the
328 screw mechanism hosting a dummy femoral and tibial component; (b) detail of one knee
329 specimen mounted on the hexapod robot through the screw mechanism; and (c) the anterior
330 incision used for resecting the cruciate ligaments.

331 Figure 2 – From the left-hand side: (a) the knee alignment rig assembled with the screw
332 mechanism, (b) the first reference configuration (i.e., 15° knee flexion), and (c) the second
333 reference configuration (i.e., 75° knee flexion).

334 Figure 3 - Bland-Altman plot for the component-by-component comparison of
335 C_{CT} and C_{6DOF} , reporting the 2.5th and 97.5th percentiles as limits of agreement.

336 Figure 4 - Bland-Altman plot for the comparison of C_{CT} and C_{6DOF} principal
337 components (CC: Compliance coefficients; S_{Sp} : Screw spring; T_{Sp} : Torsional spring),
338 reporting the 2.5th and 97.5th percentiles as limits of agreement.

318 **TABLES**
 319

| Components | | Units | Both tests ($\times 10^4$) | Lachman test ($\times 10^4$) | Pivot-shift ($\times 10^4$) |
|-------------------|--|------------------------------------|--|--|---|
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| Rotation | | N ⁻¹ | 34.7 (9.9) | 13.7 (-2.8) | 24.8 (-23.2) |
| Coupling | | N ⁻¹ × mm ⁻¹ | 0.6 (-0.3) | 1.0 (-0.5) | 1.8 (1) |

320 Table 1 – Bias (median) and dispersion (40th - 60th percentile range) of the component-by-
 321 component comparison of C_{CT} and C_{6DOF}. Translational, rotational and coupled components are
 322 grouped together. Dispersion is reported in brackets.

323

| Components | | Units | Both tests ($\times 10^4$) | Lachman test ($\times 10^4$) | Pivot-shift ($\times 10^4$) |
|-------------------------|-------------------|-----------------|--|--|---|
| Compliance coefficients | Screw springs | mm\N | 11.5 (-0.2) | 19.8 (-7.7) | 22.6 (-0.4) |
| | Torsional springs | N ⁻¹ | 74.1 (14.6) | 43.5 (23.3) | 217.7 (9.4) |
| Directions | Screw springs | | 2035.9 (1117.8) | 1359.3 (47.4) | 2395.9 (-543.8) |
| | Torsional springs | | 2319 (-1204.9) | 835.7 (40.4) | 1513.1 (-31.3) |
| Positions | | mm | 69.8 (-2.2) | 131.0 (12.9) | 168.4 (24.4) |
| Pitches | | mm | 76.8 (10.5) | 91.2 (-22) | 269.1 (88.9) |

324 Table 2 – Bias (median) and dispersion (40th - 60th percentile range) of C_{CT}'s principal
 325 components. Dispersion is reported in brackets.

326

327 **FIGURE CAPTIONS**

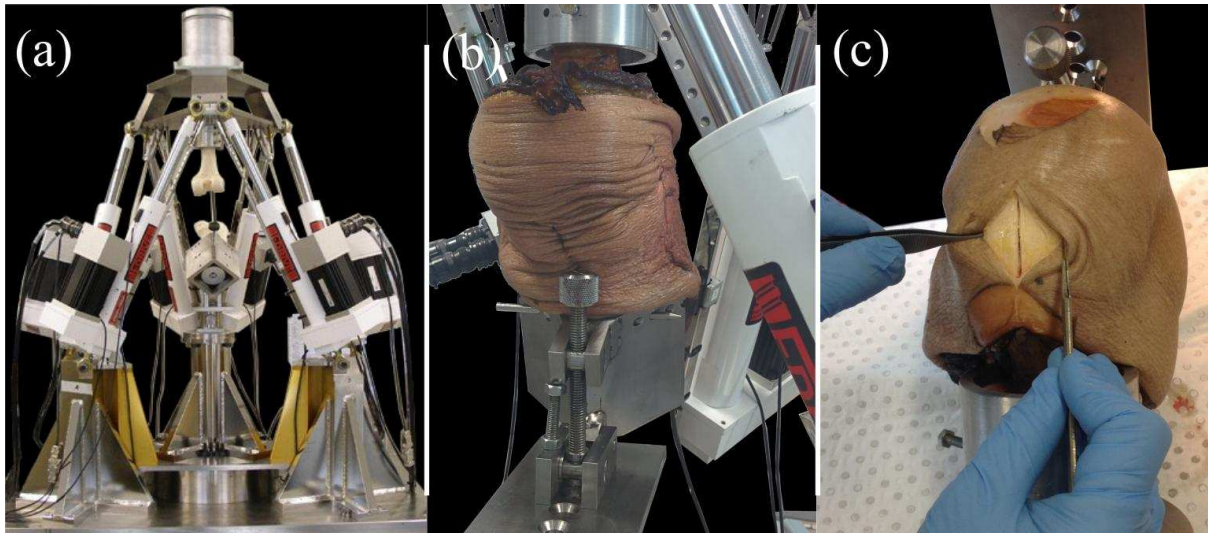
328 Figure 1 – From the left-hand side: (a) frontal view of the hexapod robot and the
329 screw mechanism hosting a dummy femoral and tibial component; (b) detail of one knee
330 specimen mounted on the hexapod robot through the screw mechanism; and (c) the anterior
331 incision used for resecting the cruciate ligaments.

332 Figure 2 – From the left-hand side: (a) the knee alignment rig assembled with the screw
333 mechanism, (b) the first reference configuration (i.e., 15° knee flexion), and (c) the second
334 reference configuration (i.e., 75° knee flexion).

335 Figure 3 - Bland-Altman plot for the component-by-component comparison of
336 C_{CT} and C_{6DOF} , reporting the 2.5th and 97.5th percentiles as limits of agreement.

337 Figure 4 - Bland-Altman plot for the comparison of C_{CT} and C_{6DOF} principal
338 components (CC: Compliance coefficients; S_{Sp} : Screw spring; T_{Sp} : Torsional spring),
339 reporting the 2.5th and 97.5th percentiles as limits of agreement.

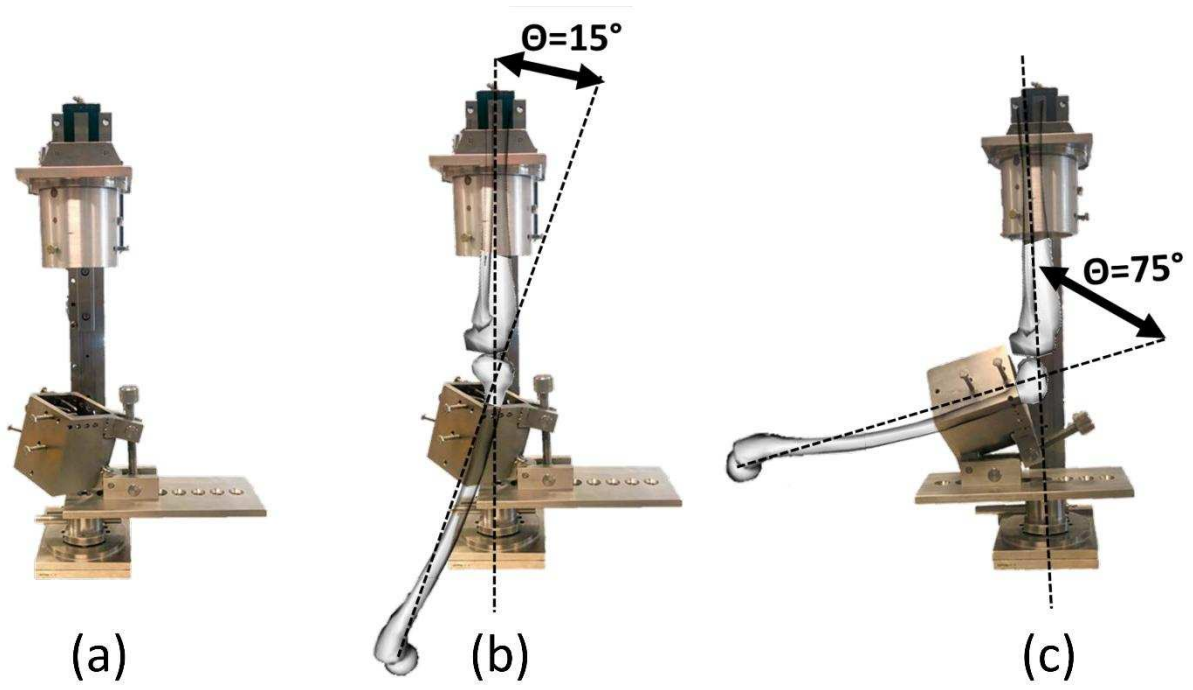
1 Figure 1



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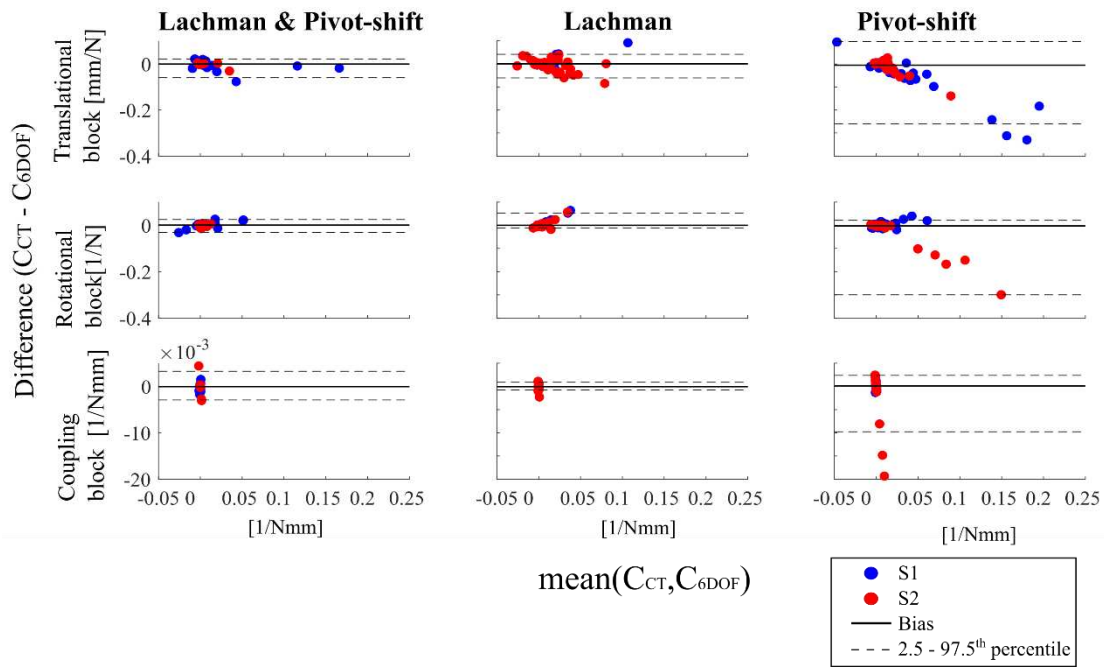
4 Figure 2



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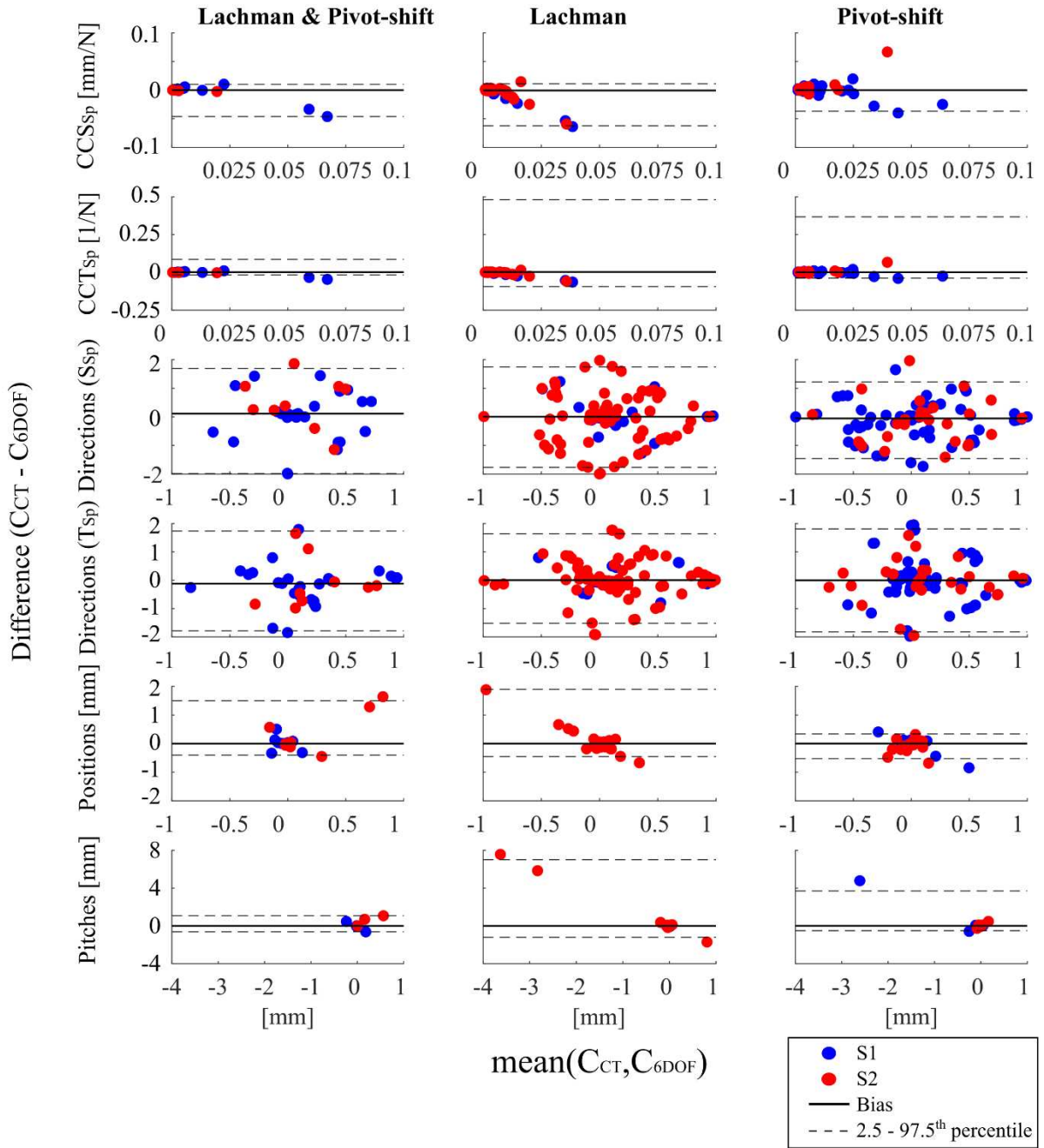
7 Figure 3



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Figure 4



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