

HOKKAIDO UNIVERSITY

Title	Stress on the posteromedial region of the proximal tibia increased over time after anterior cruciate ligament injury
Author(s)	Miura, Soya; Iwasaki, Koji; Kondo, Eiji; Endo, Kaori; Matsubara, Shinji; Matsuoka, Masatake; Onodera, Tomohiro; Iwasaki, Norimasa
Citation	Knee surgery sports traumatology arthroscopy, 30(5), 1744-1751 https://doi.org/10.1007/s00167-021-06731-4
Issue Date	2022-05-01
Doc URL	http://hdl.handle.net/2115/89277
Rights	This is a post-peer-review, pre-copyedit version of an article published in Knee Surgery, Sports Traumatology, Arthroscopy. The final authenticated version is available online at: http://dx.doi.org/org/10.1007/s00167-021-06731-4
Туре	article (author version)
File Information	KSSTA_ACL-CTOAM.pdf

% Instructions for use

Knee Surgery, Sports Traumatology, Arthroscopy (KSSTA)

Title: Stress on the Posteromedial Region of the Proximal Tibia Increased Over Time after Anterior Cruciate Ligament Injury

Soya Miura. M.D.¹, Koji Iwasaki. M. D., Ph. D.², Eiji Kondo. M. D., Ph. D.³, Kaori Endo. M. D., Ph. D.¹, Shinji Matsubara. M. D., Ph. D.¹, Masatake Matsuoka. M. D., Ph. D.¹, Tomohiro Onodera. M. D., Ph. D.¹, Norimasa Iwasaki. M. D., Ph. D.¹

- 1. Department of Orthopaedic Surgery, Faculty of Medicine and Graduate School of Medicine, Hokkaido University, Sapporo, Japan
- 2. Department of Functional Reconstruction for the Knee Joint, Faculty of Medicine, Hokkaido University, Sapporo, Japan
- 3. Centre for Sports Medicine, Hokkaido University Hospital, Sapporo, Japan

Corresponding author

- Koji Iwasaki, MD, PhD.
- Institutional address: North-15, West-7, Sapporo, Hokkaido 060-8638, Japan
- Phone: +81-11-706-5934
- Email: kojiwasaki@pop.med.hokudai.ac.jp

Declarations:

- **Conflict of interest:** The institution of an author (KI) has received funding from Olympus terumo biomaterials CORP.
- Ethical approval: This study protocol was approved by the institutional review board of Hokkaido university hospital (IRB number, 017-0163).
- Authors' contribution: SM collected the data, made the analysis and drafted the work. KI conducted this study, supervised the data analysis and completed the draft. SM, MM supported the data collection. KE advised the CT analysis. EK, OT and NI interpreted the data and revised the draft critically.

1 Abstract

Purpose Anterior cruciate ligament (ACL) injury induces anterior and rotatory instability 2 of the knee. However, the effect of this instability on the stress distribution in the knee 3 4 joint in living participants is not clear. The aim of this study was to compare the distribution pattern of subchondral bone density across the proximal tibia in the knees 5 with and without ACL injury, and to investigate the correlation between the distribution 6 patterns of the subchondral bone density and the duration of ACL-deficiency. 7 Methods Radiographic and computed tomography (CT) data pertaining to 20 patients 8 with unilateral ACL injury without combined injury (ACL-deficient group) and 19 9 nontraumatic subjects (control group) were collected retrospectively. Subchondral bone 10 density of the proximal tibia was assessed using CT-osteoabsorptiometry. Both the medial 11 12 and lateral compartments of the proximal tibia were divided into three subregions of equal width in the sagittal direction. The percentage of high subchondral bone density areas 13 (HDA%) in each subregion was quantitatively analyzed. 14 Results HDA% of the posteromedial region was significantly higher in the ACL-deficient 15 group (mean: 21.6%) than in the control group (14.7%) (p = 0.002). In contrast, HDA% 16 17 of the anteromedial region was significantly lower in the ACL-deficient group (9.4%)

18 than in the control group (15.3%) (p = 0.048). The logarithm of the time elapsed from

19 ACL injury to CT examination showed a significant correlation with HDA% in the 20 posteromedial region (p = 0.032).

21 **Conclusions** Subchondral bone density in the posteromedial region significantly 22 increased after ACL injury and correlated with the duration of ACL-deficiency in semi-23 log manner in meniscus intact knees. The increase in stress on the posteromedial region 24 after ACL injury, which induces a change in the subchondral bone density, justifies early 25 ACL reconstruction after ACL injury.

27 INTRODUCTION

Anterior cruciate ligament (ACL) injury induces anterior and rotatory instability of the 28 knee, which affects the performance level of athletes; moreover, this instability may cause 29 30 knee buckling or giving way even in non-athletes. Anterior and rotatory instability is known to alter the positional relationship between the distal femur and the proximal tibia 31 [4, 11, 26, 28, 34, 43]. This instability after ACL injury is believed to lead to abnormal 32 stress distribution across the knee joint [6, 9, 12, 42]. In cadaveric studies, the contact 33 stress on the posteromedial part of the proximal tibial articular surface in response to 34 anterior tibial load was found to be higher in ACL-deficient knee than in the intact knee 35 [6, 42]. In addition, the location of the common dynamic stress distribution on the 36 proximal tibial articular surface changed after ACL transection during simulated gait [9]. 37 38 However, it is technically challenging to measure the actual stress distribution across the knee joint in the ACL-deficient knee. Moreover, whether and how the actual in 39 vivo stress distribution changes after ACL injury is not well characterized. 40 Computed tomography (CT)-osteoabsorptiometry is an analytical method for in 41 vivo assessment of the stress distribution at joints through the subchondral bone density. 42 43 It has been demonstrated by our previous studies that CT-osteoabsorptiometry is a useful method for evaluation of in vivo stress distribution in various joints [15, 19-21, 23, 32, 44

45 33].

It was hypothesized that the stress distribution pattern of the proximal tibial 46 articular surface would change over time after ACL injury. The purpose of this study was 47 48 (1) to compare the distribution pattern of subchondral bone density across the proximal tibia with and without ACL injury, and (2) to clarify the influence of the duration of ACL 49 deficiency on the distribution of subchondral bone density. Using CT-osteoabsorptiometry, 50 the change in stress distribution within each compartment of the proximal tibia after ACL 51 injury and the influence of the time elapsed after ACL injury on the stress distribution 52 across the knee joint could be elucidated by this study. 53

54

55 MATERIAL AND METHODS

This study protocol was approved by the institutional review board of Hokkaido University Hospital (IRB number, 017-0163). Analysis was conducted by retrospectively evaluating the preoperative CT scans of the knees of patients who underwent ACL reconstruction between 2016 and 2019 at our institution. Inclusion criteria were patients who had unilateral ACL injury and had undergone CT and MRI examination prior to ACL reconstruction. The exclusion criteria were: (1) meniscal injury which was found in preoperative MRI images (≥ grade II, according to Lotysch and Mink's MRI evaluation

63	system [29]) or that was diagnosed by arthroscopic examination during the ACL
64	reconstruction surgery; (2) cartilage injury (≥International Cartilage Repair Society
65	[ICRS] grade II [8, 18]); (3) osteoarthritis (≥ Kellgren-Laurence [KL] grade II [24]); (4)
66	concomitant chondral injury or ligament injury detected by preoperative MRI or
67	arthroscopic evaluation; (5) age >35 years (Figure 1). In total, 70 patients were diagnosed
68	with ACL injury during the study's data collection period at our institution. Of those, 50
69	patients were excluded, and the remaining 20 patients were included in the study as those
70	having ACL-deficient knees (ACL-deficient group) (Figure 1). In addition, for
71	comparison of ipsilateral knee trauma, we collected the data of patients undergoing
72	simultaneous radiographic and CT examinations of the bilateral knees between 2015 and
73	2019; these patients were considered control subjects. Inclusion criteria for the control
74	group were: (1) osteoarthritis (KL grade \leq 1) in the contralateral knee, (2) age \leq 35 years
75	at the time of CT, and (3) no trauma history. Nineteen uninjured contralateral knees were
76	used as controls. There were no significant differences in age, sex, HKA angle, PTS angle,
77	and Tegner activity scale score between the control and ACL-deficient groups (Table 1).
78	

79 Clinical and radiological evaluation

80 In the ACL-deficient group, the side-to-side differences of the anterior laxity were

81	measured with a KT-2000 arthrometer (MED metric, San Diego, CA, USA) at 30° of knee
82	flexion under an anterior drawer force of 133 N. For radiological evaluation, bilateral
83	standing anteroposterior (AP), lateral views of the knee, and full-length AP radiographs
84	of the whole lower limb in full extension were assessed. Tibiofemoral osteoarthritis was
85	evaluated according to the KL grading system, Hip-knee-ankle (HKA) angle, and
86	posterior tibial slope (PTS) angle. The PTS was defined as the angle between the line
87	perpendicular to the mid-diaphysis of the tibia and the posterior inclination of the medial
88	tibial plateau. Patient activity before ACL injury was evaluated using the Tegner activity
89	scale [40].

90 Computed tomography–osteoabsorptiometry

A high-resolution helical CT scanner (Aquilion One/ViSION Edition; Toshiba Medical 91 Systems, Japan) was used to acquire axial images of the knee in full extension. Slice 92 thickness and interval were set at 0.5 mm. The acquired CT data were transferred to a 93 personal computer. The sagittal and coronal slices at 1.0-mm intervals and 3-D bone 94 models were generated from axial CT data using a commercial software (Ziocube[®]; 95 Ziosoft, Inc., Tokyo, Japan). The sagittal and coronal axes were determined with reference 96 97 to the epicondylar axis of the distal femoral condyle in the axial slice. By referring to sagittal and coronal CT images and a 3-D CT image of the articular surface of the 98

99	proximal tibia, an outline of the medial and lateral compartment of the proximal tibial
100	articular surface was manually selected to include the entire subchondral bone layer of
101	the articular surface in all slices [20]. Subsequently, the subchondral bone density of each
102	generated sagittal slice was analyzed using an original non-commercial software
103	(OsteoDens 4.0) developed at our institution [15, 19, 20, 23, 32, 33]. The maximum
104	increment point in Hounsfield units from the joint surface was set as the starting point of
105	the region of interest, and the maximum point in Hounsfield units was selected
106	automatically in the 2.5-mm region of interest from the starting point [20]. We determined
107	the radiodensity of the identified subchondral bone region at each coordinate point at 1.0-
108	mm intervals. Subsequently, a two-dimensional image that mapped the distribution of
109	subchondral bone density was obtained by stacking the sagittal slices (Figure 2A, 2B).
110	The differences between the maximum and minimum values (in Hounsfield units [HU])
111	on the mapping images were categorized into nine grades; subsequently, a surface
112	mapping image was generated using these grades to produce a color scale in which red
113	and violet indicated the greatest and lowest bone densities, respectively. The selected
114	areas of the medial and lateral plateaus included the cortical bone at the periphery of the
115	articular surface because it was impossible to exclude the cortical bone using the software.
116	However, these features were manually removed from the target area of analysis in the

117 subsequent quantitative analysis [20].

118	Quantitative analysis of the obtained mapping data focused on the location of the
119	high-density area (HDA) of the articular surface. The HDA was defined as the region
120	containing the coordinate points representing the top 30% area of HU values in each
121	medial or lateral compartment. The medial compartment of the proximal tibia was divided
122	into three subregions of equal width in the sagittal direction, denoted anteromedial (AM),
123	centromedial (CM), and posteromedial (PM) from anterior to posterior. The lateral
124	compartment was similarly divided into anterolateral (AL), centrolateral (CL), and
125	posterolateral (PL) from anterior to posterior (Figure 2C). The percentage of each
126	subregion represented by the HDA (HDA%) was calculated (see Supplemental File). The
127	measurement results in this study are presented to one decimal place of precision.
128	Quantitative analysis was performed in a blinded manner by two observers (## and ##).
129	The same set of images was measured by each examiner after 4 weeks. The averages of
130	these measurements were used in our analysis.

The reproducibility of data was evaluated using OsteoDens 4.0 software. Intraand interobserver reliability were assessed using three randomly selected knees from the control group and ACL-deficient group. HDA% was measured independently by two observers (KI and SM) in these six knees; a total of 36 subregions were measured twice

135	in a blinded manner at 4-week intervals. The intraclass correlation coefficients for
136	intraobserver reliability were 0.88 (KI) and 0.91 (SM), respectively, and the intraclass
137	correlation coefficient for interobserver reproducibility was 0.87.
138	Statistical analysis
139	Statistical analyses were performed using JMP Pro 14.0 (SAS Institute Inc., Cary, NC,
140	USA). $P < 0.05$ was considered statistically significant. Comparisons between control
141	and ACL-deficient groups were performed using the Student's <i>t</i> test or the chi-square test.
142	Pearson's correlation coefficient was used to examine the relationship between HDA% in
143	each subregion and other variables, including anterior laxity, period from ACL injury to
144	CT, HKA angle, and PTS angle, because they are believed to influence the distribution of
145	subchondral bone density [22, 36, 41] or the biomechanics of the knee joint [3, 35]. Post
146	hoc power analysis revealed that for an alpha value of 0.05, a power of 0.96 on a sample
147	size of 20 knees was achieved for the difference in HDA% in the PM region.
148	
149	RESULTS
150	
151	HDA% in each subregion
152	HDA% of the posteromedial region in the ACL-deficient group was 7% higher than in

153	the control group ($p = 0.002$). In contrast, HDA% of the anteromedial region in the ACL-
154	deficient was 6% lower than in the control group ($p = 0.048$). There were no significant
155	differences in HDA% of centromedial region and subregions of the lateral compartment
156	between the ACL-deficient and control groups (Table 2).

158 Correlation between HDA% and other variables

HDA% of the posteromedial region showed no correlation with the time elapsed from ACL injury to CT examination (n.s., r = 0.288), but showed a significant correlation with the logarithm of the time elapsed from ACL injury to CT examination (p = 0.032. r =0.480) (Figure 3). HDA% of the anteromedial region showed no correlation with the time elapsed either on the arithmetic plot or the semi-log plots. HDA% of the posteromedial region showed no correlation with other variables, including anterior laxity, HKA angle, and PTS angle.

166

167 **DISCUSSION**

The main findings of the present study were that HDA% of the posteromedial region of the proximal tibia in the ACL-deficient group with intact meniscus was significantly higher than that in the control group Furthermore, HDA% of the posteromedial region

171	showed a significant correlation with the duration of ACL-deficiency on semi-log curves.
172	Previous studies involving CT-osteoabsorptiometry have indicated that the
173	distribution pattern of subchondral bone density reflects the distribution of the stress
174	acting on the joint surface under actual loading conditions [19-21, 23, 31-33]. Funakoshi
175	et al. found high-stress distribution patterns on the anterolateral part of the capitellum and
176	the anterolateral part of the ulna in symptomatic patients with ulnar collateral ligament
177	insufficiency [15]. Therefore, CT-osteoabsorptiometry can help assess the <i>in vivo</i> stress
178	distribution across the ACL-deficient knee joint. In the present study, HDA% in the
179	posteromedial region of the proximal tibia was found to be higher in the ACL-deficient
180	knees than in the normal knees. This result suggests that ACL injury increased the stress
181	on the posteromedial region of the proximal tibia, since the changes in subchondral bone
182	density are believed to result from changes in stress distribution. Experimental studies
183	using animal models, ACL transection induced progression of osteoarthritis over time [1,
184	7, 13]. These results suggested that chronic ACL-deficiency leads to accumulation of
185	stress, which causes the initiation and progression of osteoarthritis (OA) [5]. These
186	speculations were supported by our findings in the present study.

187 There was a positive correlation between the logarithm of the time elapsed since188 ACL-deficiency and HDA% of the posteromedial region in the meniscus intact knees.

These results suggested that stress on the posteromedial region increased rapidly after ACL injury and was accumulated gradually over time, while the meniscus was intact. These findings suggested that patients with ACL injury should undergo ACL reconstruction as soon as possible from the perspective of aggressive prevention of osteoarthritis, even though the meniscus was not injured.

There are several potential mechanisms of the changes in stress distribution after 194 ACL injury including anterior translation of the tibia relative to the femoral condyle [11, 195 26, 28, 42] and anterolateral rotatory instability [11, 26, 34, 42]. Furthermore, three-196 dimensional gait analyses revealed reduced internal rotational moment in ACL-deficient 197 knees during the terminal stance phase. This gait pattern was described as a "pivot-shift 198 avoidance gait" [14, 38]. Theoretically, anterior translation is believed to increase the 199 200 stress on the posteromedial region of the tibial plateau and decrease the stress on the anteromedial region because of the concave shape of the medial tibial plateau. In addition, 201 internal rotatory instability may decrease the stress on the posteromedial region of the 202 tibial plateau and increase the stress on the anteromedial region. "Pivot shift avoidance 203 gait" may affect reciprocally compared to rotatory instability. This study suggested that 204 205 ACL injury increased the stress on the posteromedial region without any correlation with the extent of anterior instability and PTS; in addition, ACL injury led to decreased stress 206

on the anteromedial region. Taking into account both the assumed mechanisms affecting 207 the stress distribution and the obtained results in the anteromedial and posteromedial 208 region, anterior translation is believed to be the main mechanism of the altered stress 209 210 distribution. Furthermore, internal rotation may not counteract the effect of anterior 211 translation on the stress distribution, or "pivot shift avoidance gait" may play an important role in the stress distribution compared to internal rotation after ACL injury. 212 A quasi-static and dynamic biomechanical cadaveric study revealed increase of 213 dynamic contact stress on the posterior lateral tibial plateau [9], indicating that the 214 posterior tibial plateau hit against lateral femoral condyle when tibia rotated internally. In 215 the present study, we found no evidence of increased stress on the posterior lateral tibial 216 plateau. CT-OAM method indicated the resultant stress through the distribution pattern 217 218 of subchondral bone density across the joint, reflecting all movements including not only walking but the compensatory movement against internal rotatory instability. Thus, these 219 differences in the speculation of the stress distribution between the dynamic 220 biomechanical cadaveric study and this CT-OAM study demonstrated a compensatory 221 movement against rotatory instability, which could not be simulated by the knee simulator 222 223 [9].

224

Leg alignment has been reported to strongly influence the distribution of

225	subchondral bone density between the medial and lateral compartments of the proximal
226	tibia [2, 17, 41], indicating that leg alignment counteracted a change in the distribution of
227	subchondral bone density in the sagittal direction due to knee instability. Our previous
228	study demonstrated that the relative value of subchondral bone density in eight sub-
229	regions in the coronal direction among subjects increased significantly, up to 6%, and
230	shifted laterally after high tibial osteotomy (HTO) [20]. Therefore, in the present study,
231	we used the relative value of bone density within compartments in the sagittal direction
232	to detect a change in subchondral bone density distribution in the sagittal direction after
233	ACL injury. Consequently, there was a 5% decrease in the relative value of bone density,
234	compared with the control group, in the anteromedial region and an increase of 6% in the
235	posteromedial region after ACL injury, demonstrating a rearward shift of subchondral
236	bone density distribution. Taking into account the drastic change in knee biomechanics
237	before and after HTO, 5%-6% differences in the relative value of bone density in the
238	sagittal direction between ACL-deficient and control groups was thought to be a
239	substantial change. Although clinical evaluation was not performed in this study, the
240	rearward shift of stress distribution, which induced the rearward shift of subchondral bone
241	density distribution, has been reported to be a cause of the high incidence of medial
242	meniscus injury in chronically ACL-deficient knees [16, 39].

243	In addition to leg alignment, patient activity level and PTS angle could have
244	affected bone density. ACL injuries tend to affect individuals with a high activity level,
245	which could have an impact on bone density [30, 37], and PTS angle was associated with
246	knee instability in ACL-deficient knees [10]. However, there were no significant
247	differences in the activity level and PTS angle between the control and ACL-deficient
248	groups in our study. Therefore, those factors may not have contributed to the difference
249	between the ACL-deficient and control groups.
250	Regarding the influence of the initial injury itself on the bone density, ACL injury
251	is usually provoked by internal rotation and anterior translation, resulting mainly in bone
252	bruising at the posterior wall of the lateral tibial plateau [25, 43]. The posterior wall of
253	the lateral tibial plateau is outside the region of interest in the CT-OAM method. The
254	metaphyseal part of the proximal tibia is too deep to assess by CT-OAM. Furthermore,
255	HDA% of the posterolateral region was not significantly changed in the ACL-deficient
256	group compared to that in the control group. Thus, initial injury may not influence the
257	distribution of subchondral bone density assessed by the CT-OAM method.
258	In addition, the effect of any instability immediately after ACL injury on
259	subchondral bone density might be minimal; however, in a previous study, a 10%
260	decrease in the absolute BMD of the proximal tibia was seen 100 days after ACL injury

with reduced mobility and low activity [27]. Our results of a significant change in the 261 relative value of subchondral bone density in the posteromedial region 90 days after ACL 262 injury may be supported by this change in absolute BMD after ACL injury. 263 Some limitations of our study should be considered when interpreting the 264 findings. First, the stress was not measured directly but through the distribution of 265 subchondral bone density based on the CT-OAM findings [31]. Furthermore, the absolute 266 value of BMD was not evaluated; instead, the relative value in each subregion of each 267 compartment was evaluated. It should be noted that the stress distribution evaluated by 268 the CT-OAM method may not reflect the actual stress. Second, this study lacked a 269 standardized rehabilitation protocol and level of rest. Despite these limitations, the 270 strength of this study was that we matched the two groups with respect to factors that may 271 272 influence the distribution pattern of subchondral bone density (including age, BMI, and geometry of knee). Thus, a basic clarification that in vivo stress distribution changes over 273 time after ACL surgery is demonstrated by our results. 274

275

276 CONCLUSION

It has been demonstrated that HDA of the posteromedial region of the proximal tibia in
ACL-deficient knees was significantly higher than that in ACL-intact knees. Moreover, it

279	was found that HDA of the posteromedial region was correlated with the duration of ACL
280	deficiency on semi-log plots. The increase in stress on the posteromedial region over time
281	after ACL injury, which induces a change in the subchondral bone density, provides
282	orthopedic surgeons with a justification for early ACL reconstruction after ACL injury.
283	

284 Acknowledgements

285 We would like to thank Enago (www.enago.jp) for editing a draft of this manuscript.

REFERENCES

288	1.	Adams ME, Brandt KD (1991) Hypertrophic repair of canine articular cartilage in osteoarthritis
289		after anterior cruciate ligament transection. J Rheumatol 18:428-435
290	2.	Akamatsu Y, Koshino T, Saito T, Wada J (1997) Changes in osteosclerosis of the osteoarthritic
291		knee after high tibial osteotomy. Clin Orthop Relat Res 334:207-214
292	3.	Andriacchi TP, Briant PL, Bevill SL, Koo S (2006) Rotational changes at the knee after ACL injury
293		cause cartilage thinning. Clin Orthop Relat Res 442:39-44
294	4.	Andriacchi TP, Dyrby CO (2005) Interactions between kinematics and loading during walking for
295		the normal and ACL deficient knee. J Biomech 38:293-298
296	5.	Andriacchi TP, Mundermann A (2006) The role of ambulatory mechanics in the initiation and
297		progression of knee osteoarthritis. Curr Opin Rheumatol 18:514-518
298	6.	Bedi A, Chen T, Santner TJ, El-Amin S, Kelly NH, Warren RF, et al. (2013) Changes in dynamic
299		medial tibiofemoral contact mechanics and kinematics after injury of the anterior cruciate
300		ligament: a cadaveric model. Proc Inst Mech Eng H 227:1027-1037
301	7.	Brandt KD, Braunstein EM, Visco DM, O'Connor B, Heck D, Albrecht M (1991) Anterior (cranial)
302		cruciate ligament transection in the dog: a bona fide model of osteoarthritis, not merely of cartilage
303		injury and repair. J Rheumatol 18:436-446
304	8.	Brittberg M, Winalski CS (2003) Evaluation of cartilage injuries and repair. J Bone Joint Surg Am
305		85-A Suppl 2:58-69
306	9.	Chen T, Wang H, Warren R, Maher S (2017) Loss of ACL function leads to alterations in tibial
307		plateau common dynamic contact stress profiles. J Biomech 61:275-279
308	10.	Dejour D, Pungitore M, Valluy J, Nover L, Saffarini M, Demey G (2019) Preoperative laxity in
309		ACL-deficient knees increases with posterior tibial slope and medial meniscal tears. Knee Surg
310		Sports Traumatol Arthrosc 27:564-572
311	11.	Dennis DA, Mahfouz MR, Komistek RD, Hoff W (2005) In vivo determination of normal and
312		anterior cruciate ligament-deficient knee kinematics. J Biomech 38:241-253
313	12.	Du PZ, Markolf KL, Boguszewski DV, McAllister DR (2018) Femoral Contact Forces in the
314		Anterior Cruciate Ligament Deficient Knee: A Robotic Study. Arthroscopy 34:3226-3233
315	13.	Fischenich KM, Button KD, Coatney GA, Fajardo RS, Leikert KM, Haut RC, et al. (2015) Chronic
316		changes in the articular cartilage and meniscus following traumatic impact to the lapine knee. J
317		Biomech 48:246-253
318	14.	Fuentes A, Hagemeister N, Ranger P, Heron T, de Guise JA (2011) Gait adaptation in chronic
319		anterior cruciate ligament-deficient patients: Pivot-shift avoidance gait. Clin Biomech (Bristol,
320		Avon) 26:181-187
321	15.	Funakoshi T, Furushima K, Momma D, Endo K, Abe Y, Itoh Y, et al. (2016) Alteration of Stress

322 Distribution Patterns in Symptomatic Valgus Instability of the Elbow in Baseball Players: A 323 Computed Tomography Osteoabsorptiometry Study. Am J Sports Med 44:989-994 324 16. Hagino T, Ochiai S, Senga S, Yamashita T, Wako M, Ando T, et al. (2015) Meniscal tears 325 associated with anterior cruciate ligament injury. Arch Orthop Trauma Surg 135:1701-1706 326 17. Han X, Cui J, Xie K, Jiang X, He Z, Du J, et al. (2020) Association between knee alignment, 327 osteoarthritis disease severity, and subchondral trabecular bone microarchitecture in patients with 328 knee osteoarthritis: a cross-sectional study. Arthritis Res Ther 22:203 329 18. Hjelle K, Solheim E, Strand T, Muri R, Brittberg M (2002) Articular cartilage defects in 1,000 330 knee arthroscopies. Arthroscopy 18:730-734 331 19. Irie T, Takahashi D, Asano T, Arai R, Terkawi MA, Ito YM, et al. (2018) Is There an Association 332 Between Borderline-to-mild Dysplasia and Hip Osteoarthritis? Analysis of CT 333 Osteoabsorptiometry. Clin Orthop Relat Res 476:1455-1465 334 20. Iwasaki K, Kondo E, Matsubara S, Matsuoka M, Endo K, Yokota I, et al. (2021) Effect of High 335 Tibial Osteotomy on the Distribution of Subchondral Bone Density Across the Proximal Tibial 336 Articular Surface of the Knee With Medial Compartment Osteoarthritis. Am J Sports Med 337 49:1561-1569 338 21. Iwasaki N, Minami A, Miyazawa T, Kaneda K (2000) Force distribution through the wrist joint in 339 patients with different stages of Kienbock's disease: using computed tomography 340 osteoabsorptiometry. J Hand Surg Am 25:870-876 Johnston JD, Masri BA, Wilson DR (2009) Computed tomography topographic mapping of 341 22. 342 subchondral density (CT-TOMASD) in osteoarthritic and normal knees: methodological 343 development and preliminary findings. Osteoarthritis Cartilage 17:1319-1326 344 23. Kameda T, Kondo E, Onodera T, Iwasaki K, Onodera J, Yasuda K, et al. (2021) Changes in the 345 Contact Stress Distribution Pattern of the Patellofemoral Joint After Medial Open-Wedge High 346 Tibial Osteotomy: An Evaluation Using Computed Tomography Osteoabsorptiometry. Orthop J 347 Sports Med 9:2325967121998050 348 24. Kellgren JH, Lawrence JS (1957) Radiological assessment of osteo-arthrosis. Ann Rheum Dis 349 16:494-502 350 Kim-Wang SY, Scribani MB, Whiteside MB, DeFrate LE, Lassiter TE, Wittstein JR (2021) 25. 351 Distribution of Bone Contusion Patterns in Acute Noncontact Anterior Cruciate Ligament-Torn 352 Knees. Am J Sports Med 49:404-409 353 Kondo E, Merican AM, Yasuda K, Amis AA (2010) Biomechanical comparisons of knee stability 26. 354 after anterior cruciate ligament reconstruction between 2 clinically available transtibial 355 procedures: anatomic double bundle versus single bundle. Am J Sports Med 38:1349-1358 356 27. Kroker A, Besler BA, Bhatla JL, Shtil M, Salat P, Mohtadi N, et al. (2019) Longitudinal Effects 357 of Acute Anterior Cruciate Ligament Tears on Peri-Articular Bone in Human Knees Within the

358 First Year of Injury. J Orthop Res 37:2325-2336 359 28. Kvist J (2004) Sagittal plane translation during level walking in poor-functioning and well-360 functioning patients with anterior cruciate ligament deficiency. Am J Sports Med 32:1250-1255 361 29. Lotysch M, Mink J, Crues JV, Schwartz SA (1986) Magnetic resonance imaging in the detection 362 of meniscal injuries. Magn Reson Imaging 4:185 363 30. Momma D, Iwamoto W, Endo K, Sato K, Iwasaki N (2020) Stress Distribution Patterns Across the Shoulder Joint in Gymnasts: A Computed Tomography Osteoabsorptiometry Study. Orthop J 364 365 Sports Med 8:2325967120962103 Muller-Gerbl M, Putz R, Hodapp N, Schulte E, Wimmer B (1989) Computed tomography-366 31. 367 osteoabsorptiometry for assessing the density distribution of subchondral bone as a measure of 368 long-term mechanical adaptation in individual joints. Skeletal Radiol 18:507-512 Nishida K, Iwasaki N, Fujisaki K, Funakoshi T, Kamishima T, Tadano S, et al. (2012) Distribution 369 32. 370 of bone mineral density at osteochondral donor sites in the patellofemoral joint among baseball 371 players and controls. Am J Sports Med 40:909-914 372 33. Onodera T, Majima T, Iwasaki N, Kamishima T, Kasahara Y, Minami A (2012) Long-term stress 373 distribution patterns of the ankle joint in varus knee alignment assessed by computed tomography 374 osteoabsorptiometry. Int Orthop 36:1871-1876 375 34. Scarvell JM, Smith PN, Refshauge KM, Galloway HR, Woods KR (2004) Comparison of 376 kinematic analysis by mapping tibiofemoral contact with movement of the femoral condylar 377 centres in healthy and anterior cruciate ligament injured knees. J Orthop Res 22:955-962 378 35. Schatka I, Weiler A, Jung TM, Walter TC, Gwinner C (2018) High tibial slope correlates with 379 increased posterior tibial translation in healthy knees. Knee Surg Sports Traumatol Arthrosc 26:2697-2703 380 381 36. Sharma L (2001) Local factors in osteoarthritis. Curr Opin Rheumatol 13:441-446 382 37. Shiota J, Momma D, Yamaguchi T, Iwasaki N (2020) Long-term Stress Distribution Patterns 383 Across the Ankle Joint in Soccer Players: A Computed Tomography Osteoabsorptiometry Study. 384 Orthop J Sports Med 8:2325967120963085 385 38. Takeda K, Hasegawa T, Kiriyama Y, Matsumoto H, Otani T, Toyama Y, et al. (2014) Kinematic 386 motion of the anterior cruciate ligament deficient knee during functionally high and low 387 demanding tasks. J Biomech 47:2526-2530 388 39. Tashiro Y, Mori T, Kawano T, Oniduka T, Arner JW, Fu FH, et al. (2020) Meniscal ramp lesions 389 should be considered in anterior cruciate ligament-injured knees, especially with larger instability 390 or longer delay before surgery. Knee Surg Sports Traumatol Arthrosc 28:3569-3575 391 40. Tegner Y, Lysholm J (1985) Rating systems in the evaluation of knee ligament injuries. Clin 392 Orthop Relat Res 198:43-49 393 41. Wada M, Maezawa Y, Baba H, Shimada S, Sasaki S, Nose Y (2001) Relationships among bone

- mineral densities, static alignment and dynamic load in patients with medial compartment knee
 osteoarthritis. Rheumatology (Oxford) 40:499-505
- Wang D, Kent RN, 3rd, Amirtharaj MJ, Hardy BM, Nawabi DH, Wickiewicz TL, et al. (2019)
 Tibiofemoral Kinematics During Compressive Loading of the ACL-Intact and ACL-Sectioned
- Knee: Roles of Tibial Slope, Medial Eminence Volume, and Anterior Laxity. J Bone Joint Surg
 Am 101:1085-1092
- 40. 43. Willinger L, Athwal KK, Williams A, Amis AA (2021) An Anterior Cruciate Ligament In Vitro
 401 Rupture Model Based on Clinical Imaging. Am J Sports Med 49:2387-2395

403 FIGURE LEGENDS



405 Figure 1. Flowchart of study enrollment. ICRS, International Cartilage Regeneration &

406 Joint Preservation Society-Cartilage Repair Assessment system; KL, Kellgren-Laurence.



Figure 2. Identification of the subchondral bone regions of the proximal tibia using a
customized software. (A, B) The subchondral bone density of the selected region was
automatically measured at each coordinate point in each 1.0-mm sagittal slice. (C) Both
the medial and lateral compartments of the tibial articular surface were divided into three

412 subregions each from anterior to posterior for quantitative analysis of the distribution of

413 high subchondral bone density area

414 AM, anteromedial; CM, centromedial; PM, posteromedial; AL, anterolateral; CL,
415 centrolateral; PL, posterolateral



416

417 Figure 3. Semi-log plots of the time elapsed from ACL injury vs. HDA% in the

418 posteromedial region of the proximal tibia

419 ACL, anterior cruciate ligament; HDA%, percentage of high subchondral bone density

420 area

421

422 Table 1. Characteristics of the study population^a

	Control group $(n = 19)$	ACLD group $(n = 20)$	<i>p</i> value
Age, years	23.4 (21.3–26.5)	21.5 (18.5–23.6)	n.s.
Male:Female, n	10:9	10:10	n.s.
BMI, kg/m ²	24.1 (21.8–26.5)	24.3 (22.3–26.2)	n.s.
Anterior laxity, mm	n/a	3.2 (1.8–4.5)	n/a
Period from ACL injury to CT	n/a	91.4 (35.8–146.9)	n/a
examination, days			
HKA angle, degrees	-0.5 (-2.6-1.6)	-0.3 (-1.8-1.3)	n.s.
PTS angle, degrees	10.4 (8.6–12.2)	10.7 (8.9–12.5)	n.s.
Tegner activity scale score	6.9 (6.1–7.7)	6.4 (5.5–7.2)	n.s.

⁴²³ ^aData presented as frequency or mean (95% confidence interval).

424 ACL, anterior cruciate ligament; ACLD, anterior cruciate ligament deficient; Anterior

425 laxity: side-to-side anterior knee laxity at 30° flexion, BMI, body mass index; CT,

426 computed tomography; HKA, hip-knee-ankle; n/a, not applicable; n.s., not significant;

427 PTS, posterior tibial slope.

428

429 Table 2. Quantitative analysis of HDA% in each subregion^a

		Control group	ACLD group	<i>p</i> value
Madial assurements (0/)	AM	153(96-210)	94(68-120)	0.048
Medial compartment (%)	1 11/1	15.5 (5.6 21.6)	5.1 (0.0 12.0)	0.010
	СМ	52.0 (47.8–56.3)	52.4 (49.3–55.5)	n.s.
	PM	14.7 (12.5–17.0)	21.6 (18.0–25.3)	0.002
Lateral compartment (%)	AL	3.1 (1.2–5.0)	2.7 (1.3–4.1)	n.s.
	CL	38.2 (34.6–41.9)	38.9 (36.4–41.4)	n.s.

PL 43.1 (38.4–47.8) 44.7 (40.2–49.1) n.s.

- 430 ^aData presented as mean (95% confidence interval)
- 431 ACLD, anterior cruciate ligament deficient; AL, anterolateral; AM, anteromedial; CL,
- 432 centrolateral; CM, centromedial; HDA%, percentage of high subchondral bone density
- 433 area; n.s., not significant; PL, posterolateral; PM, posteromedial.