Detection of Posttraumatic Cartilage Lesions using Magnetic Resonance Imaging (MRI): An experimental Study on Canines

M Uhl, J Haberstroh, T Bley, O Wieben, M Langer, A Lahm

Citation

Abstract
Purpose: The investigation of cartilage lesions in knee joints after knock injuries with Magnetic Resonance Imaging (MRI) over a time period of six months.

Materials and Methods: A controlled force form a drop-tower was applied to one knee of 12 normal adult beagle dogs to produce a subchondral bone bruise and soft tissue compression without visible bone fracture. MR images of both knees were acquired at a magnetic field strength of 1.5 T immediately after this defined knock-trauma and again after six months. The images were based on sagittal T1-weighted spin-echo sequence, a T2-weighted turbo-spin-echo sequence with spectral fat-suppression, and a fat suppressed 3D spoiled gradient echo sequence (FLASH®, SPGR). The traumatized joints underwent an arthroscopy immediately after the second MR examination and biopsies of the cartilage were performed. The biopsies were scored histologically (Mankin score of degenerative cartilage lesions).

Results: Six months after trauma, ten out of the twelve canines had circumscribed cartilage lesions in the traumatized area of the affected knee joint and nearly all dogs had joint effusions in the affected knee joints. Furthermore, the knees with the most extending bone marrow edema developed high-grad cartilage lesions. All control scans and cartilage biopsies of the contralateral knee joints showed normal findings.

Conclusion: Joint trauma causes focal cartilage defects. The described animal model supports the hypothesis that subchondral traumatic lesions such as bone bruises are an important risk factor for early development of osteoarthritis in (knee) joints. Within a few months, severe osteoarthritis could be induced by subchondral bone bruises. Potential etiogenic mechanisms are the damage of subchondral nutrition of hyaline cartilage or changes in the biochemical composition or biomechanic properties of the cartilage.

INTRODUCTION

Over the last few years, we observed several young patients with severe osteoarthritis and damaged cartilage six to twelve months after an impact-trauma on the knee joint. These patients showed no initial cartilage lesions nor ruptures of the cruciate ligaments in MRI exams. Thompson et al. published similar experimental (1). He found subchondral lesions which were followed by cartilage damage after several months. This clinical observation raises the question which mechanisms cause cartilage degeneration and how such lesions can be identified in MRI exams. Radin et al. (2) hypothesized that subchondral bone has a crucial role in the initiation and progression of cartilage damage. After a bone bruise or subchondral fracture of trabeculae, subchondral bone changes become sclerotic with thickening of the cortex and trabeculae. Such a sclerosis results in a diminished nutrition of hyaline cartilage. Furthermore, Radin hypothesized a different elasticity of affected posttraumatic subchondral bone. Shear forces in the cartilage due to axial forces depend on the flexibility of the underlying bone matrix. A difference in shear forces within the joint cartilage may cause premature cartilage degeneration.

The purpose of this study was to generate traumas in knee-joints of canines in order to investigate whether cartilage lesions would occur as a response and whether MRI examinations of the affected joints could show such cartilage
lesions induced by subchondral traumatic bone lesions (bone bruises).

**MATERIALS AND METHODS**

**ANIMAL MODEL**

Twelve adult beagle dogs (24-30 months, weights between 14-18 kg) were exposed to a force impact of one knee such that a bone bruise was produced without essential bone fracture or cartilage damage. The dogs are weight bearing throughout the next six months.

The transarticular force was generated by a weight that is dropped onto the patella of a rigidly held knee joint of an anesthetized dog. The setup consisted of a drop-tower, a drop weight of 2.1 kg with a force-transmitting rod-tip with a diameter of 1.9 cm (adapted to the dog’s patella), a load cell (Kistler® Swiss Type 5001), and a force transducer (Kistler® Quarz). The transmitted forces are recorded on an oscilloscope with settings of 0.5 ms/div. and 0.5 V/DN (1V/1000 N). After the animal was anesthetized it was positioned in lateral recumbency with the hip abducted and 90 degrees flexed. The tibia was held in 100 degrees of flexion in the knee joint and the whole lower extremity was rigidly secured with the thigh fixed to a frame. Sagittal and axial radiographs were acquired prior to impact for proper perpendicular force application. The force was generated through gravity by the fall of the released weight over a defined distance. The maximum forces applied to each of the 12 dogs could be controlled through the distance and are presented in Table 2. The non-impacted knee was examined as a control knee for each animal.

**Figure 1**

Table 1: Modified Outerbridge classification of cartilage lesions and MRI correlation.

<table>
<thead>
<tr>
<th>Grade</th>
<th>Macroscopy</th>
<th>MRI</th>
</tr>
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<tr>
<td>1</td>
<td>cartilage swelling and softening</td>
<td>normal cartilage</td>
</tr>
<tr>
<td>2</td>
<td>less than 50% loss of cartilage thickness</td>
<td>abnormal intrachondral signal, but normal cartilage</td>
</tr>
<tr>
<td>3</td>
<td>loss of more than 50% of cartilage thickness</td>
<td>less than 50% loss of cartilage thickness, but without exposure of subchondral bone</td>
</tr>
<tr>
<td>4</td>
<td>complete loss of cartilage thickness with subchondral bone exposure</td>
<td>complete loss of cartilage thickness, but without exposure of subchondral bone</td>
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</table>

* abnormal signal: signal increase in T2-weighted images

**Figure 2**

Table 2: Cartilage lesions six months after trauma: MRI appearance.

<table>
<thead>
<tr>
<th></th>
<th>Init</th>
<th>Cartilage</th>
<th>Cartilage</th>
<th>Marked</th>
<th>Marked</th>
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<tr>
<td></td>
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<td>2D-GRE</td>
<td>2T-T2</td>
<td>score</td>
<td>score</td>
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<tr>
<td></td>
<td>lesions</td>
<td>Osteo</td>
<td>TSE</td>
<td></td>
<td>normal</td>
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<tr>
<td></td>
<td>[mm]</td>
<td>grade</td>
<td></td>
<td></td>
<td>[mm]</td>
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<td>4</td>
<td>4</td>
<td>15</td>
</tr>
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<td>2</td>
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<td>0</td>
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<tr>
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<td>0</td>
<td>2</td>
<td>0</td>
<td>0</td>
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<tr>
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<tr>
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<td>2</td>
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<td>0</td>
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<tr>
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<td>0</td>
<td>2</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
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<td>2</td>
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<tr>
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<tr>
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<tr>
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<td>11</td>
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The study was designed in accordance with the German laws for animal protection and has been approved by the German “Review Board for the Care of Animal Subjects”.

The 12 adult healthy beagle dogs of either sex had a mean weight of 14.8± 1.3 kg. General anaesthesia and intubation were performed by a specialized veterinary anesthesiologist (JH).

None of the animals was sacrificed and all dogs were alive and in good condition one year after the experiment.

**MR IMAGING METHODS**

MR imaging was performed one hour after trauma with a 1.5 T system (Vision, Siemens Medical Solutions Erlangen, Germany) and a standard head coil. The MRI examination was repeated six months after the trauma. Both examinations were performed under general anaesthesia (J.H.). The knee joints were fixed parallel in a semi-flexed position within the head coil. This setup allowed for the simultaneous acquisition of the affected and the contralateral (control) knee joint.

Scan protocol: 3 mm thick sagittal T1-weighted spin-echo sequences (SE) were acquired with a repetition time (TR) of 535 ms and an echo time (TE) of 14 ms, two excitations, and a 256 x 256 imaging matrix. Sagittal T2-weighted turbo-spin-echo (TSE) images with spectral fat-suppression were obtained with TR/TE = 2900/120 ms, echo train length = 15, two excitations, and a 256 x 256 matrix. A fat suppressed
3D-spoiled gradient echo (GRE) sequence with TR/TE/flip angle = 48ms/11ms/40°, slice thickness of 2 mm, and a 336 x 512 matrix (manufacturer's acronym: FLASH ®, fast low angle shot) was applied as a cartilage-specific scan method. In this sequence, hyaline cartilage shows a high signal intensity while bone marrow and adjacent soft tissue have a darker appearance.

The frequency-encoding direction was anterior-posterior, the field of view was 14 cm, and two signal averages were acquired with all sequences.

Two experienced radiologists semi-qualitatively evaluated the signal intensity of cartilage and subchondral bone characteristics in the T2-weighted fat-suppressed MRI-sequences. Signal intensities of the subchondral bone were classified as hypo-, iso-, or hyperintense compared to the signal intensities of the healthy contralateral knee.

A standardized form was filled out with the following categories:

- Signal intensity of traumatized subchondral bone (hypo-, iso-, or hyperintense)
- Cartilage defects (modified Outerbridge scale, Table 1) (5)
- A limitation of the study is the fact that cartilage in the joint of a canine is a thin structure with a measured thickness of only 2-3 mm. Therefore, it is not possible to differentiate between Outerbridge grades 2 and 3. Therefore, grade 2 and 3 lesions were grouped in one categorie.
- The interobserver agreement was measured using the Cohen κ (Kappa)-test. The calculated value of κ can range from 0 to +1.00. A κ of zero means there is no agreement beyond chance, and a κ of 1.00 means there is perfect agreement.
- A bone bruise was diagnosed if a circumscribed and cloudy, non-linear subchondral geographic signal increase appeared on the fat-suppressed T2-weighted images (bone marrow edema).

**BIOPSIES AND HISTOLOGY**

Immediately after the second MR imaging, the traumatized knee-joints and the contralateral knee underwent an arthroscopy and biopsies of the cartilage were performed.

The surgeon collected biopsies (osteochondral sections) of all conspicuous cartilage lesions of the traumatized knee and control biopsies of the corresponding contralateral tissue. The biopsies contained cartilage and subchondral bone. General anaesthesia was performed by a specialized veterinary anesthesiologist.

The specimens were processed according to standard protocols (6). Standard histologic stainings are hematoxylin-eosin (HE), safranin-Orange (Merck), and azan-blue (Merck). A well-known histologic score system (Mankin-Score, 7) for the evaluation of degenerative cartilage lesions was applied. This score evaluates structure, fissures, clefts, cells, vascularity, and saturation of safranin staining of articular cartilage. The maximum score of 14 points could be achieved by heavily disintegrated and degenerated cartilage. The scoring pathologist had no information whether the specimen was traumatized cartilage or normal cartilage without history of trauma.

**RESULTS**

The maximum force applied to each of the 12 canines and the associated clinical findings are summarized in Table 2. All dogs survived the procedures.

**FIRST MRI-EXAMINATION (ONE HOUR AFTER TRAUMA)**

All of the 12 traumatized knee joints showed an area of high signal intensity in the epiphysis of the femur in the fat-suppressed T2-weighted images, probably a combination of bone marrow edema, bleeding and hyperemia. The most severe bone marrow edemae with bone marrow edemae larger than 20 mm in diameter (sagittal images) were diagnosed in dogs # 1, 7, 8, and 10. All canines showed small joint effusions and localized swelling of soft tissue in the traumatized area with a slight increase of signal intensity in the fat-suppressed T2-weighted images. In one case, a non-dislocated fracture of the patella was observed.

There were no detectable cartilage lesions such as cartilage fractures, ulcers, or subchondral bone fractures. Control scans of the contralateral knee joints showed normal findings.

**SECOND MRI-EXAMINATION (SIX MONTHS AFTER TRAUMA)**

In MRI, 10 of the 12 dogs had a circumscribed cartilage lesion in the traumatized area of the affected knee joint (see Table 2). Eleven of the 12 dogs had joint effusions in the
affected knee joint. Furthermore, the knees with the most extensive bone marrow edema developed high-graded cartilage lesions (dogs 1, 7, 8, and 10). The diameter of these cartilage lesions ranged from 5 mm up to 12 mm (dog #1) with an average of 7 mm. There was no visible persisting subchondral bone marrow edema.

Again, all control scans of the contralateral knee joints showed normal findings, with one exception: Dog #7 had an Outerbridge grade 1 lesion in the contralateral joint.

The $\kappa$-interobserver agreement in the MRI film readings of all knee joints (cartilage lesion yes or no) was 0.8.

**BIOPSIES AND HISTOLOGIC FINDINGS**

There was a highly significant difference ($p<0.02$, Wilcoxon-test) between the Mankin scores of traumatized cartilage and control biopsies.

In general, the cartilage showed early signs of degeneration including loss of stainability with safranin-O in the deeper zones of articular cartilage, new vessels within the cartilage, and clefts in the superficial cartilage six months after trauma.
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Figure 4
Figure 2a: Normal appearance of cartilage in the FLASH-sequence (TR/TE/flip angle = 48ms/11ms/40°)(dog #8). Cartilage has a high signal intensity in comparison to the dark bone marrow.

Figure 5
Figure 2b: Posttraumatic cartilage lesion at imaging six months after trauma (arrow, FLASH-sequence) Outerbridge grade 4 (dog #8).

Figure 6
Figure 3a: Histologic specimen of cartilage in azan-blue staining. Normal findings with red nuclei and blue collagen-structures. The structure of the cartilage is well organized and normal (magnification 300x)
DISCUSSION

Six months after an experimental joint trauma (bone bruise, subchondral bone marrow edema), 10 of 12 affected canine knee joints developed cartilage lesions that were identified by MR imaging, biopsy, and histology. In MRI examinations, these histologically proven lesions could be correlated to changes of signal behaviour of hyaline cartilage, cartilage thinning, ulcerations, and erosions according to the Outerbridge grading system.

We hypothesize that for many years the role of subchondral bone in the pathogenesis of cartilage damage and the progression of osteoarthritis has likely been underestimated. Some recent studies show the importance of subchondral nutrition of the cartilage in autologous transplants \((\text{script}(i))\) and physiological cartilage \((\text{script}(i))\) and physiological cartilage \((\text{script}(i))\). According to Imhof et al. \((\text{script}(i))\) more than 50% of the glucose, oxygen, and water requirements of cartilage are supplied by terminal subchondral blood vessels, which have, in part, direct contact with the deepest hyaline cartilage layer. A bone bruise seems to be a limiting factor for this subchondral nutrition support of cartilage. Possible explanations for this process include break-down or thickening of the bone-cartilage interface due to bone sclerosis, vessel-damage, or local metabolic changes.

Radin et al. \((\text{script}(i))\) formulated another hypothesis. They focussed on the mechanical properties of the subchondral bone, especially its role as an effective shock absorber. They found that shear stress in the articular cartilage always occurs whenever there is a discontinuity or substantial gradient in stiffness of the subchondral plate. In former studies finite element analysis showed increasing stress in the cartilage subsequent to subchondral plate stiffening. The fact that these changes occurred without any evidence of metabolic or inflammatory changes implied that the latter follow the mechanical changes, first in the bone and then in the cartilage. More recent studies by Johnson et al. \((\text{script}(i))\) and Lahm et al. \((\text{script}(i))\) have demonstrated that osseous lesions such as subchondral fractures might heal into stiffer trabecular constructions such as subchondral sclerosis, compared with the previous normal bone. In these cases, follow-up MRI exams and arthroscopy after several months also revealed alterations of the hyaline articular cartilage, which had shown no evidence of damage during the initial examinations. Donohue \((\text{script}(i))\) described an animal in which osteoarthritic changes could be described several months after acute transarticular load and suggested that unrecognized subchondral fractures might have been responsible for this effect. However, Donohue did not determine the presence of initial subchondral damage or bone marrow edema.

The knee joints of canines have a macroscopic and histological anatomy that is similar to the human knee. Therefore, the results seem to be applicable to joint traumas in human patients.

A problematic limitation of this study is the question of causality. In this study, subchondral bone bruises are correlated positively with subsequent cartilage damages. However, it is possible that a cartilage trauma without bone bruise could cause a circumscribed cartilage lesion. Therefore, the role of the subchondral bone in developing cartilage lesions after trauma remains not crucial. There is a
possibility that subchondral bone abnormalities are not causing cartilage damage but that trauma might represent common cause of bone and cartilage disease.

In conclusion, the described animal model raises the hypothesis that subchondral traumatic lesions such as bone bruises are an important risk factor for early development of osteoarthritis in (knee) joints. It was possible to induce severe osteoarthritis through trauma within a few months. The cause of this degenerative cartilage lesion could have been the subchondral bone bruise, which was observed in all affected joints. Possible etiogenic mechanisms are the damage of subchondral nutrition of hyaline cartilage or the change of biomechanical functions (shock-absorber, shear-forces) of cartilage.

References

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Author Information

Markus Uhl
Department of Diagnostic Radiology, University Hospital Freiburg

Juergen Haberstroh
Department of Surgical Research, University Hospital Freiburg

Thorsten Bley
Department of Diagnostic Radiology, University Hospital Freiburg

Oliver Wieben
Department of Diagnostic Radiology, University Hospital Freiburg

Matthias Langer
Department of Diagnostic Radiology, University Hospital Freiburg

Andreas Lahm
Department of Orthopedic Surgery, University Hospital Freiburg