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Key Words
Cartilage · Osteochondral defect · Transplantation · Rabbit

Abstract
Regardless of their etiology, cartilage defects of articular joints remain one of the unsolved problems in medicine. Therefore, numerous techniques to enhance cartilage repair are under clinical or experimental investigation. In any serious approach experimental investigation should precede human application. If the decision is made to implement an animal model, which one should be used? What is a good experimental animal for osteochondral defects? Can chondral defects be evaluated? What is the critical size of the defect? How long should the experiment last? Which histological techniques should be used? What are the pitfalls when evaluating osteochondral defects histologically? What is the best scoring system? All these questions will be addressed to provide concise information on this topic with particular attention being paid to the rabbit as an experimental animal.

Introduction
The need for cartilage repair studies in animals before, and not after, these techniques are applied in human therapy is obvious. It is also assumed that the reader is familiar with the inherent problems of cartilage repair [Wirth and Rudert, 1996; Buckwalter and Mankin, 1998; Newman, 1998; O’Driscoll, 1998; Rudert and Wirth, 1998; Hunziker, 1999].

This article aims to encourage investigators to work with animals, and suggests ways of avoiding commonly encountered problems. This review of the multitude of current publications on experimental cartilage repair reveals serious shortcomings in the methods applied. These pitfalls not only render many studies less meaningful than they otherwise could be, but restrain often unjustified over-enthusiasm.

Articular cartilage is a highly complex biological surface structure, composed of water, collagens, glycoproteins and proteoglycans, which, with synovial fluid, allows an almost frictionless gliding of joint surfaces. It ensures mobility and the symmetrical distribution of a load to the
Fig. 1. Light micrograph of sagittal section of a rabbit femoral condyle. A Using polarized light the complex architecture of the cartilage and underlying bone can be assessed (safranin O, polarized light). B Comparable view as in A stained with Alcian blue at low pH to reveal the sulfated glycosaminoglycans (bar = 50 μm).

underlying bone. An integrated connection to the tidemark, the subchondral bone and the marrow, is another characteristic of cartilage in diarthrodial joints. The special architecture of articular cartilage can well be appreciated in histological sections examined under polarized light (see fig. 1). Along with the distinct transition from the calcified zone to the subchondral bone, the basophilic undulating tidemark, representing the boundary between uncalcified and calcified cartilage, is easily recognized. Although easily recognized, the relevance of this structure remains uncertain. The tidemark seems to play a specific role in the ‘scarless’ regeneration of articular cartilage because it has never been observed to be completely intact in repair sites, neither in our own studies nor in the literature. The tidemark, therefore, represents a good criterion for the assessment of histological sections through osteochondral repair sites. If the tidemark is visible throughout the whole defect repair area, this can only mean that the defect has not been cut correctly (see later) or that the defect repair has been very good. If the latter is the case, we will have come close to the ultimate goal of osteochondral or chondral repair.

Animal Model

Several points should be kept in mind when considering the experimental animal and defect model. The main, but not the only points of importance are the species and age of the animal, the special quality of chondral and osteochondral defects, and the duration of the experiment.

Experimental Animal

Anatomical Applicability

The anatomy of the chosen species must be sufficiently similar to human anatomy to allow for the data collected and the results obtained in these animal cartilage studies to have relevance in the development of therapies for humans. In principle, most mammals would be suitable for such studies. The disadvantage of a quadruped gait with the altered distribution of load and the adjusted biomechanics of the knee joint must be accepted in any model. Even primates have their own gaits. Potential research animals include rats [Noguchi et al., 1994], rabbits [Salter et al., 1975], pigs [Wang et al., 2000], sheep...
and goats [Bruns et al., 1992], dogs [Breinan et al., 1997] and horses [Hendrickson et al., 1994].

The rabbit knee shows a gross morphological similarity to the human knee joint, with regard to the bone geometry, cartilage and tendons. The relative length of the patellofemoral groove is greater in comparison to the human knee joint, which probably is related to the mainly squatting posture of the animal. An anatomical peculiarity of the rabbit knee is the tendon of the extensor digitorum communis muscle that arises from the distal femur and passes over the lateral femoral condyle [MacLaughlin and Chiasson, 1979].

Housing Requirements

Obviously the anatomical dimensions of small research animals and humans are different. To achieve a comparable size and dimension of cartilage defect thickness, larger animals (i.e. horses) are necessary. In most cases the costs of doing experiments with horses are prohibitive, especially if large numbers of animals are needed for statistical power; therefore, sheep or dogs are often used. Rabbits are usually housed in wire cages ranging from 0.2 to 0.4 m² per animal. Observation of animals in the 0.2-m² cages reveals that overall movement, including that of the joints, is restricted. In our own experiments we housed rabbits in cages with dimensions of 4 m². This led to wide-ranging joint motion, but had no measurable effect on osteochondral defect repair in comparison to animals housed in smaller cages (unpubl. data).

When creating cartilage defects, two peculiarities of the rabbit model should be kept in mind due to the predominantly squatting position of the animals: (1) the posterior parts of the condyles are almost constantly loaded, which is reflected in the biomechanical properties of the cartilage in these areas [Räsänen and Messner, 1996], and (2) occasional unloading of the patellofemoral groove, as in the standing human, is rather unlikely. In spite of the concave surface, the patellofemoral groove, therefore, does not belong to the less loaded regions of the joint. This is a commonly encountered mistake when deciding on where to locate a defect that is supposed to reflect a varying degree of load on the knee joint.

Critical Size of Defect

In any experimental setup, attention must be paid to the intrinsic healing capacity of the animal since a cartilage defect may heal entirely on its own or at least to an extent that makes interpretation of the results difficult. It is generally accepted that in the rabbit all joint tissues heal. This may apply to bone, menisci and cruciate ligaments. In contrast, in our experience a seamless repair, i.e. regeneration of an osteochondral defect, does not occur in the rabbit. A review of the literature supports this conclusion: only in a fetal lamb model have spontaneous repairs of superficial cartilage defects thus far been detected [Namba et al., 1998].

Rabbits in the Literature

In reviewing the literature, one finds that the rabbit is the best represented experimental animal model for cartilage research. This may be due to the above-cited reasons, and the extensive knowledge further justifies this choice. The rabbit model has been extensively investigated regarding its intrinsic healing capacity [Prudden, 1881; Fasoli, 1905; Carlson, 1957; Meachim, 1963; Fuller and Ghadially, 1972; Ghadially and Ghadially, 1975; Ghadially et al., 1977; Cheung et al., 1980; Furukawa et al., 1980; Adams and Brandt, 1991; Kim et al., 1991; Altman et al., 1992; Pineda et al., 1992; Shapiro et al., 1993; Athanasiou et al., 1995; Metsaranta et al., 1996; Wei et al., 1997]. Less frequently used is the sheep, followed by the dog and the horse. Another advantage of rabbits is the low interanimal variance due to extensive inbreeding (i.e. New Zealand White rabbits). Dogs, on the other hand, are relatively heterogeneous, if not pure-bred, and very expensive.

Experimental Defects

Juvenile or Adult?

The age of the experimental animal is of particular importance but it is often neglected. It has been well established that the healing of wounds is of a better quality and occurs faster in young than in old individuals. This is also true for the rabbit. Wei et al. [1997] created cartilage defects in rabbits of different ages without any further therapy. The superior healing capacity in young animals was confirmed, especially for subchondral bone. However, a satisfactory repair of cartilage defects was not obtained, not even in young rabbits.

According to other investigators, rabbits are mature by the age of 6 months, and may be considered to be adults [Masoud et al., 1986; Eggli et al., 1988]. In contrast, under X-ray observation, we could still detect persistent epiphyseal growth plates in 6-month-old animals (3.5–5.5 kg). In our opinion, rabbits at 6 months are not quite mature, and older animals should be used. Nevertheless, for preliminary studies this is not important, since intrinsic cartilage repair is not optimal even in younger animals. If prelimi-
nary experiments show that the repair process has improved significantly by the applied procedure, the experiments should be repeated on truly adult animals.

**Size of Defect**

What size of defect should ideally be used? The answer is often left to the investigator's preferences and technical capabilities. The defect should be large enough to be exposed to considerable loads, without risking a fracture of the condyles. Furthermore, the defect size should be reproducible. This usually leads to some type of custom-made cutting instrument with a round diameter. For us and others, a 3-mm diameter defect has proved successful, both for the condyles as well as the patellofemoral groove [Buckwalter et al., 1987; Shimizu et al., 1987; Grande et al., 1989; Shapiro et al., 1993; Freed et al., 1994; Britberg et al., 1996]. Theoretically, the patellofemoral groove would allow larger diameter defects, but the remnants of the condyles would be too weak, and fractures might occur during mobilization. The depth of the defect is difficult to standardize, especially if concave and convex surfaces are investigated simultaneously.

To create osteochondral defects, the subchondral bone, including its connection to the marrow cavity, must be opened. If care is taken and a hand drill is used (while avoiding heating the tissue!), the correct depth can be estimated by observing the small amount of bleeding that appears on the surface of the bone. The creation of larger defects (for example 3 × 3–6 mm in the trochlea) does not seem to be of any benefit, since in the literature perfect healing has never been observed, even with the common 3-mm diameter defects. In our experience, punches did not prove adequate, since they usually could not penetrate the hard subchondral plate.

**Osteochondral or Chondral?**

The cartilage thickness of the adult rabbit femoral condyle measures less than 400 μm, whilst the thickness of the human condylar cartilage is 2–3 mm [Athanasiou et al., 1991]. The idea of reexamining newer techniques of cartilage repair (i.e. chondrocyte transplantation) that require defects to be confined to the cartilage seems to be illusory after considering the rabbit anatomy. Unfortunately, the cartilage thickness in sheep is only 1.5–2 times deeper than the cartilage in rabbits, and therefore the sheep model is not really better suited to solve the problem of chondral defect repair [Hunziker, 1999]. The attempt to treat chondral defects with isolated cells and tissue-engineered constructs seems to have been a success only in dogs [Breinan et al., 1997]. However, in 50% of the controls, injury to the subchondral plate was detected [Nehrer et al., 1998]. The following question arises: Is the clinician in fact dealing with pure chondral defects? This would only be the case, if an acute cartilage fracture and avulsion have occurred. If this defect is not treated over a period of time, the subchondral plate will definitely react to the different loads, which usually results in a sclerosis of bone [Eckstein et al., 2000]. It has to be questioned whether an attempt to reconstruct the superficial cartilage layer without diminishing the subchondral sclerosis makes sense. The pure chondral defect is certainly rare and, therefore, should not be demanded as a standard for the evaluation of cartilage defects in the animal model. The potent effect of an opened marrow cavity with all its signalling substances is known [Stockwell, 1979; Wirth and Rudert, 1996; Buckwalter and Mankin, 1997].

**Localization of the Defect**

The data in the literature differs considerably with regard to the optimum localization of the defect. Some authors created a defect in the patellofemoral groove to prevent it from being overloaded postoperatively [Freed et al., 1994]. The patellofemoral joint is obviously more easily accessed than the surface of the condyles. The condyles, on the other hand, were often chosen in the literature in order to achieve a loading situation comparable to that of the weight-bearing surface of human joints [Wakitani et al., 1994]. Taking the special anatomy of the rabbit knee into account, it is apparent that the very posterior parts of the condyles must be reached because of the primarily squatting position of the rabbit [Räsänen and Messner, 1996]. This is another reason why the assumed load prevention occurring in the patellofemoral groove does not compare to the human situation. From the access point of view, the creation of 3-mm defects in both condyles and the patellofemoral groove of the rabbit knee is possible without putting undue surgical stress on the animal. However, it should be kept in mind that the tendon of the extensor digitorum muscle overlaps the lateral condyle, which might have its own effect. In our investigations we did not see significant differences in the results of osteochondral defect repair with respect to the different locations of the defect. With 3-mm defects even the operation on both legs in one session does not distress the animal as regards recovery, behavior or activity. Since the natural healing of cartilage defects is very well described in the literature, one may feel inclined to omit the creation of control defects in order to achieve a reduction in the number of animals needed for a particular study. We have, however, seen a large amount of interin-
individual variance in the healing capacity in these animals. We, therefore, strongly recommend the creation of at least one control defect per animal. Although the number of experimental animals will as a consequence be increased, this disadvantage is in our opinion offset by the increase in experience and competence obtained in evaluating the quality of the repair. A good overview of the number of animals required is given by An and Bell [1999].

A contribution of the synovium to the healing of cartilage defects has to be assumed [Hunziker and Rosenberg, 1996]. In the undiseased nonarthritic animal its effect on the healing process is the same in the treated groups and in the control groups. A significant effect of the arthroscopy alone on articular cartilage (sham operations) could not be detected in our experiments.

Follow-Up

Another important question that should be answered prior to the initiation of an experiment concerns its duration. At what time postinjury can conclusions be drawn about the healing progress? Observations regarding the intrinsic healing capacity of osteochondral defects in the rabbits constitute the standard for healing time. Shapiro et al. [1993] described impressive positive results with early repair (12 weeks) of 3-mm osteochondral defects in their model. However, an increasing extent of degenerative changes was observed after 48 weeks in all animals [Shapiro et al., 1993]. According to these authors, a reasonable follow-up period of at least 6 months is, therefore, necessary. Shahgaldi et al. [1991] reported a degeneration of osteochondral defect repairs that were still increasing 12 months after the initial operation. From these studies, it follows that a follow-up period of 6 months should be enough for a first evaluation of the experimental setup. If the defect repair appears to be satisfactory, then extending the evaluation period should be considered in order to ensure that there is no regression.

Histological Evaluation

Stains

A limited number of stains is sufficient for an adequate evaluation of the repair tissue quality. Tissue sampling and preservation should be done in a manner which prevents the loss of proteoglycans, i.e. by fast processing and through the use of cationic dyes in the fixation solution [Hunziker, 1990]. Fixation is followed by decalcification, dehydration and embedding in paraffin wax. The common paraffin sections are only a few microns thick. To reduce the risk of detachment, these sections can be mounted on 3-tri-ethoxysilyl-propylamine-coated slides. Sections can be dewaxed in xylol and stained according to the following techniques: hematoxylin-eosin (HE) for an overview of the tissue section [Romeis, 1989; Kiernan, 1999]. The tidemark visibility is influenced by the choice of hematoxylin. The toluidine blue stain may also be used to get an overview of the tissue structure with a high contrast (see fig. 2) [Romeis, 1989; Chayen and Bitensky, 1991]. Safranin O stains cartilage in different shades of red to orange, often combined with fast green [Rosenberg, 1971; Romeis, 1989].

Alcian blue, a cationic water-soluble dye, selectively stains sulfated glycosaminoglycans, when applied at low pH (~1.0) (fig. 1B). Nuclei require counterstaining. Mallory azan as an unspecific dye gives the impression of collagen production [Yasui et al., 1982; Rudert et al., 2000].

These few staining methods provide a thorough evaluation of the gross histomorphology of osteochondral defect repair sites. Experimentally created osteochondral defects provide the advantage of having the repair tissue and the reference tissue (i.e. uninjured cartilage) in one section. One can choose between the toluidine blue and HE stain, as well as between the safranin O and the Alcian blue stain. It should be stressed that the Alcian blue stain varies in quality. We recommend repeating this stain until consistent results are obtained.

These stains are all that is necessary for evaluating the repair tissue using one of the common histological scores. In addition, one should include immunohistochemical techniques to investigate the major collagen types (fig. 3). It is not easy to get good antibodies that do not reveal a high cross-reactivity between the collagen types. Although the importance of collagen type II is always emphasized as being the major component of cartilage collagens, the amount of or presence of collagen type I is even more important. As long as a significant amount of collagen type I is found in the tissue, the repair tissue is comprised of fibrous cartilage. While the tissue may contain more or less fibrous cartilage, it still is definitely not hyaline articular cartilage.

In order to distinguish scar tissue from invasive connective tissue and vessels, marker proteins can be looked for, for example using antilaminin antibodies to visualize the basement membrane component of blood and lymph vessels [Rudert and Tillmann, 1993].
Fig. 2. Light micrograph of an overview section of an osteochondral trochlea defect treated with a poly-L-lactic acid fleece 6 months after the initial operation (toluidine blue, bar = 500 μm). The high contrast of the stain makes it possible to easily distinguish between the original cartilage and the fibrous repair tissue. Remnants of the implanted material can be seen in the depth of the defect.

Fig. 3. Immunohistochemical detection of collagen type II (ChC1, mouse IgG2a, Developmental Studies Hybridoma Bank, Iowa, USA; 1:20) [Holmdahl et al., 1986] (A), and collagen type I (COL-1, mouse IgG1, C2456, Sigma; 1:500) [Mayne, 1988] (B) with monoclonal antibodies using the diaminobenzidine method. A, B Bar = 100 μm.
**Parts of Figures and Sections**

The presentation of histological data represents a serious problem leading to misinterpretation. High magnifications of tissue sections may mislead if they are presented in the absence of an overview of the entire defect. As an example, we offer a sequence of pictures of the same defect at different magnifications, showing good hyaline cartilage in the highest magnification (fig. 4). The lower magnification clearly shows that the subchondral plate has not been reconstituted properly, and the defect tissue extends down to the subchondral space. In the overall view, one can see that only a part of the defect is filled with cartilage; other areas of the defect reveal shortcomings, such as remnants of the implanted carrier material.

![Image of histological section](image)

(For fig. 4B, C see page 236.)

**Fig. 4.** Overview and different magnifications of a defect in the patellofemoral groove 12 months after treatment with a resorbable fleece cultured with chondrocytes. **A** High magnification reveals good hyaline tissue (bar = 50 µm); slight initial degenerative changes may be recognized on the surface.

Another problem associated with the creation of histological sections is the position of the cut and the orientation of the specimens. Different potential mistakes that could be made are shown schematically (fig. 5). A proper cut, which lies approximately in the center of the defect and is not obliquely orientated (fig. 5, row 1, columns A and B), should reveal the whole diameter of the 3-mm defect and its complete depth (fig. 5, column C). One obvious prerequisite for this is that the defect is detectable. If an area next to the center of the defect is cut (fig. 5, columns A and B), the entire diameter of the defect cannot be seen on the slide. If one bears the whole diameter of the defect in mind as a reference, the smaller defect diameter in the off-center cut may misleadingly suggest that the
Fig. 4. B The lower magnification already shows the minor defect repair. The repair tissue on the right side reaches below the subchondral bone plate of the uninjured condyle (bar = 80 μm). C Overview of the defect. The whole area of the defect filled with repair tissue can be evaluated. Remnants of the fleece material are visible in the center of the defect (bar = 500 μm).
Fig. 5. Schematic drawing of the different cutting positions (column A) and angles (column B) and their corresponding effect on the histological sections (column C). Row 1 = Central perpendicular cut through defect; row 2 = cut next to central position; the defect on the histological slide is not shown in its whole diameter; row 3 = marginal straight cut through defect; the histological slide shows only small remnants of the original defect diameter; row 4 = oblique cut through defect. In the histological section the surface looks completely reconstituted, while repair tissue is visible in the depth of the defect.

Repair tissue has consolidated to a small residual part (fig. 5, column C) and an erroneous conclusion might all too easily be drawn from an examination of the edges of the defect (fig. 5, columns A, C). It should be kept in mind that the person who produces the sections may not necessarily be the same person who evaluates them.

As already mentioned, a complete and regular tide-mark should arouse suspicion about the possibility of mistakes having been made in the cutting technique or choice of sections. The following example demonstrates how easy it is to arrive at an erroneous conclusion. If the orientation of the cut is oblique to the defect (fig. 5, columns A, B), the superficial part of the section may reveal original cartilage which was not injured, while the depth of the defect is still filled with repair tissue (fig. 5, column C). This case falsely suggests a perfect reconstruction of the defect surface to the observer who believes that he/she is viewing the actual defect, of which a part is still visible.

The elucidation of potential mistakes may sharpen the investigator’s awareness of potential pitfalls not only in respect of his own data but also with regard to published data.
Table 1. Score introduced by O'Driscoll et al. [1988]

<table>
<thead>
<tr>
<th>Nature of the predominant tissue</th>
<th>Score</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Score</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Comments</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cellular morphology</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hyaline articular cartilage</td>
<td>4</td>
<td>round cell morphology, chondrones</td>
</tr>
<tr>
<td>Incompletely differentiated mesenchyme</td>
<td>2</td>
<td>difficult to distinguish from fibrous tissue, high cellularity, chondrocytes and fibroblasts typical cells and tissue (fibrous)</td>
</tr>
<tr>
<td>Fibrous tissue or bone</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Safranin-O staining of the matrix</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal or nearly normal</td>
<td>3</td>
<td>easy to evaluate because reference tissue = normal tissue is visible next to the defect</td>
</tr>
<tr>
<td>Moderate</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Slight</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Structural characteristics</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Surface regularity</td>
<td></td>
<td>only regard surface ! (see next topic)</td>
</tr>
<tr>
<td>Smooth and intact</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Superficial horizontal lamination</td>
<td>2</td>
<td>typical of beginning degeneration</td>
</tr>
<tr>
<td>Fissures: 25–100% of the thickness</td>
<td>1</td>
<td>deteriorating tissue</td>
</tr>
<tr>
<td>Severe disruption, including fibrillation</td>
<td>0</td>
<td>easily recognizable</td>
</tr>
<tr>
<td>Structural integrity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>2</td>
<td>does not necessarily involve surface</td>
</tr>
<tr>
<td>Slight disruption, including cysts</td>
<td>1</td>
<td>hint to biomechanical stability of the tissue</td>
</tr>
<tr>
<td>Severe disintegration</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Thickness</td>
<td></td>
<td></td>
</tr>
<tr>
<td>100% of normal adjacent cartilage</td>
<td>2</td>
<td>easy to evaluate applies to filling of more than 100% also if tissue is cartilage (2 points), if tissue is bone (0 points)</td>
</tr>
<tr>
<td>50–100% of normal cartilage</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>&lt;50% of normal cartilage</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Bonding to the adjacent cartilage</td>
<td></td>
<td>and to subchondral bone</td>
</tr>
<tr>
<td>Bonded at both ends of graft</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Bonded at one end, or partially at both ends</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Not bonded</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Absence of cellular changes resulting from degeneration</td>
<td>= evaluation of degeneration</td>
<td></td>
</tr>
<tr>
<td>Hypocellularity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal cellularity</td>
<td>3</td>
<td>compare to reference cartilage</td>
</tr>
<tr>
<td>Slight hypocellularity</td>
<td>2</td>
<td>difficult to assess, this characteristic should apply only to hyaline cartilage</td>
</tr>
<tr>
<td>Moderate hypocellularity</td>
<td>1</td>
<td>also applies to high cellularity in fibrous tissue</td>
</tr>
<tr>
<td>Severe hypocellularity</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Chondrocyte clustering</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No clusters</td>
<td>2</td>
<td>typical degenerative changes in cartilage</td>
</tr>
<tr>
<td>&lt;25% of the cells</td>
<td>1</td>
<td>higher magnification necessary for evaluation</td>
</tr>
<tr>
<td>5–100% of the cells</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Absence of degenerative changes in adjacent cartilage</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal cellularity, no clusters, normal staining</td>
<td>3</td>
<td>degeneration of the adjacent cartilage is an important feature for assessing the biomechanical function of the repair tissue!</td>
</tr>
<tr>
<td>Normal cellularity, mild clusters, moderate staining</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Mild or moderate hypocellularity, slight staining</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Severe hypocellularity, poor or no staining</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>24</td>
<td></td>
</tr>
</tbody>
</table>
Scoring Damage and Repair

Unfortunately several different scoring schemes with a variety of implementations are in use when evaluating osteochondral defect repair. In the rabbit model two scoring systems tend to dominate: (1) the scoring system of O’Driscoll et al. [1988], and (2) that described by Wakitani et al. [1994] modified from Pineda et al. [1992]. The O’Driscoll scoring system requires two stains, one for overview (HE) and the safranin O stain to reveal the sulfated glycosaminoglycans. This scoring system is in widespread use, and its advantage over the Wakitani scoring system resides in its inclusion of degenerative changes. These aspects are of special interest when evaluating cartilage defects in order to determine the long-term stability of the repair tissue. Wakitani et al. have, therefore, proposed that their scoring system should only be used for the short-term follow-up of cartilage defects. Of note is that this simple-to-use commonly applied scoring system by Wakitani et al. is an ‘inverse’ scoring system in that it assigns less points in the case of better results. Rather than presenting another modification to an existing scoring system, we suggest using the O’Driscoll scoring system in order to achieve better comparability of results in future studies (table 1, our comments).

Conclusion

The rabbit is a suitable experimental animal for the studies of articular cartilage repair. It remains, however, unclear to what extent the data determined can be applied by means of extrapolation to humans. The experimental investigation of repair in animal articular cartilage is nevertheless necessary, especially given that repair in animals is generally more successful than in humans.

The duration of the follow-up should be about 6 months after primary experiments. If the results are promising, a follow-up period of at least 12 months should be chosen. When carrying out histological evaluations, focusing on specific parts of the defects is important, but for the critical evaluation of the repair overviews of the whole defect should also be evaluated. The histological scoring system by O’Driscoll et al. is suitable for evaluation. It is not simple but it includes degenerative changes and it is commonly used.

References


Histological Evaluation of Osteochondral Defects

Cells Tissues Organs 2002;171:229–240

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