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<td>磁気共鳴画像と組織学的異常との関連についての研究</td>
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Correlation of histopathology with magnetic resonance imaging in Kienböck disease

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**A running title**
Correlation of histopathology with MRI in Kienböck disease

**Key words**
Kienböck disease, histopathology, magnetic resonance imaging, lunate, bone necrosis

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Introduction

The treatment of Kienböck disease remains controversial; however, it is agreed that early diagnosis is important. Magnetic resonance imaging (MRI) of Kienböck disease typically gives a uniformly low signal on T1-weighted images. MRI is essential for an early diagnosis. However, it is difficult to understand the detail of the actual histology, which can enable the selection of appropriate treatment options. Few reports have correlated MRI scans and histopathological appearances of biopsy specimens or comparisons with sagittal sections of whole lunate bones. As compared to the histological findings, low-intensity areas on MRI did not correlate closely with the extent of the necrotic areas and did not distinguish between new bone formation and granulation tissue. Moreover, Hashizume et al. said that this disagreement was due to the poor quality of the MRI. Schmitt et al. summarized the pathoanatomic processes and the corresponding MRI findings in the natural course of lunate osteonecrosis. In close correlation with the underlying pathoanatomic processes, 3 different signal and contrast enhancement patterns can be identified in lunate osteonecrosis with the use of contrast-enhanced, T1-weighted MRI. This imaging technique clearly shows the different enhancement patterns and differentiation between bone marrow edema and partial and complete bone marrow necrosis.

The purpose of this study was to compare in the detail pre-surgery MRI scans with the corresponding coronal sections of extirpated lunates of patients with Kienböck disease. Our hypothesis is that the MRI scans taken with 47-mm microscopy surface coil are reflected the histopathology of Kienböck disease.

Materials and methods

Six patients (3 men and 3 women; aged 21–64 years; average 38 years) with Kienböck
disease underwent tendon-ball replacement or the Graner surgical procedure (lunate excision, capitate osteotomy, and intercarpal arthrodesis) between 2005 and 2008 at our Hospital. Each patient was examined by radiography and MRI. Lichtman’s criteria were used to identify stage 3b Kienböck disease on the x-ray.

MRI was performed within 1 month before surgery using a 1.5-T system (Gyroscan NT Intera; Phillips Medical Systems, Best, The Netherlands). Coronal 2-dimensional proton-density weighted (PDW) (T1-weighted) (repetition time [TR][msec]/echo time [TE][msec] = 1697-1852/17.0) images, and fast-field echo (FFE) (T2-weighted) (TR/TE = 392-396/13.8-14.0) images of the wrist were acquired using a 47-mm microscopy surface coil (Philips Medical Systems, Best, The Netherlands). The microscopy coil is intended for a range of applications requiring a small field of view while maintaining a high signal-to-noise ratio and is well suited to examine small anatomical lesions. The slice thickness was 1.5-mm, and the slice interval was 0.1-mm with a field of view of 50-mm. Under these conditions, the lunate bones were imaged in 8 slices of the coronal view. A radiologist (Y.O.) and the author (T.O.) observed all preparations and evaluated the images.

The whole lunate bones were extirpated during replacement surgery and were fixed in a 10% buffered neutral formalin solution (Wako®, Osaka, Japan). After decalcification in 0.5 M EDTA, 0.1 M Tris and NaOH for 4 months, the samples were embedded in paraffin. The decalcified whole lunates were sectioned roughly into 8 coronal specimens (Fig. 1) correlating with the coronal MRI and were stained with hematoxylin-eosin. Given that a long axis of the lunate was about 20mm, the width of 8 coronal specimens was about 2mm. Since the slice thickness of MRI was 1.5mm, the error was presumed to be up to about 1mm.
Assessment points of histopathological osteonecrosis included observations of empty lacunae, fatty marrow, and vascular structures, and the findings were compared with the signal levels of the PDW- and FFE-coronal MRI at the same slice levels. The author (T.O.) and another researcher (Y.H.) familiar with histopathological evaluations made the histological observations of the slices. In total, 8 views from the MRI and 8 slices of the histopathological specimens that were similar in shape macroscopically were compared by the author (T.O.) with regards to the assessment points of histopathological osteonecrosis.

Results

Generally, PDW images of normal lunates exhibit high signal intensities, whereas FFE images exhibit intermediate intensities. In comparison, the PDW images of the necrotic lunate in this study demonstrated lower signal intensities, and the FFE images exhibited higher or lower intensities. The overall MRI and histopathological observations of each diseased lunate are shown in Table 1. Sagittal diagrams include images taken from the central part of the coronal view (Fig. 2). Histopathological analyses revealed disrupted trabecular and degraded fatty marrows towards the center of the lunates. However, on the dorsal and palmar aspects of the lunates, the trabecular structures, fatty marrows, and blood vessels appeared normal. Likewise, the palmar and dorsal aspects of the lunates maintained near-normal intensities as observed in the PDW images.

The pre-surgical MRI and histopathological images of a representative case are shown Figure 3. Towards the center of the lunate, the signal intensity of the PDW images was reduced, and segmented trabecular structures were observed in the corresponding
histopathological views. The details of a representative slice level are shown (Fig. 3c, k, s). Within the solid outline (Fig. 4, upper row), the region appeared nearly normal histopathologically because we could observe trabecular structures and fatty marrow (Fig. 4a). This region also exhibited high intensity PDW images and moderate intensity FFE images. Furthermore, the observed signal was equal to the signal of the normal osseous tissue in the MRI. Conversely, within the dotted outline (Fig. 4, upper row), the region was filled with fibrous granular tissue and blood vessels, and no fatty marrow or osteocyte nuclei were observed histopathologically (Fig. 4b). This region also exhibited slightly low intensity PDW images and high intensity FFE images. In all specimens, we observed a signal change on the MRI, as well as changes in the histopathology. In the dorsal distal region (Fig. 3a, i, q), near-normal signal intensities were observed on the MRI, and normal trabecular structures were observed in the histopathological analyses, including osteocyte nuclei, fatty marrow, and blood vessels. This region also exhibited high intensity PDW images and intermediate intensity FFE images (Fig. 3a, i, q). In the volar 1/3 area (Fig. 3f, n, v) of the lunate, there were fibrous granular tissues and blood vessels but an absence of fatty marrow, and this area exhibited low intensity PDW images and high intensity FFE images.

Of the 6 patients having Kienböck disease (stage 3b), osteocyte nuclei, fatty marrow, and blood vessels were present within the corresponding high intensity areas of the PDW images. In the low intensity areas of the PDWs, osteocyte nuclei and fatty marrow were absent, and blood vessels were only present in some of the histopathological findings. The intensities of the FFE images and the histopathological findings did not always correlate (Table 2).
Discussion

In normal bone, T1-weighted MRI images have a high signal, and T2-weighted MRI images show an intermediate signal. However, in the early stages of osteonecrosis, T1-weighted images exhibit a low signal, and T2-weighted images show a high signal. This intensity change reflects a loss of fatty marrow affecting the T1 signal and possible edema contributing to a high signal in the T2-weighted images. In the more advanced stages of osteonecrosis, T1- and T2-weighted images both show low signal intensities.\(^\text{16}\)

In the present cases, the lunate conditions were assumed to be advanced osteonecrosis because of stage 3b on x-ray; however, the MRI scans using a 47-mm microscopy coil showed a variety of focal changes.

Desser et al. (1990) showed that MRI was able to distinguish areas of viable and nonviable bone within the lunate. They further demonstrated that undecalcified, fluorescently-labeled histological sections of lunate biopsies exhibited tetracycline uptake.\(^\text{7}\) Trumble et al. (1990) showed that 6 patients having a diagnosis of Kienböck disease demonstrated a correlation between the loss of signal intensity on T1- and T2-weighted MRI images and evidence of osteonecrosis by histology. However, the extent of marrow changes that must be present for signal intensity alterations in MRI scans has not been determined.\(^\text{6}\) Hashizume et al. (1996) histologically examined extracted whole lunates from 10 patients with Kienböck disease (stage 3). All of the patients showed a markedly decreased intensity of the lunate on MRI in sagittal T1-weighted images. In T2-weighted images, 2 cases showed complete low intensity, and 3 cases yielded diffuse images that included mixed high and low areas. MRI (T1- and T2-weighted images) low-intensity areas did not correlate closely with the extent of the necrotic areas in the histological findings and did not distinguish between new bone
formation and granulation tissue in detail. Moreover, they said that this disagreement was due to the poor quality of the MR images. In our 6 cases, empty lacunae and a reduction of fatty marrow, but not the presence of blood vessels, correlated with the signal intensities of the PDW images taken with a 47-mm microscopy coil.

Kienböck disease is denoted as an avascular necrosis because blood vessels are usually not present. In the lunates of our study, the trabecular bone structures were segmented, and fatty marrows were absent, which potentially allowed the formation of fibrous granulation tissues, although with the presence of blood vessels. Hashizume et al. (1996) reported that necrotic areas were invaded with new bone formation and granulation. The necrotic tissue then changed into fibrous scar tissue and necrotic debris. Around the necrotic area, non-necrotic tissues under hypervascularized conditions were reactive to the necrosis. Even if there are blood vessels histopathologically, it is unknown whether there is effective blood flow or interosseous pressure when evaluated by MRI. If we can know the effective blood flow in the lunate, it may be useful for selecting treatment or elucidating the etiology of Kienböck disease.

Schmitt et al. (2007) classified 3 patterns for Kienböck disease by using contrast-enhanced MRI and described this classification as the best evaluation for the viability of bone marrow. Certainly, to evaluate blood flow and the bone marrow edema of the lunate in detail, gadolinium enhanced MRI is necessary.

The absence of gadolinium enhancement in our study is a limitation. Additional limitations include the small number of cases, low field strength, and minimal imaging conditions.
References


**Figure legends**

Figure 1. Whole lunate with a schema of the 8 coronal slices scanned using MRI.

Figure 2. MRI analysis of each patient. Sagittal diagrams include images taken from the central part of the coronal view.

Figure 3. Pre-surgical PDW images (a–h) and FFE images (i–p) and HE stained sections (q–x) (x 12.5) taken from the dorsal to palmar side of the lunate from a 21-year-old left-handed woman that underwent a Graner surgical procedure for Kienböck disease (stage 3b).

Figure 4. Representative slice levels (taken from Fig. 2c, k, s) and correlating histology. Within the solid outline (upper row), the region appeared nearly normal histopathologically because we could observe trabecular structures and fatty marrow (a). This region also exhibited high intensity PDW images and moderate intensity FFE images and was equal to the signal of the normal osseous tissue in the MRI. Conversely, within the dotted outline (upper row), this region contained fibrous granular tissue and blood vessels, and no fatty marrow or osteocyte nuclei were observed histopathologically (b). (a) A high magnification image of the squared encircled area in (c, k and s). Osteocyte nuclei, fatty marrow, and blood vessels are present within the vitalized focal area of the solid line. (b) Fibrous granular tissues and blood vessels are present, whereas there is an absence of fatty marrow within the dotted line.

Table 1. MRI and histopathological analysis of each patient.

Table 2. Correlation of the histopathology with the MRI scans: (+), presence; (±), discordance; (−), absence.
### Table 1: MRI Findings

<table>
<thead>
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<tr>
<td>PDW</td>
<td>FFE</td>
</tr>
<tr>
<td>1</td>
<td>normal or partial low (dorsal 1/3 and volar 1/3), low (central 1/3)</td>
</tr>
<tr>
<td>2</td>
<td>normal (dorsal1/2), low (volar1/2)</td>
</tr>
<tr>
<td>3</td>
<td>normal (dorsal1/4 and volar-ulnar sides), low (dorsal 1/4 to volar-radial sides)</td>
</tr>
<tr>
<td>4</td>
<td>all slices are slightly low</td>
</tr>
<tr>
<td>5</td>
<td>low (volar1/4), another slices are slightly low</td>
</tr>
<tr>
<td>6</td>
<td>normal or partially slight low (dorsal 1/3 and volar 1/3), low (central 1/3)</td>
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**Normal**
- **hyperintense signal**
- **intermediate signal**
Figure 3.
Figure 4.
### Table 1

<table>
<thead>
<tr>
<th>Patient</th>
<th>Gender</th>
<th>Age</th>
<th>X-ray finding</th>
<th>Empty lacunae</th>
<th>Fatty marrow</th>
<th>Blood vessel</th>
<th>MRI finding</th>
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<tr>
<td>1</td>
<td>F</td>
<td>65</td>
<td>segmentation and comminuted fracture at central 1/3</td>
<td>partially presence (central 1/3), a few (dorsal 1/3 and volar 1/3)</td>
<td>absence (central 1/3), partially presence (dorsal 1/3 and volar 1/3)</td>
<td>partially presence in all slices</td>
<td>normal or partially slightly low (dorsal 1/3 and volar 1/3), low (central 1/3)</td>
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<tr>
<td>2</td>
<td>M</td>
<td>24</td>
<td>segmentation at volar 1/3</td>
<td>presence (dorsal1/3), absence (volar2/3)</td>
<td>presence (dorsal1/3), absence (volar2/3)</td>
<td>presence (dorsal1/3), absence (volar2/3)</td>
<td>normal (dorsal1/2), low (volar1/2)</td>
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<tr>
<td>3</td>
<td>M</td>
<td>21</td>
<td>severe collapse, especially radial side</td>
<td>partially presence in all slices</td>
<td>partial presence (dorsal1/4 and volar-ulnar side)</td>
<td>partially presence in all slices</td>
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<tr>
<td>4</td>
<td>M</td>
<td>33</td>
<td>segmentation (+) colonal and sagittal plane on center</td>
<td>partially presence in all slices</td>
<td>partially presence (dorsal 1/3), absence (central to volar 1/3)</td>
<td>partially presence in all slices</td>
<td>all slices are slightly low</td>
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<tr>
<td>5</td>
<td>F</td>
<td>64</td>
<td>segmentation at volar 1/3</td>
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<td>low (volar1/4), another slices are slightly low</td>
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<tr>
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<td>21</td>
<td>segmentation and comminuted fracture at volar 1/3</td>
<td>partially presence (central 1/3), a few (dorsal 1/3 and volar 1/3)</td>
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<td>partially presence in all slices</td>
<td>normal or partially slight low (dorsal 1/3 and volar 1/3), low (central 1/3)</td>
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**Histopathological finding**

- Normal
- Scoliotic change (-)
- Collapse (-)
- Segmentation (+)

**MRI finding**

- Absence
- Presence
- Hyperintense signal
- Intermediate signal
Table 2.

<table>
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<tr>
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<th>Blood vessel</th>
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<td>+</td>
<td>+</td>
<td>-</td>
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<td>slightly low</td>
<td>-</td>
<td>-</td>
<td>±</td>
<td>+</td>
</tr>
<tr>
<td></td>
<td>low</td>
<td>-</td>
<td>-</td>
<td>±</td>
<td>+</td>
</tr>
<tr>
<td>FFE image</td>
<td>high</td>
<td>±</td>
<td>±</td>
<td>±</td>
<td>±</td>
</tr>
<tr>
<td></td>
<td>intermediate</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>low</td>
<td>±</td>
<td>±</td>
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Abstract

Purpose  Diagnosis and treatment remain controversial for Kienböck disease. A few reports have correlated magnetic resonance imaging (MRI), which is essential for early diagnosis, and histopathology of Kienböck biopsy specimens, but histopathological correlations of whole lunate bones or histological slices compared with MRI images are lacking. The purpose of this study was to compare pre-surgical MRI scans taken with a 47-mm microscopy surface coil with corresponding histological slices of Kienböck diseased lunates.

Materials and methods  Extirpated whole lunates were harvested at the time of surgery from 6 patients with Kienböck disease (stage 3b) undergoing tendon-ball replacement or a Graner surgical procedure. Paraffin-embedded, coronally sectioned specimens were stained with hematoxylin-eosin and compared with pre-surgical coronal scans using MRI with a 47-mm microscopy surface coil.

Results  Towards the center of the lunates, the signal intensity in the proton-density weighted (PDW) images was reduced, whereas the dorsal and palmar sides of the lunates exhibited no changes in intensity. In correlation, histopathological findings revealed strongly disrupted trabeculae toward the center of the lunates and intact trabeculae in the dorsal side of the lunates. Likewise, the necrotic and vitalized bone exhibited low and high signal intensities, respectively, in the PDW images; however, in the fast-field echo (FFE) images, there were no correlations with the histopathological observations.

Conclusions  MRI (PDW images, but not FFE images) using a 47-mm microscopy coil reflected the extent and localization of the necrotic area in Kienböck diseased lunates, as evidenced by comparison with histological analyses of the lunate specimens.