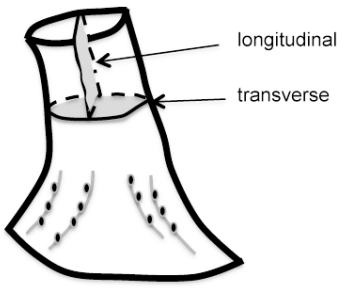
Number	65 donors with 120 knees
Female/male	35/30
Age, mean ± SD years	66.7 ± 19.0 (23 - 92)
Body height, mean ± SD cm	170.4 ± 12.4 (132.1 − 198.1)
Body weight, mean ± SD kg	72.7 ± 23.9 (27.2 − 147.2)
Body mass index, mean ± SD kg/m^2	24.8 ± 7.0 (12.5 − 43.8)

Supplementary Table 1. Donor information.

Cartilage grade	Normal	Abnormal	Ruptured
0 (n=9)	9 (100.0)	0 (0.0)	0 (0.0)
I (n=51)	38 (74.5)	13 (25.5)	0 (0.0)
II (n=31)	16 (51.5)	10 (32.3)	5 (16.1)
III (n=18)	2 (11.1)	12 (66.7)	4 (22.2)
IV (n=11)	3 (27.3)	5 (45.5)	3 (27.3)

Supplementary Table 2. Macroscopic grading of ACL and articular cartilage.
Cartilage grades indicate the degree of macroscopic articular cartilage degeneration. Grade 0: normal when total cartilage score was 39, grade I: minimal change when total score was 40 to 58, grade II: mild change when total score was 59 to 78, grade III: moderate change when total score was 79 to 97, and grade IV: severe change when total score was higher than 98. Values in parenthesis represent number of knees with each cartilage grade. For normal, abnormal and ruptured ACL the number of cases and (%) are shown.

A



B

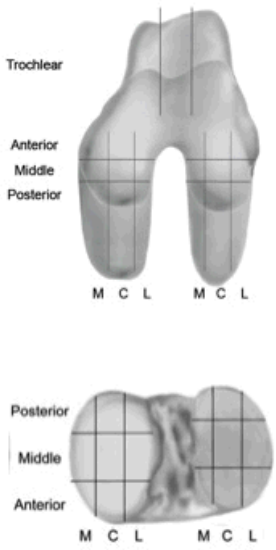
Inflammation
Mucoid degeneration
Chondroid metaplasia
Cystic changes
Orientation of collagen fibers

C

	score
No changes	0
Minimal changes	0.5
Mild changes	1
Moderate changes	2
Severe changes	3

Supplementary Figure 1. Histological analysis of ACL.
A) Sample preparation for histological analysis. Diagram indicates femoral attachment site and areas in the midsubstance of the ACL where longitudinal and transverse sections were collected.
B) Categories for histological analysis.
C) Scoring system for each category listed in B.

A



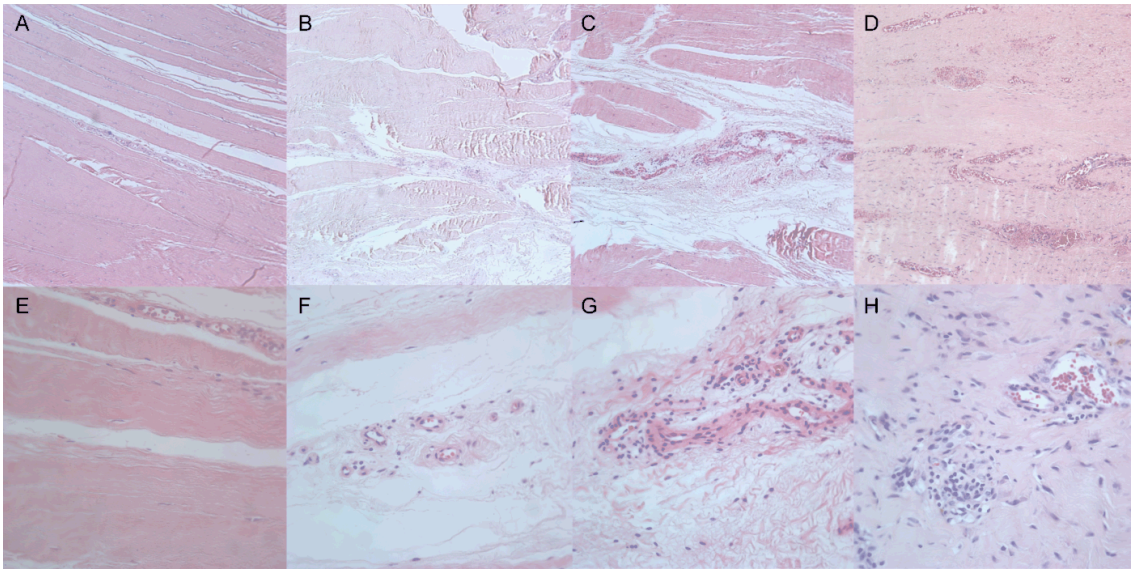
B

Modified Outerbridge classification	score
Intact surface	1
Fibrillation	2
Fissuring	3
Erosion	4

C

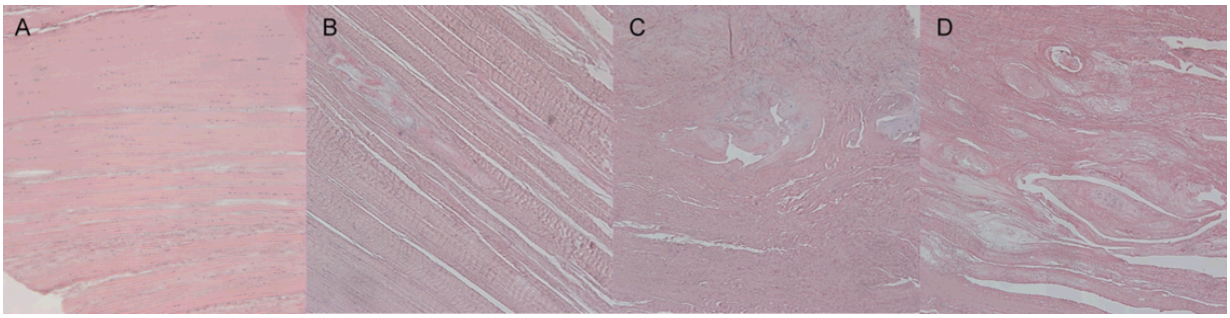
Cartilage grade	total score
Grade 0	: 39
Grade I	: 40 - 58
Grade II	: 59 - 78
Grade III	: 79 - 97
Grade IV	: 98 -

Supplementary Figure 2. Macroscopic grading of cartilage.
A) ICRS map
B) Modified Outerbridge classification
C) Cartilage grading



Supplementary Figure 3. ACL inflammation

(A) – (D) H&E staining (magnification x10).
(E) – (H) H&E staining (magnification x40).
(A)(E) Section of ACL showing no inflammation. No leukocyte infiltration is observed.
(B)(F) Section of ACL showing mild inflammation. A few leukocytes are present.
(C)(G) Section of ACL showing moderate inflammation. Leukocyte infiltration and neovascularization is present.
(D)(H) Section of ACL showing severe inflammation. Leukocyte aggregation and neovascularization is present.



Supplementary Figure 4. Mucoid degeneration in ACL.

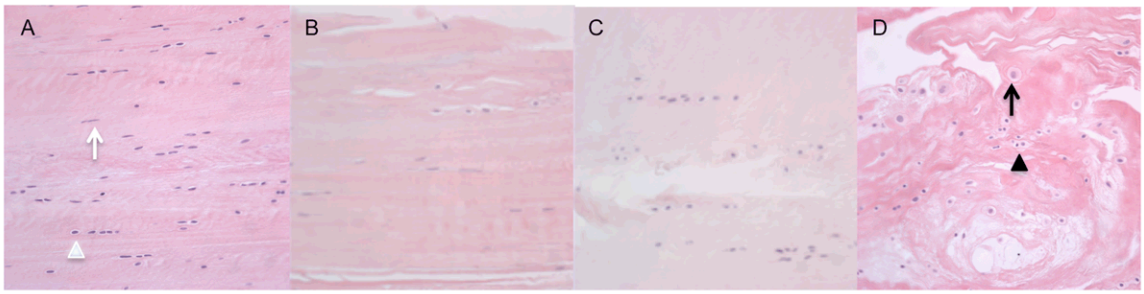
A) Section of ACL showing no mucoid degeneration.

B) Section of ACL showing mild mucoid degeneration. Mild degeneration starting between the collagen bundles.

C) Section of ACL showing moderate mucoid degeneration. Moderate foci of mucoid matrix are observed.

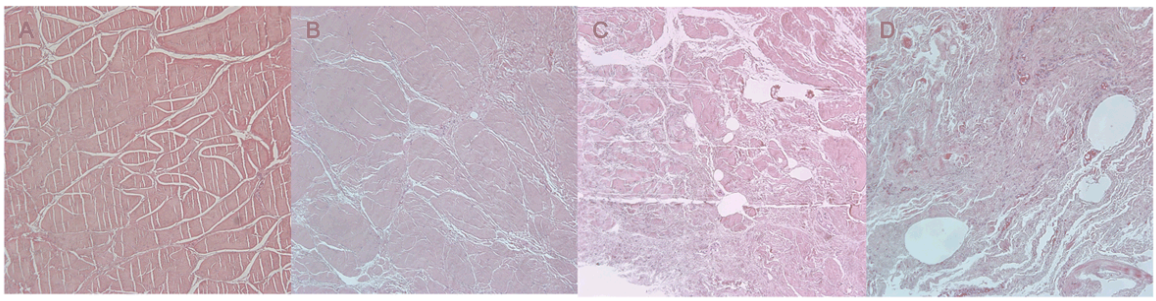
D) Section of ACL showing severe mucoid degeneration. Extensive degradation of collagen fibers and foci of mucoid matrix are observed.

H&E staining (magnification x10).



Supplementary Figure 5. Chondroid metaplasia in ACL.

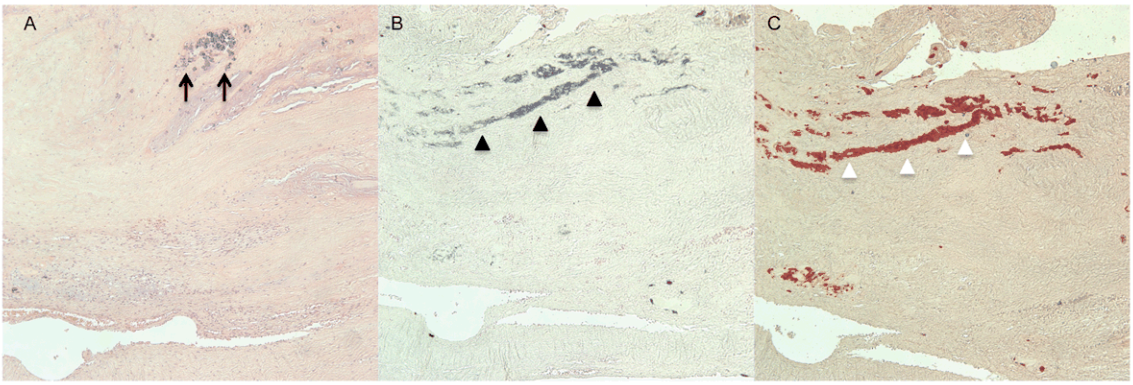
A) Section of ACL showing no chondroid metaplasia. Only fusiform (white arrow) and ovoid cells (white arrowhead) are observed.
B) Section of ACL showing mild chondroid metaplasia. A few spheroid cells are observed.
C) Section of ACL showing moderate chondroid metaplasia. Spheroid cells are dominantly observed.
D) Section of ACL showing severe chondroid metaplasia. Only spheroid cells (black arrow) and pseudo-cloning (black arrowhead) that suggest chondroid metaplasia are observed and associated with mucoid degeneration.
H&E staining (magnification x40).



Supplementary Figure 6. Cystic changes in ACL

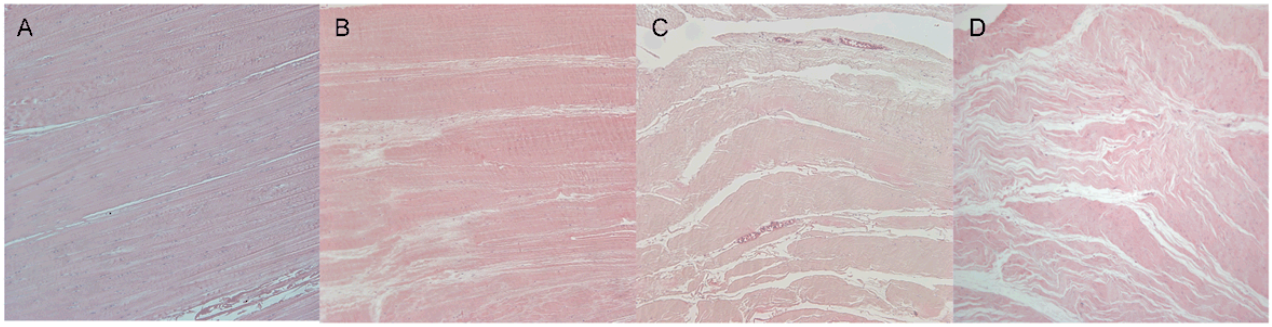
A) Section of ACL showing no cystic change.
B) Section of ACL showing mild cystic changes. A few small cysts are observed.
C) Section of ACL showing moderate cystic changes. Moderate size cysts are observed.
D) Section of ACL showing severe cystic changes. Large size cysts are observed.

H&E staining (magnification x10)



Supplementary Figure 7. Calcium deposition in ACL.

A) Section of ACL stained with H&E showing calcium deposition (black arrows).
B) Section of ACL stained with Von Kossa showing calcium deposition (black arrowheads).
C) Section of ACL stained with Alizarin Red S showing calcium deposition (white arrowheads).



Supplementary Figure 8. Collagen fiber organization in ACL.

A) Section of ACL showing normal orientation of collagen fibers.

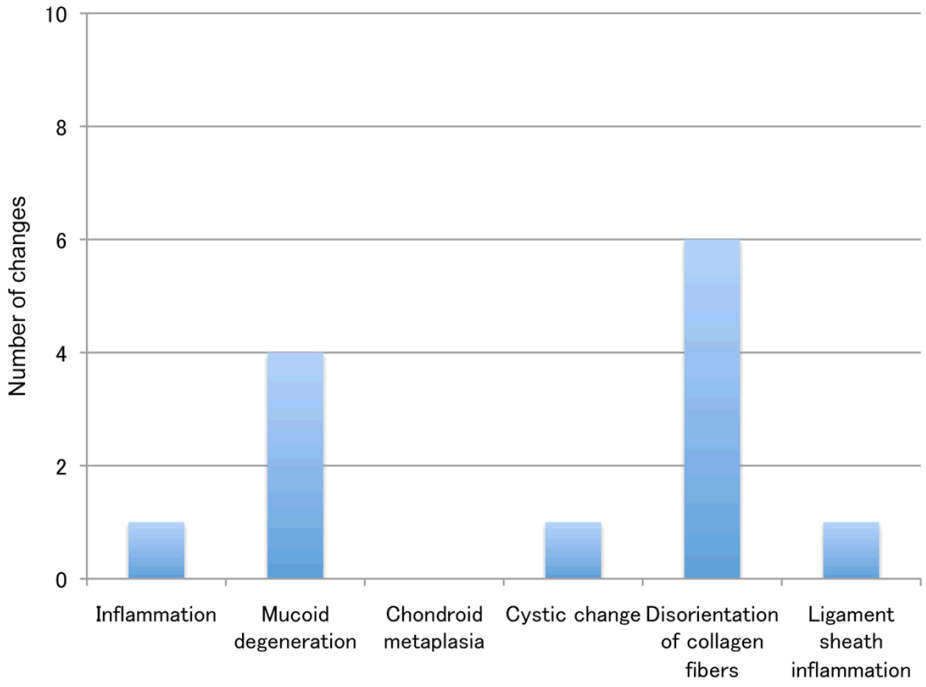
B) Section of ACL showing mild disorientation of collagen fibers.

Disorientation of the collagen fibers in less than one third of the ligament is observed.

C) Section of ACL showing moderate disorientation of collagen fibers. Disorientation of the collagen fibers between one third and two thirds is observed.

D) Section of ACL showing severe disorganization of collagen fibers. Disorientation of the collagen fibers in more than two third of the ligament is observed.

H&E staining (magnification x10).



Supplementary Figure 9. The earliest changes in the ACL
The disorientation of collagen fibers and mucoid degeneration were observed most frequently in the ACL from young (< 45 years old) donors with grade 0 cartilage.