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Biomaterials 26 (2005) 611–619
Biomaterials
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Feasibility of chitosan-based hyaluronic acid hybrid biomaterial for a novel scaffold in cartilage tissue engineering ☆

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Received 14 October 2003; accepted 13 March 2004

Abstract

In this study, we hypothesized that hyaluronic acid could provide superior biological effects on the chondrocytes in a three-dimensional culture system. To test this hypothesis, we investigated the in vitro behavior of rabbit chondrocytes on a novel chitosan-based hyaluronic acid hybrid polymer fiber. The goal of the current study was to show the superiority of this novel fiber as a scaffold biomaterial for cartilage tissue engineering. Chitosan polymer fibers (chitosan group) and chitosan-based hyaluronic acid hybrid polymer fibers (HA 0.04% and HA 0.07% groups, chitosan coated with hyaluronic acid 0.04% and 0.07%, respectively) were originally developed by the wetspinning method. Articular chondrocytes were isolated from Japanese white rabbits and cultured in the sheets consisting of each polymer fiber. The effects of each polymer fiber on cell adhesivity, proliferation, morphological changes, and synthesis of the extracellular matrix were analyzed by quantitative a cell attachment test, DNA quantification, light and scanning electron microscopy, semi-quantitative RT-PCR, and immunohistochemical analysis. Cell adhesivity, proliferation and the synthesis of aggrecan were significantly higher in the hybrid fiber (HA 0.04% and 0.07%) groups than in the chitosan group. On the cultured hybrid polymer materials, scanning electron microscopic observation showed that chondrocytes proliferated while maintaining their morphological phenotype and with a rich extracellular matrix synthesis around the cells. Immunohistochemical staining with an anti-type II collagen antibody demonstrated rich production of the type II collagen in the pericellular matrix from the chondrocytes. The chitosan-based hyaluronic acid hybrid polymer fibers show great potential as a desirable biomaterial for cartilaginous tissue scaffolds.

Keywords: Chitin/chitosan; Chondrocyte; Hyaluronic acid/hyaluronan; Cell culture; Cell adhesion

1. Introduction

In Living organisms, the authentic substrate for most cells is the extracellular matrix (ECM). The ECM adheres to cells via integrins, which are membrane-spanning heterodimeric receptors [1]. Through the cell–matrix adhesions, the ECM transduces physiological signals regulating cell growth, cell proliferation, cell differentiation, and matrix remodeling to the cells [1]. Therefore, the ECM plays an important role in living tissue development and regeneration.

In a tissue engineering technique, tissue regeneration is achieved by culturing isolated cells on biocompatible and biodegradable materials as scafollds onto which cells are seeded. A large number of studies have shown the importance of selecting the appropriate biomaterials as scaffolds for the cell adhesion and supporting the proliferation [2–10]. For the reason given above, the ideal scaffold material should be one which closely mimics the natural environment in the tissue-specific ECM [9].

Once damaged, the articular cartilage consisting of hyaline cartilage tissue has little capacity for spontaneous

☆ Supported by Regional Consortium Research Development Work.
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doi:10.1016/j.biomaterials.2004.03.013

healing. Although the limited potential for self-repair of the articular cartilage necessitates operations to treat injured cartilage, no current procedures for cartilage repair have successfully regenerated long-lasting hyaline cartilage tissue to replace a cartilaginous lesion [11,12]. To solve this limitation, tissue engineering techniques by culturing isolated chondrocytes on a variety of scaffold materials, including naturally occurring and synthetic, have been developed [4–10]. However, there have been no ideal materials for cartilage tissue engineering.

One of the considerable characteristics in the cartilage tissue is that a small number of chondrocytes are embedded in the rich ECM. Therefore, cell–matrix interactions play a crucial role in the development and regeneration of the cartilage tissue. To successfully achieve cartilage tissue regeneration, a cell-carrier substance which closely mimics the natural environment in the cartilage-specific ECM must be developed. In the current study, hyaluronic acid, which is a main component of the proteoglycans (PGAs) in the cartilage, was applied to chitosan as a fundamental biomaterial.

Recently, several studies have demonstrated that cellular functions differ in two-dimensional and three-dimensional (3D) systems [13,14]. In cartilage tissue engineering, a closer approximation to in vivo environments should be attained by culturing cells in 3D materials. Additionally, the articular cartilage must be considered for its mobility as an excessively stressed tissue. To structurally mimic the environments of the cartilage tissue, the fundamental structure of a scaffold should be a 3D system with adequate mechanical strength. In the current study, the authors have structurally developed a novel polymer fiber—chitosan-based hyaluronic acid hybrid fiber—as a biomaterial to easily fabricate 3D scaffolds.

In this study, we hypothesized that hyaluronic acid could provide superior biological effects on the chondrocytes in a 3D culture system. To test this hypothesis, we investigated the in vitro behavior of rabbit chondrocytes on a novel chitosan-based hyaluronic acid hybrid polymer fiber. The objectives of the current study were to evaluate the chondrocyte adhesion, proliferation, and the synthesis of the ECMs in the chitosan-based hyaluronic acid hybrid polymer fiber and to show the superiority of this novel fiber as a scaffold biomaterial for cartilage tissue engineering.

2. Materials and methods

2.1. Polymer fibers

Polymer fibers were developed by the wet spinning method as described by Tamura et al. [15] with the following modification. Fig. 1 shows the process of

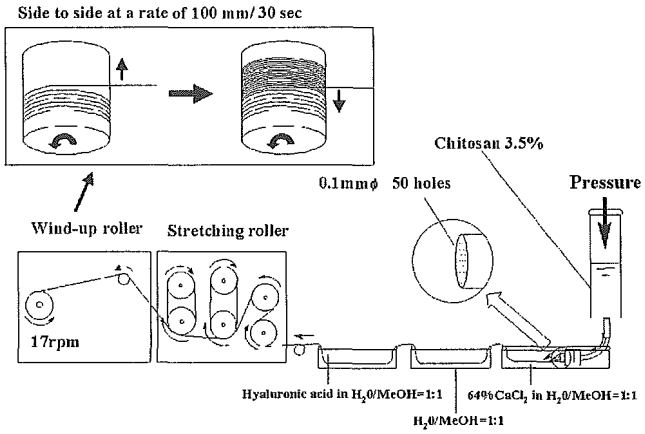


Fig. 1. The original roller system.

developing the fibers using an original apparatus [15]. Chitosan is a commercial material purchased from Kimitu Chemical Co. Inc., (Tokyo, Japan). Hyaluronic acid produced by lactic acid bacteria, with a viscosity average molecular weight of 2,400,000, was gifted from DENKI KAGAKU KOUGYO Co. Ltd. (Tokyo, Japan). The degree of deacetylation of the chitosan was 81%, and viscosity average molecular weight was 600,000. To prepare the polymer fiber 7 g of chitosan powder was dissolved in 200 ml of 2% aqueous acetic acid solution to give 3.5% of polymer concentration. Dope of chitosan was spun into a calcium coagulant bath (64% $CaCl_2$ dissolved in 50% aqueous methanol solution) through a stainless steel spinnlet (0.1 mm diameter, 50 holes) at a winding speed of 4.4 m/min at room temperature. Then, 50% aqueous methanol solution was used as a second coagulation bath and 0.04 or 0.07% hyaluronic acid dissolved in 50% aqueous methanol solution was a third coagulation bath. Using an original roller system (Okada Co. Inc., Sapporo, Japan), the resulting fibers were stretched and treated with 0.8% sodium hydroxide (NaOH) dissolved in 90% aqueous methanol solution to neutralize the acidity of the fibers. The fibers wound in the roller were washed with methanol and dried at room temperature. The diameter of each fiber was 0.03 mm.In the current study, chitosan polymer fiber (chitosan group) and chitosan-based hyaluronic acid hybrid polymer fiber (chitosan coated with hyaluronic acid 0.04%, HA0.04% group; chitosan coated hyaluronic acid 0.07%, HA0.07% group) were originally developed. For further investigations of the chondrocyte culture system, we automatically made a fiber sheet using the original apparatus (Fig. 1). Coagulated fibers were passed through a cross feeding guide and wound onto a stainless roller (120 mm diameter and 120 mm wide) at the rate of 17 rpm. The cross feeding guide set forward in the roller was moved from side to side at a rate of 100 mm/30 s. The cross-feed length and rotation count were 100 mm and 40 times,

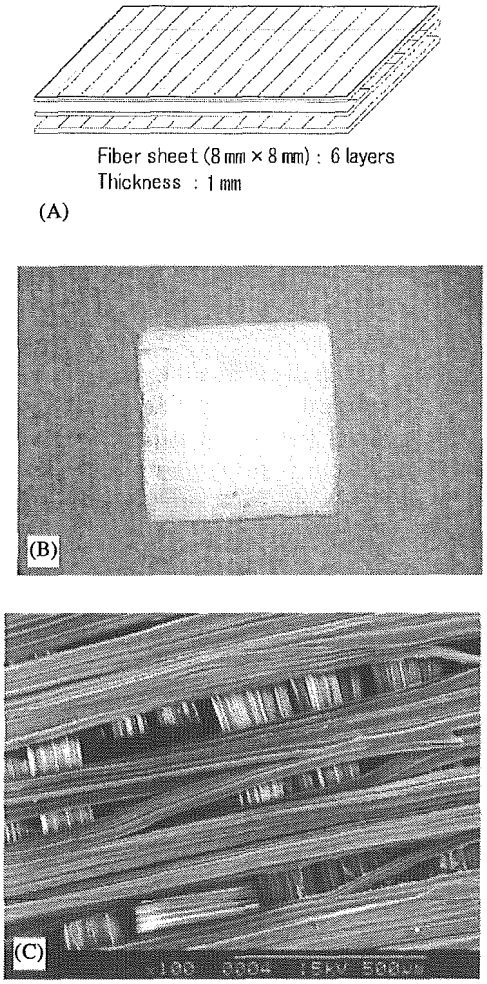


Fig. 2. (A,B) Three-dimensional (3D) scaffold material for the chondrocyte culture. Sheets consisting of each polymer fiber are stacked in a perpendicular pattern with six layers (8 × 8 mm, 1 mm thickness). (C) Scanning electron micrograph of the 3D scaffold material.

respectively. The fibers wound onto the roller were washed and dehydrated with methanol, and then dried at room temperature. The dry filaments were cut from the roller and a sheet fiber of filaments were piled 40 high (380 mm length, 100 mm wide and 0.25 mm thickness). The sheets consisting of each polymer fiber were cut into small sheets and stacked in a perpendicular pattern with six layers (8 × 8 mm, 1 mm thickness) (Fig. 2A,B,C). Each sheet was peripherally adhered with 2% chitosan gel and dried at 40°C for over night. During this process, we constantly obtained the same 3D fabrications. These 3D materials were sterilized in autoclave at 135°C for 20 minutes for the chondrocyte culture.

2.2. Measurement of material properties

Material properties of five samples in each fiber group were measured according to the Japanese Industrial Standards L1015. Tensile tests for each fiber group were performed at a crosshead speed of 20 mm/min using a material testing machine (P/N346-51299-02, SHIMADZU, Kyoto, Japan). The cross-sectional area was determined using a microscope (BX50, OLYMPUS, Tokyo, Japan) and a video dimension analyzer (VM-30, OLYMPUS, Tokyo, Japan).

2.3. Chondrocyte suspension

Ten week old Japanese white rabbits with a mean body weight of 2.0 kg (Hokudo, Sapporo, Japan) were used in this study. Articular cartilage slices, gathered from the knee, the hip, and the shoulder joints of each animal, were detached from the adherent connective tissues. Cartilage specimens were minced like paste and washed three times in sterile 0.9% sodium chloride. Then, the chondrocytes were isolated with 0.25% trypsin (Difco Lab., Detroit, MI) in sterile saline for 30 minutes followed by 0.25% collagenase (Worthington, Freehold, NJ) in Dullbecco's modified Eagle's medium (SIGMA Chemical Co., St. Louise, MO) supplemented with 10% fetal bovine serum (Invitrogen Corp., Carlsbad, CA), 100 IU/ml penicillin, 100 μg/ml streptomycin, and 0.25 μg/ml fungizone (BIOWHITTAKER, Walkersville, MD) for 6 h at 37°C in a culture bottle.Finally, the isolated cells were collected by centrifugation (1,500 g, 37°C, 5 min) after removal from the culture bottle and washed three times with the culture medium. The final cell density of chondrocyte suspension was adjusted for further investigations.

2.4. Cell adhesion study

Chondrocyte adhesion to the polymer fibers was assessed by the method as previously reported by Nishimura et al. [16]. The polymer fibers of Polyglactin 910, a 90:10 copolymer of glycolide and lactide, coated with polyglactin 370 (9-0 Vicryl suture material, Ethicon Co., Somerville, NJ), were used as control materials. The fibrous samples were cut into 10 mm pieces and packed in Teflon tubes (25 mm length, 4.8 mm inner diameter) and then 0.1 ml of chondrocyte suspension containing 0.5×10^6 cells was loaded on the column at room temperature. The cells were allowed to adhere in a humidified incubator (37°C, 5% CO_2) for 1 h. Each column was gently rinsed with 1 ml of 1 M phosphate-buffered saline (PBS), and the number of unattached cells in the rinsed solution was quantified by microscopic observation using a hemocytometer. Parallel samples of $n = 5$ were used for each group of polymer fiber.

2.5. Chondrocyte culture

The 3D scaffold materials mentioned previously were used for the chondrocyte culture. Chondrcyte suspension

containing 0.6×10^6 cells was embedded on the materials. These samples were placed in a 37°C, humidified 5% CO_2 incubator for 1 h and then overlaid with 2 ml of the culture medium. Chondrocyte cultures were placed in a humidified incubator and replaced with a fresh medium twice a week..

2.6. DNA quantification

At 1, 7, and 14 days after cultivation, 5 cultured materials of each fiber group were harvested to quantify the total amount of DNA. The DNA content (μg/sample) was measured in aliquots of the sodium citrate (0.05 M phosphoric acid, 2 M NaCl) dissolved powdered samples by the modified fluorometric assay using a bisbenzididazole dye (Hoechst dye 33258, Polyscience Inc., Northampton, UK) [17]. In fluorescence measurements, disposable cuvettes were used; the excitation wavelength was 356 nm and the emission wavelength was 458 nm. The results were extrapolated from a standard curve using salmon testis DNA (Worthington, Freehold, NJ).

2.7. RNA isolation

After 14 days of culture, samples of each fiber group were frozen in liquid nitrogen prior to RNA extraction. Total RNA was extracted by the TRIspin method described previously [18]. Briefly, frozen samples were powdered in liquid nitrogen cooled with Brown Dismembrater vessels (B. Braun Biotech., Allentown, PA). The TRIzole reagent (Life Technologies, Gaitherburg, MD) was added to the powdered tissue at the rate of 1 ml/100 mg sample weight and the samples warmed to room temperature. The samples, to which chloroform was added, were centrifuged at 12,000 g for 15 min at 4°C. Then, the upper aqueous phase containing the RNA was obtained and mixed with 70% ethanol. Finally, total RNA was isolated using the RNeasy total RNA kit (Qiagen, Chatsworth, CA) according to the manufacturer's protocol.

2.8. Semiquantitative reverse transcriptase-polymerase chain reaction (RT–PCR) analysis

Total RNA yield was fluorometrically quantified with the SYBR® Green reagent (Molecular Probes, Eugene, OR) according to the manufacturer's recommendations. According to the previous reports, semiquantitative RT–PCR analysis was performed using rabbit specific primer sets for type I collagen, type II collagen, aggrecan, and a housekeeping gene, glyceraldehyde-3-phosphate dehydrogenase (GAPDH) [19–22]. First, 1 μg of total RNA was reverse-transcribed into cDNA using the StratScript RNase H^- kit (Stratagene, La Jolla, CA). Second, aliquots (1.5 μl of 50 μl total value) of the resulting cDNA were amplified in a total volume of 50 μl containing PCR buffer, 0.2 μM dNTP mixture, 1.5 mM MgCl, 0.5 μM of each primer, and 1 unit of the Taq DNA polymerase (Life Technologies Inc., Gaithersburg, MD). As reported previously, conditions were determined to be in the linear range for both the PCR amplification and the image analysis system [19–22]. The PCR products were separated by electrophoresis of 20 μl of each reaction mixture in a 2% agarose gel at 100 V/cm in 1 × Tris-acetate-EDTA buffer. Following electrophoresis, the gels were stained with ethidium bromide, destained in distilled water and photographed using a charge coupled device (CCD) camera. Comparison to the standard 1 kb DNA ladder (Life Technologies Inc., Gaithersburg, MD) ensured proper size of PCR products. Then, the PCR products were separated by electrophoresis. Finally, the images were captured with a CCD camera and analyzed with Quantity One (PDI., Inc., Huntington Station, NY). To yield a semi-quantitative assessment of the gene expression, the data were expressed as normalized ratios by comparing the integrated density values for the genes in question with those for GAPDH.

2.9. Morphological and immunohistochemical analysis

Cell morphology in the 3D scaffold material was observed by light microscopy and scanning electron microscopy (SEM) at 14 days after cultivation. At the end of the cultivation period, all samples were rinsed with Ringer's solution to remove nonattached cells. The cells in the material were fixed over night with 2.5% glutaraldehyde supplemented with 0.1 M phosphate buffer. After fixation, the SEM specimens were rinsed with 0.1 M phosphate buffer and fixed in 1% OsO_4 for 1 h, then soaked in 1% tannic acid for an additional 1 h. These processes were repeated three times. The specimens were dehydrated through a graded ethanol series and dried at the critical point of CO_2. The specimens were then mounted on an aluminum stub and sputtered with argon using an ion coater (Hitachi, Tokyo, Japan), and viewed with a SEM (Hitachi S-4500, Hitachi, Tokyo, Japan) immediately after preparation. Immunohistochemical stains were performed with anti-type I and anti-type II collagen antibodies (Fuji Pharm. Lab., Toyama, Japan) to detect expression of the type I and type II collagen products.

2.10. Statistical analysis

All data were represented as mean ± standard error. Statistical comparisons were performed using one-way analysis of variance (ANOVA) and Fisher's PLSD test. Differences were considered significant for $p < 0.05$.

3. Results

3.1. Material properties

The tensile strength of each fiber group was $87.4 \pm 2.0\,N/mm^2$ in the chitosan group, $168.2 \pm 7.0\,N/mm^2$ in the HA0.04% group, and $144.4 \pm 2.1\,N/mm^2$ in the HA0.07% group. The values of the hyaluronic acid hybrid fiber significantly increased as compared with that of the chitosan fiber ($p < 0.0001$). The strain at failure was $11.2 \pm 1.7\%$ in the chitosan group, $9.8\% \pm 2.4\%$ in the HA0.04% group, and $9.7 \pm 1.9\%$ in the HA0.07% group. There were no significant differences among the 3 groups.

3.2. Cell adhesion

Adhesivities of the chondrocytes were expressed by the percentage of chondrocytes trapped in the column to the total chondrocytes loaded on the column (0.5×10^6 cells). The percentage was $53.3 \pm 7.1\%$ in the control group, $79.3 \pm 2.2\%$ in the chitosan group, 95.1 ± 1.3 in the HA0.04% group, and $90.5 \pm 3.2\%$ in the HA0.07% group. The values in the HA 0.04% and HA 0.07% groups were significantly higher than that in the control ($p < 0.0001$) and in the chitosan groups ($p < 0.05$).

3.3. Cell proliferation

Light micrographs (Fig. 4) showed the proliferation of chondrocytes on all the fibers at 14 days after cultivation. From day 1 to day 14 of the culture period, the total amount of DNA increased in all the fiber groups (Fig. 3). After 7days in culture, the total amount of DNA in each group was $134.5 \pm 3.9\,\mu g$/sample in the chitosan group, $142.2 \pm 11.2\,\mu g$/sample in the HA0.04% group, and $240.1 \pm 23.0\,\mu g$/sample in the HA0.07% group. The value in the HA 0.07% group was significantly higher than that in the chitosan and HA0.04% groups ($p < 0.05$). On the other hand, at 14 days after cultivation, there were no significant differences among the 3 groups.

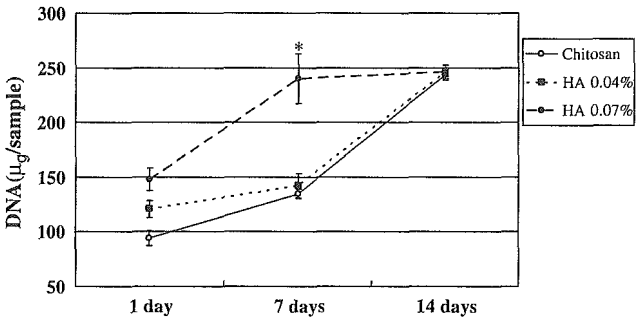


Fig. 3. The increase of DNA content per sample (μg/sample) in the chitosan and hybrid 3D scaffolds seeded with chondrocytes. $^*p < 0.05$ versus the other groups. $N = 5$, mean ± standard error.

3.4. Cell morphology

There was no effect of fiber material on cell morphology at 14 days after cultivation. Light micrographs (Fig. 4) and SEM micrographs (Fig. 5A,B) revealed the characteristic round morphology of the chondrocytes on all the fibers.

3.5. Extracellular matrix products

The SEM micrographs revealed the dense fiber, which indicated the type II collagen, in interstitial space between the fibers (Fig. 5B). At 14 days after cultivation, the quantity of total mRNA yield per mg wet weight in the chitosan group, in the HA0.04% group, and in the HA0.07% group were 0.27 ± 0.02, 0.24 ± 0.02, and $0.15 \pm 0.02\,\mu g/mg$, respectively. The mRNA for GAPDH was well expressed in all samples. Based on the analysis of 1 μg of total RNA converted to cDNA by RT from each sample, integrated density values of GAPDH in the linear PCR range (25 cycles) of the chitosan group, of the HA0.04% group, and of the HA0.07% group were 0.20 ± 0.01, 0.22 ± 0.01, and 0.20 ± 0.01 integrated density units, respectively. There were no significant differences in GAPDH band density among the 3 groups. These results support the normalization of subsequent assessments to this gene. At 14 days the culture materials, normalized ratio of mRNA of type I collagen, of type II collagen, and of aggrecan to that of GAPDH is summarized in Table 1. In the values of type I and type II collagen, there were no statistically significant differences among the 3 groups (Table 1 and Fig. 6). On the other hand, no expression of the mRNA of the aggrecan was identified in the chitosan group (Table 1 and Fig. 6). The normalized ratio of the HA0.07% group significantly increased, as compared to that in the HA0.04% group ($p < 0.05$). In a histochemical study, safranin O lightly stained the pericellular matrix around the chondrocytes in all the fibers at 14

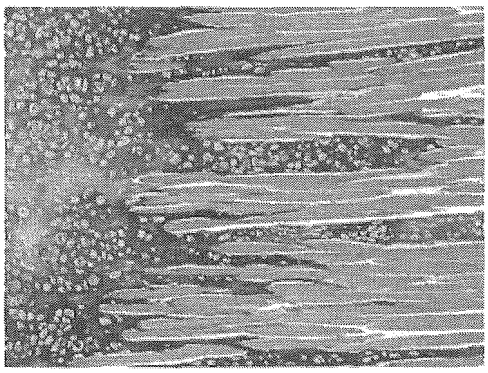
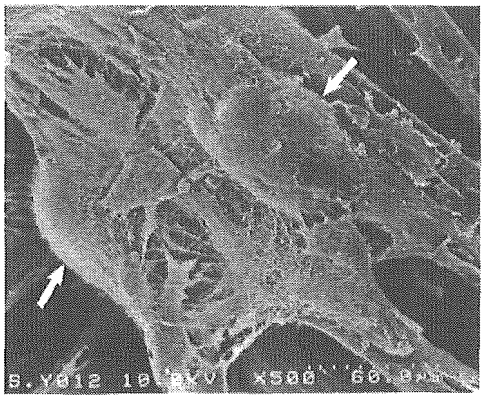
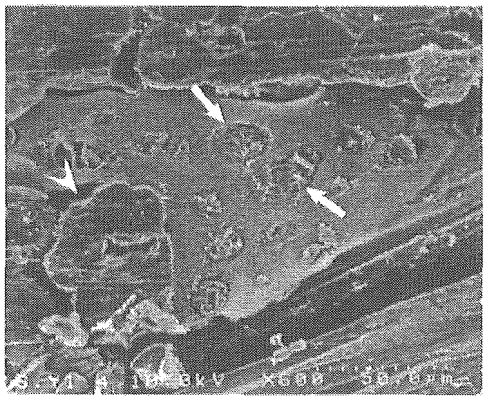


Fig. 4. Light micrograph of chondrocytes proliferated in the 3D scaffold material consisting of the chitosan-based 0.04% hyaluronic acid hybrid polymer fiber at 14 days after cultivation (hematoxylin–eosin staining, original magnification × 50).



(A)



(B)

Fig. 5. Scanning electron micrographs of the chondrocytes seeded on the 3D scaffold material consisting of the chitosan-based 0.07% hyaluronic acid hybrid polymer fiber at 14 days after cultivation. (A) Scaffold superficial surface; (B) scaffold sagittal surface. The characteristic round morphology of the chondrocytes (white arrows) and the dense fibers of the type II collagen can be found around the chondrocytes. Arrow heads, polymer fiber.

Table 1

Material groups ($n = 5$)	Type II collagen	Aggrecan	Type I collagen
Chitosan group	1.51±0.07	No expression	0.45±0.04
HA 0.04% group	1.59±0.07	1.07±0.17	0.60±0.11
HA 0.07% group	1.37±0.12	1.59±0.09*	0.43±0.11

*$p = 0.025$ versus HA 0.04% group.

days after cultivation. Immunohistochemical staining with an anti-type II collagen antibody demonstrated rich type II collagen production in the pericellular matrix (Fig. 7A). However, there was no staining for type I collagen in all the fibers (Fig. 7B).

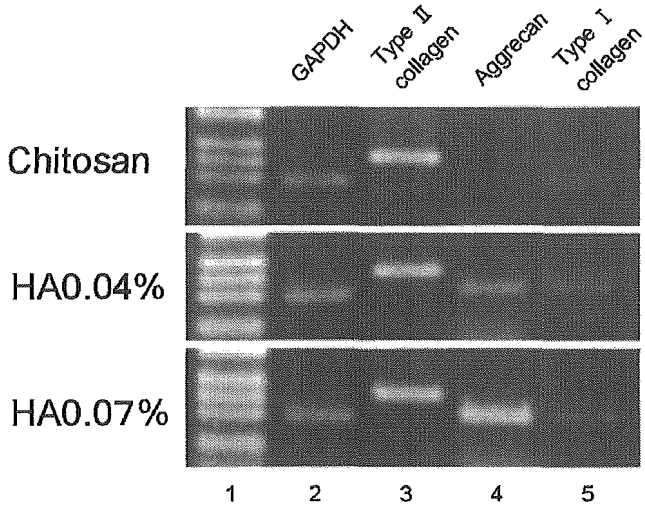


Fig. 6. Reverse transcriptase-polymerase chain reaction (RT-PCR) analysis in the chitosan, the HA0.04%, and the HA0.07% group specimens. Lane 1, ladder marker; lane 2,GAPDH; lane 3, type II collagen; lane 4, aggrecan; lane 5, type I collagen. At 14 days after cultivation, the mRNA for type II collagen was well expressed in all specimens. On the other hand, no expression of the mRNA of the aggrecan was identified in the chitosan group specimens.

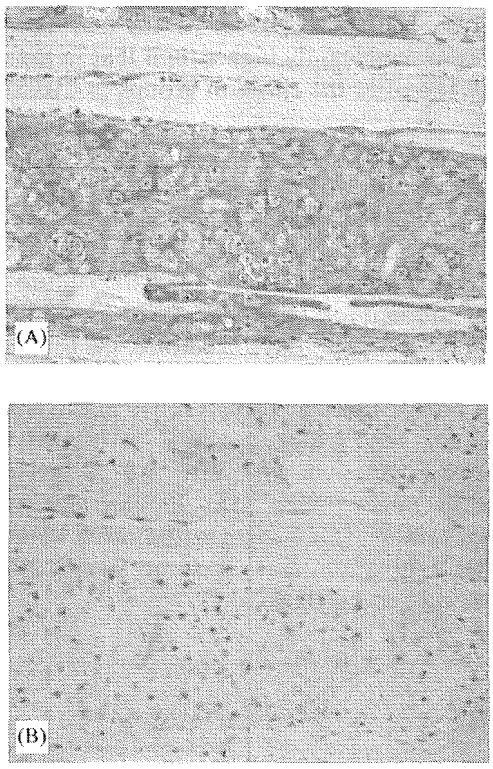


Fig. 7. Immunohistochemical stainings with anti-type I and II collagen antibodies. A, Rich production of type II collagen is indicated in the HA0.07% group. B, No staining of type I collagen is found in the HA0.07% group. (original magnification × 100).

4. Discussion

The final goal of the current study was to clarify the feasibility of the novel chitosan-based hyaluronic acid hybrid polymer fibers as a scaffold biomaterial for cartilage tissue engineering. Recently, several reports have shown the potential of chitosan scaffold biomaterial for cartilage tissue engineering [6,8,9,44]. Suh and

Matthew [9] reported that chitosan is well suited as a carrier material for the transplant of autologous chondrocytes. Our results demonstrated that adhesion, proliferation, and ECM products of the chondrocytes were significantly higher on the hybrid polymer fibers than on the non-hybrid chitosan polymer fiber, which is well accepted as a scaffold material. Based on these previous and our current results, we reasonably conclude that the chitosan-based hyaluronic acid hybrid polymer fibers have a great potential as a desirable biomaterial in cartilage tissue scaffolds.

Of emphasis in our novel biomaterial is that hyaluronic acid, which is a main component of cartilage glycosaminoglycans (GAGs), is applied to chitosan as a fundamental substance. The ideal cell-carrier substance should be one which closely mimics the natural environment in the cartilage ECM. Glycosaminoglycans, which are parts of the cartilage ECM components, play an important role in regulating expression of the chondrocyte phenotype and in supporting chondrogenesis [8,23–26]. Therefore, the application of hyaluronic acid as a component of the cartilage scaffold biomaterial must be a reasonable approach for enhancing chondrogenesis. Concerning the cell adhesivity of hyaluronic acid, Zimmerman et al. [27] showed that hyaluronic acid is an adhesion modulator molecule, which can mediate the early stage of cell-substrate interaction. On the other hand, CD44 is well known as a cell surface receptor for hyaluronic acid [28,29]. CD44 is a transmembrane glycoprotein expressed in a variety of cell types in connective tissues and a major cell surface protein in chondrocytes. This has been postulated to have a function as the principal receptor for hyaluronic acid, a common GAG component of the ECMs [29–31]. Murdoch et al. [32] demonstrated that there was a dramatic increase of CD44 expression on the isolated chondrocytes from the cartilage. Based on these previous data and the current results, we reasonably conclude that scaffold biomaterials introducing hyaluronic acid can provide excellent chondrocyte adhesive activity.

In the current study, another important point is that a polymer fiber has been applied to the scaffold biomaterial. A scaffold for cartilage tissue engineering requires adequate mechanical strength to maintain the initial shape of the implanted scaffold. Several studies have demonstrated the chondrogenic potential of GAGs-augumented chitosan hydrogels [8,45]. However, these hydrogels do not have the required mechanical strength as mentioned above. Therefore, scaffolds consisting of these hydrogels cannot be transplanted into large cartilaginous lesions in advanced degenerative diseases such as osteoarthritis and rheumatoid arthritis. To solve this drawback, we have developed a new polymer fiber as a fundamental material for 3D fabric. The obtained data showed a significant increase of mechanical strength in the hyaluronic acid hybrid fibers. This indicates that introducing hyaluronic acid to the fundamental materials plays an important role in increasing the material properties of the scaffold. Tamura et al. [15] reported the enhancement of tensile strength by the coating of alginate fiber with chitosan. Ionic interaction is the most convenient way to form a tight bond between two molecules. They concluded that the tight bond of chitosan to alginate increased the tensile strength of the hybrid fibers. In the current study, the tensile strength of a chitosan polymer fiber increased by applying hyaluronic acid coating. As chitosan is a cationic polysaccharide consisting of glucosamine residues and hyaluronic acid has anionic behavior, a tight bond between both molecules was expected. The main reason for the increase of mechanical strength in the novel hybrid fiber is this tight bond between chitosan and hyaluronic acid polymers. The novel fabric consisting of chitosan-based hyaluronic acid hybrid polymer fibers will serve as an ideal scaffold with adequate strength for cartilage tissue engineering.

Chitosan is a partially deacetylated derivative of chitin, the primary structural polymer in arthropod exoskeletons. Structurally, chitosan is a linear polysaccharide consisting of $\beta(1\rightarrow4)$ linked D-glucosamine residues with a variable number of randomly located *N*-acetyl-glucosamine groups. The average molecular weight ranges from 50 to 1000 kDa. The potential of chitosan as a biomaterial is based on its cationic nature and high charge density in solution. Madihally et al. [6] reported that the cationic nature of chitosan allowed for electrostatic interactions with anionic GAGs, PGAs, and other negatively charged species. These ionic interactions may serve as a mechanism for retaining and recruiting cells, growth factors, and cytokines within a tissue scaffold. Consequently, chitosan has been already employed as an excellent biomaterial for wound healing and tissue repair [33–35]. Since chitosan is regarded as a cationic polysaccharide showing excellent cell supporting properties, a hybrid material composed of chitosan combined with hyaluronic acid might prove to be a novel class of polyion complex effective for cartilage specific scaffolds.

The current strategies for the treatment of damaged adult articular cartilage are limited. To solve the limitations of the current operations such as osteotomies and total joint arthroplasties, several tissue engineering techniques have been developed and clinically applied to such lesions [42,43]. However, because of the mechanical weakness of scaffold materials and the limited number of donor cells, the present techniques can be used only for relatively small cartilaginous lesions following traumatic injuries and osteochondritis dessecans. Ideally, a tissue engineering technique could be available as an alternative to the current operations mentioned above for the treatment of large cartilaginous lesions

in degenerative diseases, including osteoarthritis and rheumatoid arthritis. In articular cartilage tissue engineering, we must consider that the articular cartilage is subject to excessive compression and shear stress. Therefore, to maintain the initial shape of the scaffold surface and the number of attached chondrocytes, adequate mechanical strength and highly cellular adhesivity are requirements for scaffold materials in cartilage tissue engineering. The other consideration is that the chondrocytes exhibit a profound change in their phenotype after isolation from the ECM. They show the development of a fibroblastic morphology and a switch in production from type II collagen to type I collagen. To maintain the chondrocyte phenotype through the process of cartilage regeneration, scaffold material must have the potential to support the chondrogenesis while maintaining the chondrocyte phenotype. Based on the current data, for cartilage tissue engineering, we may reasonably conclude that our novel chitosan-based hyaluronic acid hybrid polymer fiber serves as an ideal biomaterial to create a 3D fabricated scaffold with adequate strength, high cellular adhesivity, and excellent support for chondrogenesis. In the current study, we focused not on the shape or structure of the 3D fabrication for cartilage tissue, but on the development and assessment of the chitosan-based hyaluronic acid hybrid fiber as a cartilage tissue engineering scaffold. Using the novel 3D scaffold material with these properties, this tissue engineering technique would be applied to the treatment of large cartilaginous lesions in a variety of diseases such as osteoarthritis and rheumatoid arthritis.

A considerable limitation of this study is that the results were derived from an in vitro experimental model. Therefore, the biocompatibility of the current fibrous material in living joints is still unclear. A number of studies have reported the tissue response to various chitosan-based materials [36–41]. In general, these chitosan materials have been observed to evoke a minimal foreign body reaction. Sue and Matthew [9] stated that this reaction may play a role in inducing local cell proliferation and ultimately integration of the implanted material with the host tissue. However, the biocompatibility or immunological reaction of fibrous chitosan material to the joint tissue remains unclear. In addition, the process of degradation or absorption of the current fibrous material in the articular environment is still unknown. A further direction of our study will be to clarify these points using animal experimental models. Finally, further research will be needed to determine the adequate shape, pore size and mechanical properties of a 3D fabrication for cartilage tissue regeneration.

Although there is a considerable limitation as mentioned above, the data derived from this study suggest great promise for the future of chitosan-based hyaluronic acid hybrid polymer fibers as a scaffold biomaterial. The novel scaffold material will be applied to cartilage tissue engineering for relatively wide cartilaginous lesions caused by various joint diseases, including osteoarthritis and rheumatoid arthritis.

Acknowledgements

This work was partly supported by the Hokkaido Bureau of Economy, Trade and Industry, Northern Advancement Center for Science & Technology in Hokkaido, and Grant-in Aid for Scientific Research (B-1539044) from Japan Society for the Promotion of Science. Also, the authors would like to thank Mr. Tohru Mitsuno and Mr. Shouzo Miyoshi (General Research Center, DENKI KAGAKU KOUGYO Co. Ltd., Tokyo, Japan) for their excellent technical assistance in fiber preparation.

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特集 RA上肢の手術—最近の動向

RA手関節の手術

石川淳一* 三浪明男 岩崎倫政

要旨：リウマチ手関節では病期の進行に従って特有の変形を呈する。手術方法としては滑膜切除を基本として遠位橈尺関節の破壊に対してはDarrach法，Sauvé-Kapandji法，hemiresection interposition arthroplastyなどが行われ，橈骨手根関節の破壊に対しては部分手関節固定，全手関節固定，人工関節置換などがある。それぞれ有効な手術法であり，筆者らが行っている方法を中心に詳述した。言うまでもなく関節リウマチは全身性疾患であり，手術治療を考える際は手関節のみの状態にとらわれず，隣接関節をはじめ他の関節の状態を総合的に検討し，患者のADL上の改善が期待される場合のみそれぞれの病期に応じて手術適応，方法を吟味することが重要であると考える。

はじめに

手関節は関節リウマチ（RA）で侵される頻度の高い関節であり，手のかなめ石としての手関節の変形はその末梢のMP，PIP関節の機能および変形の発生にも重要な影響を及ぼす。さらに手関節の伸展，屈曲のみならず遠位橈尺関節の破壊は前腕の回旋運動の障害をもたらす。

RA手関節の初期のX線変化としては骨萎縮像，骨嚢胞の形成などであるが，病期の進行とともに滑膜増殖は手関節を支持する靱帯の破壊，機能消失をもたらし，手関節特有のX線学的変化をもたらす。最も高頻度に滑膜増殖がみられるのは尺側部のいわゆるprestyloid recessといわれる部位であり，この部と遠位橈尺関節での滑膜増殖により尺骨頭の破壊と三角線維軟骨複合体（TFCC）の尺側手根骨の支持機能が失われ，手根骨は回外方向へ回旋し，尺骨頭は背側へ脱臼する。また掌側の橈骨手根靱帯（radiocapitate, radiolunate ligament）の機能消失により舟状骨は掌側回転を生じ，手根骨は橈側へ回転する。舟状月状骨間靱帯の破壊により舟状月状骨間の離開がみられる場合もある。さらに背側の橈骨手根靱帯（dorsal radiotriquetral ligament）の機能不全とあいまって手根骨の尺側偏位および掌側亜脱臼が生じる。また手根骨の橈側回転に伴って中手骨も橈屈することになり，結果としてMP関節での尺側偏位が助長される。

RA手関節に対しては上記の病期の進行によるX線変化に応じて種々の手術的治療が考慮されるが，大きく分けると，(1) 滑膜切除，(2) 尺骨遠位端切除（Darrach法）や遠位橈尺関節（DRUJ）の再建術，(3) 橈骨手根関節の再建術などが挙げられる。以下各手術法の適応および方法について述べる。

I．滑膜切除術

抗リウマチ薬による内科的治療の進歩により滑膜切除術の適応となる例は減少傾向である。しかし，薬物治療や装具療法などあらゆる保存的治療

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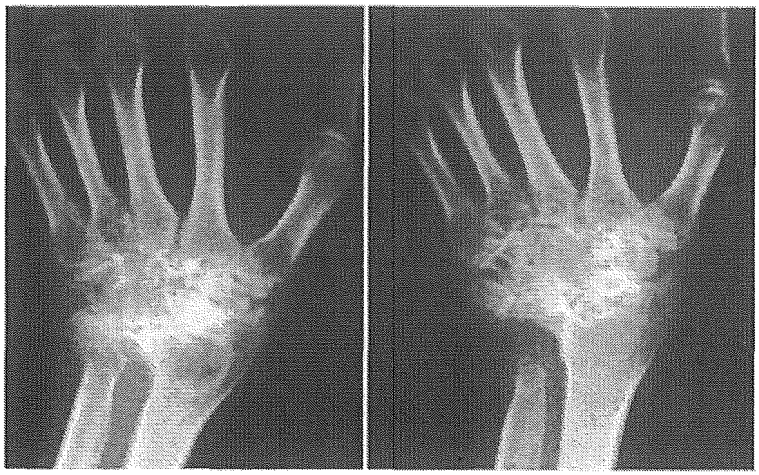
Key words：Surgical treatment, Rheumatoid arthritis, Wrist



術　前　　術後 7 年

図 1　Darrach 法

71 歳女性，stage IV。橈骨手根関節は骨性強直であり，手根骨尺側偏位の進行はない。

に抵抗する疼痛のある滑膜炎が 4〜6 カ月以上持続しており，X 線像上関節破壊が進行しておらず関節裂隙が保たれている例では，関節変形の進行防止，除痛効果，伸筋腱断裂の発生防止などの観点より，滑膜切除はなお有効な方法と考えられる。滑膜切除により炎症の場の排除を行うことにより薬物治療の有効性を高めることも期待できる。ほとんどの例では，有痛性の尺骨遠位端背側脱臼，亜脱臼を伴っており，後に述べる尺骨遠位端切除（Darrach 法）を併用して行う。また伸筋腱の皮下断裂を伴う例では伸筋腱の再建が必要となる。

第 2 中手骨基部より手関節中央を通り，尺骨頭の近位尺側 3〜4 cm に至る直線状の皮膚切開を用いる。背側の静脈は術後の腫脹を抑えるため可能な限り温存することが重要である。橈骨神経浅枝，尺骨神経背側枝は術野の橈尺側にてそれぞれ確認しておく。伸筋支帯は第 6 コンパートメント上で縦切し，橈側をベースとしてコの字形に橈側へ反転する。伸筋腱を確認し，腱周囲および腱内への滑膜増生を認める場合滑膜切除を行う。

関節包は H 字状に切開し，橈骨手根関節，手根中央関節，遠位橈尺関節の滑膜切除をマイクロリューエル，関節鏡用パンチなどを用いて行う。特に尺骨手根骨間は滑膜増生が強く，入念に切除を行う必要がある。尺骨頭の不安定性が著明な場合は Darrach 法を合併して行う。駆血帯を解除し，止血操作を丁寧に行った後，関節包を閉鎖縫合する。腱断裂に対する処置を行った例以外，伸筋支帯を腱の下敷きにする操作は行っていない。皮下にドレーンを留置し，皮下，皮膚を縫合する。術後は約 2 週間のシーネ固定の後，手関節の自他動運動を開始する。

小川ら[1]は平均 13 年の長期成績を報告し，無痛は 78%，腫脹の消失は 92%で得られていたが，X 線像上での関節破壊の進行は 81%でみられたとしている。長期での関節破壊の進行は避けられないが，滑膜切除は先に述べた適応症例を厳格に選べば除痛，腫脹の消失において良好な成績が得られると考える。

II．遠位橈尺関節の再建術

1．尺骨遠位端切除（Darrach 法）

遠位橈尺関節の破壊があり，回内外時の疼痛が著明な場合や背側への尺骨頭脱臼により伸筋腱の断裂が存在する場合，滑膜切除と併用して行う。問題点として尺骨遠位切除端の不安定性による痛みや尺側の支持の消失による手根骨の尺側偏位の出現が指摘されている。したがって活動性の低い，

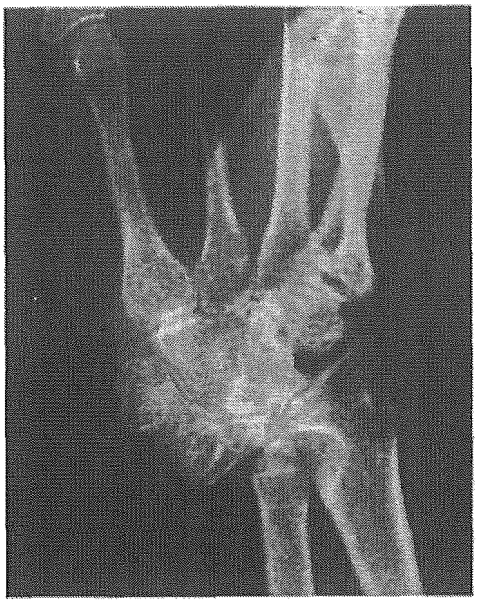


図 2
著明な手根骨の尺側偏位を認め，手根骨は掌尺側へ脱臼している。

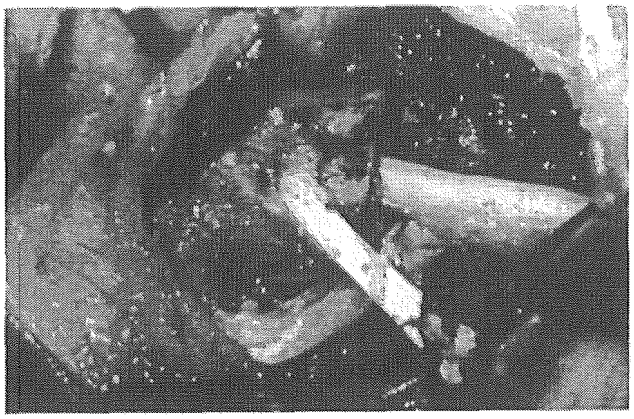


図 3　尺骨切除端に対する安定化手術
ECU の半裁腱を，近位を基部として作成し，骨孔を通してもとの腱に縫合する。

比較的高齢者や橈骨手根関節が強直位にある例が最もよい適応となる(図 1)。術前 X 線像にてすでに手根骨の尺側偏位が存在したり，橈骨遠位尺側縁が近位尺側へ傾斜している例では Darrach 法単独は禁忌である（図 2)。

手術方法は先に述べた滑膜切除施行後，尺骨遠位を骨膜下に展開し，遠位尺側から近位橈側へボーンソーを用いて切除する。切除量は回内外にて橈骨とぶつからない程度の最小限（通常 15 mm 程度)でよい。切除端はヤスリにて滑らかにする。近年切除端の不安定性による疼痛が問題点として指摘され，種々の安定化術が報告されている。筆者らは尺側手根伸筋腱（ECU 腱）を用いた再建を行っている[2]。ECU 腱の遠位橈側に近位を基部とする half slip を作成し，切除端の背側に 3.5 mm ドリルであけた骨孔に通し，反転して最大緊張下に同腱に interlacing 縫合を行う(図 3)。術後は約 2 週間のシーネ固定を行う。

2．Sauvé-Kapandji（S-K）法

DRUJ の破壊により前腕回旋時痛がある例が適応となる。Darrach 法では握力の低下をきたす場合があることと，手関節の横幅が狭くなる点が欠点であり，比較的若年者で活動性が高い場合は S-K 法が選択される。S-K 法後長期経過例では尺骨頭と尺側手根骨が癒合することが多く，手関節の安定性に寄与しうると考えられる。しかしすでに橈骨手根関節が強直位にある場合は S-K 法の必要はない。

DRUJ の滑膜切除を行ったのち，骨膜下に尺骨の骨幹端部を展開する。ボーンソーにて約 15 mm 尺骨頭を残して 10～15 mm 幅で骨切除する。尺骨頭および橈骨の尺骨切痕を海綿骨がでるまで新鮮化する。先に切除した尺骨を残存する尺骨頭の幅に応じて円盤状に採型し，間に介在するよう移植する。Kirschner wire にて固定したのちキャニュレイテッド海綿骨ネジ 1 本にて固定する（図 4)。尺骨切除部の骨膜は完全に切除し，再癒合を防止する。術後は軽度回外位にて肘上シーネ固定を 2 週間行う。

S-K 法の問題点として Darrach 法と同様に近位端の不安定性によるクリック，疼痛があげられる。不安定性が著明な場合，近位端と橈骨が衝突(impinge)する。筆者らは先に述べた ECU の半裁腱を用いた遠位端安定化術を追加して行っており[2]，不安定性をきたした例は経験していない(図 5)。

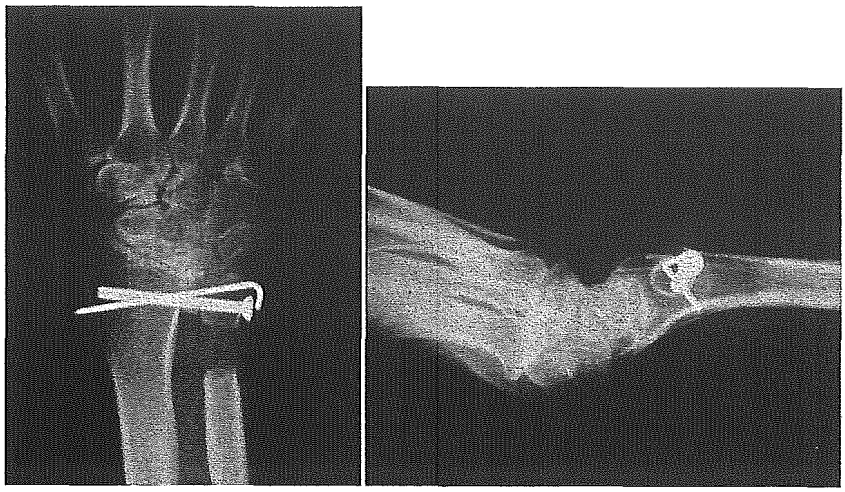


図 4　S-K 法
52 歳女性，stage III。術後 2 年。尺側手根骨の支持が得られている。

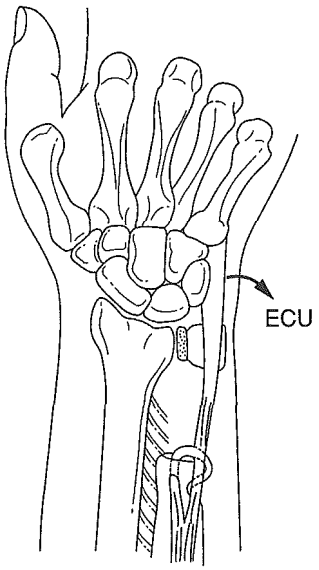


図 5　S-K 法＋ECU tenodesis
ECU の half slip を用いて腱固定を行い，尺骨近位端の安定化を図る。

3．Hemiresection interposition arthroplasty（Bowers 法），Matched distal ulnar resection（Watson 法）

比較的早期の RA で TFCC の機能が温存されているが DRUJ 関節面の破壊による回旋時痛が著明な場合が適応となる。したがって RA に対する適応は極めて少ないと思われる。

手術方法は尺骨の TFCC 付着部を温存して尺骨頭の橈骨との関節面を切除し，切離した関節包および伸筋支帯を尺骨頭の切除面に介在するように縫合する。長掌筋腱の腱球を挿入する場合もある。手技の詳細については他書にゆずる[3]（図 6）。

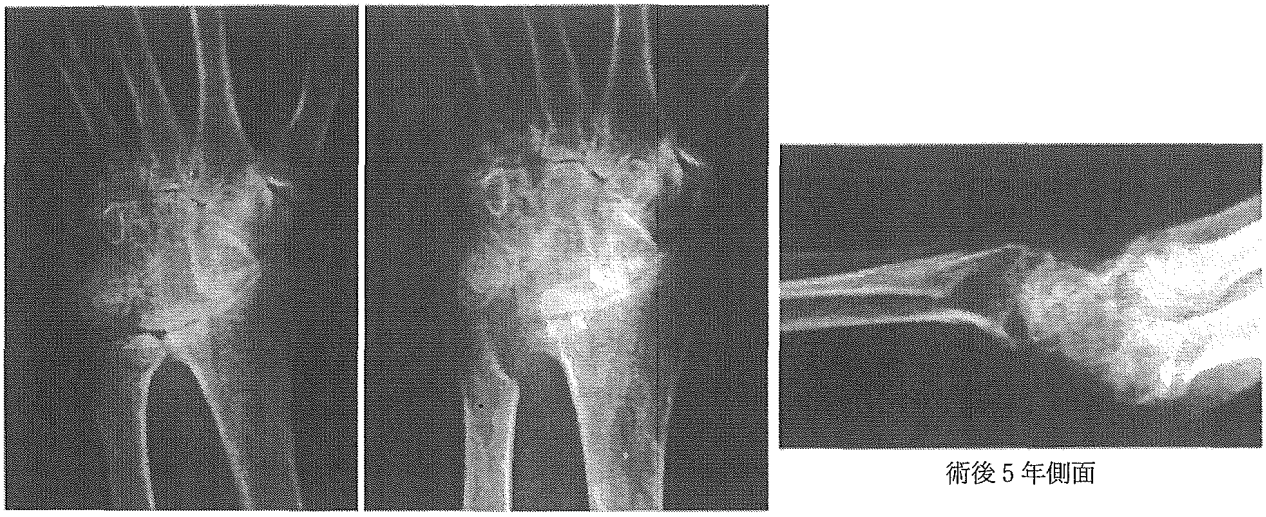
III．橈骨手根関節の再建術

1．橈骨月状骨間固定術

橈骨手根関節の破壊による手関節掌背屈での疼痛が強く，手根中央関節は比較的保たれている例が適応となる。また術前手根骨の尺側偏位や橈側回転がみられる場合に Darrach 法を行う際は手関節のアライメントの矯正と変形の進行を防止する目的で橈骨月状骨間固定を追加する。

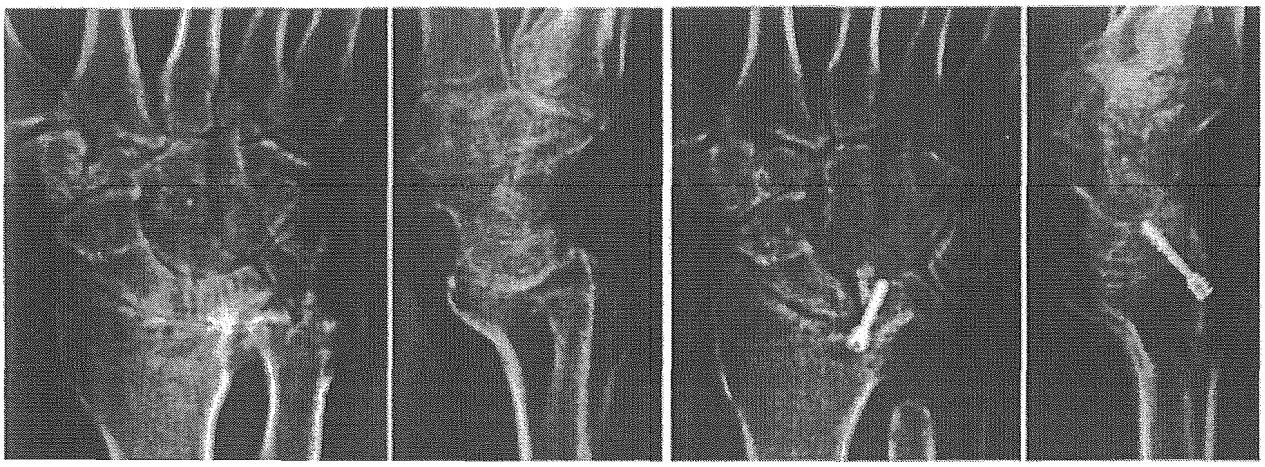
手術方法は橈骨月状骨窩および月状骨関節面を海綿骨が露出するまでリューエルで切除したのち月状骨を可及的に解剖学的位置に整復する。手根骨の尺側偏位，橈側回転を矯正するように留意する。腸骨を採取し，ブロック状に橈骨月状骨関節の高さを保持するような形で移植する。内固定として Kirschner wire や Herbert screw，ステープルを用いる[4)5)]（図 7）。術後は 6 週間の外固定を行う。

橈骨月状骨間固定術で最も問題となるのは可動域の減少である。しかし当科で行った 13 例の術後



術　前　　術後5年正面　　術後5年側面

図 6　Hemiresection interposition arthroplasty
62歳女性，stage IV。術後5年。尺骨遠位端の不安定性はない。



術　前　　術後2年

図 7　橈骨月状骨間固定
43歳男性。術前 stage IIIが術後2年 stage IIIと進行を認めない。伸展-屈曲は術前 40°-60°が術後 25°-50°と軽度低下した。

平均4年の調査では伸展が術前36°から術後27°，屈曲は術前36°が術後26°と各々約10°の低下を認めたのみであった。また Stanley ら[6]の術後評価でも Excellent が64%，Good が36%と良好であり，X線像での病期の進行を認めなかった[7]。Darrach 法単独では X 線像での病期の進行を認める例があり，橈骨月状骨間固定術の追加はより安定した手関節の獲得と破壊の進行を防ぐ可能性があると思われ，極めて有用な方法である。

2．全手関節固定術

手関節リウマチでは手根中央関節の関節破壊は痛みの原因となることが少なく，全手関節固定術が適応となる場合は少ないと考えられる。また手関節可動域は腱の滑動（excursion）の増加にとっ

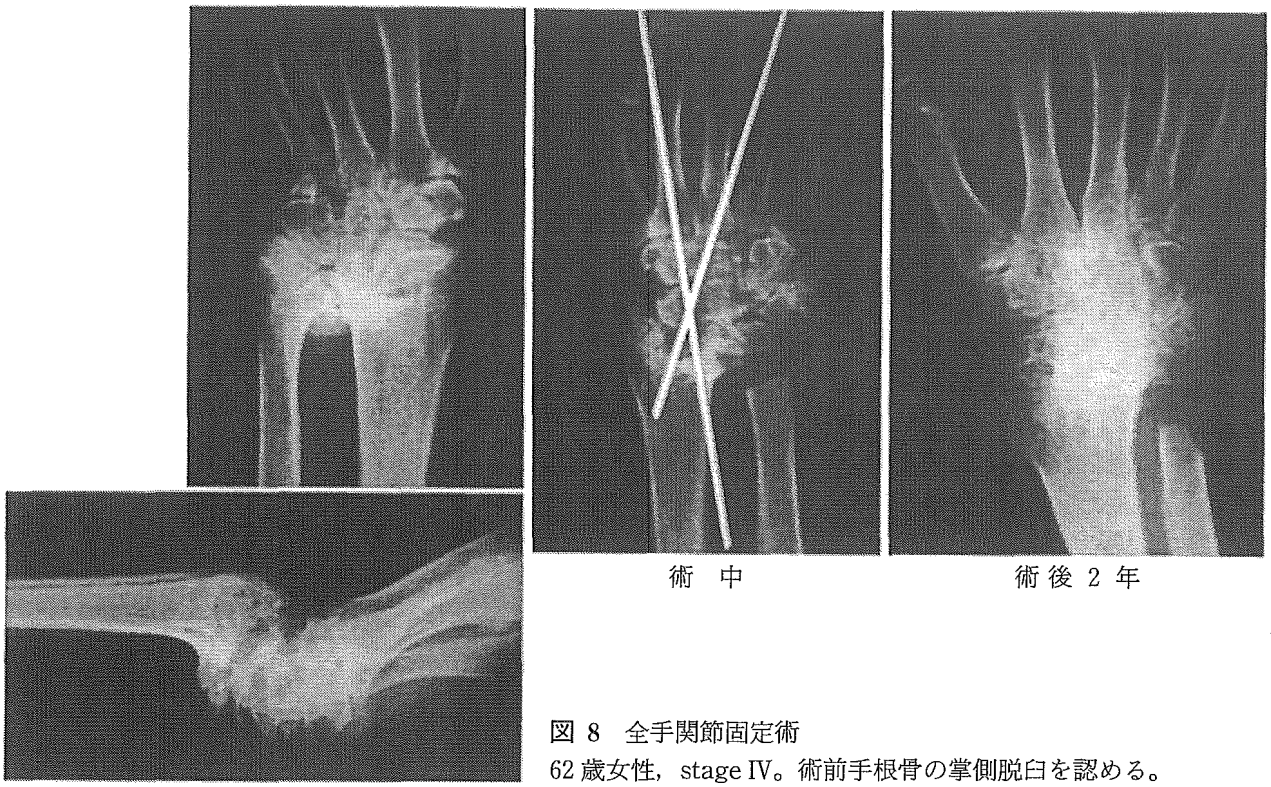


図 8　全手関節固定術
62 歳女性，stage IV。術前手根骨の掌側脱臼を認める。

て極めて重要であり，とくに手指伸筋腱の腱断裂を伴う例では全固定術により十分な腱の滑動が得られず，手指の運動機能の損失が大きくなる。また同側の肩，肘関節にも機能障害が存在する場合は全固定術によって ADL が著明に障害されてしまう。したがって全固定術が適応となるのは全手関節の破壊があり，同側の肩，肘，手指の機能が温存されている活動性の高い若年者や手関節伸筋腱群が断裂した有痛性の高度の屈曲拘縮が存在する場合に限られる。

手関節の固定肢位に関しては意見の分かれるところである。筆者らは屈曲伸展および橈尺屈中間位での固定を原則としているが，両側例では片側は中間位で，対側は 20°程度の屈曲位で固定するのがよい。

手術方法も様々な手技が報告されている。筆者らは Carroll ら[8]の方法に準じて行っている。手根骨背側をリューエルなどで切除したのち，腸骨より皮質海綿骨をウサギの顔のように採型し，両方の耳に該当する部分は第 2，3 中手骨基部髄腔へ，顔の顎の部分は橈骨遠位髄腔へ挿入する。さらに 2 本の 1.8 mm の Kirschner wire を腸骨背側で交叉させて第 2，3 中手骨と橈骨間を固定する。これにより移植骨を手根骨に押さえ込むように強固に固定することができる（図 8）。必要であれば 3 本目の鋼線を追加する[9][10]。

3．人工関節置換術

同側の肩，肘，手指の破壊が存在し，手関節の可動域が必要な活動性の低い例で適応となるが，現在のところ長期にわたり安定した成績は得られていない。

1967 年に Swanson が手関節に対して flexible なシリコン人工関節（図 9）を応用したが，シリコン滑膜炎やインプラントの破損など大きな問題点があった[11]。1970 年代後半に全人工関節として Meuli[12]や Volz[13]などの ball and socket 人工関節が開発され臨床応用された。1〜2 年の短期成績は良好であったが，5 年前後の長期では遠位コン

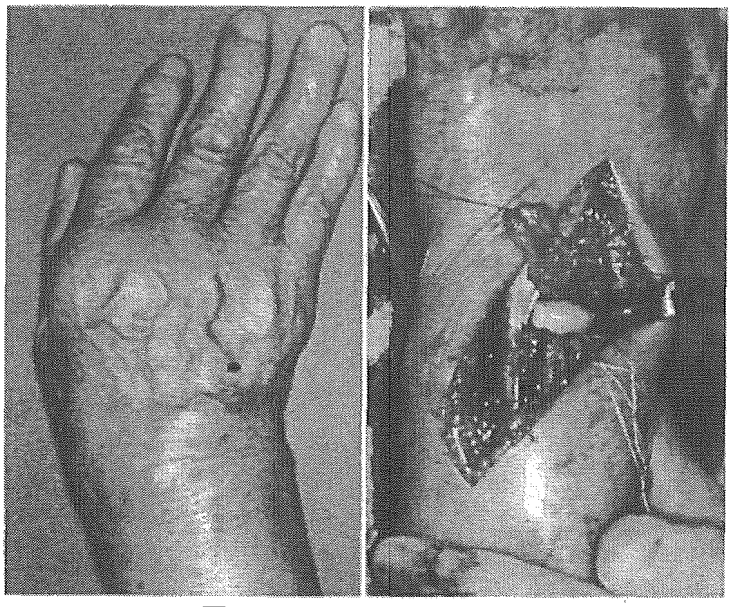


図 9 Swanson インプラント
60歳女性，stage IV。

ポーネントのゆるみや脱臼などを生じ，failure rate は30%前後にのぼると報告されている。また骨切除量が多く，手関節固定術など salvage 手術が困難であることも大きな問題点である。

1983年より Mayo Clinic で開発され使用されている biaxial wrist prosthesis の5年以上の成績の報告では46例中8例で遠位コンポーネントのゆるみ，1例で脱臼が生じたとしており[14]，成績は向上しているものと考えられる。今後さらに手技および機種の改善による長期成績の向上が望まれる。

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Summary

Surgical treatment for rheumatoid arthritis of the wrist

Surgical treatment for rheumatoid arthritis of the wrist is detailed. Synovectomy of the wrist joint is effective for the prolonged synovitis that resists medicinal treatment with retained joint space. Darrach, Sauvé-Kapandji and hemiresection interposition arthroplasty are indicated for painful forearm rotation due to the destruction of distal radio-ulnar joint. Limited wrist fusion, especially radiolunate fusion is a reliable method for pain relief and the stability of the joint. Each operative intervention should be selected according to the radiographic stages and demands of the patients, considering the condition of the other joints.

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II 代表的疾患のリハビリテーション

1．上肢・肩甲帯

5）手関節周辺外傷*

石川淳一　三浪明男**

[整形外科 56巻8号：940～944，2005]

はじめに

手関節周辺の外傷としては橈骨遠位端骨折，舟状骨骨折をはじめとする手根骨骨折，月状骨周囲脱臼，三角線維軟骨（TFC）損傷，遠位橈尺関節（DRUJ）脱臼などが代表的である．これらの外傷に対するリハビリテーションにあたっては，まず手関節の複雑なバイオメカニクスに対する知識が必要であると考える．本稿ではじめに手関節のバイオメカニクスについて触れたあと，手関節外傷全般および先に列挙した代表的外傷に対する理学療法の実際について述べることとする．

1．手関節のバイオメカニクス

手関節は8つの手根骨および橈尺骨により構成される．手根骨は近位手根列として舟状骨，月状骨，三角骨の3つがあり，橈骨と橈骨手根関節（radiocarpal joint）を形成する．豆状骨は尺側手根屈筋腱付着部に存在し種子骨と考えられ，三角骨とのみ関節面を有する．遠位手根列は大菱形骨，小菱形骨，有頭骨，有鉤骨より構成され，近位手根列とのあいだで手根中央関節（midcarpal joint）を形成する（図1）．手関節運動は中手骨基部に付着する橈尺側の手根伸筋，屈筋腱により作動し，遠位手根列から近位手根列へ伝わり，それぞれの手根骨の解剖学的形態や手関節の諸靱帯の制御により複雑かつ精巧な運動がもたらされる（図2）．手関節運動は主に掌背屈および橈尺屈であり，橈骨手根関節，手根中央関節の両方が関与する．それぞれの関節が掌背屈運動に関与する割合は，一般に背屈で橈骨手根関節：手根中央関節＝6：4，掌屈では逆に4：6と考えられている．また橈尺屈運動のうち橈屈は約70%が手根中央関節において行われ，尺屈ではそれぞれ約50%である．近位手根列は橈屈では尺側移動とともに

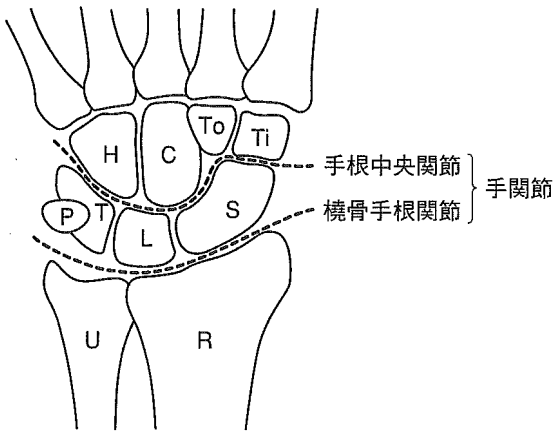

図1．手関節の骨格構造．R：橈骨，U：尺骨，S：舟状骨，L：月状骨，T：三角骨，P：豆状骨，H：有鉤骨，C：有頭骨，To：小菱形骨，Ti：大菱形骨

Key words：wrist, kinematics, physiotherapy

* Rehabilitation after traumatic injuries of the wrist

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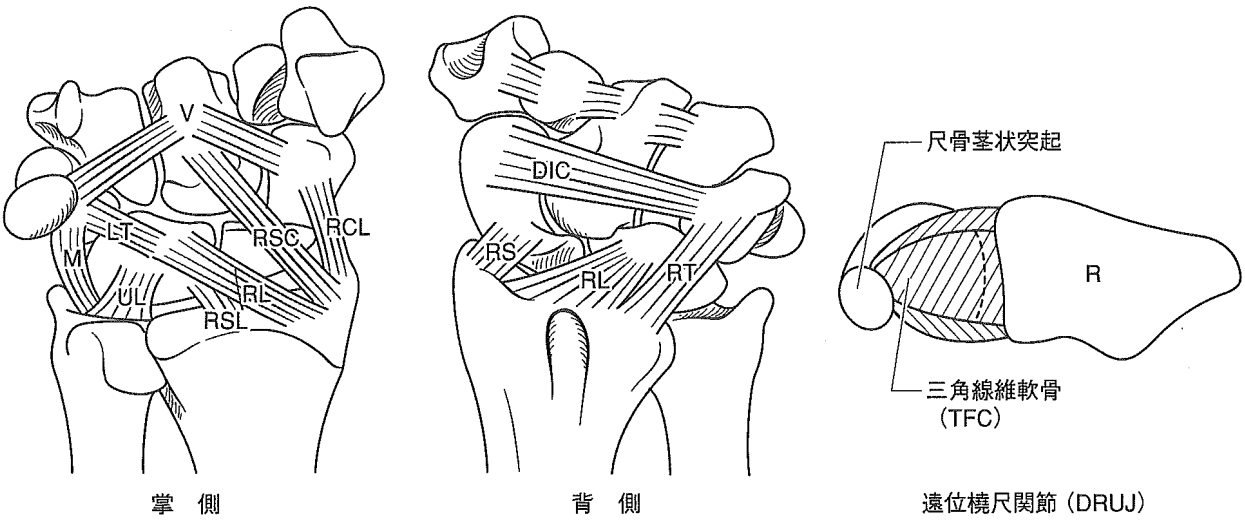

図 2. 手関節の靱帯構造．それぞれ起始および付着する骨の頭文字にて呼称する．V：V 靱帯，M：メニスクス，LT：月状三角骨靱帯，UL：尺骨月状骨靱帯，RSL：橈骨舟状月状骨間靱帯，RL：橈骨月状骨靱帯，RSC：橈骨舟状有頭骨間靱帯，RCL：橈側側副靱帯，RS：橈骨舟状骨靱帯，RT：橈骨三角骨靱帯，DIC：背側手根間靱帯

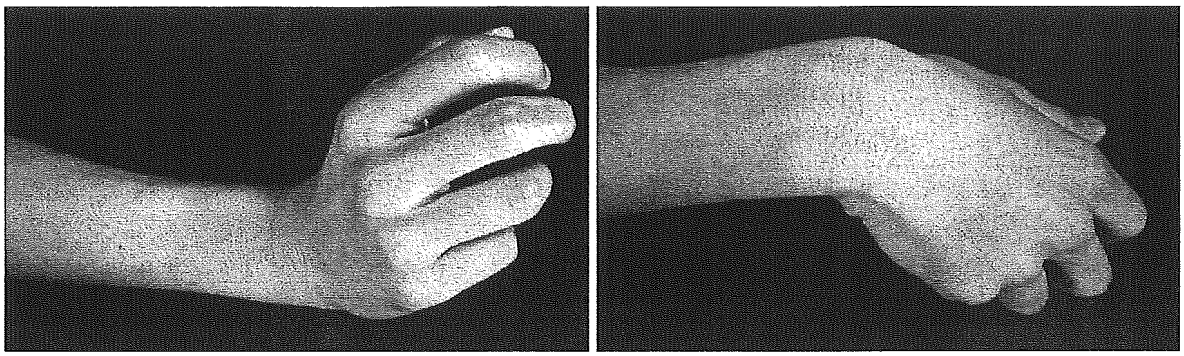

図 3. Dart throwers motion．手関節橈背屈から掌尺屈への運動

掌屈し，逆に尺屈では橈側移動するとともに背屈する．遠位手根骨同士は強固に連結されており相互の運動はわずかであるが，近位手根列間すなわち舟状骨月状骨間，月状骨三角骨間は手関節運動に伴いある程度の動きが生じる．近位手根列のうち舟状骨は mechanical link としてもっとも重要であり，手関節動作筋によりもたらされる遠位手根列の動きは舟状骨を介して近位手根列に伝わる．このことより舟状骨の動きは近位手根列の中でもっとも大きく，手関節背屈では舟状骨は月状骨に対して約 20°背屈し，手関節掌屈では 10°～15°掌屈する[1]．したがって，手関節の靱帯でもっとも損傷頻度が高いのが舟状骨月状骨間靱帯である．もともと舟状骨長軸は掌屈しているうえに，遠位手根列からの軸圧により掌屈する力が加わっている．一方月状骨は形態的に側面からみて背側が薄く，掌側が厚い非対称の三日月形のため，遠位手根列からの軸圧は月状骨を背屈させる力となる．月状骨（周囲）脱臼などで舟状骨月状骨間靱帯が広範囲に損傷されたり，舟状骨偽関節により舟状骨の動きが月状骨に伝わらなくなることで，月状骨が背屈，舟状骨が掌屈する，いわゆる dorsiflexed intercalated segment instability (DISI) 変形が発生することとなる．

最近では手関節の掌背屈運動に関して，矢状面ではなく投げ矢面（dart throwers plane）での運動がより生理的であることが証明されてきている[2]．これは橈背屈から掌尺屈の運動（いわゆるダーツを投げるさいの運動）であり，日常での手関節の動きはほとんどこの面での動きであるといってもよいかもしれない（図 3）．

筆者らは新鮮凍結死体を用いた手関節の運動解析にて，矢状面と投げ矢面での手関節運動を比較した．その結果，投げ矢面では矢状面に比し，手根中央関節の動きが橈骨手根関節の動きより大きくなり，また舟状骨月状骨間の動きは少なくなることがわかった[1]．このことは橈骨遠位端骨折や舟状骨月状骨間損傷後の関節可動域（ROM）訓練として，投げ矢面での運動がより安全で有効であることを示していると考えられる．

DRUJは凹面をなす橈骨の尺骨切痕（sigmoid notch）と凸面の尺骨頭による関節であり，前腕の回内外運動にさいし，橈骨頭と尺骨茎状突起基部を結ぶ線を回転軸として尺骨頭周囲を橈骨が回旋する．その安定性に関しては骨性の関与は少なく，関節包，三角線維軟骨複合体（TFCC），尺側手根伸筋腱，骨間膜，方形回内筋など，主に周囲軟部組織が安定化機構として重要である（図2）．尺骨切痕の曲率は尺骨頭の曲率より大きいため，回内外にさいしては回転運動に加えすべり運動が生じる．一般に回外では尺骨頭は掌側に，回内では背側に位置する．このすべり運動は前述した軟部組織により制動される．このうちTFCはDRUJの安定性にもっとも重要であり，尺骨茎状突起基部付着部のTFC断裂はDRUJの不安定性をもたらす．

II．手関節外傷後のリハビリテーション

1 急性期

手関節周囲の外傷後は当然ながら手関節の腫脹をきたすが，加えて手部および手指にまで浮腫が及ぶ．外傷直後あるいは手術直後の急性期はギプスシーネあるいはスプリントによる手関節部の固定が行われる．腫脹をいかに抑えるかが急性期のリハビリテーションにおいてはきわめて重要であり，三角巾による患肢挙上と局所のクーリングが必要である．三角巾は患肢挙上のため広く行われるが，患者にはあまり三角巾に頼らず，常に心臓より高い位置で手を挙上し，肩，肘，手指の自動運動を積極的に行うよう指導する．このことは上肢の外傷後に起りやすいcomplex regional pain syndrome（CRPS）の発生防止の点でもきわめて重要である．外固定の遠位の範囲は手関節のみとすることは当然であり，手指が完全に屈曲・伸展できることを確認する．中手指節（MP）関節は伸展拘縮を起しやすく，完全屈曲可能とするためには外固定は手掌中央皮皺線を越えないよう注意する．また近位指節間（PIP）関節は屈曲拘縮を起しやすく，拘縮が完成してしまうと改善が困難となるため，早期より他動的に完全伸展させる必要がある．さらに母指の内転拘縮にも注意が必要である．腫脹の消退のためには自動運動が重要であり，テニスボールなどなるべく軟らかいものを使って積極的に行わせる．ゆっくりと最大屈曲させ，屈曲位をしばらく保持するように指導する．数時間ごとに10分など時間を決めて行ってもらうと有効である[3]．

2 回復期

外傷の種類にもよるが，外固定期間は通常4～6週であり，その後手関節のROM訓練を開始する．最初は痛みのない範囲での自動運動が中心であり，物理療法として気泡浴や渦流浴を行う．自宅でも入浴時などの自動運動を指導する．ROM訓練後の腫脹の状況をみつつ，腫脹の増強がなければ徐々に他動でのROM訓練を始める．もし訓練後腫脹，熱感の増強があるようなら無理な継続はせず，冷水中での自動運動や訓練後のアイシングを行う．手関節のROM訓練は掌背屈が中心であるが，前述した投げ矢面でのROM訓練が運動生理学的にもっとも安全で有効であると考えられる．獲得ROMの増加と平行して手関節伸筋・屈筋の筋力訓練を行う．

III．代表的手関節外傷疾患とリハビリテーションの注意点

1 橈骨遠位端骨折

高齢者など骨萎縮がすすんだ例では，手をついて転倒したさいなどに容易に本骨折が発生する．一般に手関節背屈位で転倒したさいは遠位