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Arthroscopic International Cartilage Repair Society Classification System Has Only Moderate Reliability in a Porcine Cartilage Repair Model

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Background: The International Cartilage Repair Society (ICRS) score was designed for arthroscopic use to evaluate the quality of cartilage repair.

Purpose: To evaluate the reliability of the ICRS scoring system using an animal cartilage repair model.

Study Design: Controlled laboratory study.

Methods: A chondral defect with an area of 1.5 cm² was made in the medial femoral condyle of 18 domestic pigs. Five weeks later, 9 pigs were treated using a novel recombinant human type III collagen/poly lactide scaffold, and 9 were left to heal spontaneously. After 4 months, the pigs were sacrificed, then 3 arthroscopic surgeons evaluated the medial femoral condyles via video-recorded simulated arthroscopy using the ICRS scoring system. The surgeons repeated the evaluation twice within a 9-month period using their recorded arthroscopy.

Results: The porcine cartilage repair model produced cartilage repair tissue of poor to good quality. The mean ICRS total scores for all observations were 6.6 (SD, 2.6) in arthroscopy, 5.9 (SD, 2.7) in the first reevaluation, and 6.2 (SD, 2.8) in the second reevaluation. The interrater reliability with the intraclass correlation coefficient (ICC) for the ICRS total scores (ICC, 0.46-0.60) and for each individual subscore (ICC, 0.26-0.71) showed poor to moderate reliability. The intrarater reliability with the ICC also showed poor to moderate reliability for ICRS total scores (ICC, 0.52-0.59) and for each individual subscore (ICC, 0.29-0.58). A modified Bland-Altman plot for the initial arthroscopy and for the 2 reevaluations showed an evident disagreement among the observers.

Conclusion: In an animal cartilage repair model, the ICRS scoring system seems to have poor to moderate reliability.

Clinical Relevance: Arthroscopic assessment of cartilage repair using the ICRS scoring method has limited reliability. We need more objective methods with acceptable reliability to evaluate cartilage repair outcomes.

Keywords: cartilage repair; the International Cartilage Repair Society (ICRS) score; arthroscopy; animal cartilage repair model

Cartilage injuries of the knee may cause pain and decreased function with disability. To relieve these symptoms, cartilage repair aims to fill a defect with repair tissue that has a structure and biomechanical function equal to the original cartilage.^{1,6} As higher quality of repair tissue is correlated with better clinical outcomes, repair quality may serve as an objective measure to evaluate the repair technique.^{4,5,27} Arthroscopy may be used to evaluate cartilage pathologies and structural outcome of cartilage repair in vivo.^{1,6,21,22}

Additionally, repair tissue quality may serve as a primary outcome measure in studies without achievable clinical outcome (eg, feasibility studies and animal studies).³¹

The International Cartilage Repair Society (ICRS) score was designed for arthroscopic use to macroscopically assess the repair tissue quality after cartilage repair.^{4,31} In the ICRS score, the repair quality is assessed according to lesion fill, integration into the surrounding cartilage, and the appearance of the repair tissue surface during arthroscopy. The ICRS score has been used in several studies to evaluate the outcome of cartilage repair.^{8,13,25,32,34}

Previous validation studies of the ICRS score after autologous chondrocyte implantation in humans have shown limitations in score performance, but the reasons for these deficiencies have remained unclear.^{7,8,31,33} The

inter- and intrarater reliability values of the ICRS score are also lacking in the present literature.^{23,31,33} As the ICRS score was designed for arthroscopic use, a simulated arthroscopic environment has been used in most validation experiments. However, previous studies have acknowledged the challenge of replicating an authentic arthroscopic assessment for validation.^{23,31,33}

The purpose of this study was to evaluate the reliability of the ICRS score for arthroscopic use. To test the inter- and intrarater reliability, a novel study model was designed where different individuals performed multiple video-recorded arthroscopies on the same animal study subjects.

METHODS

Experimental Animals and Ethical Considerations

Four-month-old female domestic pigs (*Sus scrofa domestica*; $n = 18$) obtained from a local farmer were used for this study. The animals were acclimatized to the experimental facility and handlers 14 days before any treatment. The animals were housed in groups and allowed free movement in pens with bedding throughout the experiment. A veterinarian supervised the well-being of the animals during the study. The study was authorized by the National Animal Experiment Board (ESAVI/6113/04.10.07/2015) and conducted according to the ethical guidelines and regulations of the Finnish Act on the Protection of Animals Used for Scientific or Educational Purposes (497/2013) and Government Decree on the Protection of Animals Used for Scientific or Educational Purposes (564/2013).

Surgical Procedure

For the initial procedure, animals were anesthetized using 0.2 mg/kg of medetomidine, 10 mg/kg of ketamine, and 3 mg/kg of propofol followed by 1.5% to 2.5% isoflurane. Preoperative analgesia of 0.05 mg/kg of buprenorphine and 3 mg/kg of carprofen and antibiotic prophylaxis of 3.0 g of cefuroxime were administered. The animals were intubated and set in a supine position on the operating table. A medial parapatellar arthrotomy was made to the right hind leg, and the patella was dislocated laterally. The aim was to create and repair as large as possible full-thickness cartilage lesions to the weightbearing surface of

the medial femoral condyle. With the help of anatomic samples, an oval lesion size of 11×17 mm was considered the largest lesion size that was safe to produce through a medial parapatellar arthrotomy. To standardize the defect size, an oval-shaped custom-made hollow punch (size, 11×17 mm; area, 1.5 cm^2) was designed. The surgeon marked the outer margins of the lesion with this hollow punch and made a full-thickness oval-shaped chondral defect in the right medial femoral condyle of all 18 pigs. The subchondral bone at the defect area was left intact. The animals were allowed free weightbearing and unrestricted movement after the operation. Postoperative analgesia of carprofen and buprenorphine, together with microbiological prophylaxis of cephalexin, was continued for 3 days.

Five weeks later, using the described anesthesia protocol, the fibrous tissue of the defect area of each of the 18 pigs was debrided to the subchondral bone, the subchondral bone was left intact, and 9 of those pigs were treated using a novel recombinant human type III collagen/poly lactide scaffold.^{19,28} The scaffold was made of recombinant human type III collagen (FibroGen Inc) and poly L/D-lactide (96/4) (Corbion Purac). The manufacturing process of these rhCo-PLA scaffolds has been described previously.¹⁹ The scaffold was cut to fit the defect and secured using absorbable sutures (Monocryl 6-0; Ethicon Inc, Johnson & Johnson) to the surrounding cartilage. Nine pigs did not receive the scaffold after the debridement, and the defect was left to heal spontaneously. All surgical procedures were made by 2 experienced orthopaedic knee surgeons (A.V. and T.P.).

Four months after the second procedure, the pigs were sacrificed using intravenous anesthetic, then the medial condyles were excised and evaluated during a simulated video-recorded arthroscopy.

Simulated Arthroscopic and Video Evaluations

Simulation was done by immersing the specimens in an 8×12 -cm container filled with phosphate-buffered saline containing metalloprotease inhibitors (PBSI): 5 mM of ethylenediaminetetraacetic acid disodium salt (VWR International) and 5 mM of benzamidine hydrochloride (Sigma-Aldrich) (Figure 1). The excised medial condyles were fixed at the bottom of the container and arthroscopy was performed and video recorded using a standard arthroscopy tower (Karl Storz Endoscopy), with a standard 4.0 mm and 30° angled optic and a standard arthroscopic probe.

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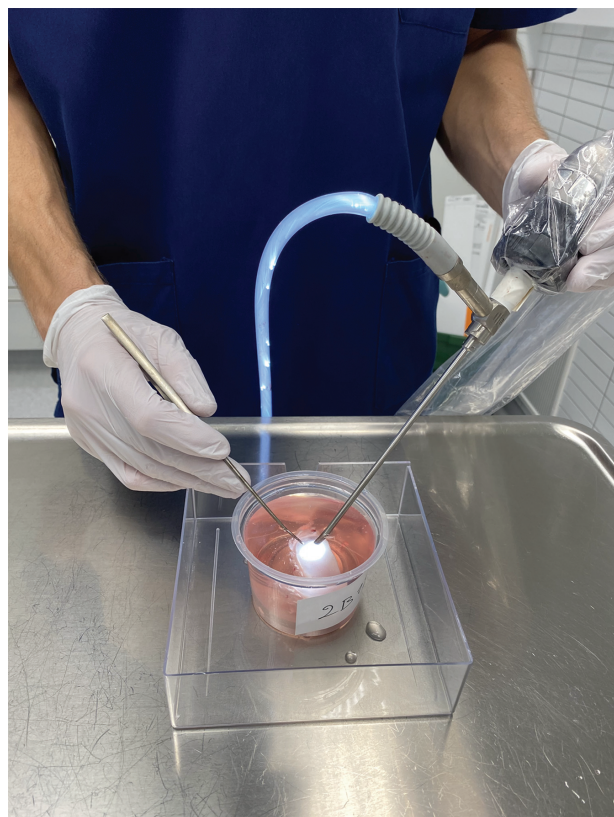


Figure 1. Simulated video-recorded arthroscopy using a camera and a probe.

The simulated arthroscopy of the repaired tissue was performed by 3 independent surgeons using the ICRS scoring method. The surgeons made their evaluations without knowledge of the results of the others. The surgeons had different levels of experience with arthroscopic knee procedures. The first evaluator was an orthopaedic resident with 1 year of experience in knee arthroscopy, the second was an orthopaedic fellow with 6 years of experience in knee arthroscopy, and the third was an orthopaedic consultant with more than 10 years of experience in arthroscopy (E.S., J.P. and T.P.). All of the evaluators were familiar with the ICRS scoring method, but they were also re-educated on using the grading system before the initial arthroscopic assessments. During the arthroscopies, the evaluators filled a blank ICRS formula with all the ICRS subclasses (Table 1). All evaluators reevaluated their own video-recorded arthroscopies twice after the initial arthroscopy within a 9-month period in a randomized and blinded manner using a web-based survey (SurveyMonkey). The first reevaluation was made 6 months after the arthroscopy, and the second followed 3 months later.

Statistical Analysis

Three reliability measures were used to evaluate the inter-rater reliability of the ICRS score. Internal consistency was estimated using Cronbach alpha coefficient, with an α

TABLE 1
Macroscopic Evaluation of Cartilage Repair
Using the International Cartilage Repair Society
(ICRS) Scoring System³³

Cartilage Repair Assessment (ICRS)	Points
Degree of defect repair	
In level with surrounding cartilage	4
75% repair of defect depth	3
50% repair of defect depth	2
25% repair of defect depth	1
0% repair of defect depth	0
Integration into border zone	
Complete integration with surrounding cartilage	4
Demarcating border <1 mm	3
3/4 of graft integrated, 1/4 with a notable border >1 mm width	2
1/2 of graft integrated with surrounding cartilage, 1/2 with a notable border >1 mm	1
From no contact to 1/4 of graft integrated with surrounding cartilage	0
Macroscopic appearance	
Intact smooth surface	4
Fibrillated surface	3
Small, scattered fissures or cracks	2
Several, small, or few but large fissures	1
Total degeneration of grafted area	0
Overall repair assessment	
Grade I: normal	12
Grade II: nearly normal	11-8
Grade III: abnormal	7-4
Grade IV: severely abnormal	3-1

value of .7 to .8 being interpreted as satisfactory; for clinical application, the α value should be $\geq .9$.³ Intraclass correlation coefficients (ICCs) were calculated using a single-rater, absolute-agreement, 2-way random effects model. Also, a modified Bland-Altman plotting method for more than 2 observers was used.⁹

To evaluate the intrarater reliability of the ICRS score, a reliability analysis was made using the ICCs based on a single-rater, absolute-agreement, 2-way mixed-effects model. ICC values <0.5 indicate poor reliability; between 0.5 and 0.75, moderate reliability; between >0.75 and 0.9, good reliability; and >0.90, excellent reliability.^{14,24}

All statistical analyses were performed using Stata Version 16.0 (StataCorp).

RESULTS

The porcine cartilage repair model produced repair tissue from poor to good quality with good defect fill (Figure 2).

The mean total score of the ICRS for all observations was 6.6 (SD, 2.6) in the first recorded arthroscopy, 5.9 (SD, 2.7) in the first reevaluation, and 6.2 (SD, 2.8) in the second reevaluation. The internal consistency (Cronbach alpha) for the ICRS items was 0.82 in the first recorded arthroscopy. The interrater reliability with the ICC for ICRS total scores (ICC, 0.46-0.60) and for each individual subscore (ICC, 0.26-0.71) showed poor to moderate reliability (Table 2). The intrarater reliability with the ICC also showed poor to moderate reliability for ICRS total scores (ICC, 0.52-0.59) and for each individual subscore (ICC, 0.29-0.58) (Table 3).

TABLE 2
Interrater Reliability of Evaluating Repaired Cartilage Using the ICRS Scoring System and Its Subscores^a

	Evaluation at Arthroscopy	Reevaluation 1 (Video)	Reevaluation 2 (Video)
ICRS total score	0.60 (0.34 to 0.81)	0.57 (0.30 to 0.79)	0.46 (0.17 to 0.72)
Degree of defect subscore	0.46 (0.18 to 0.72)	0.33 (0.07 to 0.63)	0.38 (0.08 to 0.67)
Integration into border zone subscore	0.32 (0.05 to 0.61)	0.45 (0.17 to 0.72)	0.27 (-0.01 to 0.59)
Macroscopic appearance subscore	0.26 (0.13 to 0.54)	0.71 (0.48 to 0.87)	0.47 (0.18 to 0.73)

^aRepresented are intraclass correlation coefficient (ICC) estimates and their 95% CIs based on a single-rater, absolute-agreement, 2-way random effects model. ICRS, International Cartilage Repair Society.

TABLE 3
Intrarater Reliability of Evaluating Repaired Cartilage Using the ICRS Scoring System^a

	Resident	Fellow	Consultant
ICRS total score	0.54 (0.26-0.78)	0.52 (0.25-0.76)	0.59 (0.33-0.80)
Degree of defect subscore	0.58 (0.32-0.80)	0.49 (0.21-0.74)	0.58 (0.31-0.80)
Integration into border zone subscore	0.31 (0.04-0.61)	0.40 (0.11-0.68)	0.58 (0.31-0.79)
Macroscopic appearance subscore	0.45 (0.17-0.71)	0.44 (0.16-0.71)	0.29 (0.03-0.59)

^aRepresented are intraclass correlation coefficient (ICC) estimates and their 95% CIs based on a single-rater, absolute-agreement, 2-way mixed effects model. ICRS, International Cartilage Repair Society.

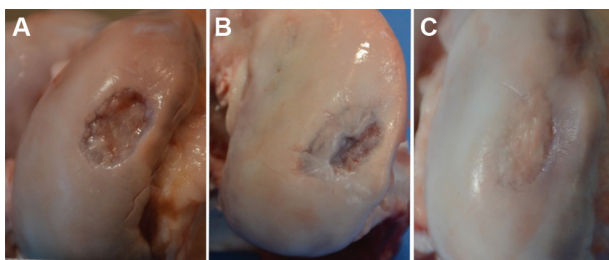


Figure 2. Examples of macroscopic cartilage repair results. (A) Poor-quality repair: low volume of repair cartilage. (B) Average quality repair: some regenerated cartilage. (C) Good-quality repair: good-quality repair tissue with good defect fill.

The modified Bland-Altman plot for the initial recorded arthroscopy and for the 2 reevaluations showed an evident disagreement among the observers within the whole range of possible ICRS scores from 0 to 12 (Figure 3). Midlevel results are prone to more interpretation resulting in bigger differences among the observers than around poor (ICRS score near 0) or excellent cartilage repair results (ICRS score near 12) (Figure 3).

DISCUSSION

This animal study for testing the reliability of the arthroscopic ICRS repair tissue scoring system showed poor to moderate inter- and intrarater reliability. To our knowledge, this is the first animal study in which the reliability of the ICRS score for cartilage repair has been investigated.

In the previous reliability studies, the initial arthroscopic assessment is often done by a single surgeon, and the actual

study of reliability is based either on still images or videos with a small sample size.^{23,31,33} The ICRS repair tissue scoring system has previously been validated for use in assessing cartilage repair tissue during human knee arthroscopies.^{23,31,33} In the study by Smith et al,³¹ the performance of the ICRS score was evaluated by 6 reviewers using 5 videos recorded during a knee arthroscopy in patients who had previously undergone an autologous chondrocyte implantation procedure. Smith et al reported an interrater reliability of 0.83 and an intrarater reliability of 0.94 using the ICC. The authors concluded that the ICRS score is an effective tool in the evaluation of cartilage repair. In a study by Van den Borne et al,³³ still images of 101 cartilage repair sites were presented for 7 observers. They reported an interrater reliability of 0.62 and an intrarater reliability of 0.73 using the ICC. A conclusion was made that the ICRS repair tissue scoring system is a useful tool for the macroscopic evaluation of cartilage repair for research purposes but not for individual clinical testing.³³ In a study by Paatela et al,²³ 2 observers assessed arthroscopic images of repair tissue from 62 patients. They calculated an ICC of 0.89 for ICRS repair tissue score. However, a modified Bland-Altman score showed marked disagreement among the observers, suggesting that the reliability was probably not as good as the ICC value suggested. All 3 of these studies had substantially better reliability than did our study. The most likely explanations for this difference could relate to differences in the statistical methods, visual material from the repair tissue, or lesion properties (eg, differences between species in repair tissue morphology).

Recently, improvements to statistical methods have been introduced to assess the reliability of a score. The ICC can be calculated in 10 different ways depending on the study design.¹⁴ Smith et al³¹ and Van den Borne et al³³ did not report the form of the ICC that was used, and no subsequent

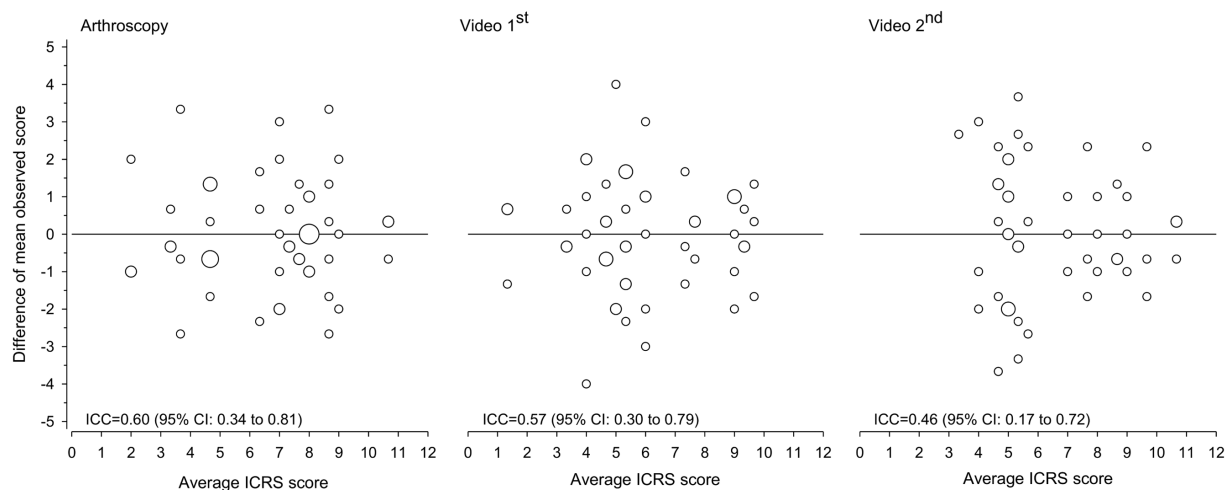


Figure 3. Modified Bland-Altman plot comparing the scoring of 3 independent observers using the International Cartilage Repair Society (ICRS) scoring system. Circle size represents the number of samples. ICC, intraclass correlation coefficient.

plot to visualize the level of agreement among the raters was shown. Therefore, the statistical method might be different compared with that used in our study. Furthermore, ICC alone may be an insufficient method to assess intraobserver reliability. As Jones et al⁹ demonstrate in a series of lung cancer samples, the ICC may calculate surprisingly high values, although a Bland-Altman plot might simultaneously show clinically significant unreliability. A recent study demonstrated similar wide disagreement in a Bland-Altman compared with the reported ICC in the reliability of the ICRS score.²³ Therefore, reliability should be assessed using an exactly specified ICC, together with a modified Bland-Altman plot, and both methods should be used to interpret reliability.⁹ In the present study, the interrater reliability ranged from 0.46 to 0.60 and the intrarater reliability ranged from 0.52 to 0.59, which we conclude to be poor to moderate according to a recent interpretation guideline for the ICC.^{14,24} The modified Bland-Altman plot also supported this interpretation, with the wide disagreement among the raters. The level of experience did not seem to alter the results. There were 3 raters with different experience levels. The intrarater reliability was almost the same among the 3 raters, and no trend was observed between the intrarater reliability and the experience of the surgeon.

A previous study suggested that the reliability of the score seems to degrade as the lesion size increases, possibly due to more heterogeneous repair tissue in larger lesions.²³ Therefore, the relatively larger lesion size in our study might also partly explain the inferior reliability of the ICRS score in our study compared with that in the human studies.

As our results suggest, the ICRS score has limitations in reliably assessing repair results, and thus more objective methods should be developed. Several novel arthroscopic methods have been introduced to assess the severity of damage in hyaline cartilage, including mechanical testing of cartilage stiffness,^{15,16} high-frequency ultrasound,^{10,26} mechanoacoustical testing,^{11,12} optical coherence tomography,²⁰ and electromechanical testing.^{2,29,30} These methods could possibly make the arthroscopic assessment of

cartilage repair more accurate and reliable. However, none of them has been validated to assess repair tissue quality. Their validity has been only studied to assess damage of native hyaline cartilage. It is unknown if good ability to detect damage in hyaline cartilage also makes a method a valid tool to assess the quality of repair tissue.

The limitations of the present study are a rather small sample size and a small number of raters. The repair tissue was evaluated through arthroscopy in a simulated setup and not in the joint, and this may have impaired the generalization of the results. In the present study, a simulated arthroscopy setting was used because the stifle joints of pigs are small and the experience of the surgeon might affect the diagnostic accuracy of stifle joint arthroscopy of pigs.¹⁷ Furthermore, our observers were not familiar with arthroscopies of the stifle joint of a domestic pig. The simulated setting was considered to minimize technical difficulties and to provide equal visualization of the repair site for all observers with different arthroscopic surgery skills. A simulated arthroscopy can also be seen as a benefit because it made the evaluation possible for more than 1 surgeon and ensured that no iatrogenic damage was done to the studied cartilage. Each surgeon performed the primary arthroscopic cartilage evaluation and performed the reevaluations twice from her or his recorded video. We consider that the simulated setup enabled a reproducible and standardized environment that very closely resembled a normal arthroscopy. Evaluation using the recorded videos can cause bias, and no impression about tactile assessment can be made using a video alone. A surgeon is expected to have more reliable test results when using the scoring systems during arthroscopy via a probe than when evaluating repair results solely via videos. However, the results of this study indicate that the evaluations using the initial arthroscopy and reevaluations using the videos seemed comparable, giving rather similar interrater reliability values for both evaluation types.

The strengths of this study were the use of an animal model that allowed the creation of a standardized lesion size and location and the initial arthroscopic assessment

made by multiple surgeons. Also, there was a wide variation in repair results from poor to good repair tissue, which can be regarded as a benefit of the present animal model. Additionally, the porcine joint is considered to be one of the closest approximations to the human joint.¹⁸

CONCLUSION

Based on the present study, the ICRS scoring system seems to have only poor to moderate reliability for evaluating cartilage repair in the porcine cartilage repair model. This study highlights the need for novel objective methods to evaluate cartilage repair outcomes in animal repair cartilage models.

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