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Review

Complex and elementary histological scoring systems for articular cartilage repair

Patrick Orth[1,2] and Henning Madry[1,2]

[1]Center of Experimental Orthopaedics and Osteoarthritis Research, Saarland University and

[2]Department of Orthopaedic Surgery, Saarland University Medical Center, Homburg/Saar, Germany

Summary. The repair of articular cartilage defects is increasingly moving into the focus of experimental and clinical investigations. Histological analysis is the gold standard for a valid and objective evaluation of cartilaginous repair tissue and predominantly relies on the use of established scoring systems. In the past three decades, numerous elementary and complex scoring systems have been described and modified, including those of O'Driscoll, Pineda, Wakitani, Sellers and Fortier for entire defects as well as those according to the International Cartilage Repair Society (ICRS-I/II) for osteochondral tissue biopsies. Yet, this coexistence of different grading scales inconsistently addressing diverse parameters may impede comparability between reported study outcomes. Furthermore, validation of these histological scoring systems has only seldom been performed to date. The aim of this review is (1) to give a comprehensive overview and to compare the most important established histological scoring systems for articular cartilage repair, (2) to describe their specific advantages and pitfalls, and (3) to provide valid recommendations for their use in translational and clinical studies of articular cartilage repair.

Key words: Articular cartilage, Subchondral bone, Cartilage repair, Histology, Scoring system

Offprint requests to: Henning Madry, Center of Experimental Orthopaedics and Osteoarthritis Research, University of Saarland, Kirrberger Strasse, Building 37-38, D-66421 Homburg/Saar, Germany. e-mail address: henning.madry@uks.eu

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Introduction

Hyaline articular cartilage covers all diarthrodial joints and provides a gliding surface for joint movements (Hunziker, 2002). Focal lesions of this smooth joint surface may occur as a consequence of direct trauma, osteonecrosis, or osteochondritis dissecans (Madry et al., 2010). The resulting articular cartilage defect is characterized as being either chondral, involving only the cartilaginous zones, or osteochondral, reaching further into the subchondral bone (Orth et al., 2014).

Both defect types exhibit essential differences in the history of natural repair. Due to a lack of access to marrow elements of the underlying subchondral bone, chondral defects are mainly repopulated by cells that migrate from the synovial membrane (Hunziker and Rosenberg, 1996). However, filling of such defects is insufficient, frequently inducing gradual degeneration of the repair tissue and an increase in the size of the defect (Hunziker, 2002). In contrast, osteochondral defects are filled with a blood clot that forms if the bone marrow communicates with the defect (Shapiro et al., 1993; Jackson et al., 2001). Pluripotent mesenchymal cells present therein differentiate into chondrocytes and osteoblasts that later form the cartilaginous repair tissue and the reconstituted subchondral bone. Despite such advantageous biological circumstances, the fibro-cartilaginous repair tissue does not withstand mechanical loads over time and may degenerate after several years, possibly inducing secondary osteoarthritis.

Numerous histological scoring systems have been developed and are in widespread use to grade such articular cartilage defects, serving as the main pillar in

the important evaluation of cartilage repair. Although histological grading of osteoarthritic (OA) lesions was established as early as 1971 by Mankin et al. (1971), the first scoring system for circumscribed (non-OA) articular cartilage defects was proposed by O'Driscoll and colleagues in 1986 (O'Driscoll et al., 1986). Since then, a number of other methods have been suggested, such as those established by Pineda et al. (1992), Wakitani and co-workers (1994), Sellers et al. (1997), or Fortier and colleagues (2002). To analyse human osteochondral core biopsies, two histological scoring systems were recently developed by the International Cartilage Repair Society (ICRS) (Mainil-Varlet et al., 2003, 2010).

The aim of this review is (1) to give a comprehensive overview and to compare the most important established histological scoring systems for the evaluation of repair tissue in focal chondral and osteochondral defects in animal models and patients, (2) to describe their specific advantages and pitfalls, and (3) to provide valid recommendations for their use in translational and clinical studies of articular cartilage repair.

Table 1. Histological scoring system according to O'Driscoll et al. (O'Driscoll et al., 1986)

Nature of predominant tissue	
Cellular morphology	
Hyaline articular cartilage	4
Incompletely differentiated mesenchyme	2
Fibrous tissue or bone	0
Safranin-O staining of matrix	
Normal or nearly normal	3
Moderate	2
Slight	1
None	0
Structural characteristics	
Surface regularity	
Smooth and intact	3
Superficial horizontal lamination	2
Fissures 25 to 100 percent of the thickness	1
Severe disruption, including fibrillation	0
Structural integrity	
Normal	2
Slight disruption including cysts	1
Severe disintegration	0
Thickness	
100 percent of normal adjacent cartilage	2
50-100 percent of normal cartilage	1
0-50 percent of normal cartilage	0
Bonding to the adjacent cartilage	
Bonded at both ends of graft	2
Bonded at one end or partially at both ends	1
Not bonded	0
Freedom from cellular changes or degeneration	
Hypocellularity	
Normal cellularity	3
Slight hypocellularity	2
Moderate hypocellularity	1
Severe hypocellularity	0
Chondrocyte clustering	
No clusters	2
<25 percent of the cells	1
25-100 percent of the cells	0
Freedom from degenerative changes in adjacent cartilage	
Normal cellularity, no clusters, normal staining	3
Normal cellularity, mild clusters, moderate staining	2
Moderate cellularity, mild clusters, moderate staining	1
Severe hypocellularity, poor or no staining	0

Presentation of scoring systems

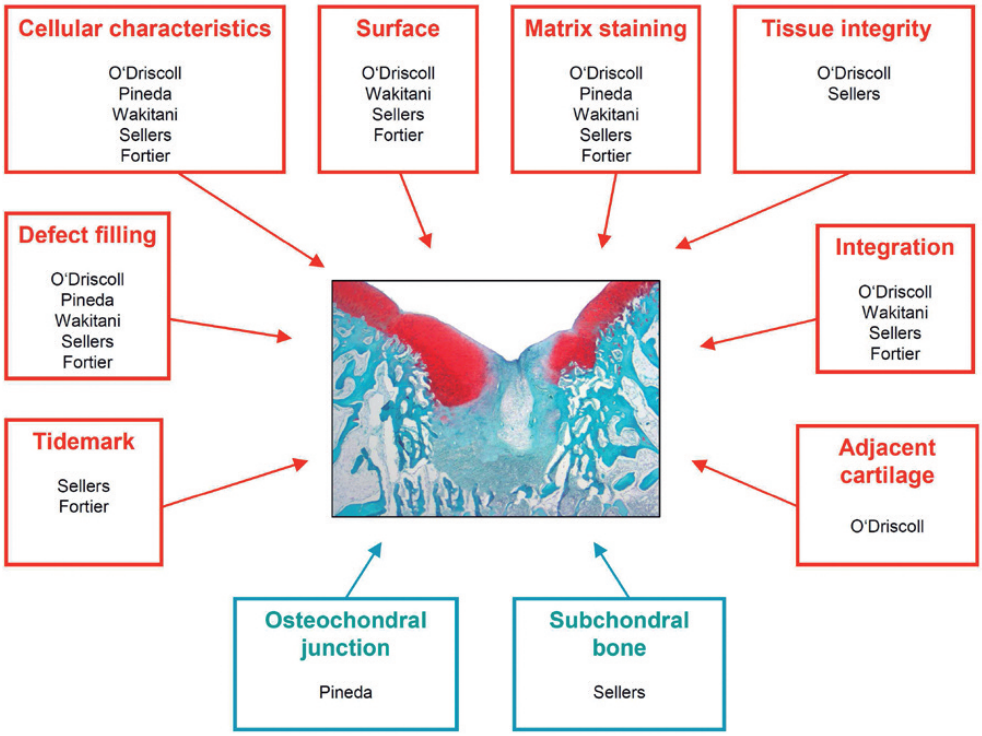
This section gives a detailed presentation of all histological scoring systems. Considering the complexity of the osteochondral unit, distinct structural aspects of osteochondral repair that merit attention are discussed (Fig. 1).

O'Driscoll scoring system

Historically, the first histological grading system for circumscribed articular cartilage defects was developed in 1986 by Shawn O'Driscoll (O'Driscoll et al., 1986). Originally, it was applied to analyze the effect of periosteal grafts in the treatment of full-thickness chondral defects in rabbits following safranin O staining. The initial scoring system comprised the single parameters of (1) nature of the predominant tissue, (2) affinity of its matrix for the safranin-O stain, (3) surface regularity, (4) structural integrity, (5) bonding to the adjacent articular cartilage, and (6) surface level of the newly formed tissue. In their follow-up study on durability of the cartilaginous repair tissue in the same animals (O'Driscoll et al., 1988), O'Driscoll and colleagues extended this score by adding the parameters of (7) hypocellularity, (8) chondrocyte clustering, and (9) freedom from degenerative changes in the adjacent cartilage (Table 1). The total point value of this complex scoring system ranges from 0 (no signs of cartilage repair) to 24 points (complete regeneration). Maximum point values for single histological parameters range between 2 and 4.

Pineda scoring system

In 1992, Stephen Pineda and co-workers developed an elementary scoring system for the grading of articular cartilage repair in the rabbit model using Safranin O staining (Pineda et al., 1992). The scale is composed of four parameters: (1) filling of the defect, (2) reconstitution of the osteochondral junction, (3) matrix staining, and (4) cell morphology (Table 2). The resulting total score value ranges from 0 (complete regeneration) to 14 points (no repair) while maximum point values for single parameters range between 2 and 4. The Pineda score is an inverse system as low point values represent a good repair response and vice versa.



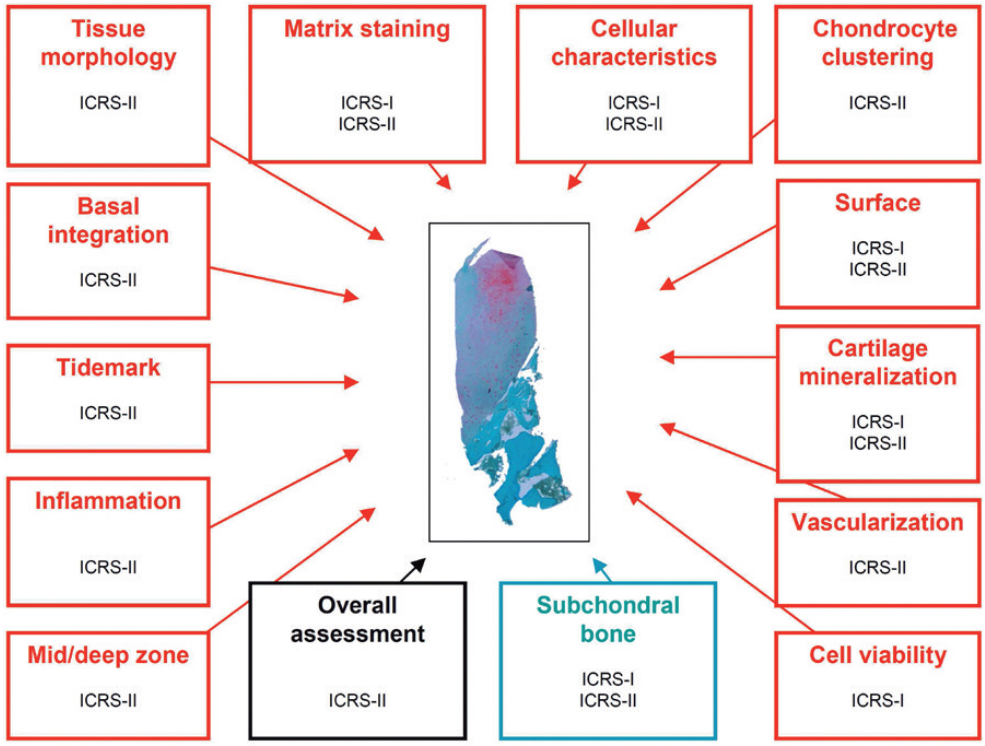


Fig. 1. When contemplating about which individual score to apply for the evaluation of an osteochondral repair tissue, the fundamental question is whether the entire cartilage defect can be inspected (usually in the case of experimental animal models), or whether only a tissue biopsy can be obtained (usually taken with a Jamshidi needle with an approximate diameter of 1.8 - 3.2 mm). This is the most important guiding principle on whether to use one of the classical scores described for animal studies (O'Driscoll, Pineda, Wakitani, Sellers, or Fortier score), or for the evaluation of biopsies such as the ICRS scores. Next, individual parameters reflecting the different categories can be taken into account. For example, the evaluation of subchondral bone reconstruction is of minor importance in studies focusing on partial thickness chondral defects, while studies that induce osteochondral defects require analysis of subchondral bone reconstruction.

Wakitani scoring system

The group of Shigeyuki Wakitani performed an investigation on the effect of bone marrow or periosteum derived mesenchymal cells in the repair of full-thickness chondral defects in the medial femoral condyle in rabbits in 1994 (Wakitani et al., 1994). For the histological analysis of toluidine blue stained sections, the authors developed an elementary scoring system, including the parameters of (1) cell morphology, (2) matrix staining, (3) surface regularity, (4) thickness of cartilage, and (5) integration of donor with host cartilage (Table 3). Maximum score values for single parameters range

Table 2. Histological scoring system according to Pineda et al. (Pineda et al., 1992)

Filling of defect	
125 %	1
100 %	0
75 %	1
50 %	2
25 %	3
0 %	4
Reconstruction of osteochondral junction	
Yes	0
Almost	1
Not close	2
Matrix staining	
Normal	0
Reduced staining	1
Significantly reduced staining	2
Faint staining	3
No stain	4
Cell morphology	
Normal	0
Most hyaline and fibrocartilage	1
Mostly fibrocartilage	2
Some fibrocartilage, but mostly nonchondrocytic cells	3
Nonchondrocytic cells only	4

Table 3. Histological scoring system according to Wakitani et al. (Wakitani et al., 1994)

Cell morphology	
Hyaline cartilage	0
Mostly hyaline cartilage	1
Mostly fibrocartilage	2
Mostly non-cartilage	3
Non-cartilage only	4
Matrix staining (metachromasia)	
Normal (compared with host adjacent cartilage)	0
Slightly reduced	1
Markedly reduced	2
No metachromatic stain	3
Surface regularity (total smooth area compared with entire area of cartilage defect)	
Smooth (> 3/4)	0
Moderate (> 1/2 - 3/4)	1
Irregular (1/4 - 1/2)	2
Severely irregular (< 1/4)	3
Thickness of cartilage (compared with that of surrounding cartilage)	
> 2/3	0
1/3 - 2/3	1
<1/3	2
Integration of donor with host adjacent cartilage	
Both edges integrated	0
One end integrated	1
Neither edge integrated	2

Table 4. Histological scoring system according to Sellers et al. (Sellers et al., 1997)

Filling of the defect relative to surface of normal adjacent cartilage	
111-125 %	1
91-110 %	0
76-90 %	1
51-75 %	2
26-50 %	3
<25 %	4
Integration of repair tissue with surrounding articular cartilage	
normal continuity and integration	0
decreased cellularity	1
gap or lack of continuity on one side	2
gap or lack of continuity on two sides	3
Matrix staining with Safranin O-fast green	
normal	0
slightly reduced	1
moderately reduced	2
substantially reduced	3
none	4
Cellular morphology (choose first between a-b-c-d)	
(a) normal	0
(b) mostly round cells with the morphology of chondrocytes	
>75 % of tissue with columns in radial zone	0
25-75 % of tissue with columns in radial zone	1
<25 % of tissue with columns in radial zone (disorganized)	2
(c) 50 % round cells with the morphology of chondrocytes	
>75 % of tissue with columns in radial zone	2
25-75 % of tissue with columns in radial zone	3
<25 % of tissue with columns in radial zone (disorganized)	4
(d) mostly spindle-shape (fibroblast-like) cells	5
Architecture within entire defect (not including margins)	
normal	0
1-3 small voids	1
1-3 large voids	2
>3 large voids	3
clefts or fibrillations	4
Architecture of surface	
normal	0
slight fibrillation or irregularity	1
moderate fibrillation or irregularity	2
severe fibrillation or disruption	3
Percentage of new subchondral bone	
90-100 %	0
75-89 %	1
50-74 %	2
25-49 %	3
<25 %	4
Formation of tidemark	
Complete	0
75-99 %	1
50-74 %	2
25-49 %	3
<25 %	4

between 2 and 4, with lower point values reflecting better repair. Similar to the Pineda score, total point values in the inverse Wakitani score range between 0 and 14.

Sellers scoring system

The Sellers score was established in 1997 and originally attempted to determine the effect of recombinant human bone morphogenetic protein 2 (rhBMP-2) on the repair of osteochondral defects in the lapine trochlea (Sellers et al., 1997). As reported by Rani Sellers, Diane Peluso, and Elisabeth Morris, their histological grading scale was modified from those of Pineda and Wakitani and designed to reduce observer bias and identify subtle changes during repair. The score evaluates eight single aspects of articular cartilage repair: (1) filling of the defect, (2) integration of the repair tissue, (3) matrix staining with safranin O, (4) cellular morphology, architecture (5) within the entire defect and (6) of the surface, (7) percent of new subchondral bone, and (8) formation of the tidemark (Table 4). For each of these single criteria, a maximum point value between 3 and 5 is provided, resulting in an inverse total score value ranging from 0 (complete regeneration) to 31 points (no repair tissue).

Fortier scoring system

In 2002, Lisa Fortier and colleagues developed a complex scoring system for the histological analysis of articular cartilage repair in horses following transplantation of fibrin/chondrocyte-composites supplemented with insulin-like growth factor-I (IGF-I) (Fortier et al., 2002). Originally performed using toluidine blue stained sections, the score incorporates seven single parameters of cartilage repair, each ranging between 2 and 4 maximum point values. These include (1) depth of defect filling, (2) integration with adjacent cartilage, (3) surface architecture, (4) cellular morphology and organisation, (5) cellularity, (6) tidemark formation, (7) intensity of toluidine blue staining. Constructed as an inverse scoring system, the minimum total point value of 0 is reflective of tissue regeneration while 20 points indicate a complete lack of cartilage repair (Table 5).

ICRS-I scoring system

In 2001, the ICRS established a Histological Endpoint Committee with the aim of providing a standardized histological scoring system for human articular cartilage repair tissue. In 2003, the Committee

Table 5. Histological scoring system according to Fortier et al. (Fortier et al., 2002)

Depth of defect filled (%)	
111 to 125	1
91 to 110	0
76 to 90	1
51 to 75	2
26 to 50	3
<25	4
Integration with adjacent cartilage	
Normal continuity	0
Gap on one side	1
Gap on both sides	2
Surface architecture	
Normal, smooth	0
Slight fibrillation or irregularity	1
Moderate fibrillation	2
Severe fibrillation	3
Cellular morphology and organisation (%)	
100 normal	0
>75 normal	1
25 to 75 normal	2
<25 normal	3
Cellularity relative to adjacent cartilage (%)	
Decreased >10	2
Decreased <10	1
Normal	0
Increased <10	1
Increased >10	2
Tidemark formation (%)	
Complete	0
75 to 90 complete	1
50 to 74 complete	2
25 to 49 complete	3
<25 complete	4
Toluidine Blue staining relative to adjacent cartilage (%)	
Normal	0
Decreased <25	1
Decreased >25	2

Table 6. Histological scoring system according to ICRS-I (Mainil-Varlet et al., 2003).

Surface	
Smooth/continuous	3
Discontinuities/irregularities	0
Matrix	
Hyaline	3
Mixture: hyaline/fibrocartilage	2
Fibrocartilage	1
Fibrous tissue	0
Cell distribution	
Columnar	3
Mixed/columnar-clusters	2
Clusters	1
Individual cells/disorganized	0
Cell population viability	
Predominantly viable	3
Partially viable	1
<10% viable	0
Subchondral bone	
Normal	3
Increased remodelling	2
Bone necrosis/granulation tissue	1
Detached/fracture/callus at base	0
Cartilage mineralization	
Normal	3
Abnormal/inappropriate location	0

recommended a score applicable only to small core biopsies (Mainil-Varlet et al., 2003). The single criteria of the grading system evaluate (1) surface, (2) matrix, (3) cell distribution, (4) cell population viability, (5) subchondral bone, and (6) cartilage mineralization of the repair tissue (Table 6). The score is based on a system of visual patterns (rather than on verbal descriptions) with each parameter being scored against a series of example images. For single criteria, the highest score (3 points) is applied to the ideal repair result (i.e. complete regeneration), whereas the lowest score (0 points) is assigned to the worst repair result. Yet, as the relative importance of these criteria is unknown, the single scores should not be summed; impeding the calculation of an overall score value. No specific recommendation on staining method is given by the ICRS Committee.

ICRS-II scoring system

In order to further increase the reproducibility of histological evaluations, the Histological Endpoint Committee of the ICRS proposed a second complex grading system in 2010 (Mainil-Varlet et al., 2010). The ICRS-II scoring system was developed based on core biopsy specimens obtained from femoral condyles of patients who underwent microfracture treatment or autologous chondrocyte implantation. Staining with hematoxylin/eosin, safranin O, or toluidine blue was recommended. This score consists of 14 criteria relating to (1) tissue morphology, (2) matrix staining, (3) cell morphology, (4) chondrocyte clustering, (5) surface architecture, (6) basal integration, (7) tidemark formation, (8) subchondral bone abnormalities/marrow fibrosis, (9) inflammation, (10) abnormal calcification/ossification, (11) vascularisation, (12) surface, and (13) mid/deep zone assessment as well as (14) an overall assessment subscale (Table 7). Each ICRS-II parameter is separately scored using a 100 mm visual analogue scale (VAS). Interestingly, summation of values is not intended, rendering any comparison to categorical numerical grading systems difficult.

Comparison between scoring systems

Comparison between scoring systems may be based on a complete versus a partial defect evaluation, depending on the extent of the retrieved repair tissue. Moreover, characteristics of single parameters that may be reflected in either elementary or complex scores allow a comprehensive structural evaluation of the osteochondral repair tissue. The most commonly included criteria in all scores include tissue morphology, defect filling, matrix staining, cellular morphology, surface structure, and repair tissue integration.

Complete versus partial defect evaluation

Out of the 7 established histological scoring systems for focal articular cartilage repair, the 5 scores according to O'Driscoll, Pineda, Wakitani, Sellers, and Fortier are designed for the evaluation of entire defects including integration sites and adjacent cartilage (Fig. 1). Because of ethical and technical reasons, retrieval of entire defects and adjacent tissue for diagnostic purposes is only seldom practicable in patients (e.g. during the course of total joint replacement or post mortem), and these 5 scoring systems are usually applied to experimental animal models. In contrast, the ICRS-I and ICRS-II grading scales were developed for the histological analysis of human core biopsy specimens. Therefore, only intralesional characteristics of the repair tissue are included in both systems, while grading of horizontal integration sites or the adjacent cartilage is not intended.

Table 7. Histological scoring system according to ICRS-II (Mainil-Varlet et al., 2010)

Tissue morphology (viewed under polarized light)	
Full-thickness collagen fibers	0%
Normal cartilage birefringence	100%
Matrix staining (metachromasia)	
No staining	0%
Full metachromasia	100%
Cell morphology	
No round/oval cells	0%
Mostly round/oval cells	100%
Chondrocyte clustering (4 or more grouped cells)	
Present	0%
Absent	100%
Surface architecture	
Delamination, or major irregularity	0%
Smooth surface	100%
Basal integration	
No integration	0%
Complete integration	100%
Formation of a tidemark	
No calcification front	0%
Tidemark	100%
Subchondral bone abnormalities/marrow fibrosis	
Abnormal	0%
Normal marrow	100%
Inflammation	
Present	0%
Absent	100%
Abnormal calcification/ossification	
Present	0%
Absent	100%
Vascularisation (within the repaired tissue)	
Present	0%
Absent	100%
Surface/superficial assessment	
Total loss or complete disruption	0%
Resembles intact articular cartilage	100%
Mid/deep zone assessment	
Fibrous tissue	0%
Normal hyaline cartilage	100%
Overall assessment	
Bad (fibrous tissue)	0%
Good (hyaline cartilage)	100%

Elementary versus complex scores

An eye-catching difference between the various histological grading systems is the number of single criteria included. The grading systems according to Pineda and Wakitani consist of only 4 or 5 single criteria of evaluation, respectively, and may therefore be classified as elementary scores. On the other hand, the complex systems according to O'Driscoll, Sellers, or Fortier comprise 9, 8, or 7 single parameters, respectively. The ICRS scores include 6 (ICRS-I) or even 14 (ICRS-II) single parameters and may also be classified as complex scales.

Recently, we applied elementary (Pineda and Wakitani) and complex (O'Driscoll, Sellers, and Fortier) scores to evaluate cartilage repair on histological sections of standardized osteochondral defects in rabbits by three observers (Orth et al., 2012b). No significant disparity in reliability and reproducibility was detected between elementary and complex scores. Despite different levels of experience in cartilage research, all investigators obtained similar results for each type of grading system. Remarkably, neither training level nor the presence of cartilage-specific histomorphometric parameters (e.g. chondrocyte clustering or tidemark formation) influenced reproducibility, in good agreement with previous findings (Ostergaard et al., 1999; Moojen et al., 2002). This suggests that all these scores represent relatively robust tools to evaluate articular cartilage repair. However, complex scoring systems provide more descriptive information regarding the nature of the repair tissue, especially about structural and cellular characteristics or the presence of degenerative changes. In good accordance, minute differences are best reflected by the complex Sellers score, while elementary scores do not illustrate the real extent of such differences (Orth et al., 2012b).

Characteristics of single parameters

Not only number, but also the nature of the single criteria allows for a comparison between the scoring systems (Fig. 1). The scoring systems of O'Driscoll, Pineda, Wakitani, ICRS-I, and ICRS-II classify the overall tissue morphology and differentiate between hyaline cartilage, fibrocartilage, and fibrous tissue.

The parameter of defect filling/tissue thickness is included in all 5 scores that address evaluation of the entire defect (i.e. the O'Driscoll, Pineda, Wakitani, Sellers, and Fortier score). This parameter cannot be judged when only core biopsy specimens are obtained and comparison with the adjacent tissue is not feasible.

Matrix staining and cellular morphology are criteria which are included in all grading systems except for the ICRS-I. However, these parameters can also be addressed in core biopsies and therefore are incorporated in the ICRS-II. Other criteria related to the cells constituting the repair tissue include cellularity (O'Driscoll and Fortier score), cell distribution and chondrocyte clustering (O'Driscoll, Sellers, ICRS-I, and ICRS-II score).

Except for the Pineda score, all systems address the structural aspect of the repair tissue surface. However, structural integrity of the entire repair tissue (appearance of cysts, voids, or clefts) is only represented in the complex scoring systems of O'Driscoll and Sellers.

All grading scales evaluating entire defects (O'Driscoll, Pineda, Wakitani, Sellers, and Fortier score) include the parameter of repair tissue integration. While Pineda and co-workers focused on vertical (basal) integration of the repair cartilage (i.e. reconstitution of the osteochondral junction), the remaining 4 systems grade integration of the repair tissue with the adjacent cartilage (horizontal or chondral integration). As only core biopsies from within the defect site are analyzed by both ICRS scores, the parameter of horizontal integration cannot be included here. Vertical integration of repair tissue with the subchondral bone compartment is however reflected in the ICRS-II score. In the clinical situation, both horizontal and vertical integration are relevant for the success of articular cartilage repair.

Regarding the evaluation of the subchondral bone within the affected osteochondral unit, only the complex Sellers score provides grading of its reconstitution. Of note, this parameter is not applicable for the evaluation of chondral lesions with an intact and untreated subchondral bone compartment. Thus, utilization of the Sellers score is restricted to osteochondral defects and chondral defects with additional therapeutic or accidental subchondral bone affection (e.g. due to marrow stimulation techniques or subchondral bone cysts). Subchondral bone abnormalities such as marrow fibrosis, bone necrosis, fracture, or callus formation as well as cartilage mineralization are explicitly displayed in both ICRS scores. The formation of the tidemark, the basophilic line that separates hyaline from calcified cartilage on histological sections, is addressed by the Sellers, Fortier, and ICRS-II score (Fig. 1).

Validation of scoring systems

Scoring systems for articular cartilage repair need to be sensitive, reliable, objective, and reproducible (Mainil-Varlet et al., 2010). To assess sensitivity or reliability, validation of a scoring system is required. However, prior to any validation, a reference standard and cut-off value for the discrimination between good and poor outcome is mandatory.

In patients, the retrieval of cartilaginous repair tissue is complicated and usually requires second-look surgery, while joint function or pain level are easy to monitor and may thus serve as reference standards. In contrast, the entire repair tissue is usually retrieved in experimental animal models, but grading of functional outcome measures is more complicated, inevitably necessitating the definition of an objective reference standard for validation. For example, collagen or glycosaminoglycan content (Grogan et al., 2006; Orth et al., 2012b),

computerized histomorphometry (Juvin et al., 1990; O'Driscoll et al., 2001; Moussavi-Harami et al., 2009), biomechanical testing (Vasara et al., 2004), macroscopic assessments (van den Borne et al., 2007; Goebel et al., 2012), non-destructive imaging of the repair tissue (Link, 2009; Orth et al., 2012a; Eldracher et al., 2014; Goebel et al., 2014), or other established histological grading scales (Moojen et al., 2002) may serve as such a reference standard in animal models.

To date, validation of histological scoring systems for *in vivo* cartilage repair strategies has seldom been performed (Mainil-Varlet et al., 2010; Orth et al., 2012b). In 2002, Moojen et al. (Moojen et al., 2002) compared the complex O'Driscoll score and the elementary Pineda score using samples with variable cartilage quality assessed by 3 observers at 2 time points. The authors reported a high intra- and interobserver reliability as well as a good correlation (r=0.71) between both scores. As this comparative analysis lacks a reference standard of cartilage repair, it does not allow for score validation.

Of note, the ICRS-II score was validated using the type II collagen content of the repair tissue as reference standard (Mainil-Varlet et al., 2010). Here, human core biopsy samples were taken arthroscopically from the centre of the repair tissue. The correlation coefficient between computer-assisted histomorphometrical assessment of type II collagen staining and the overall assessment criterion in the ICRS-II score was moderate (r=0.56) while intra- and interobserver reliability for the overall assessment parameter was high (r>0.74).

In our recent comparison between elementary (Pineda and Wakitani) and complex (O'Driscoll, Sellers, and Fortier) scoring systems of experimental cartilage repair in rabbits (Orth et al., 2012b), all 5 scores provided high intra- (r>0.91) and interobserver reliability (intra-class correlation >0.93) and high internal correlations (Spearman's ϱ>0.62). For validation purposes, DNA and proteoglycan contents of the repair tissues were correlated with histological overall score values. Interestingly, histological grading did not correlate with proteoglycan contents but with DNA contents (O'Driscoll, Wakitani, and Sellers score).

Conclusions

The repair of articular cartilage defects is increasingly moving into the focus of experimental and clinical investigations. Histological analysis is the gold standard for a valid and objective evaluation of cartilaginous repair tissue and predominantly relies on the use of established scoring systems. The following key messages regarding the histological grading of focal articular cartilage defects in experimental animal models and patients deserve special attention:

(1) The most commonly applied histological scoring systems for experimental cartilage repair are those according to O'Driscoll, Pineda, Wakitani, Sellers, and Fortier, dictating the evaluation of entire defect and the adjacent cartilaginous tissue.

(2) The ICRS-I and ICRS-II scores are primarily designed for human core biopsies of osteochondral repair tissue, thus allowing for only partial defect evaluation.

(3) Histological scoring systems are either elementary (Pineda or Wakitani) or complex (O'Driscoll, Sellers, Fortier, ICRS-I, ICRS-II). While both types are equally reliable, elementary systems are less time-consuming. However, complex scores provide more structural information and better display minute differences of articular cartilage repair.

(4) The most commonly included criteria in all scores comprise tissue morphology, defect filling, matrix staining, cellular morphology, surface structure, and repair tissue integration.

(5) Chondral defects that do not involve the subchondral bone may not be graded with scores addressing subchondral bone reconstitution or abnormalities.

(6) Validation of histological scoring systems requires a reference standard. Such validation has only seldom been performed to date.

Future work focusing on further validation of the scores based on commonly accepted reference standards will contribute to a better comparability of individual preclinical and clinical studies in articular cartilage repair.

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