

Supplementary Materials: Cartilage Repair Activity during Joint-Preserving Treatment May be Accompanied by Osteophyte Formation

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Table S1. Pearson correlation coefficients between the osteophyte Altman scores and the osteophyte size as measured by KIDA.

	Medial femur KIDA	Medial tibial KIDA	Medial total KIDA	Lateral femur KIDA	Lateral tibial KIDA	Lateral total KIDA	Total KIDA
Medial femur Altman	R = 0.560 $p < 0.001$	R = 0.489 $p < 0.001$	R = 0.633 $p < 0.001$	R = 0.382 $p < 0.001$	R = 0.347 $p < 0.001$	R = 0.404 $p < 0.001$	R = 0.569 $p < 0.001$
Medial tibial Altman	R = 0.422 $p < 0.001$	R = 0.602 $p < 0.001$	R = 0.580 $p < 0.001$	R = 0.291 $p < 0.001$	R = 0.260 $p < 0.001$	R = 0.339 $p < 0.001$	R = 0.463 $p < 0.001$
Medial total Altman	R = 0.545 $p < 0.001$	R = 0.586 $p < 0.001$	R = 0.664 $p < 0.001$	R = 0.373 $p < 0.001$	R = 0.337 $p < 0.001$	R = 0.410 $p < 0.001$	R = 0.570 $p < 0.001$
Lateral femur Altman	R = 0.390 $p < 0.001$	R = 0.403 $p < 0.001$	R = 0.469 $p < 0.001$	R = 0.623 $p < 0.001$	R = 0.622 $p < 0.001$	R = 0.600 $p < 0.001$	R = 0.671 $p < 0.001$
Lateral tibial Altman	R = 0.357 $p < 0.001$	R = 0.325 $p < 0.001$	R = 0.410 $p < 0.001$	R = 0.473 $p < 0.001$	R = 0.739 $p < 0.001$	R = 0.646 $p < 0.001$	R = 0.629 $p < 0.001$
Lateral total Altman	R = 0.414 $p < 0.001$	R = 0.406 $p < 0.001$	R = 0.488 $p < 0.001$	R = 0.614 $p < 0.001$	R = 0.741 $p < 0.001$	R = 0.683 $p < 0.001$	R = 0.719 $p < 0.001$
Total Altman	R = 0.495 $p < 0.001$	R = 0.587 $p < 0.001$	R = 0.628 $p < 0.001$	R = 0.497 $p < 0.001$	R = 0.528 $p < 0.001$	R = 0.697 $p < 0.001$	R = 0.669 $p < 0.001$

Cells with thicker borders indicate the correlations between KIDA and Altman for the same part of the joint. All correlations were statistically significant ($p < 0.001$).

Table S2. Baseline characteristics of the different patient groups for male and female patients separately.

Parameter	KJD (n = 58)		KJD _{HTO} (n = 20)		HTO (n = 36)		CHECK (n = 44)		SF (n = 17)	
	Male (n = 34)	Female (n = 24)	Male (n = 15)	Female (n = 5)	Male (n = 23)	Female (n = 13)	Male (n = 5)	Female (n = 39)	Male (n = 10)	Female (n = 7)
Age, mean (SD)	51.4 (6.8)	51.4 (9.5)	50.9 (5.6)	51.8 (6.9)	49.9 (6.6)	47.8 (6.2)	67.6 (1.5)	63.6 (4.3)	52.7 (4.9)	55.3 (4.3)
BMI, mean (SD)	28.1 (2.9)	27.9 (4.6)	27.8 (3.4)	26.3 (3.2)	27.2 (3.1)	26.7 (4.1)	33.4 (3.7)	28.9 (4.8)	29.4 (3.4)	28.5 (3.5)
KL-grade, n (%)										
Grade 0	0 (0)	0 (0)	0 (0)	0 (0)	1 (4)	0 (0)	0 (0)	2 (5)	0 (0)	0 (0)
Grade 1	4 (12)	4 (17)	4 (27)	1 (20)	2 (9)	2 (15)	2 (40)	16 (41)	0 (0)	0 (0)
Grade 2	7 (21)	2 (8)	4 (27)	0 (0)	7 (30)	3 (23)	2 (40)	14 (36)	2 (20)	0 (0)
Grade 3	15 (44)	13 (54)	6 (40)	4 (80)	10 (44)	8 (62)	1 (20)	7 (18)	3 (30)	4 (57)
Grade 4	8 (24)	5 (21)	1 (7)	0 (0)	3 (13)	0 (0)	0 (0)	0 (0)	5 (50)	3 (43)

KJD = all knee joint distraction patients with available osteophyte measurements; KJD_{HTO} = subgroup of KJD patients who were included in the KJD vs HTO clinical trial; HTO = high tibial osteotomy patients from the KJD vs HTO clinical trial; CHECK = untreated knee osteoarthritis patients from the cohort hip and cohort knee trial who received a total knee arthroplasty during follow-up; SF = KJD patients from a separate clinical study who underwent synovial fluid aspirations.

Table S3. Influence of baseline characteristics on two-year osteophyte change after knee joint distraction treatment.

Parameter	Unstandardized coefficient (B)	Standardized coefficient (β)	p-value
Age	0.166	0.092	0.495
Gender	−2.158	−0.075	0.570
BMI	−0.071	−0.018	0.890
Kellgren-Lawrence grade	2.423	0.160	0.330

Analyses performed using linear regression; the influence of baseline characteristics (age, gender, BMI, Kellgren-Lawrence grade) was corrected for baseline osteophyte size. Not correcting for baseline values did not change significance.

Table S4. Pearson correlations between baseline osteophyte size and baseline WOMAC and joint space width.

	Osteophyte size	WOMAC total	WOMAC pain	WOMAC stiffness	WOMAC function	JSW
Osteophyte size	1	R = −0.063 p = 0.641	R = −0.086 p = 0.521	R = −0.070 p = 0.604	R = −0.048 p = 0.720	R = −0.315 p = 0.016
WOMAC total	R = −0.063 p = 0.641	1	R = 0.923 p < 0.001	R = 0.824 p < 0.001	R = 0.989 p < 0.001	R = −0.210 p = 0.113
WOMAC pain	R = −0.086 p = 0.521	R = 0.923 p < 0.001	1	R = 0.757 p < 0.001	R = 0.870 p < 0.001	R = −0.114 p = 0.393
WOMAC stiffness	R = −0.070 p = 0.604	R = 0.824 p < 0.001	R = 0.757 p < 0.001	1	R = 0.779 p < 0.001	R = −0.188 p = 0.158
WOMAC function	R = −0.048 p = 0.720	R = 0.989 p < 0.001	R = 0.870 p < 0.001	R = 0.779 p < 0.001	1	R = −0.227 p = 0.087
JSW	R = −0.315 p = 0.016	R = −0.210 p = 0.113	R = −0.114 p = 0.393	R = −0.188 p = 0.158	R = −0.227 p = 0.087	1

The row and column with thicker borders indicate the relevant correlations. Cells with bold text indicate statistically significant correlations (p < 0.001). JSW = joint space width; WOMAC = Western Ontario and McMaster Universities Osteoarthritis Index.

Table S5. Pearson correlations between one- and two-year changes in osteophyte size and WOMAC and joint space width.

One-year changes						
	Δ Osteophyte size	Δ WOMAC total	Δ WOMAC pain	Δ WOMAC stiffness	Δ WOMAC function	Δ JSW
Δ Osteophyte size	1	R = 0.031 <i>p</i> = 0.818	R = 0.121 <i>p</i> = 0.372	R = 0.139 <i>p</i> = 0.302	R = 0.113 <i>p</i> = 0.404	R = -0.062 <i>p</i> = 0.646
Δ WOMAC total	R = 0.031 <i>p</i> = 0.818	1	R = 0.639 <i>p</i> < 0.001	R = 0.897 <i>p</i> < 0.001	R = 0.924 <i>p</i> < 0.001	R = 0.100 <i>p</i> = 0.459
Δ WOMAC pain	R = 0.121 <i>p</i> = 0.372	R = 0.639 <i>p</i> < 0.001	1	R = 0.666 <i>p</i> < 0.001	R = 0.750 <i>p</i> < 0.001	R = -0.071 <i>p</i> = 0.601
Δ WOMAC stiffness	R = 0.139 <i>p</i> = 0.302	R = 0.897 <i>p</i> < 0.001	R = 0.666 <i>p</i> < 0.001	1	R = 0.985 <i>p</i> < 0.001	R = 0.159 <i>p</i> = 0.239
Δ WOMAC function	R = 0.113 <i>p</i> = 0.404	R = 0.924 <i>p</i> < 0.001	R = 0.750 <i>p</i> < 0.001	R = 0.985 <i>p</i> < 0.001	1	R = 0.122 <i>p</i> = 0.366
Δ JSW	R = -0.062 <i>p</i> = 0.646	R = 0.100 <i>p</i> = 0.459	R = -0.071 <i>p</i> = 0.601	R = 0.159 <i>p</i> = 0.239	R = 0.122 <i>p</i> = 0.366	1
Two-year changes						
	Δ Osteophyte size	Δ WOMAC total	Δ WOMAC pain	Δ WOMAC stiffness	Δ WOMAC function	Δ JSW
Δ Osteophyte size	1	R = 0.080 <i>p</i> = 0.557	R = 0.146 <i>p</i> = 0.283	R = 0.165 <i>p</i> = 0.224	R = 0.158 <i>p</i> = 0.244	R = -0.106 <i>p</i> = 0.438
Δ WOMAC total	R = 0.080 <i>p</i> = 0.557	1	R = 0.584 <i>p</i> < 0.001	R = 0.861 <i>p</i> < 0.001	R = 0.910 <i>p</i> < 0.001	R = 0.162 <i>p</i> = 0.234
Δ WOMAC pain	R = 0.146 <i>p</i> = 0.283	R = 0.584 <i>p</i> < 0.001	1	R = 0.639 <i>p</i> < 0.001	R = 0.692 <i>p</i> < 0.001	R = -0.162 <i>p</i> = 0.234
Δ WOMAC stiffness	R = 0.165 <i>p</i> = 0.224	R = 0.861 <i>p</i> < 0.001	R = 0.639 <i>p</i> < 0.001	1	R = 0.989 <i>p</i> < 0.001	R = 0.193 <i>p</i> = 0.153
Δ WOMAC function	R = 0.158 <i>p</i> = 0.244	R = 0.910 <i>p</i> < 0.001	R = 0.692 <i>p</i> < 0.001	R = 0.989 <i>p</i> < 0.001	1	R = 0.158 <i>p</i> = 0.246
Δ JSW	R = -0.106 <i>p</i> = 0.438	R = 0.162 <i>p</i> = 0.234	R = -0.162 <i>p</i> = 0.234	R = 0.193 <i>p</i> = 0.153	R = 0.158 <i>p</i> = 0.246	1

The row and column with thicker borders indicate the relevant correlations. Cells with bold text indicate statistically significant correlations (*p* < 0.001). JSW = joint space width; WOMAC = Western Ontario and McMaster Universities Osteoarthritis Index.

Table S6. Baseline and one-year Altman scores for patients with synovial fluid aspirations.

	Baseline	One year	<i>p</i> -value
Medial femur (0–3)	2.0 (0.5)	2.1 (1.1)	0.075
Lateral femur (0–3)	2.0 (1.0)	2.0 (1.5)	0.500
Medial tibia (0–3)	2.0 (0.8)	2.0 (0.8)	0.401
Lateral tibia (0–3)	1.0 (1.3)	1.0 (1.7)	0.260
Total (0–12) *	6.7 (2.0)	6.9 (1.8)	0.653

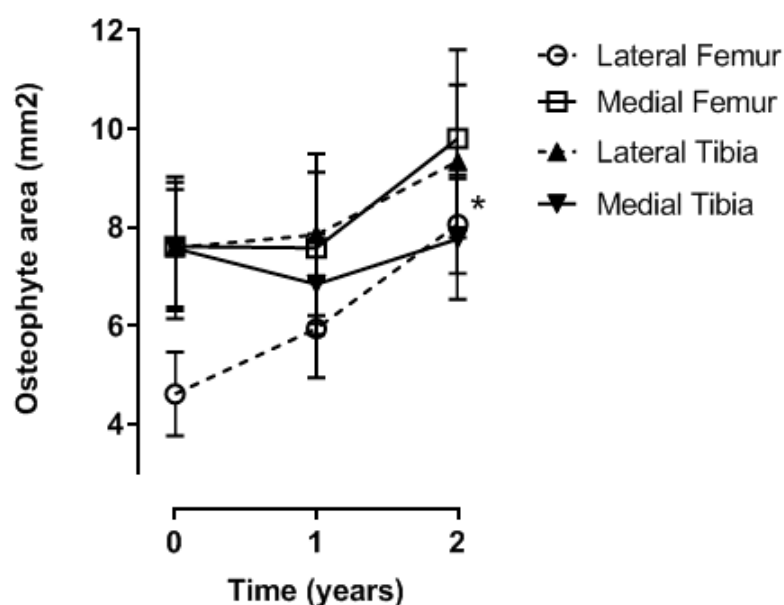
For the four compartments, the median and interquartile range are given and *p*-values are calculated with Wilcoxon Signed Rank tests. *For the total Altman score, the mean and standard deviation are given and the *p*-value is calculated with a paired *t*-tests.

Table S7. Pearson correlations between baseline total Altman score and TGF β -1 and IL-6, and between one-year changes.

<i>Baseline values</i>			
	Total Altman	TGF β -1	IL-6
Total Altman	1	R = -0.380 <i>p</i> = 0.147	R = 0.209 <i>p</i> = 0.422
TGF β -1	R = -0.380 <i>p</i> = 0.147	1	R = 0.130 <i>p</i> = 0.632
IL-6	R = 0.209 <i>p</i> = 0.422	R = 0.130 <i>p</i> = 0.632	1
<i>One-year changes</i>			
	Δ Total Altman	Δ TGF β -1	Δ IL-6
Δ Total Altman	1	R = 0.305 <i>p</i> = 0.289	R = 0.299 <i>p</i> = 0.280
Δ TGF β -1	R = 0.305 <i>p</i> = 0.289	1	R = -0.438 <i>p</i> = 0.118
Δ IL-6	R = 0.299 <i>p</i> = 0.280	R = -0.438 <i>p</i> = 0.118	1

The row and column with thicker borders indicate the relevant correlations. TGF β -1 = transforming growth factor- β 1; IL-6 = interleukin-6.

Total osteophyte size per region for KJD_{HTO}



Supplementary Figure S1. Change in osteophyte size in mm² per region before and one and two years after treatment with knee joint distraction, for patients indicated for high tibial osteotomy (KJD_{HTO}, n = 20). Mean and standard error of the mean (SEM) are shown, * indicates significant changes compared to baseline using repeated measures ANOVA (*p* < 0.05).