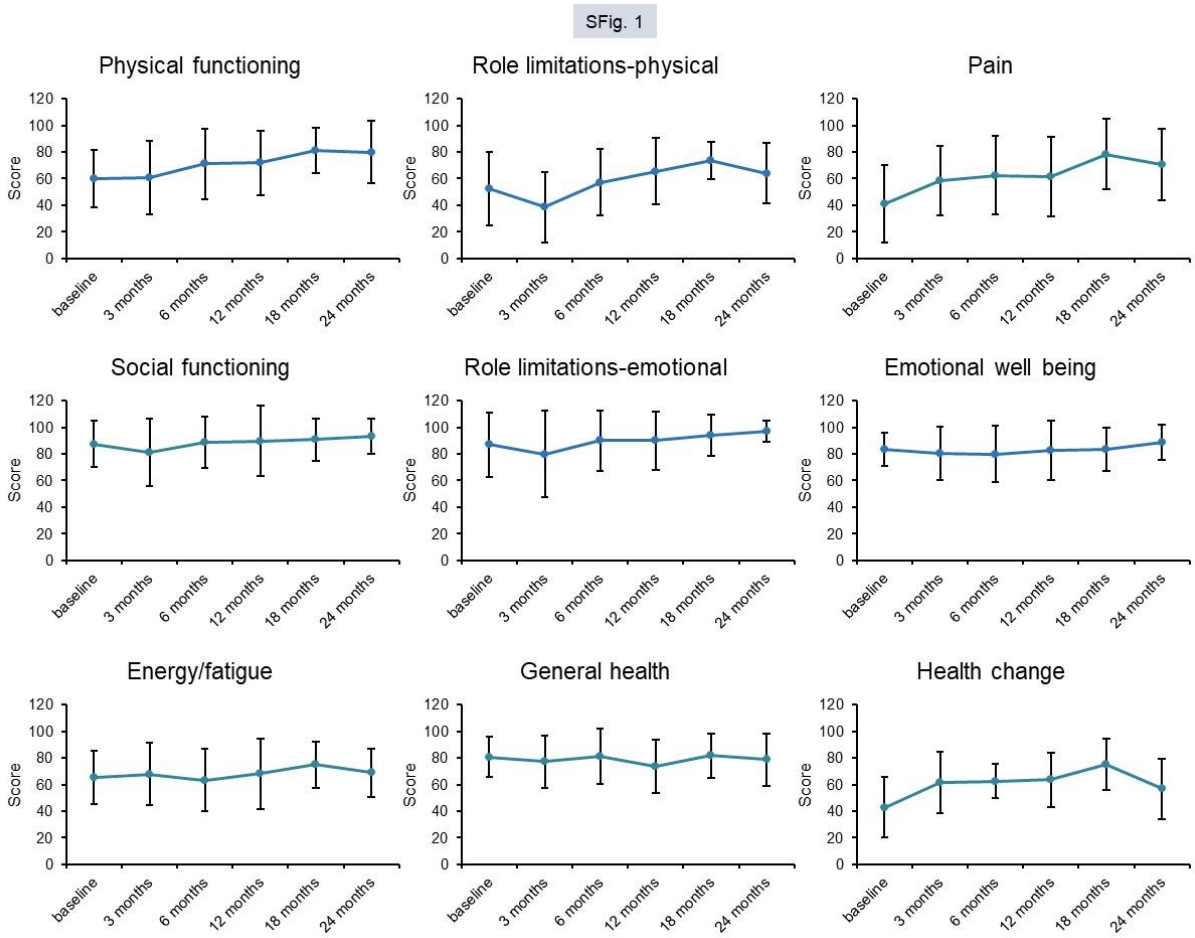
Supplementary Figures and Tables



Supplementary Figure 1. SF-36 survey results over the course of the study.

Supplementary Table 1. Detailed classification of adverse events in ChonDux patients

	ChonDux adverse events: N (%) of ChonDux patients			
System Organ Class Preferred term	**Mild**	**Moderate**	**Severe**	**Total**
Ear and labyrinth disorders	**2 (11.1%)**	**1 (5.6%)**	**0 (0.0%)**	**3 (16.7%)**
Endolymphatic hydrops	2 (11.1%)	1 (5.6%)	0 (0.0%)	3 (16.7%)
General disorders and administration site conditions	**4; 22.2%**	**4 (22.2%)**	**0 (0.0%)**	**8 (44.4%)**
Pain	3; 16.7%	5 (27.8%)	0 (0.0%)	4 (44.4%)
Swelling	2; 11.1%	1 (5.6%)	0 (0.0%)	3 (16.7%)
Injury, poisoning and procedural complications	**5; 27.8%**	**3 (16.7%)**	**0 (0.0%)**	**8 (44.4%)**
Fall	3 16.7%	2 (11.1%)	0 (0.0%)	5 (27.8%)
Fracture	0 (0.0%)	1 (5.6%)	0 (0.0%)	1 (5.6%)
Joint injury	1; 5.6%	0 (0.0%)	0 (0.0%)	1 (5.6%)
Procedural complication	1; 5.6%	0 (0.0%)	0 (0.0%)	1 (5.6%)
Wound haemorrhage	1; 5.6%	0 (0.0%)	0 (0.0%)	1 (5.6%)
Wound secretion	1; 5.6%	0 (0.0%)	0 (0.0%)	1 (5.6%)
Musculoskeletal and connective tissue disorder	**5 (27.8%)**	**3 (16.7%)**	**1 (5.6%)**	**9 (50.0%)**
Arthralgia	3 (16.7%)	1 (5.6%)	0 (0.0%)	4 (22.2%)
Back pain	0 (0.0%)	1 (5.6%)	0 (0.0%)	1 (5.6%)
Lumbar spinal stenosis	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Haemarthrosis	0 (0.0%)	0 (0.0%)	1 (5.6%)	1 (5.6%)
Joint crepitation	1 (5.6%)	0 (0.0%)	0 (0.0%)	1 (5.6%)
Joint instability	1 (5.6%)	1 (5.6%)	0 (0.0%)	2 (11.1%)
Nervous system disorders	**0 (0.0%)**	**0 (0.0%)**	**0 (0.0%)**	**0 (0.0%)**
Transient ischemic attack	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Psychiatric disorders	1 (5.6%)	**0 (0.0%)**	**0 (0.0%)**	1 (5.6%)
Insomnia	1 (5.6%)	0 (0.0%)	0 (0.0%)	1 (5.6%)

Supplementary Table 1. Detailed classification of adverse events in ChonDux™ treated patients. Adverse events were grouped by system organ class preferred term and classified as mild, moderate, or severe. The number of events and the % of patients experiencing that event are presented. Patients experiencing adverse events of more than 1 severity were summarized according to the maximum severity experienced over all episodes of that adverse event.

Supplementary Table 2. Patient demographics and safety

	Microfracture	
Participants	**N**	
Total	3	
Age	**years**	
mean	50.0	
standard deviation	3.6	
median	51.0	
range	46 – 53	
Sex	**N**	**%**
Male	2	66.7
Female	1	33.3
Subjects reporting any adverse events	**N**	**%**
Mild	0	0.0
Moderate	2	66.7
Severe	1	33.3
Total	3	100.0
Total number of adverse events	**reports**	**%**
Mild	6	66.7
Moderate	2	22.2
Severe	1	11.1
Total	9	100.0

Supplementary Table 3. MRI participation at each visit

	Microfracture
Time point	**N**
baseline	3
3 month	3
6 month	3
12 month	3
18 month	2
24 month	2

Supplementary Table 4. VAS pain scoring

	Microfracture		
VAS pain frequency	**Day 4-7**	**Week 6**	**Change**
mean	4.1	19.8	15.7
standard deviation	3.5	27.8	25.9
median	5.9	5.0	2.5
range	0.0 – 6.3	2.5 – 51.9	-0.9 – 45.6
VAS pain severity	**Day 4-7**	**Week 6**	**Change**
mean	6.5	15.6	9.1
standard deviation	9.6	15.2	5.8
median	2.0	10.7	8.7
range	0.0 – 17.6	3.5 – 32.7	3.5 – 15.1

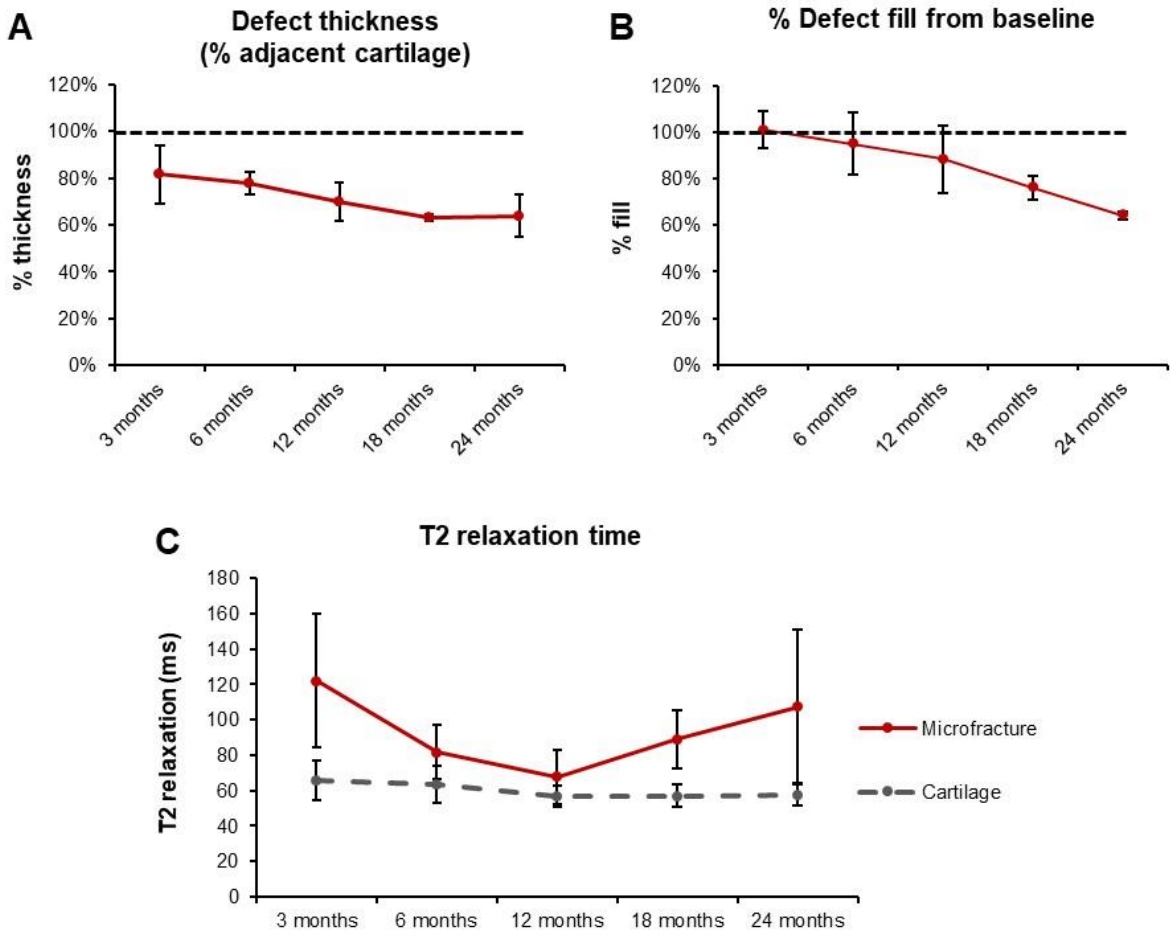
Supplementary Tables 2-4. (1) Patient demographics and safety with arthroscopic microfracture. (2) MRI participation of arthroscopic microfracture patients. (3) VAS pain frequency and severity with arthroscopic microfracture.

Supplementary Table 5. Detailed classification of adverse events in microfracture patients

	Microfracture adverse events: N (%) of microfracture patients			
System Organ Class Preferred term	**Mild**	**Moderate**	**Severe**	**Total**
Ear and labyrinth disorders	**3 (100.0%)**	**0 (0.0%)**	**0 (0.0%)**	**3 (100.0%)**
Endolymphatic hydrops	3 (100.0%)	0 (0.0%)	0 (0.0%)	3 (100.0%)
General disorders and administration site conditions	**2 (66.7%)**	**1 (33.3%)**	**0 (0.0%)**	**3 (100.0%)**
Pain	2 (66.7%)	1 (33.3%)	0 (0.0%)	3 (100.0%)
Swelling	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Injury, poisoning and procedural complications	**0 (0.0%)**	**0 (0.0%)**	**0 (0.0%)**	**0 (0.0%)**
Fall	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Fracture	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Joint injury	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Procedural complication	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Wound haemorrhage	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Wound secretion	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Musculoskeletal and connective tissue disorder	**0 (0.0%)**	**0 (0.0%)**	**1 (33.3%)**	**1 (33.3%)**
Arthralgia	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Back pain	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Lumbar spinal stenosis	0 (0.0%)	0 (0.0%)	1 (33.3%)	1 (33.3%)
Haemarthrosis	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Joint crepitation	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Joint instability	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Nervous system disorders	**0 (0.0%)**	**1 (33.3%)**	**0 (0.0%)**	**1 (33.3%)**
Transient ischemic attack	0 (0.0%)	1 (33.3%)	0 (0.0%)	1 (33.3%)
Psychiatric disorders	**0 (0.0%)**	**0 (0.0%)**	**0 (0.0%)**	**0 (0.0%)**
Insomnia	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Renal and urinary disorders	**1 (33.3%)**	**0 (0.0%)**	**0 (0.0%)**	**1 (33.3%)**
Nephrolithiasis	1 (33.3%)	0 (0.0%)	0 (0.0%)	1 (33.3%)

Supplementary Table 5. Detailed classification of adverse events in arthroscopic microfracture treated patients. Adverse events were grouped by system organ class preferred term and classified as mild, moderate, or severe. The number of events and the % of patients experiencing that event are presented. Patients experiencing adverse events of more than 1 severity were summarized according to the maximum severity experienced over all episodes of that adverse event.

SFig. 2



Supplementary Figure 2. MRI analysis of articular cartilage defect structural remodeling with arthroscopic microfracture treatment. Full MRI image processing workflow to quantify defect fill are provided in the Materials and Methods section. (A) Quantified defect thickness normalized to adjacent uninjured cartilage and (B) % defect fill normalized to initial defect size at baseline over the full 24 month time course with arthroscopic microfracture treatment (mean ± SD). Dashed lines reference 100% defect thickness and fill. (C) T2 relaxation time of arthroscopic microfracture treated defects compared to adjacent uninjured cartilage (pooled from all patients in study, mean ± SD).