

Supplementary Materials: Identifying Consensus and Open Questions around Assessing or Predicting the Quality and Success of Cartilage Repair: A Delphi Study

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Supplementary Table S1. A full list of the Likert-scale-rated single statements and results from the round 2 questionnaire.

Statement	Round 2 Statement Number	None (n)	Somewhat (n)	Middling (n)	Largely (n)	Completely (n)	Total answers (n)	Median	% Positive	IQR	Consensus Reached?
The size and depth of the lesion should both be measured.	1a	0	1	0	4	18	23	C	95.65	0	✓
We should measure the lacunae (cysts) in the bone.	1b	1	5	3	3	9	21	L	57.14	3	X
We should measure the area of bone marrow oedema-like (BML) signal.	1c	2	5	3	4	6	20	M/L	50	3	X
We should take disease status (e.g. synovial fibrosis, bone sclerosis, inflammation) into account for efficient repair.	2a	0	1	0	2	21	24	C	95.83	0	✓
Patients should be better stratified prior to clinical trial entry.	2b	0	1	2	8	13	24	C	87.5	1	✓
Environmental factors are important in influencing repair (e.g. age, exercise, gender).	2c	0	0	0	9	15	24	C	100	1	✓
Access to specialist rehabilitation programs would be useful for all patients, pre- and post- cartilage repair.	3	0	1	3	6	14	24	C	83.33	1	✓
An increase in collagen type II expression is a key marker of cartilage quality in pellet culture.	4a	0	1	2	9	10	22	L	86.36	1	✓

An increase in collagen type II expression is a key marker of cartilage quality in animal models.	4b	0	0	0	10	12	22	C	100	1	✓
An increase in collagen type II expression is a key marker of cartilage quality in humans.	4c	0	1	1	7	14	23	C	91.30	1	✓
An increase in aggrecan expression is a key marker of cartilage quality in pellet culture.	5a	0	1	4	9	8	22	L	77.27	1	X
An increase in aggrecan expression is a key marker of cartilage quality in animal models.	5b	0	1	1	12	8	22	L	90.91	1	✓
An increase in aggrecan expression is a key marker of cartilage quality in humans.	5c	0	2	2	10	9	23	L	82.61	1	✓
An increase in lubricin expression is a key marker of cartilage quality in pellet culture.	6a	0	0	6	9	5	20	L	70	1.25	X
An increase in lubricin expression is a key marker of cartilage quality in animal models.	6b	0	0	5	11	5	21	L	76.19	0	X
An increase in lubricin expression is a key marker of cartilage quality in humans.	6c	0	1	4	10	7	22	L	77.27	1	X
Any functional fibrocartilage is sufficient.	7	3	5	10	3	3	24	M	25	1.25	X
Hyaline cartilage is absolutely necessary.	8	2	0	6	10	6	24	L	66.67	1.25	X
Collagen type X expression should not be present at mRNA level.	9	2	2	10	6	3	23	M	39.13	1	X
Collagen type X expression should not be present in the repair.	10	1	1	7	9	4	22	L	59.09	1	X
Measuring cartilage changes is irrelevant, the pathogenic mechanisms that lead to the changes are more important and may be largely cartilage dependant.	11	3	6	8	4	1	22	M	22.72	1	X
Collagen type VI is a useful marker for cartilage repair quality.	12	2	0	4	0	8	14	C	57.14	2	X
A more extensive histology scoring system is needed for pellet culture.	13a	4	1	6	5	6	22	M	50	1.5	X
A more extensive histology scoring system is needed for animal models.	13b	4	2	2	8	8	24	L	66.67	2.25	X
A more extensive histology scoring system is needed for human tissue.	13c	4	2	2	7	9	24	L	66.67	2.25	X
A simpler scoring system is best for MRI in animal models.	14a	1	2	7	5	5	20	M/L	50	1.25	X

A simpler scoring system is best for MRI in human research.	14b	2	3	7	5	6	23	M	47.82	1.5	X
Scoring systems should include both structural and inflammatory features in animal models.	15a	2	2	3	8	6	21	L	66.67	2	X
Scoring systems should include both structural and inflammatory features in human research.	15b	2	2	2	9	8	23	L	73.91	1.5	X
It is important to assess all tissues in the joint in animal models.	16a	0	0	5	10	9	24	L	79.17	2	X
It is important to assess all tissues in the joint in human research.	16b	0	0	4	8	12	24	L/C	83.33	1.5	✓
Non-invasive measures provide a way to reduce time and cost.	19	1	1	5	5	12	24	L/C	70.83	1	X
The advancement of the bone front is negative.	21	1	2	9	2	3	17	M	29.41	1	X
It is important to assess the identity and quality of both repair cartilage and the bone-cartilage interface in animal models.	23a	0	0	2	8	13	23	C	91.30	2	✓
It is important to assess the identity and quality of both repair cartilage and the bone-cartilage interface in humans.	23b	0	1	4	7	11	23	L	78.26	1	X
The repair has an effect on the surrounding cells in animal models.	24a	0	0	5	5	13	23	C	78.26	1	X
The repair has an effect on the surrounding cells in humans.	24b	0	0	5	5	13	23	C	78.26	1	X
Determining the mechanism of damage repair response is important in animal models.	25a	0	2	2	6	13	22	C	90.91	1	✓
Determining the mechanism of damage repair response is important in human research.	25b	0	2	2	6	13	23	C	82.61	1	✓
MRI should be used in short bursts to keep costs down in animal models.	26a	2	2	5	6	2	17	M	47.06	1	X
MRI should be used in short bursts to keep costs down in human research.	26b	1	1	8	5	2	17	M	41.18	1	X
Treatment costs should be justifiable.	27	0	1	2	7	13	23	C	86.96	1	✓

Any technique or product for cartilage repair has to be scalable.	28	0	2	4	9	8	23	L	73.91	1.5	X
The cell type should raise as few ethical and safety issues as possible.	29	3	4	5	3	8	23	L	47.83	2	X
Laboratory research should push the boundaries, not slow down for clinics. There is a need for clinical innovation.	30	0	1	1	8	13	23	C	91.30	1	✓
More investment in cell therapies is needed.	31	0	1	4	5	13	23	C	78.26	1	X

Supplementary Table S2. A full list of the Likert-scale-rated single statements and results from the round 3 questionnaire.

Statement	Round 3 Statement Number	None (n)	Somewhat (n)	Middling (n)	Largely (n)	Completely (n)	Total answers (n)	Median	% Positive	IQR	Consensus Reached?
We should measure the lacunae (cysts) in the bone.	1a	1	1	4	3	6	15	L	60.00	2	X
We should measure the area of bone marrow oedema-like (BML) signal.	1b	0	2	3	5	4	14	L	64.29	1.75	X
An increase in aggrecan expression is a key marker of cartilage quality in pellet culture.	2a	0	0	0	8	7	15	L	100	1	✓
An increase in lubricin expression is a key marker of cartilage quality in pellet culture.	3a	0	0	7	4	2	13	M	46.15	1	X
An increase in lubricin expression is a key marker of cartilage quality in animal models.	3b	0	0	3	11	1	15	L	80.00	0	✓
An increase in lubricin expression is a key marker of cartilage quality in humans.	3c	0	0	3	9	3	15	L	80.00	0	✓
Any functional fibrocartilage is sufficient.	4	0	4	6	3	2	15	M	33.33	1.5	X
Hyaline cartilage is absolutely necessary.	5	1	1	3	7	3	15	L	66.67	1	X
Collagen type X expression should not be present in the repair at mRNA level.	6	0	4	6	5	0	15	M	33.33	1.5	X
Collagen type X expression should not be present in the repair.	7	0	2	5	7	1	15	L	53.33	1	X
Measuring cartilage changes is irrelevant, the pathogenic mechanisms that lead to the	8	3	4	5	2	1	15	M	20.00	1	X

changes are more important and may be largely cartilage dependant.											
Collagen type VI is a useful marker for cartilage repair quality.	9	0	2	6	1	6	15	M	46.67	2	X
A more extensive histology scoring system is needed for pellet culture.	10a	1	2	4	4	4	15	L	53.33	1.5	X
A more extensive histology scoring system is needed for animal models.	10b	1	1	2	4	7	15	L	73.33	1.5	X
A more extensive histology scoring system is needed for human tissue.	10c	1	1	1	2	9	14	C	78.57	1	✓
A simpler scoring system is best for MRI in animal models.	11a	1	0	6	6	1	14	M/L	50.00	1	X
A simpler scoring system is best for MRI in human research.	11b	1	0	7	5	1	14	M	42.86	1	X
Scoring systems should include both structural and inflammatory features in animal models.	12a	0	0	1	8	5	14	L	92.86	1	✓
Scoring systems should include both structural and inflammatory features in human research.	12b	0	0	1	7	7	15	L	93.33	1	✓
It is important to assess all tissues in the joint in animal models.	13	0	0	1	3	11	15	C	93.33	0.5	✓
Non-invasive measures provide a way to reduce time and cost.	14	0	0	1	0	14	15	C	93.33	0	✓
The advancement of the bone front is negative.	15	0	0	8	4	2	14	M	42.86	1	X
It is important to assess the identity and quality of both the repair cartilage and the bone-cartilage interface in humans.	16	0	0	0	4	11	15	C	100	0.5	✓
The repair has an effect on the surrounding cells in animal models.	17a	0	0	0	2	13	15	C	100	0	✓
The repair has an effect on the surrounding cells in humans.	17b	0	0	0	2	13	15	C	100	0	✓
MRI should be used in short bursts to keep costs down in animal models.	18a	1	0	8	4	0	13	M	30.77	1	X
MRI should be used in short bursts to keep costs down in human research.	18b	1	2	7	2	1	13	M	23.08	0	X

Any technique or product for cartilage repair has to be scalable.	19	0	0	0	7	8	15	C	100	1	✓
The cell type should raise as few ethical and safety issues as possible.	20	0	0	1	5	9	15	C	93.33	1	✓
More investment in cell therapies is needed.	21	0	0	1	1	12	14	C	92.86	0	✓

Supplementary Table S3. A full list of the statement series and results from the round 2 questionnaire'

Round 2 Ranked Series	Options	Number of respondents	Number that ranked as most important	Mean Rank	Mode Rank	Kendall's coefficient of concordance	Consensus Reached?
Tissue Type	Cartilage	24	23	1.10	1	0.736	✓
	Meniscus		1	4.21	5		
	Fat Pad		0	5.79	6		
	Subchondral Bone		0	2.40	2		
	Synovium (focal to defect)		0	3.60	4		
	Synovium (general)		0	3.90	4		
Treatment Choice Basis	Patient Expectations	24	12	2.13	1	0.049	X
	Clinician Expectations		5	2.44	2		
	Biomarkers		4	2.67	3		
	Baseline		3	2.77	3		
Repair Quality Assessment	Filling of defect area	20	6	3.98	1	0.182	X
	Filling of defect depth		0	4.73	2		
	Quality measures by stiffness		0	6.60	10		
	Lateral integration		1	5.93	5		
	Attachment to bone		0	5.83	6		
	Smooth surface		0	7.15	9		
	Low friction surface		0	7.55	8		
	Durability over time		4	4.23	1		
	Functionality (lack of pain)		3	4.33	3		

Functionality (delayed OA progression)		3	4.70	7			
Treatment Outcome	Regain function	24	9	1.96	2	0.172	X
	Movement without pain		7	2.13	2		
	Return to baseline (or better) quality of life		3	2.92	3		
	Patient specific goals		4	3.00	4		

Supplementary Table S4. A full list of the statement series and results from the round 3 questionnaire'

Round 3 Ranked Series	Options	Number of respondents	Number that ranked as most important	Mean Rank	Mode Rank	Kendall's coefficient of concordance (W)	Consensus Reached?
Treatment Outcome	Movement without pain	15	6	1.77	1	0.437	X
	Return to baseline (or better) quality of life		0	3.10	3		
	Patient specific goals		1	3.37	4		
	Regain function		6	1.77	2		
Treatment Choice Basis	Biomarkers	15	0	2.87	3	0.376	X
	Patient expectations		10	1.73	1		
	Baseline imaging		1	3.43	4		
	Clinician expectations		3	1.97	2		
Repair Quality Assessment	Attachment	15	2	3.27	3	0.287	X
	Stiffness		1	4.27	5		
	Durability		6	2.23	1		
	Filling		1	2.53	2		
	Surface		1	4.80	6		
	Lateral integration		0	3.90	4		