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ACL deficiency influences medio-lateral tibial alignment and knee varus-valgus during in vivo activities

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(Article begins on next page)

1 **ACL deficiency influences medio-lateral tibial**
2 **alignment and knee varus—valgus during in-vivo**
3 **activities**

4 **Abstract**

5 **Purpose:** The role of the anterior cruciate ligament (ACL) in
6 knee biomechanics in vivo and under weight-bearing is still
7 unclear. The purpose of this study was to compare the
8 tibiofemoral kinematics of ACL—deficient knees to healthy
9 contralateral ones during the execution of weight-bearing
10 activities.

11 **Methods:** Eight patients with isolated ACL injury and
12 healthy contralateral knees were included in the study.
13 Patients were asked to perform a single step forward and a
14 single leg squat first with the injured knee and then with the
15 contralateral one. Knee motion was determined using a

16 validated model-based tracking process that matched
17 subject-specific MRI bone models to dynamic biplane
18 radiographic images, under the principles of Roentgen
19 stereophotogrammetric analysis (RSA). Data processing was
20 performed in a specific software developed in Matlab.

21 **Results:** Statistically significant differences ($p<0.05$) were
22 found for single leg squat along the frontal plane: ACL-
23 deficient knees showed a more varus angle, especially at the
24 highest knee flexion angles (40-50° on average), compared
25 to the contralateral knees. Furthermore, ACL-deficient knees
26 showed tibial medialization along the entire task, while
27 contralateral knees were always laterally aligned. This
28 difference became statistically relevant ($p<0.05$) for knee
29 flexion angles included between 0° and about 30°.

30 **Conclusion:** ACL-deficient knees showed an abnormal
31 tibial medialization and increased varus angle during single
32 leg squat when compared to the contralateral knees. These
33 biomechanical anomalies could cause a different force
34 distribution on tibial plateau, explaining the higher risk of
35 early osteoarthritis in ACL deficiency. The clinical relevance
36 of this study is that also safe activities used in ACL
37 rehabilitation protocols are significantly altered in ACL
38 deficiency.

39 **Level of evidence:** Level III

40 **Keywords:** Anterior cruciate ligament, Knee kinematics, In
41 vivo, Single leg squat, Biplane radiography

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64 **Introduction**

65 The role of anterior cruciate ligament (ACL) in knee
66 kinematics has been largely investigated. ACL function as a
67 primary restraint of the anterior tibial displacement in static
68 conditions is widely accepted, like its probable role in acting
69 like a secondary restraint of internal tibial rotation [1, 5, 8–
70 11, 17–19, 24, 31]. The relevance of biomechanical studies
71 and the importance of their constant technological
72 improvement derives from the necessity of a better
73 comprehension of mechanisms that lead to an improved risk
74 of osteoarthritis in patients affected by ACL deficiency [1, 2,
75 5, 6, 9, 10, 14, 18, 23, 33].

76 In particular, the comprehension of how the lack of ACL
77 modifies knee biomechanics not only in vivo and
78 dynamically, but also under weight-bearing conditions, is

79 crucial to gain information as close as possible to what
80 happens in daily life motion.

81 Motion capture tools such as video- analysis and
82 radiostereometry are valuable tools to understand better the
83 biomechanics of the knee during common movements of
84 daily and sport activities [1, 5, 8–10, 15, 18, 26, 33]. The
85 main limits of these methods are related to their accuracy,
86 because reconstruction of joint kinematics is based on skins
87 sensors, which are affected by relevant artifacts. Double
88 fluoroscopy overcomes the previous problem, because it
89 allows studying directly bone movements through
90 radiographs' exposition of patients executing motor tasks [3,
91 4, 6, 14, 29, 33]. In this scenario, joints biomechanical
92 anomalies following distinct pathologies could be
93 investigated in a more accurate way, thanks to dynamic

94 Roentgen stereophotogrammetric analysis (RSA) [3, 4].

95 Biomechanical differences between the anterior cruciate
96 ligament-deficient (ACL_D) knees and contralateral of the
97 same subjects could be identified using a biplane
98 radiographic system. In the present study, gait and single leg
99 squat were analyzed, since the first one is a basic activity of
100 daily living and the second one is a more demanding motor
101 task, but safe and easy to perform for the patients [17, 31].

102 The aim of the present study was to identify knee
103 biomechanical anomalies following ACL rupture, during the
104 execution of in vivo under weight-bearing activities, to
105 investigate mechanisms that lead to improved risk of
106 osteoarthritis in ACL deficiency.

107 It was hypothesized that knee tibiofemoral kinematics is
108 altered after ACL tear and that the alteration probably does

109 not involve only anterior posterior laxity or internal—
110 external rotation, but also flexion—extension and medio-
111 lateral tibial alignment, as previously reported by other
112 investigators [1, 5, 9, 15, 18, 19].

113 The clinical relevance of this work is that proving a
114 significant impairment and altered patterns in gait kinematics
115 could support a wider recourse to surgery, because walking
116 is a basilar activity and its constant alteration could influence
117 knee degeneration more than sport activities, which most of
118 the people do occasionally. Moreover, an altered knee
119 kinematics in single leg squat could confirm the necessity of
120 surgery for athletes.

121

122 **Materials and methods**

123 All the patients involved in this research study signed
124 informed consent forms. This study obtained the approval
125 from the Institutional Review Board (IRB) of Rizzoli
126 Orthopaedic Institute (ID: 40/CE/US/ml—Clinical Trial
127 Gov ID: NCT02323386). This study represents the
128 secondary analysis of data collected from a prospective
129 study, aimed to evaluate the outcome of ACL reconstruction.
130 Based on the original study protocol, 62 patients were
131 included and assessed preoperatively with 1.5 T MRI
132 analysis and dynamic RSA of injured and contralateral knee.

133 The inclusion criteria for the original study were:

- 134 - Age 16–50 years._
- 135 - Complete, traumatic and unilateral ACL injury._
- 136 - No previous knee ligament reconstruction or repair._

- 137 - No concomitant posterior cruciate ligament, postero-
138 lateral corner, lateral collateral ligament or medial
139 collateral ligament lesion._
140 - Absence of mild or advanced knee osteoarthritis
141 (Kellgren–Lawrence III–IV)._

142 For the purpose of the present study, the inclusion criteria
143 were:

- 144 - Isolated ACL tear._
145 - No injury of contralateral knee._

146 Exclusion criteria were:

- 147 - Concomitant other ligamentous or meniscal injuries._
148 - Incomplete kinematic data._
149 - Unwillingness to take part in the study. _

150 From the 62 patients of the initial cohort, 10 patients
151 underwent dynamic RSA of the contralateral knee. Two

152 more patients were then excluded because of incomplete
153 kinematic data. Overall, eight patients (5 men, 3 women, 30
154 \pm 12 years old) matched the inclusion criteria and were
155 included in the study.

156

157 *Motor tasks*

158 The patients were asked to perform two motor tasks: a single
159 step and a single leg squat. The tasks were performed with
160 the ACLD limb and subsequently with the contralateral one.
161 Patients were asked to perform the tasks according to their
162 possibilities. The investigators carefully checked the initial
163 position of the foot to limit the bias caused by
164 internal—external alignment: the foot had to be aligned with
165 the ideal antero-posterior axis of the knee, thus pointing
166 forward. The acquisition was performed in a specialized

167 radiographic room. The tasks were performed three times
168 per limb, the first two to gain comfort with the experimental
169 set-up (no X-ray exposure) and the third one for data
170 acquisition (X-ray exposure).

171

172 *Data acquisition*

173 The data were collected using a radiographic set-up for
174 dynamic RSA. The device used (BI-STAND DRX 2) was
175 developed in our institute, in collaboration with ASSING
176 (ASSING Group, Rome, Italy). The specifics of the RSA
177 radiographic set-up were -analogous to the ones already
178 published in previous articles from the same study group [3,
179 4] (Figure 1A).

180 Bone models of tibia and femur were obtained from a 1.5T
181 MRI of either the affected or the contralateral knee. When

182 MRI images of the contralateral knees were not available, the
183 models were derived from a process of mirroring of the ones
184 of the affected knee and of their correspondent reference
185 systems. The radiographic images were processed in a
186 dedicated software in Matlab[®] (R2016a, MathWorks Inc.,
187 Natick, MA, USA) developed at our institute, applying
188 algorithms related to the Model-Based Dynamic RSA. A 3D
189 virtual environment was used for semi-automatic
190 segmentation of bone contours on radiographic images
191 and, subsequently, to place the bone models according to the
192 contours (Figure 1B).

193 The dynamic RSA was validated before to start the clinical
194 study. The validation protocol was based on radiograph
195 computer simulations of the radiological setup and images,
196 with different quality and noise level. The accuracy of the

197 radiological scene reconstruction and of the model position
198 was assessed according to the ISO-5725 regulation [34]. The
199 global accuracy of model positioning and orientation,
200 evaluated in terms of “trueness \pm precision”, resulted to be
201 sub-millimetric, respectively, 0.22 ± 0.46 mm and 0.26 ± 0.2
202 $^{\circ}$. Kinematics data are presented as mean \pm standard error
203 over the percentage of the task. Figure 2 shows the reference
204 systems of the tibial and femoral models in the RSA
205 software. The kinematical quantitative data for each patient,
206 in 6 degrees-of -freedom, were calculated using the Grood
207 and Suntay decomposition [13].

208 Since it was impossible to standardize the time elapsed to
209 perform the motor task by each patient, we normalized the
210 data on the percentage of the task (% task), based on specific
211 moments to determine the beginning, the middle and the end

212 (Table 1). Regarding the gait, only the stance phase was
213 taken into account.

214

215 *Statistical analysis*

216 The kinematic data were processed using Matlab. The paired
217 *t*- test was used to compare the data of the ACLD an
218 contralateral knees along each frame of the entire motor task
219 for all the parameters. Differences were considered
220 statistically significant for $p < 0.05$.

221 An a-priori power analysis was conducted, based on
222 previous studies using fluoroscopic technique to evaluate
223 knee kinematics in ACLD conditions [6, 29, 30].
224 Considering a medio-lateral translation of 2.51 ± 1.30 mm
225 for ACLD knee and of 0.89 ± 1.47 mm for contralateral knee,

226 to achieve a power of 0.8 and an alpha level of 0.05, the
227 minimum number of patients required was set to seven.

228

229 **Results**

230 *Frontal plane*

231 Regarding the joint angles and translations on the frontal
232 plane, there were statistically significant differences between
233 ACLD and contralateral knee ($p < 0.05$) (Table 2). In
234 particular, varus—valgus rotations were statistically different
235 from the 50% to the 80% of the squat (Figure 3B): ACLD
236 knee showed, on average, a more varus rotation compared to
237 the contralateral knee. Furthermore, medio-lateral
238 translations showed a more medial tibial alignment for
239 ACLD knees with respect to the frontal plane. This trend was
240 present both in the squat and in the step (Figs. 3A, -

241 4): in the squat, the difference was statistically
242 significant from 0% to 35% and from 65% to 100% of the
243 task; no statistical differences were found in the step.

244

245 *Sagittal and transverse plane*

246 Regarding sagittal and transverse plane joint angles and
247 translation, no statistical differences were found between
248 ACLD and contralateral knee kinematics along the entire
249 percentage of both motor tasks (n.s.).

250

251 **Discussion**

252 The main findings of the present study were:

- 253 • Statistically significant differences were found ~~in~~
254 medio-lateral translations between ACL~~–~~deficient and
255 contralateral knees during single leg squat from 0% to

256 35% and from 75% to 100% of the motor task (that
257 correspond to an average flexion value from 0° to 30°); -

- 258 • During single leg squat, significant differences were
259 found in varus--valgus angle from 50% to 80% of
260 motor task; -
- 261 • No differences were observed between afflicted and
262 contralateral knee during the stance phase of the gait.

263 The influence of ACL deficiency on knee kinematics is a hot
264 topic in recent orthopedic researches, due to the
265 correlation altered biomechanics is supposed to have with
266 increased risk of early osteoarthritis [1, 2, 5, 6, 9, 10, 14, 18,
267 23, 33]. To the best of our knowledge, this is one of the first
268 studies aimed to analyze, with an advanced and highly
269 accurate technology, the translations and rotations of ACLD
270 and contralateral knee joint in vivo and under weight-bearing

271 conditions. On purpose, two tasks that differed in terms of
272 closed (squat) and open (step) kinetic chain were analyzed.

273 Onthe one hand, gait is one of the commonest daily
274 activities, easily performed by ACLD patients too. On the
275 other hand, the squat was chosen since it is more demanding
276 but, at the same time-safe to perform [17,
277 31].

278 Other investigators have already observed the concept of
279 tibial medialization (Figure 5) after ACL injury, inferring
280 this is due to the oblique orientation of ACL. Li et al. [18],
281 analyzsed single leg weight-bearing lunge through double
282 fluoroscopy and found a significant lateral shift of tibio-
283 femoral cartilage contact points, both in the medial (between
284 0° and 60° of flexion) and the lateral compartment of the tibia
285 (between 15° and 30° of flexion). This finding was

286 reproduced also in a cadaveric study [19], where the
287 application of different loading conditions in specimens with
288 ACLD knee led to a significant tibial medialization between
289 15° and 30° of flexion. Furthermore, DeFrate et al. [5] found
290 a greater tibia medialization in ACLD knees from 0° to 90°
291 of flexion during the execution of a quasi-static lunge. These
292 results are in accordance with the findings of the present
293 study, since a significant tibial medialization was observed
294 in correspondence to a knee range of flexion between 0° and
295 30°. This abnormal position could explain the high incidence
296 of osteoarthritis on the medial femoral condyle and anterior
297 tibial spine in chronic ACL deficiency [7, 23]: medial shift
298 of the tibia could reduce the distance between these two knee
299 structures, leading to an altered force distribution on their
300 surfaces [18].

301 The contribution of ACL in varus—valgus laxity is also a
302 controversial topic [12, 22, 29, 32]. In the present study,
303 ACLD knees were found significantly more varus than the
304 contralateral ones in the first degrees of the re-extension
305 phase of the squat, after they reach the maximum flexion. A
306 crucial role of ACL in frontal plane knee rotations can
307 therefore be supposed. Previous literature studies drew the
308 same conclusion. Yamazaky et al. [32] demonstrated ACL
309 injured limbs had a more knee varus than uninjured of about
310 5° at the maximum flexion angle of a single leg squat, using
311 an electromagnetic device. In another study [29], performed
312 with fluoroscopy, knees after ACL reconstruction were
313 shown to be more varus than contralateral during downhill
314 running. This aspect could endorse the surgical techniques’
315 inability to restore physiologic knee varus—valgus after

316 ACL tear. Lastly, there is the recent concept of valgus
317 collapse as a frequent mechanism involved in ACL non-
318 contact injury [25], which could bring to suppose knee
319 valgus as a position of discomfort for patients simulating the
320 ligament rupture biomechanics. ACL-injured patients could
321 probably maintain an easier balance keeping a more varus
322 position [32].

323 Differently than expected, no differences were found neither
324 in tibial anterior—posterior translation nor in knee internal—
325 external rotation. Closed kinetic chain exercises like squat
326 are considered safer than open kinetic chain ones in ACL
327 injury rehabilitation programs, especially when patients need
328 to increase muscle activity, because they are supposed to
329 cause less ligament strain [20]. For this reason, squat
330 exercises have a role in ACL deficiency rehabilitation: the

331 high muscular co-activation of quadriceps and hamstrings

332 provides a greater anterior—posterior tibial stability [17, 31].

333 This consideration could justify the absence of differences in

334 tibial position in anterior—posterior knee laxity and in

335 internal—external rotation in our data. Moreover, some

336 previous studies described a higher tibial internal rotation in

337 ACLD knees, but for motor task different from the squat [5,

338 10].

339 In step, we did not found any statistical difference between

340 ACLD knee kinematics and contralateral one. These results

341 are partially in contrast with literature: several studies [9, 15]

342 identified anomalies in knee flexion—extension during

343 walking, but showed neither significantly more anterior

344 tibial translation nor an increased antero-posterior laxity

345 range. Gao et al. [9] described an increased tendency of the

346 ACLD knees to remain in flexion at the end of the stance
347 phase of the gait, while Hurd and Snyder-Mackler [15]
348 described a “joint stiffness strategy” as a combination of
349 reduced peak knee flexion and lack of extension during the
350 mid-stance. The main thesis for this altered knee flexion
351 pattern relies on abnormal muscle activation in patients
352 with ACL tear, aimed to better control knee anterior—
353 posterior laxity. Indeed, many studies based on
354 electromyography highlighted differences in activation of
355 quadriceps and hamstrings after ACL injury, even if there is
356 no consensus regarding the adaptation mechanism [15, 26,
357 27].

358 In the present study, no flexion—extension anomalies were
359 identified. The step was executed at a low speed and usually
360 with small step length. Previous investigators demonstrated

361 that small spatiotemporal parameters influence knee flexion
362 during stance, thus resulting in a stiff knee strategy [21, 28]
363 and an almost full extension, similar to our results.

364 In brief, the findings of the present study could indicate
365 ~~on top of~~ the role of ACL in knee biomechanics: in vivo and
366 under weight-bearing conditions, the ACL could decisively
367 contribute to medio-lateral tibial alignment and knee varus-
368 -valgus. **So** far, the ACL reconstruction techniques have
369 focused on the restoration of anterior-posterior and
370 internal-external rotation knee stability, without
371 considering the anomalies on frontal plane. Actually,
372 previous studies reported that ACL reconstruction does not
373 restore these parameters [6, 29]. According to the present
374 study, surgeons should observe ACL injury from a wider
375 perspective, thus considering also ACLD knee motion

376 anomalies in the frontal plane, to develop reconstruction
377 techniques aimed to reproduce physiological knee stability.

378 The present study has several limitations. First, due to the
379 controlled nature of the tasks (especially the step), the small
380 sample size could have affected the statistical analysis and
381 probably failed to reveal other differences between the two
382 groups. However, it was possible to demonstrate some
383 consistent trends. A second, intrinsic limitation linked to the
384 sample size relied upon the high intra-subject knee motion
385 variability. The choice to acquire, under radiograph
386 exposure, only one repetition per task, was made due to
387 ethical reasons. This issue was minimized through a direct
388 comparison of healthy and unhealthy limbs of the same
389 patients.

390 The other two considerations include the selection of
391 patients based on time from injury and the choice of
392 contralateral limbs as gold standard. When debating on
393 ACL-deficient knee biomechanics, the time from injury is
394 crucial, because patients may progressively develop
395 muscular asymmetries to stabilize the joint [33].
396 Nevertheless, the present study was mainly focused on how
397 the injury affected the biomechanics and not on how
398 rehabilitation could restore knee stability. The contralateral
399 knees might not reproduce a normal knee kinematics [16].
400 Anyhow, obtaining a pool of healthy controls would have
401 been highly unethical due to radiograph exposure;
402 furthermore, the evaluation of contralateral knees as controls
403 is typical of nearly all the fluoroscopic studies.

404 Lastly, the choice of the tasks was related to the actual
405 radiographic set-up: due to the limited spaces and the
406 obstacles represented by the medical devices around, it
407 would have been unsafe and impossible to analyze high-
408 dynamics tasks, such as jumps or cut-maneuvers.

409 These last tasks could have stressed the knee joint more, and
410 maybe underlined further differences from the contralateral.

411 A future set-up development will permit acquire more
412 complex and stressing tasks.

413

414 **Conclusion**

415 ACL-deficient knees showed an abnormal tibial
416 medialization and increased varus angle compared to the
417 contralateral knees. These biomechanical anomalies may
418 lead to different forces distributions on the tibial plateau,

419 explaining the higher risk of early osteoarthritis in ACL
420 deficiency. Clinicians should take into account the influence
421 of ACL tear on frontal plane knee kinematics in movement
422 commonly used in ACL rehabilitation protocols.

423

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427

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601 **Figures Legend**

602 **Figure 1** Radiological set-up of the RSA device, where
603 patients performed motor tasks. The orthogonal arrangement
604 of flat panels and X-ray tubes allows a 3D reconstruction of
605 bones movements (A); vVirtual reconstruction of a motor
606 task in the RSA software, where mathematical data
607 describing tibio-femoral kinematics were extrapolated (B).

608 **Figure 2** Anatomical reference systems of tibia and femur in
609 the RSA software. X-axis: flexion angle and the medio-
610 lateral translation; Y-axis: varus—valgus rotation and
611 anterior—posterior translations; Z-axis: internal—external
612 rotations and proximal—distal translation.

613 **Figure 3** Medio-lateral translations (mean \pm SEM) of the
614 tibia with respect to the femur during single leg squat; notice
615 that significant differences were found from 0% to 35% and
616 from 75% to 100% of the motor task (that correspond to an
617 average flexion value from 0° to 30°) (A). Varus—valgus
618 rotations (mean \pm SEM) of the tibia with respect to the femur
619 during single leg squat; notice that significant differences
620 were found from 50% to 80% of the motor task (B).

621 **Figure 4** Medio-lateral translations (mean \pm SEM) of the
622 tibia with respect to the femur during the stance phase of the

623 gait; notice that, despite no significant differences being~~were~~
624 found, the tibias of ACLD knees were on average shifted to
625 a more medial position than the ones of the contralateral
626 knees.

627 **Figure 5** Difference in medio-lateral tibial position between
628 the normal knee (A) and the ACL- deficient knee (B).

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630 **Tables**

| Motor task normalization | | |
|---------------------------------|--------------------------|---------------------------|
| Time percentage | Phase of the step | Phase of the squat |
| 0% | Heel <u>-</u> strike | Initial extension |
| 50% | Midstance | Maximum flexion |
| 100% | Heel <u>-</u> off | Terminal extension |

631 *Table 1 - List and value of the specific moments used to*
 632 *normalize the data for the execution of the motor tasks.*

633

| Significant differences | | | | |
|--|----------------------|----------------|---------------------------|----------------|
| | % of the task | Injured | Contralatera l | p value |
| Squat medio- lateral translation s (mm) | 0 - 35 % | 1.4 ± 0.4 | -1.2 ± 0.7 | < 0.05 |
| | 65 - 100 % | 1.5 ± 0.6 | -1.9 ± 0.9 | < 0.001 |

| | | | | |
|---|--------------|------------|------------|--------|
| Squat varus= valgus angles (°) | 50 - 80 % | -0.9 ± 1.3 | -5.3 ± 2.2 | < 0.05 |
|---|--------------|------------|------------|--------|

634 *Table 2: Average ± standard error values of the*
635 *significant differences between ACL-deficient and*
636 *contralateral knee*

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638

639 **List of abbreviations**

640 **ACL** Anterior cruciate ligament

641 **ACLD** Anterior cruciate ligament deficient

642 **RSA** Roentgen stereophotogrammetric analysis