Ⅱ－3 低出力超音波パルス治療の骨癒合強度に対する効果
―マイクロ CT を用いた仮骨の強度予測と 4 点曲げ試験による実測値の比較―

Effect of low-intensity pulsed ultrasound stimulation on gap healing in a rabbit osteotomy model evaluated by four-point bending test and quantitative micro computed tomography-based 3-dimensional cross-sectional moment of inertia

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【目的】ウサギ脛骨 Gap モデルを作製し、LIPUS が仮骨強度に及ぼす効果をマイクロ CT と 4 点曲げ試験を行い定量的に評価する。
【方法】21-23 週齢、体重約 4kg で雄の日本白色家兎 56 羽を用いた。右脛骨に骨切りを行い、2mm の Gap を作製し両側式の創外固定を行った。LIPUS の照射／非照射群に分け、観察期間を 4、6、8 及び 12 週とした。術後 3 日より 1 週間に 6 日、吸入麻酔下に 20 分間照射し、非照射群も同様の条件でダミーの振動子を用いて模擬照射を行った。観察終了後と殺し、μCT 撮影と 4 点曲げ試験を行った。μCT の関心領域は gap の中心 1mm とし、XYZ 空間上に設置した。X,Y 及び Z 軸周りの断面 2 次モーメント（CSM）と慣性モーメント（CSMI）を求め、Y 軸周りのモーメントと曲げ剛性・強度との相関関係を評価した。統計には Pearson の積算相関係数を求め、有意水準は $p<0.05$ とした。更に X,Z 軸周りの CSM と CSMI から LIPUS 効果の異方性を予測した。
【結果】骨折した個体を除く 56 羽中 46 羽に対し評価した。曲げ剛性と CSMy 及び CSMIy との相関はそれぞれ $r = 0.75$（$p<0.001$）、$r = 0.707$（$p<0.001$）で、曲げ強度との相関はそれぞれ $r = 0.679$（$p<0.001$）、$r = 0.71$（$p<0.001$）であった。また 8 週において LIPUS 照射群の CSM は非照射群と比べて y, z 軸方向で有意に高値（$p<0.001$）であり、CSMI は x, y 及び z 軸の 3 方向で有意に高値（$p<0.001$）であった。
【考察】観血的手術で gap を施したモデルに対し 4 点曲げ試験と 3 方向のモーメントを比較し評価した。LIPUS は剛性の回復を促進し、その効果は等方性である可能性を示唆した。

[Introduction] Low-intensity pulsed ultrasound (LIPUS) is usually radiated transversely from the lateral aspect of long bones. The stimulation is thus uni-directional. If the effect depends on the direction, the result could vary depending on the direction. The use of μCT allows 3-dimensional (3D) images and strength-related structural parameters such as cross-sectional moment (CSM) and cross-sectional moment of inertia (CSMI) to be calculated. These strength-related parameters from μCT correlate well with bending or torsional stiffness by mechanical testing. The purpose of this study was to evaluate the effects of LIPUS on restoration of mechanical properties calculating the 3D structural parameters obtained from quantitative μCT scans and making a comparison with four-point bending test.
[Material and Methods] Bilateral, transverse, mid-tibial osteotomies with a 2-mm gap were performed in 56 rabbits. LIPUS was continued for both the treatment group and the control group, for 20 min, six times / week, for 4, 6, 8 or 12 weeks. After the tibia was scanned by μCT, region of interest was set at the center of the osteotomy gap with a width of 1 mm and the XYZ coordinate was calculated. The axial CSMIs were defined as CSMIx and CSMIy, whereas the polar CSMI was also defined as CSMIz. Using Pearson's correlation analysis, we tested for statistically significant correlations between CSMIy and mechanical properties ($p < 0.05$).
[Results] Of the 56 rabbits, 46 were available for mechanical analysis. Positive correlations were demonstrated between bending stiffness versus CSMy ($r = 0.75$, $p < 0.001$) and CSMIy ($r = 0.707$, $p < 0.001$) and also bending strength versus CSMy ($r = 0.679$, $p < 0.001$) and CSMIy ($r = 0.71$, $p < 0.001$). When comparing the results of CSMs and CSMIs between control and LIPUS groups, the CSMy and CSMz in LIPUS groups were significantly larger than that in the control group at 8 weeks and the CSMIs of the LIPUS groups were significantly larger than that in the control group in all direction at 8 weeks.
[Discussion] μCT scans evaluated strength-related parameters in three independent planes. Mechanical testing can evaluate strength in only one plane for one specimen. Our results demonstrated that LIPUS improves initial restoration of stiffness at the healing site in bending in anteroposterior and mediolateral planes, as well as torsion.

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different skill levels, gender and age, in different workspaces and in the presence of dynamic obstacles.

D-8

The Development of a Custom-made Intra-medullary Nail for Use in an Ovine Tibial Segmental Defect Model

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The aim of this study was the development and manufacture of an intra-medullary nailing system to stabilise a tibial segmental defect in an ovine model, in order to study bone regeneration strategies. Tissue engineering is well established in orthopaedic research in vitro, and small animal studies have demonstrated the therapeutic effect of synthetic scaffolds seeded with mesenchymal stem cells in bone regeneration [1]. Upscaling to a large animal (ovine) model is necessary prior to translation to human clinical trials.

Difficulties in ovine models include strong and consistent methods of maintaining the critical bone defect in a fully weight bearing sheep. Potential methods are plating, external fixation or intra-medullary (IM) nailing, the latter two being the most clinically relevant. External fixation requires meticulous and labour-intensive post-operative care, thus the development of an intuitive, robust ovine IM device would be beneficial.

The breed of sheep selected, the Northern Mule, has a body mass up to 100 kg. The typical tibial medullary canal for this animal is 20 cm long and 8–9 mm in diameter. Reaming of the medullary canal affects the bone biology at the defect site which may confound results, therefore an oversized nail, though more stable, is undesirable for this model. The weakest points in the nail are the locking screw holes due to the removed material at these points and stress raisers. Increasing the nail diameter adds strength and an 8 mm diameter nail is the minimum possible diameter to accommodate holes for 3.5 mm diameter locking screws whilst maintaining enough strength to not buckle or bend over the defect length.

For human IM nail insertion, and previous ovine IM nail studies, distal locking screws are inserted freehand which requires intra-operative imaging. This adds time and expense to the procedure and increases personnel and equipment requirements and costs [2,3]. A jig was developed to align the drill and locking screws with the internal screw holes both proximally and distally. The novel insertion apparatus and technique presented in this paper consists of an external guide attached to the proximal end of the nail which is aligned with the screw holes and can be rotated and re-aligned with perpendicular holes allowing full locking of the nail within the bone.

This technique simplifies surgery and significantly reduces costs when compared to existing intra-medullary nailing systems.

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D-9

Interpositional Knee Devices: The Way Forward?

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Osteoarthritis is the most common progressive degenerative disorder of the cartilage of joints. Treatment of osteoarthritis (OA) is evolving, allowing the Orthopaedic surgeon and patient more options including the choice of surgical intervention at an earlier stage of the disease. The interpositional knee device is a recently developed patient specific implant used for the treatment of uni-compartmental OA and the correction of leg axis deformity. It is designed for use in mild to moderate osteo-arthritis only. It offers benefits over the traditional surgical management methods of uni-compartmental OA. It is less invasive, can be performed as a day procedure and does not limit future options. The National Institute for Clinical Excellence (NICE) recently issued guidance on the use of this device as experimental.

A young adult with uni-compartmental arthritis is suitable for this implant instead of a uni-compartmental knee replacement or a high tibial osteotomy. A Magnetic Resonance Imaging (MRI) scan of the patient's knee is reviewed by the local radiologists along with a radiologist in the US to decide if the patient is suitable for the implant based on a number of factors. A bespoke implant, based on the MRI data, is produced. Prior to insertion of the device an arthroscopic procedure is undertaken to allow proper positioning of the implant in the knee.

We have treated 26 patients with the iForma Conformis interpositional knee implant in South Wales at the Princess of Wales Hospital, Bridgend and the Royal Glamorgan Hospital, Llantrisant since November 2007. The pre- and post-operative Western Ontario and McMaster Universities (WOMAC) Osteoarthritis Index scores were recorded prior to surgery and at the last follow up appointment. The average age was 54.7 years, Body Mass Index (BMI) 32; there were 9 females and 17 males. The average pre-operative WOMAC score was 42.2 with an improvement to 62.9 post-operatively. A total of 33 implants were used (20 right, 13 left). Only 5 lateral compartment implants were used. 7 patients experienced post-operative problems (5 implants removed and 2 MUAs). No dislocations were reported. The average follow-up time was 19.2 months (range 10–27 months).

Our early experience suggests patient selection plays a vital role in the outcome of patients following surgery. It indicates that the interpositional knee device is a viable and safe alternative to a uni-compartmental knee replacement. A further study is underway to compare this procedure with the uni-compartmental knee device.

D-10

A Navigated Unilateral External Fixation System for Deformity Correction Incorporating Preoperative Surgical Simulation and Intraoperative Razor Guidance

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Ring frames like Ilizarov or Taylor Spatial Frame[1] are preferred for correction of severe and complex multi-plane deformities. However, the available frames are heavy and bulky leading to poor compliance by patients. Also, the mounting procedure requires considerable expertise and skill, and it is technically demanding to insert penetrating wires for application to the proximal femur. On the other hand, a unilateral external fixator has the advantages of less bulk and a lighter weight. Thus, it causes less disability and can achieve better patient compliance even with bilateral application. However, previous unilateral fixators have had various limitations with respect to deformity correction, such as restricted placement of hinges, restricted correction planes, and a limited range of correction angles. In addition, it was impossible to achieve progressive correction while fixation was maintained. To overcome these disadvantages of existing unilateral fixators, a new unilateral external fixator with a universal bar link system has been developed that can achieve acute and gradual correction of multi-plane deformities, including rotational and translational deformities.

Preoperative surgical planning for determining optimal mounting of the fixator is performed using a 3D STL model of the bone created from preoperative CT scans and CAD data of the fixator. A correction hinge can be placed exactly right on the centre of rotational angulation (CORA) or at any desired location with the preoperative planning. Virtual deformity correction can be performed and final outcome after correction can be assured in 3D plane.

A laser-beam projection system has been developed, which allows us to obtain surgical guidance information. Utilizing the system, pin insertion sites and direction as well as placement of the fixator can be determined intraoperatively as exactly as preoperatively planned. Laser beams are directly projected onto the surgical field so that the surgeons are able to obtain accurate guidance information. Two laser-beam lines are projected onto the cylindrical tool surface. When two beams align parallel, precise insertion of the tool can be done as previously planned. With this guidance system, we don't have to look at a monitor to make sure that insertion direction is precise or not. We are able to just keep on looking at the devices we hold.

Gradual correction of the deformity can be performed by rotating three dials mounted on the link using a warm geared goniometer that is temporarily attached to the apparatus, while fixation is maintained. The fixator is manipulated by rotating each of the three dials to the predetermined angles calculated by computer software. The goal of treatment is to restore physiological orientation of the knee and ankle joints, as well as to restore physiological alignment of the mechanical axis.

Mechanical testing demonstrated that this new fixator had sufficient strength for full weight bearing as well as sufficient fatigue resistance for repeated or prolonged use. The results of clinical application in patients with multi-plane femoral deformities were excellent, and correction with very small residual deformity was achieved in each plane.

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D-11

A Combined Passive and Active Joints Robotic System for Photodynamic Therapy for Port Wine Stains

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Port Wine Stain (PWS) birthmarks are congenital vascular malformations, which usually appear at birth and tend to become darker and thicker with age's growth. Vascular-targeted Photodynamic Therapy (PDT) is an effective approach among the treatments for PWS. However, due to the arbitrariness of manual operation and pole points existing in laser radiation, the PWS zone was always cured unevenly in clinics. This paper presents a novel robotic system, which consists of a passive arm and an active wrist, for assisting doctors to exert PDT treatments. In clinics, compared to the fully actuated robot, the passive arm is more convenient and safer to be operated; the two Degrees of Freedom (DOFs) active wrist can automate PDT under the guidance of binocular vision, so the doctors can focus more concentration on clinical judgments and treatments rather than do heavy manual work. The workflow to use the robotic system is as follows. In pre-treatment, the doctor should firstly adjust the passive arm to an appropriate pose (position and orientation), after that the robotic system should acquire enough images around the lesion by the binocular vision, and then the doctor could segment the lesion easily on a Liquid Crystal Display (LCD) panel with a mouse, finally the workstation could reconstruct the lesion's 3-Dimensional (3-D) models with surface rendering method. During the treatment, based on the 3-D positions of the boundary of the lesion, the workstation will manipulate the active wrist to move the laser tip according to the doctor's setting. This paper, firstly, introduced the mechanism of PWS and its treatments. Based on the prosperities of PDT, we designed the robotic system architecture, which consists of the medical robot, binocular vision and workstation. Then the detailed mechanical design on the robot with combined passive and active joints was given. The passive arm has four joints, each of which has a built-in electromagnetic brake, which can lock the joint at any angle during the treatment and loose it by pushing an electrical button when needed to revolute. The active wrist has two joints, which can automatically manipulate the laser tip in PDT. Furthermore, we discussed the kinematic analysis and uniform radiation, which is the key direct factor for PDT. To validate the robotic system, we have done three experiments to assess the accuracy respectively on the robot, the binocular vision and the whole robotic system. Experimental results showed that the robotic system could reduce much more work burden and realize more uniform radiation than manual work could. The clinical results will be given after the accomplishment of the ongoing clinical experiments. Obviously, this robotic system can also be employed in other laser-based therapy for uniform radiation.

D-12

Mechanism Design Issues for Minimally Invasive Surgical Robots

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Introduction and Objectives: Design of minimally invasive surgical (MIS) robots is a great challenge because it involves multiple specialties spread in the fields of medicine and engineering. From the engineering side, the robot design can be further managed into various aspects such as the manipulator design, actuation strategy, motion control, vision acquisition and processing, etc. Among the various specialties, mechanism design plays a predominated role in the whole design process; however, there is still no literature dedicated to the mechanism design of MIS robots. This paper, therefore, aims at providing a figure to the mechanism design of MIS robots.

Material and Methods: Based on the exhaustive review of the literatures in MIS robot design, the challenges for mechanism design of MIS robots are studied. First, an exclusive kinematic feature in MIS robots, namely "remote center-of-motion (RCM)", is revisited. Secondly, the design issues for mechanism design of MIS robots are discussed.

Results: A general mechanism design procedure for MIS robots is summarized. Accordingly, eleven design issues for the mechanism design of MIS robots, including the RCM function, ergonomics, kinematic redundancy, backdrivability, modularity, safety, accuracy, workspace, dexterity, singularity, and isotropy, are concluded.

Conclusions: As a result, this paper provides a comprehensive overview to the mechanism design of robotic manipulators used for minimally invasive surgery. It suggests researchers a way to follow-up when designing the manipulator structure of MIS robots. It contributes to both mechanisms and medical communities for the kinematic analysis and mechanism design of MIS robots.

D-13

A Metamorphic Instrumental Hand for Robot Assisted Minimally Invasive Surgery

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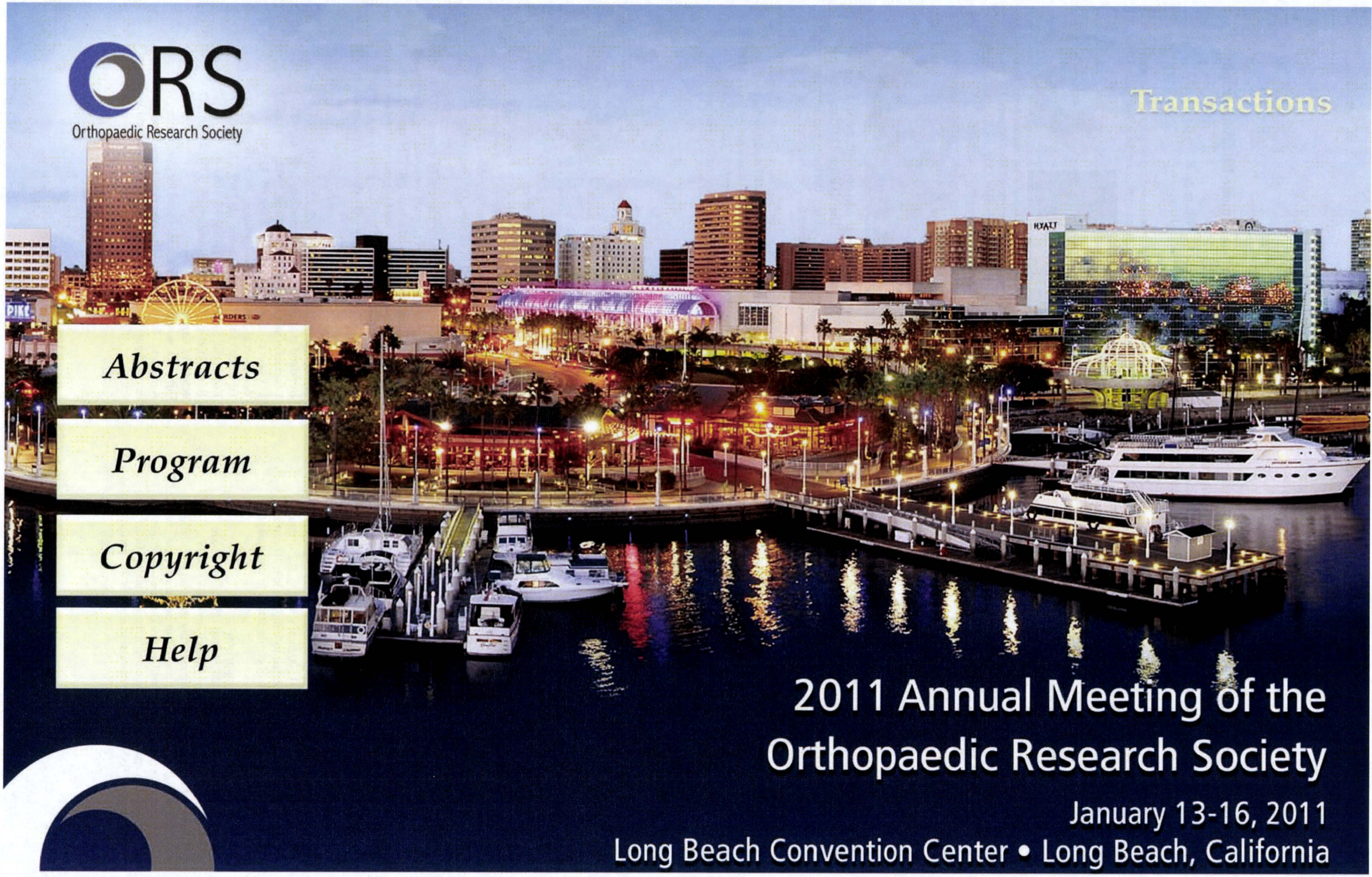
Instrumental hands for robot assisted minimally invasive surgery (MIS) perform surgical operation inside the abdomen of the patient under a surgeon's control. In this paper, a three-fingered metamorphic instrumental hand derived from the planar four bar mechanism is proposed for the robot assisted MIS. The metamorphic instrumental hand is aimed to improve the robot assisted MIS manipulation. It is composed of one metamorphic mechanism and three independent operational fingers. The metamorphic mechanism is capable of changing the topological structure of the device from a pole to a three fingered instrumental hand during operation, and return to a pole again after operation. The metamorphic characteristic enables the instrumental hand to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Measurement of Articular Cartilage Thickness Using a 3D Image Reconstructed from B-mode Ultrasonography Mechanical Scans -Comparison with MRI-derived Data-

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INTRODUCTION

Although articular cartilage thickness has previously been quantified using B-mode ultrasonography (US) [1, 2], thicknesses in those studies were measured 2-dimensionally using B-mode slice images. Cartilage thickness has also been quantified by creation of 3-dimensional (3D) models from MRI data [3, 4], but this approach has not been adapted to US. The purpose of this study was to develop a method to measure 3D articular cartilage thickness at the femoral condyle using B-mode US and to compare results with 3D measurements using MRI to clarify the feasibility of US in clinical evaluations of articular cartilage.

OBJECTIVES AND METHODS

US B-mode image acquisition

Subjects comprised 2 healthy male volunteers (age, 37 and 59 years) and 2 male patients with knee osteoarthritis (age, 73 and 81 years) who provided written informed consent prior to participation in the study. The study protocol was approved by the ethics committee of our institution. A B-mode 10.0-MHz linear ultrasound probe (UST-5411; Aloka, Tokyo, Japan) connected to an ultrasound device (Prosound ALPHA 10; Aloka) was attached to a probe scanner stabilized by a holding arm, allowing the ultrasound probe to move along the surface of the flexed knee (Fig. 1A). The base of the holding arm was rotated by a gear and data on angle of rotation of the arm was transferred to the ultrasound device by an encoder. Scans with angle data were recorded. The medial surface of the right knee of each participant was scanned using the ultrasound probe with the knee flexed at 120° (Fig. 1B) so the cartilage surface of the femoral medial condyle could be visualized by US. The US probe was attached to the arm so the US imaging plane was parallel to the arm plane, allowing the imaging plane to rotate around the center axis of the encoder, which was coaxial with the medial-lateral axis of the femoral condyle. The range of the angle of rotation for the arm was 0-80° and the US B-mode images (total, 101 images) were acquired every 0.8° (Fig. 2A). System settings were optimized to image the cartilage surface (tissue harmonic, 420 pixels × 468 pixels; pixel size, 0.0855 mm × 0.0855 mm).

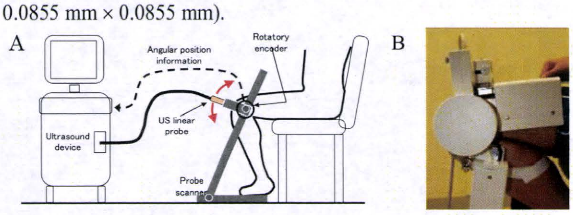

Figure 1. A) Illustration of the entire US system for knee cartilage image acquisition. **B)** Side view of a knee in the probe scanner.

Cartilage area extraction and 3D model creation (US and MRI)

Image and position data were imported to the originally developed software and slice images were aligned in 3D in the proper position (Fig. 2B, C). Parallel slice images were then created using the multiple plane reconstruction method and imported to the 3D model creation software (Mimics; Materialize, Leuven, Belgium). Cartilage area was extracted in each image using the Livewire method of the software [5] and a 3D cartilage model was created from the extracted cartilage area. MR images of the knees were acquired using the sequence previously described [4] from the MRI device (Achieva 3.0T X-series; Philips, Eindhoven, the Netherlands; 512 pixels × 512 pixels; pixel size, 0.313 mm × 0.313 mm; slice thickness, 0.600 mm; slice gap, 0.291 mm). DICOM data from MRI were imported to Mimics and a 3D cartilage model was created after extraction of cartilage area in each image as similarly done for US.

Articular cartilage thickness comparison

The 3D data for 3D cartilage models from US and MRI were imported to 3D inspection software (Rapidform XOV; INUS Technology, Seoul, Korea) and aligned using the point registration method (Fig. 3C). Cartilage thickness (Tc) in each model was visualized by color mapping (Fig. 3A, B). Cartilage thickness was determined at 400 points 1 mm apart from one another in the US model (Tc-US) and the MRI model (Tc-MRI). Linear regression analysis was performed and Pearson's coefficient of correlation was used to compare Tc-US with Tc-MRI. A correlation was considered significant for values of $p<0.05$.

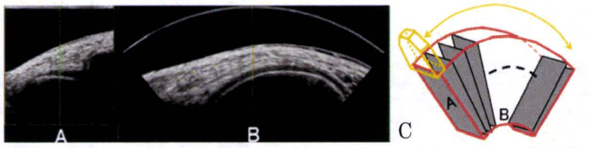

Figure 2. A) Original B-mode US image of a participant knee. **B)** US image of the knee from the side, reconstructed from original US images in A). **C)** Illustration of US image alignment. Original US images in A) were aligned three dimensionally in the proper position.

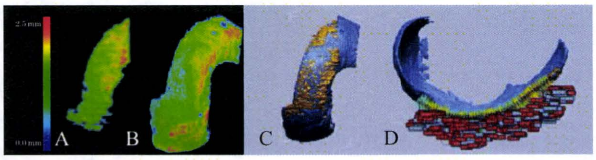

Figure 3. Color mapping of cartilage thickness with the 3D US model **(A)** and the 3D MRI model **(B)**. **C)** The 3D US and MRI models were aligned by point registration. **D)** Cartilage thickness measurements from both models at 400 points 1 mm apart from one another.

RESULTS

With color mapping of articular cartilage thickness, the US model exhibited relatively good similarity to the MRI model in thickness distribution (Fig. 3A, B). Tc-US correlated significantly with Tc-MRI in all participants ($p<0.0001$, each) (Fig. 4). Pearson's coefficient of correlation tended to be slightly higher in volunteers than in patients with osteoarthritis.

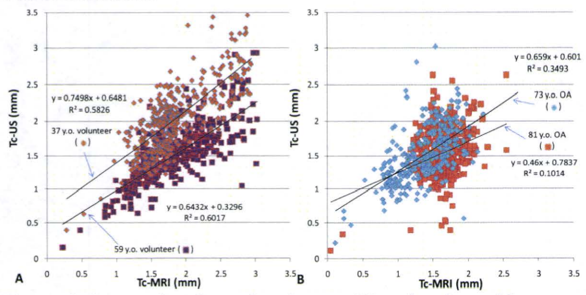

Figure 4. Scatter plots for each volunteer **(A)** and patient with osteoarthritis **(B)**. Linear regression analysis shows good agreement between Tc-US and Tc-MRI in all plots. OA: osteoarthritis.

DISCUSSION

This is the first study to clinically measure Tc using a 3D US cartilage model, although 3D US has been adopted for evaluating other tissues, such as the Achilles tendon [6] and rotator cuff [7].Considering the high accuracy of Tc measurement using MRI [8], our results show that, like MRI, Tc-US measurement using 3D models also allow accurate measurement of Tc, in both healthy individuals and patients with osteoarthritis.

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Effect of low-intensity pulsed ultrasound stimulation on callus remodeling in a gap healing model
- Evaluation by bone morphometry using 3-dimensional quantitative micro computed tomography -

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INTRODUCTION

Low-intensity pulsed ultrasound stimulation (LIPUS) effects are reportedly derived from the promotion of cell differentiation, which induces acceleration of fracture healing, resulting in earlier restoration of strength at the fracture healing site.

Previous studies have attempted to determine which stages of fracture healing are affected by LIPUS. Many basic studies suggested that LIPUS affected the inflammation, angiogenesis and soft callus formation stages. However, several studies suggested that LIPUS had no promoting effect in hard callus formation and remodeling stages [1]. Most previous basic studies have investigated the effects of LIPUS by histological evaluation, which is useful in clarifying cell differentiation and the formation of tissue morphology/arrangement, but is limited to observation in a 2-dimensional (2D) plane. Another method adopted has been mechanical testing of harvested specimens, but this is limited in that the testing is destructive and the strength of the healing site is evaluated in only one of multiple spatial planes.

In recent years, several basic studies have investigated fracture healing site morphology using micro-computed tomography (μCT). The advantage of μCT lies in the non-destructive morphological and densitometric assessments in 3-dimensional (3D) planes. In evaluating the effects of LIPUS on fracture healing by means of μCT, assessment is only possible after the healing stage has formed mineralized fracture callus.

The purpose of the present study was to quantitatively evaluate the effect of LIPUS on bone healing by means of μCT throughout both modeling and remodeling processes using a gap healing model in rabbits.

MATERIALS AND METHODS

Surgical Procedures

A total of 42 skeletally mature between 21 and 23-week-old male Japanese white rabbits (Kitayama Labes, Nagano, Japan), weighing 3.4-4.0 kg, were used for this study. Under general anesthesia, four transfixation pins (diameter, 2 mm; length, 50 mm) were inserted at the metaphyseal regions of the tibia in the frontal plane using a custom-made surgical pin driver. Transverse osteotomy was performed using a T-saw (blade thickness, 0.36 mm) with continuous irrigation with saline solution across the mid-shaft of the tibia at 12 mm distal to the tibio-fibular junction. The osteotomy with a 2-mm gap was immobilized with four pins fixed to an external fixator with double side bars. All procedures were performed in accordance with the guidelines of the Association for Assessment and Accreditation of Laboratory Animal Care (AAALAC).

LIPUS Treatment

The LIPUS system (model SAFHS®2000J, Teijin Pharma, Tokyo, Japan), which transmits 200-μsec burst of 1.5-MHz sine waves repeated at 1kHz with an average intensity of 30mW/cm^2, was used. After postoperative day 3, LIPUS was continued under general anesthesia for both the treatment group (n=7/group/time point) and the control group (n=7/group/time point). The transducer was placed onto the anterior surface of the operated leg with ultrasound coupling gel, for 20 min, six times/week, for 4, 6, or 8 weeks. The control group also received a sham inactive transducer under exactly the same condition as the LIPUS group.

μCT Analysis

All animals were euthanized with CO_2 asphyxiation and the entire right tibia was removed. After removal of soft tissues, the harvested tibia was scanned by μCT (Scan X mate-E090; Comscantecno, Kanagawa, Japan). The scan was performed along the long axis of the diaphysis, with a voltage of 60 kVp and a current of 80 μA. Scan range covered 5 mm proximal and 5 mm distal to the center of the gap, with a resolution of 28.57 μm^3 voxel size. The region of interest (ROI) was set at the callus healing area (Fig. 1) defined by the gap filled with callus in 2D-CT scans and extended 0.5 mm proximally and distally from the center of the osteotomy gap with a total of 36 CT axial scans. 3D reconstruction of mineralized tissue was performed using a TRI-BONE system (Ratoc System Engineering, Tokyo, Japan). A threshold for newly formed mineralized callus was set as 200 mg/cm^3 [2].

Morphometric parameters used for evaluation were mineralized callus volume (BV, cm^3) and volumetric bone mineral density of mineralized tissue comprising the callus (mBMD, mBMD = BMC/BV, mgHA/cm^3). The whole ROI was measured and was subdivided into three zones (Fig. 1): a periosteal callus zone (External; red zone); a medullary callus zone (Endosteal; green zone); and the cortical gap zone as the remaining zone (Intercortical: yellow zone). For each zone, BV and mBMD were measured.

Statistical Analysis

The μCT evaluations were analyzed using a one-way ANOVA test. If that correction did not achieve normality, then a Kruskall-Wallis ANOVA on ranks was utilized. Data were all presented in mean and standard error of the estimate. Values of $p<0.05$ were considered statistically significant.

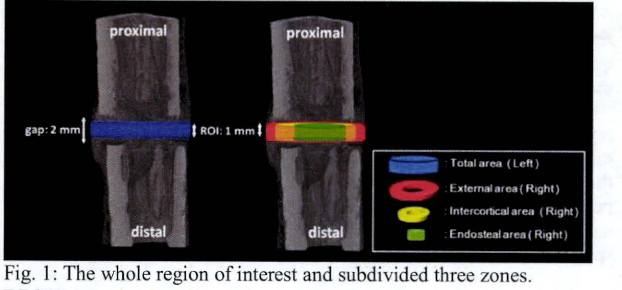

Fig. 1: The whole region of interest and subdivided three zones.

RESULTS

Callus Volume

The results of BV were shown in Fig.2. The control groups showed no significant differences. However, in the LIPUS groups, mean BV for the Endosteal zone was significantly lower for the 8-week group than for the 4-week group ($p < 0.05$). Comparing results at the same time point, the LIPUS group at 8 weeks was significantly higher than that of the control group in the Intercortical zone ($p<0.001$).

Volumetric Bone Mineral Density of Mineralized Tissue

The results of mBMD were shown in Fig. 3. The control groups showed no significant differences. However, in the LIPUS groups, the 8-week group was significantly higher than the 4-week group for Total, External, Internal, and Endosteal zones, respectively ($p < 0.001$, 0.001, 0.001, and 0.05). Comparing results at the same time point, the LIPUS group at 8 weeks was significantly higher than that of the control group in both External ($p < 0.05$) and Intercortical ($p < 0.05$) zones.

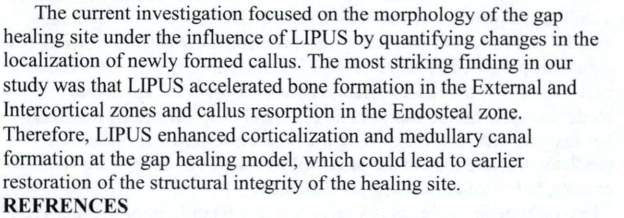

Fig.2-3: The result of BV (left) and mBMD (right) were showed.
*= $p < 0.05$, ***= $p < 0.001$

DISCUSSION

The current investigation focused on the morphology of the gap healing site under the influence of LIPUS by quantifying changes in the localization of newly formed callus. The most striking finding in our study was that LIPUS accelerated bone formation in the External and Intercortical zones and callus resorption in the Endosteal zone. Therefore, LIPUS enhanced corticalization and medullary canal formation at the gap healing model, which could lead to earlier restoration of the structural integrity of the healing site.

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CT-based finite element method for predicting the strength of the proximal femur in patients with postmenopausal osteoporosis
- Evaluation of inter- and intra-observer reliabilities and reproducibility -

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Introduction:

The increase in fragility fractures of the proximal femur has become one of the major problems of an aging society. It has now become much more significant to accurately assess fracture risk and to establish effective prevention strategies in each individual osteoporotic patient.

Clinically available methods for estimating bone strength include bone densitometry, such as DXA (dual energy X-ray absorptiometry) or pQCT (peripheral quantitative computed tomography), and imaging modalities, such as X-ray or CT. Such techniques evaluate regional bone density and morphology, which are partly related to fracture risk, but they are of limited value for quantifying structural strength [1, 2]. Therefore, it is necessary to develop a noninvasive method to accurately quantify bone strength, incorporating information on the three-dimensional distribution of morphology, density, and material properties.

We established a quantitative computed tomography (QCT)-based finite element method (QCT/FEM) that was able to more accurately quantify the structural strength of the proximal femur than previous methods [3].

QCT/FEM must have a high accuracy and reproducibility if it is to be repeatedly used in longitudinal clinical studies. Therefore, the purpose of this study was to investigate the inter- and intra-observer reliabilities of the analysis of the strength of the proximal femur in patients with postmenopausal osteoporosis. Moreover, the reproducibility of the method was also evaluated by repeated analyses of a fresh cadaver specimen of the proximal femur.

Materials and Methods:

The study protocol was approved by our ethics committee, and the patients were enrolled after giving their informed consent. Axial CT scans of the proximal right femur were obtained in 12 female patients (mean age, 78 years) with postmenopausal osteoporosis (Aquilion Super 4, Toshiba Medical Systems Co., Tokyo, Japan; 120 kVp, 75 mAs, 512×512 matrix, pixel spacing 0.683 mm, slice thickness 3 mm), as well as scans of a calibration phantom.

A right femur with no skeletal pathology was collected within 24 hours of death from a 72-year-old female. A bone specimen was stored at -70 °C after each step of the protocol. The specimen was trimmed with a handsaw 14 cm distal to the midpoint of the lesser trochanter, and the proximal part was used for the experiments. After thawing, the trimmed specimen was cleaned of all soft tissues [1]. The specimen was then immersed in water, and axial CT scans were obtained with a slice thickness of 3 mm and a pixel width of 0.625 mm using the Aquilion Super 4 (Toshiba Medical Systems Co.; 120 kVp, 75 mAs, 512×512 matrix), as well as a calibration phantom. Repeated QCT scans were performed with repositioning of the specimen, and 6 data sets were obtained for analyzing reproducibility.

From the QCT data, FE models were created using triangular shell elements with a thickness of 0.4 mm and a size of 3 mm for the outer surface of the cortical bone and tetrahedral solid elements with a size of 3 mm for the rest of the bone [3]. To allow for bone heterogeneity, the mechanical properties of each element were computed from the Hounsfield unit value. Ash density for each voxel was determined from the linear regression equation derived by relating the Hounsfield unit of a calibration phantom to the equivalent ash density. Young's modulus and the yield stress of each tetrahedral element were calculated using the equations proposed by Keyak et al. [4] and Keller [5]. Poisson's ratio for each element was set at 0.4. Boundary conditions were applied to this model to represent the stance configuration [4, 6]. Materially nonlinear FE analysis was performed using the Newton-Raphson method. The predicted fracture load of the proximal femur was defined as the load causing failure of at least one shell element [3].

Two orthopedic surgeons (Observers A and B) independently analyzed strength from the same data of the proximal femur for each patient. According to the method of Feldman, each observer analyzed the same data twice [7]. The time interval between the first and second analyses was more than 3 weeks. Intra-class correlation (ICC) coefficients were used as indices for inter- and intra-observer reliabilities. From the strength data acquired by Observer A, with scans and analyses of the proximal femur specimen repeated six times, the coefficient of variation was calculated.

Results:

Strength data analyzed by Observers A and B are shown on Table 1. There was no significant difference in the mean analyzed strength between the first and second analyses for Observer A ($p = 0.591$). Likewise, there was no significant difference for Observer B ($p = 0.259$). In addition, there was no significant difference in the mean analyzed strength between Observers A and B ($p = 0.917$). Intra-observer reliability as assessed by the intra-class correlation coefficient was 0.924 for Observer A and 0.956 for Observer B. Inter-observer reliability as assessed by the intra-class correlation coefficient was 0.905. The mean analyzed strength and the standard deviation of the specimen for the repeated analyses were 3675 N and 52.4 N, respectively. Reproducibility as assessed by the coefficient of variation was 1.43%.

Table 1: Analyzed strengths by Observers A and B (N)

Observer A

	First trial		Second trial	
	M	SD	M	SD
Predicted Fracture Load (N)	4390	320	4365	380

Observer B

	First trial		Second trial	
	M	SD	M	SD
Predicted Fracture Load (N)	4385	370	4345	350

M: mean, SD: Standard Deviation

Discussion:

Altman et al. classified reliability as assessed by the ICC coefficient as good with a coefficient of 0.61-0.81 and as very good with a coefficient of 0.81-1.00 [8]. Therefore, the reliability of our method was considered to be very good. Cody et al. reported that the reproducibility of their QCT/FEM was 1.85% from repeated analyses of the QCT scans from 10 volunteers [9]. The result for the reproducibility of our method appears to be nearly identical. The reproducibility of DXA for the proximal femur has been reported to be 2-3% [10]; the reproducibility of QCT/FEM can attain the same level. In conclusion, QCT/FEM can be used in a longitudinal cohort study investigating the change in strength analyzed over time.

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第35回日本整形外科スポーツ医学会シンポジウム「Locomotive Syndromeを予防するためのスポーツ医学的アプローチ」

骨粗鬆症を有する中高年者をLocomotive Syndromeにしないために—骨折高リスク高齢者への対策—

Prevention for the Locomotive Syndrome in Elderly Persons with Osteoporosis

遠藤 直人 Naoto Endo

●Key words

Osteoporosis：Fracture risk：QOL

●要旨

骨粗鬆症では骨強度の低下により骨が脆弱化し，軽微な外力で骨折をきたす．骨粗鬆症性骨折の転帰は，骨折直後には疼痛があり，活動が制限される．脊椎椎体圧迫骨折例では脊椎椎体変形は残存し，身体的な障害や心理的な障害をきたす．大腿骨頚部骨折は高齢者に多く，とくに75歳以降，年齢とともに急増する．大腿骨頚部骨折者数は今後とも一層の増加が予測される．したがって骨粗鬆症では自立が障害されることから，ロコモティブシンドロームの主要な疾患の1つと捉えられている．

骨粗鬆症患者個別に骨折危険因子の有無，程度を評価し，それに基づいて個別に対応をすることが必要である．骨密度増強および骨折防止のために食事，運動，また必要に応じ薬物が推奨される．さらに骨折リスクの高い人には積極的に介入し，骨折を防ぐことが必要である．整形外科医が積極的な役割を果たすことが求められる．

骨粗鬆症は自立を障害：ADLとQOLの低下

骨粗鬆症の定義は“骨折リスクを増すような骨強度上の問題をすでに持っている人に起こる骨格の疾患”(2000年，NIHコンセンサス会議)である．骨粗鬆症では骨強度(＝骨密度＋骨質)の低下により骨が脆弱化し，軽微な外力で骨折をきたす．高齢者に多く，骨粗鬆症が高度では外傷歴がはっきりしない骨折症例もみられる．

骨粗鬆症での骨折部位は脊椎椎体が最も多く，次いで大腿骨頚部，橈骨遠位，上腕骨頚部に骨折をきたす．

骨粗鬆症性骨折の転帰は，骨折直後には疼痛があり，活動が制限される．それに加えて脊椎椎体圧迫骨折例では，脊椎椎体変形は残存する．脊椎椎体は前方が後方に比してより圧潰することが多く，脊柱後弯変形をきたす．高度な後弯変形は胸郭が腹部へ

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表1 高齢者における骨折リスク

寝たきり，不動・低活動
認知症，認知機能低下
脳血管障害
施設入居
栄養障害，低栄養状態
肝，腎，消化器障害

食い込むようになり，腹部の圧迫症状，逆流性食道炎(GERD：gastroesophageal reflux disease)などを伴う．このように脊椎椎体骨折は骨折時のみでなく，骨癒合後においても身体的な障害をきたし，転倒や再骨折への不安を抱く心理的な障害をもきたす[1~3](表1).

大腿骨頚部骨折

日本における大腿骨頚部骨折数は年およそ16万件と推定されている．大腿骨頚部骨折は歩行障害に直結し，通常，骨折直後から移動・歩行ができなくなる．わが国の高齢化は急速に進んでおり，とくに75歳以上のいわゆる後期高齢者の増加が著しい．大腿骨頚部骨折は高齢者に多く，とくに75歳以降，年齢とともに急増する．大腿骨頚部骨折者数は，今後とも一層の増加が予測される．

生命予後

生命予後の面で大腿骨頚部骨折は不良であり，骨折後1年で10%の方は亡くなると報告されている．

脊椎椎体骨折症例においても医療機関で受診される骨折例では大腿骨頚部骨折症例と同程度に不良であると報告されている．

骨粗鬆症は健康寿命を阻害する

骨粗鬆症では自立が障害される．骨折により，移動，活動などの基本的日常生活動作(ADL)ができず，生活の質(QOL：quality of life)も低下する．健康長寿，すなわち"痴呆(認知症)，寝たきりにならない状態，心身ともに自立した生活・活動期間"を阻害する要因である．このように骨粗鬆症はロコモティブシンドローム(以下，ロコモ)の主要な疾患の1つである[1~4].

骨粗鬆症治療と予防の目的

骨粗鬆症の予防と治療ガイドライン，2006年版で示されているが，骨粗鬆症の治療と予防の目的は，骨折を予防し，骨折危険性を低減し，QOLの維持・向上を図ることである[3, 4](表2).

骨折危険因子とその評価

FRAX〔fracture risk assessment tool〕(WHO)は，骨粗鬆症患者の骨折リスクの評価に基づき，個人レベルにおける10年間の骨折確率を推計する．FRAXで使われている骨折危険因子は"年齢，性別，大腿骨頚部骨密度[骨密度がない例ではBMI(body mass index)]，既存骨折，両親の大腿骨近位部骨折歴，喫煙，飲酒，ステロイド使用，関節リウマチ，続発性骨粗鬆症"である．この結果は治療開始基準として用いられている[5].

骨粗鬆症の予防と治療ガイドライン，2006年版において治療開始基準に用いられている骨折危険因子は"低骨密度，既存骨折，年齢"，"過度のアルコール摂取，現在の喫煙，大腿骨頚部骨折の家族歴"である[3](表2).

その他の骨折危険因子：25(OH)Dなど[6~11]

新潟県佐渡市における骨折疫学調査結果では，大腿骨頚部骨折群の血中25(OH)D値は非骨折群に比較して有意に低く，intact PTHは有意に高かった．したがって"血中25(OH)D低値"，"PTH高値"は大腿骨頚部骨折のリスク因子である．

血清ucOCはビタミンK摂取量の指標である．ucOC高値はビタミンK不足を意味し，"ucOC高値(ビタミンK不足)"は大腿骨頚部骨折リスクである(WHO technical report 921).

その他の危険因子として，"ホモシステイン高値"は大腿骨近位部骨折発症率と関連していることが報告されている．

認知症，認知機能低下も骨折危険因子と考えられ

表2 脆弱性骨折予防のための薬物治療開始基準[3)]

I	脆弱性骨折がない場合 1）腰椎，大腿骨，橈骨または中手骨BMDがYAM 70%未満 2）YAM 70%以上80%未満，閉経後女性，50歳以上の男性 過度のアルコール摂取，現在の喫煙，大腿骨頚部骨折の家族歴のいずれか1つを有する場合
II	脆弱性既存骨折がある場合(男女とも50歳以上)

表3 各種薬剤の特徴とエビデンス[3)]

	除痛	骨密度	骨折防止効果		総合評価
			椎体	非椎体	
カルシウム製剤		C	C	C	C
女性ホルモン		A	A	A	C
活性型ビタミンD		B	B	B	B
ビタミンK	B	B	B	B	B
エチドロネート		A	B	B	B
アレンドロネート	*	A	A	A	A
リセドロネート	*	A	A	A	A
ラロキシフェン	A	A	B	A	A
カルシトニン	A	B	B	C	B

る(表1)．

ロコモにしないために：骨粗鬆症の予防[12〜14)]

1. 骨粗鬆症の予防と治療としてはまず骨折危険因子の評価を行ない，除くことが可能な因子については除くように対処する．

 骨折リスクとしては前述のように低骨密度，高齢，既存骨折，飲酒，現在の喫煙などがあり，さらに近年注目されているビタミンD〔血液中25(OH)D〕低値，ucOC，ホモシステインにも注目する．骨粗鬆症患者個別に骨折危険因子の有無，程度を評価し，それに基づいて個別に対応をすることが必要であろう．

2. 骨強度低下により，軽微な外力で骨折することからそれに対する適切な対策が必要である．
3. 骨密度増強(および骨折防止)のためには食事，運動，必要に応じ薬物が推奨される．

 食事ではカルシウム，ビタミンD，ビタミン類を充分に摂取することが必要である．とくに高齢者ではたんぱく質不足の人が多い．骨粗鬆症治療のためのカルシウム摂取目標量として800 mg以上が推奨される(骨粗鬆症の治療と予防のガイドライン，2006年版)．

 運動として，散歩がよい．長く続けられる運動として，散歩は望ましい．高齢者では背筋訓練は椎体骨折予防効果がある．また開眼片足立ち訓練は転倒防止効果がある[15)]．運動は個別の能力に基づいて量，強度を含めて処方することが大切である．

4. 薬剤選択：脆弱性骨折予防のための薬物開始基準，各薬剤の特徴とエビデンスが骨粗鬆症の予防と治療ガイドライン，2006年版で示されている．

 近年，ビスホスホネート治療に際し，ビタミンDの併用が重症骨粗鬆症例において効果的と報告されている(表3)．

5. QOLへの配慮：骨折はADLを障害するのみでなく，“再骨折への不安，寝たきりへの懸念”をもきたす．これはQOLの低下である．患者の愁訴，不満として疼痛が大きな要因である．したがってQOLの維持向上を図るうえで，疼痛対策が第

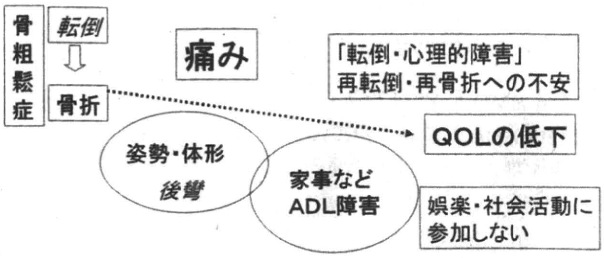

図1 骨粗鬆症患者の転帰
骨折によりADL，QOL低下が低下する．QOLの維持・向上をめざすことが必要でそのためにも疼痛対策が重要である．

一に重要である(図1)．

6. 骨折の連鎖を予防：骨粗鬆症による骨折には連鎖がある．新潟県佐渡市での疫学調査によれば，脊椎骨折，大腿骨近位部骨折ともに60歳～70歳台以降に急増する．脊椎骨折者の半数は，その後に大腿骨近位部骨折を起こすと推定されていることから"骨折の連鎖：脊椎骨折⇒大腿骨頚部骨折"をきたすと考えられている．したがって，大腿骨頚部骨折の予防には脊椎骨折時点から対応し，"骨折の連鎖を断つこと"が必要である．

まとめ

骨粗鬆症を予防し，ロコモに至らないようにするためには"骨粗鬆症検診(X線検査，骨密度測定，危険因子調査など)"をすすめることが第1歩である．とくに骨折高リスクの高齢者を早期に発見し，適切な対策を行なうことが重要と考えられる．

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ビタミンDと骨折リスク

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ビタミンDは骨密度（bone mineral density：BMD）増加効果は低いものの骨折予防効果がある。この作用機序としてはBMDに必ずしも依存しない骨強度改善の機序が考えられている。大腿骨近位部骨折患者においては非骨折者に比して血清25(OH)Dが低値であり，骨折の背景にビタミンDの不足が示唆される。ビタミンDは骨格筋や神経細胞に作用し，転倒予防効果も報告されている。さらに近年，認知機能やそのほかの骨外組織に対してもビタミンDの果たす役割が注目されている。

Hip fracture：assessment of fracture risk for treatment.

Vitamin D and risk of fracture.

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Although an increase in vitamin D has a small effect on bone mineral density, it has an influence on fracture prevention. This may be explained by a mechanism of improvement of bone strength that does not necessarily depend on bone mineral density. The level of serum 25 (OH) D is low in hip fracture patients compared with non-fracture controls, which suggests that a background of vitamin D insufficiency may be

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involved in hip fracture. Vitamin D acts on skeletal muscle and nerve cells, and it has been reported that this has an effect on fall prevention. Furthermore, recent reports suggest a role of vitamin D in cognitive function and in other tissues not involving bone.

はじめに

骨粗鬆症の治療薬として活性型ビタミンDの存在はよく知られているところであるが，近年，ビタミンDが骨だけではなく骨格筋や神経に作用して筋力やバランスを改善し，転倒を抑制することや，さらに認知機能や骨外組織においてもその関連を示す報告が多くみられている。ビタミンDと骨折との関係を中心に，多様な広がりをみせるビタミンDの働きについて考察する。

骨折予防とビタミンD

活性型ビタミンD_3は，著明な骨密度（bone mineral density：**BMD**）増加効果はないものの，椎体および非椎体骨折の防止効果があるとの報告がみられる[1)~4)]。WHO（World Health Organization）テクニカルレポートでは，カルシトリオール，αカルシドールのいずれにおいても，BMD増加作用，椎体骨折防止効果，非椎体骨折防止効果については「結果が一定しない」と評価されている。また，骨粗鬆症の予防と治療ガイドラインによれば，活性型ビタミンD_3は椎体骨折・非椎体骨折ともにグレードB（行うよう勧められる）となっている。また「特にカルシウム（Ca）不足が主体となっている症例や，転倒頻度が高く骨折を起こしやすい高齢者への使用が推奨される。高Ca血症には注意が必要」と記載されている。

骨折予防効果について，椎体骨折ではTilyardら[1)]の報告で既存の女性椎体骨折患者において3年間の活性型ビタミンD_3投与により，椎体骨折発生の有意な抑制が示された。国内ではOrimoら[2)]の報告において，1年間の二重盲検比較試験の結果，活性化ビタミンD投与群で椎体骨折が有意に減少した。これらの臨床試験を含む8試験のメタアナリシス[3)]においても，椎体骨折での骨折抑制は相対リスク0.63（0.45～0.88，$p < 0.01$）となっている。

非椎体骨折では，6試験のメタ解析で相対骨折リスクは0.77（0.57～1.04，$p = 0.09$）で，抑制傾向はあるが有意ではなかった[3)]。Tanizawaら[4)]の報告では新潟県佐渡市の住民約1万人を対象にした検討で，活性型ビタミンD_3 0.5 μg/日以上の服用は非服用に比べて大腿骨近位部骨折の発生リスクを1/4程度に有意に減少させることが示された。また，この研究ではビタミンD投与を中止すると，骨折発生率が非治療群と同等に上昇することが報告され，治療の継続が重要であることが示された。

同じ佐渡市で2004年，1年間の大腿骨近位部骨折症例全例を調査した結果，大腿骨近位部骨折症例の血清25(OH)Dレベルが骨折を有しない同地域の方に比べて低値であった[5)]。骨折群の平均値は20 ng/mLを下回っており，ビタミンD不足の存在が示唆された。大腿骨近位部骨折におけるビタミンD不足は諸外国においても報告されている[6)7)]。また，大腿骨近位部骨折患者の約80%はX線検査上，既存の椎体骨折を有していたため，椎体骨折発生後，数年後に大腿骨近位部骨折を起こしているケースが多いことが推察される。椎体骨折の段階で既にビタミンD不足が存在する可能性があると考えられる。

BMD：bone mineral density（骨密度）

さらに，高齢女性のおよそ半数がビタミンD不足であるとの報告[8)9)]や，施設入居者では自立高齢者よりビタミンDが低値であるとの報告がされている[10)]。

活性型ビタミンD_3はBMD上昇効果という点ではビスホスホネート製剤と比べ決して高くはない。骨粗鬆症の予防と治療ガイドラインにおいても「BMD増加についてはわずかな増加効果がある」（グレードB）となっている。ビタミンDの骨折抑制効果について，必ずしもその機序のすべてが明らかとなってはいない。

骨強度＝BMD＋骨質であることから，BMDに対する作用とは独立した作用として，骨質に対してもビタミンDが何らかの作用を有するのではないかと推察されている。Saitoら[11)]は，骨コラーゲンの架橋組成比（非生理的架橋／生理的架橋）の異常に対するビタミンD不足の関連を指摘している。骨コラーゲン架橋には，ホモシステイン，ビタミンB_6などほかにも種々の因子が関与しており，ビタミンDもそのうちのひとつの因子として役割を担っていると考えられている。

転倒と25(OH)D

大腿骨近位部骨折の原因は，転倒によるものがその大部分を占める。従って，高齢者における易転倒性，動揺性，筋力低下などは骨折の大きなリスク因子となる。この転倒予防に関してもビタミンDとの関連が指摘されている。Bischoff-Ferrariら[12)]らのメタアナリシスによれば，ビタミンD投与群は非投与群に比し，有意に転倒の発生を抑制すると報告されている。またPfeiferら[13)]は閉経後女性237名について血清25(OH)Dレベルが体幹動揺性と負の相関をすることを示した。(すなわち25〔OH〕Dレベルが高いほど動揺しにくい。)これらのメカニズムとして，筋線維ビタミンD受容体を介したビタミンDの筋への直接作用や，筋細胞・神経細胞のビタミンD受容体を介して筋と神経の協調性を高め，重心動揺を減少させる作用などの機序が考えられている。日本国内では鈴木ら[14)]の報告によれば，2,957例の地域在住高齢者の25(OH)Dを測定した結果，男性の4.8%，女性の17.7%でビタミンDが不足（<20 ng/mL）しており，特に女性では低レベルの25(OH)Dが転倒と関係していた（OR＝0.97，95% CI＝0.94～0.99，p＝0.01）。転倒予防に対しても血清25(OH)Dが適切なレベルであることが重要であると考えられる。

ビタミンDの骨外での作用

1．認知症

ビタミンDと認知症に関して，Satoら[15)]はアルツハイマー患者における25(OH)D低値を報告している。この要因として，日光曝露の減少や栄養不良などが影響している可能性が示唆された。アルツハイマー病になった結果としてビタミンDが不足することが考えられるが，一方でビタミンD受容体（**VDR**）は認知機能に関わる大脳皮質，海馬などの中枢神経系に存在しており，近年，neurologistの間でもビタミンD不足と認知機能の関係について関心が高まっている。しかし，一口に認知機能といっても幅広く，25(OH)Dが高齢者の遂行機能とは関係するが記憶テストとは関係しないとの研究結果があり[16)]，特に認知機能のどの部分がビタミンDと深く関係しているのか，また分子レベルでの機序などについても今後のさらに詳細な報告が待たれる。

筆者らが佐渡市で行った研究でも，大腿骨近位部骨折患者において，介護保険の認知症高齢者の日常生活自立度が低いほど血清25(OH)Dが低値との結果が出ている（**図1**）[5)]。

VDR：ビタミンD受容体

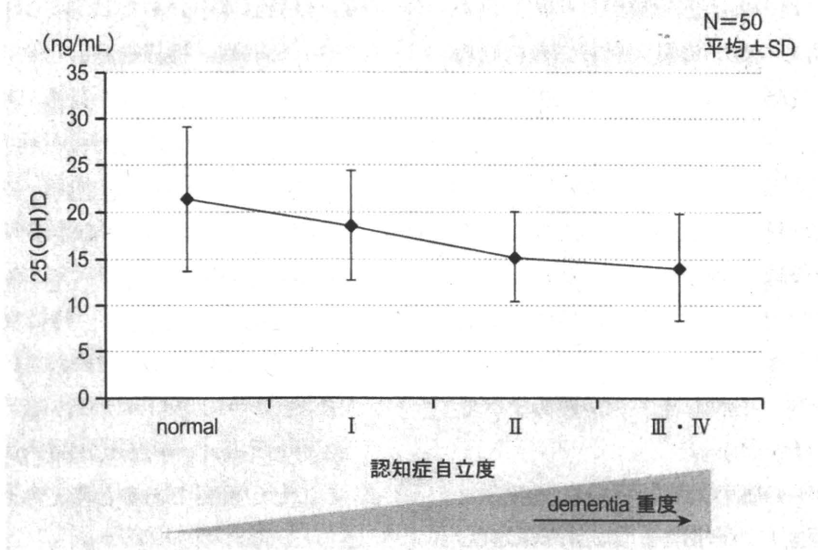

図1　大腿骨近位部骨折患者の認知症自立度と25(OH)D

認知症自立度が低下しているほど血清25(OH)Dが低値であった ($p < 0.05$)。
(文献5より引用改変)

表1　低ビタミンD状態が関与する疾患

骨粗鬆症	＋＋＋＋
転倒	＋＋＋＋
1型糖尿病	＋＋
腫瘍	＋＋＋＋
自己免疫疾患	＋＋
高血圧	＋＋＋
歯周病	＋＋＋＋
易感染性／感染への応答低下	＋＋＋＋
多発性硬化症	＋＋
変形性関節症	＋＋

＋＋＋＋：ひとつ以上の無作為試験を含む強いエビデンス。
＋＋＋：無作為試験はないが強い疫学的根拠。
＋＋または＋：強い根拠はないが疑われる。　(文献17より引用)

2．そのほかの骨外作用と生命予後

ビタミンD不足状態が関与していると考えられる疾患は，骨粗鬆症のほかにも，悪性腫瘍，自己免疫疾患，糖尿病，高血圧，心疾患と全身の多岐にわたる慢性疾患での関与が疫学研究やRCT (randomized controlled trial：ランダム化比較

RCT：randomized controlled trial (ランダム化比較試験)

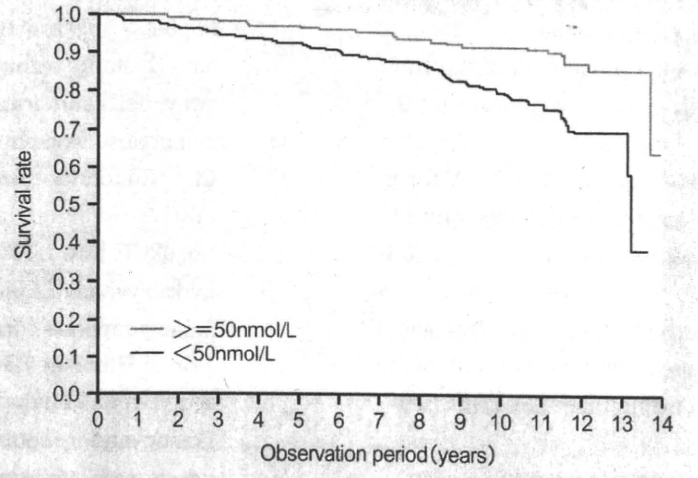

図2 血清25(OH)Dレベルと生命予後

25(OH)D < 50 nmol/L vs.25(OH)D ≧ 50 nmol/Lで生存率に有意差がみられた。($p < 0.01$)

(文献20より引用)

試験)の結果から指摘されている(**表1**)[17]。心血管系において，ビタミンD不足は動脈硬化を悪化させる報告がみられている。Giovannucciら[18]によると，米国で25(OH)D < 15 ng/mLの低ビタミンD群の男性は，ビタミンD充足群に比べて心筋梗塞のリスクが有意に高値であった。腫瘍においても，大腸がん，乳がん，前立腺がんなどとの関係が報告されている[19]。ビタミンD受容体は全身の臓器に分布しているため，骨以外にも全身にさまざまな作用を及ぼしていることが考えられる。

血清25(OH)Dレベルと生命予後に関して，歩行可能な閉経後女性1,232名を調査した結果，25(OH)D < 50 nmol/L(= 20 ng/mL)は生命予後のリスクファクターとなると報告されている[20](**図2**)。大腿骨近位部骨折や脊椎骨折の受傷は生命予後に影響を与えることが報告されているが，骨折だけではなく全身の脆弱性にビタミンDが何らかの関与をしている可能性が示唆される。

おわりに

ビタミンDはBMDへの効果を含め，それ以外の機序(骨質)も合わせて骨折の抑制に寄与するとみられる。また筋・神経においては転倒抑制効果，さらにそのほかの骨外組織や生命予後へのビタミンDの影響に関して，近年関心が高まっている。

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地域の指導者とともに実施した骨粗鬆症と転倒の予防教室の効果

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遠藤直人[2)]

はじめに

地域在住の65歳以上の住民1,039名(男性419名，女性620名)を対象に骨量と体力特性の関係を分析した結果，骨量は握力，下肢筋力(膝伸展筋力)，上体起こし(体幹筋力)，長座体前屈(柔軟性)，開眼片足立ち，10m障害物歩行(歩行能力)，6分間歩行(歩行持久力)と有意な相関があった[1)]。この結果をもとに骨粗鬆症と転倒の予防プログラムを開発し，2003年度に埼玉県K市とS市の住民に対し，6ヵ月間13回の骨粗鬆症と転倒の予防教室(以下，予防教室)を実施し，その前後で測定を行った。その結果，すべての測定に参加した女性54名は骨量には有意な変化はなかったが，下肢筋力，障害物歩行，上体起こしは有意に改善した[2)]。次に予防教室に参加し，すべてのプログラムを終了した住民66名を対象に，2007年に骨量と体力を測定した。その結果，2003年の予防教室参加前後，4年後のすべての結果が得られた39名は，骨量は年齢相応に低下したものの，下肢筋力，開眼片足立ち，長座体前屈は増加していた。また，握力，6分間歩行能力は維持しており，上体起こしと障害物歩行は，実施前と比べ有意に増加していた[3)]。それらの経過を踏まえ，この参加者が地域の指導者(以下，指導者)となる住民主体の教室を支援するために，指導者研修会を実施し，その指導者とともに予防教室を開催した。そこで，今回の予防教室が地域在住高齢者の骨量・体力・QOLに及ぼす効果を分析し報告する。

1　方　法

1)対　象

対象となる指導者は，S市とK市での2003年度の予防教室参加者から募った。また，予防教室の参加者は60～75歳までの地域住民103名であった。

2)指導者研修会

研修会は医師，看護師・保健師，栄養士，理学療法士，作業療法士が医学的注意，予防教室の目的・原則・運営方法，介護予防，栄養と食事，実施する各運動の原理・目的などについて講演し，理学療法士，作業療法士が運動やレクリエーションについて実技指導を行った。同時に2007年10月以降の予防教室の運営について協議し

Effects of Preventive Programs for Osteoporosis and Falls Practiced with the Community Leaders
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Key words：骨量，体力，QOL，地域指導者

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表1　前期参加者の骨量・QOL・体力の変化($n=30$)

	実施前(平均±SD)	実施後(平均±SD)	有意確率
骨量			
音響的骨評価値(×10⁶)	2.21±0.241	2.29±0.240	NS
若年成人平均値(YAM%)	78.1±8.72	81.2±8.42	NS
同年齢平均値(%)	95.1±10.18	99.3±9.44	NS
JOQOL点数(100点満点)	81.4±7.29	81.5±6.48	NS
体力			
握力(kg)	24.6±6.17	25.8±5.75	0.042
下肢筋力(kg)	21.1±3.98	21.4±3.54	NS
開眼片足立ち(秒)	73.0±43.05	87.2±38.74	0.003
6分間歩行(m)	541.7±62.05	557.2±114.43	NS
10m障害物歩行(秒)	8.4±1.75	7.5±1.77	＜0.001
長座体前屈(cm)	37.1±8.47	38.6±7.69	NS
上体起こし(回)	5.2±5.78	8.0±6.72	＜0.001

準備を行った。

3) 支援体制の構築と実施スケジュール

2008年5月から指導プログラムと配布資料を作成し，支援体制を作った。同年6月に住民指導者募集を行い，準備会議および研修会は7～9月に各4回開催した。同年10～12月までを予防教室前期，2009年1～3月までを予防教室後期とし，両市でそれぞれ週1回，3ヵ月間に10回開催した。指導者研修会と予防教室は，S市とは協力を，K市とは共催を得て，埼玉県立大学の公開講座として両市の保健センターで実施した。

4) 予防教室の指導内容

指導は運動方法だけでなく，運動継続の重要性，地域住民が自立して運動や健康維持に取り組む必要性，医学的注意，運動やレクリエーションの原則，運動と栄養・食事の関係，個々の体操およびレクリエーションの目的とその原理を講演により理解してもらった。さらに，歩数計を配布しその使用方法を指導し，資料に添付した日誌に歩数，運動や活動を記録してもらい，運動を習慣づけ，生活の中での活動量向上を目指した。

5) 予防教室の効果判定

骨量・体力測定とQOL評価を行い，前期・後期とも各予防教室実施前後と，さらに前期の参加者は教室終了3ヵ月後との効果を比較した。骨量測定は超音波法による踵骨の音響的骨評価値(OSI)を測定し，若年成人平均値(YAM)%と同年齢平均値%を求めた。体力は文部科学省スポーツ・青少年局新体力テスト(65～79歳対象)により握力，上体起こし，長座体前屈，開眼片足立ち，障害物歩行，6分間歩行を，把持型筋力計により下肢筋力を測定した。QOL評価は日本骨代謝学会骨粗鬆症患者QOL評価質問表(JOQOL)で行った。

統計学的分析は統計解析ソフトPASW18.0を用いて，前期と後期の予防教室前後の比較は対応のあるt-検定を，前期の予防教室前後と3ヵ月後の効果は一元配置分散分析を行った。

2　結　　果

1) 受講者数と指導者数

受講者は前期36名，後期67名の計103名，指導者は前期16名，後期23名となった。なお，後期の指導者は，両市とも前期参加者の一部が担当した。

2) 参加者の体力と骨量およびQOLの変化

前期参加者36名中30名が予防教室前後の測定に参加した。体力測定の結果(**表1**)，握力(平均±SD：24.6±6.17～25.8±5.75kg，$p=0.042$)，開眼片足立ち(73.0±43.05～87.2±38.74秒，$p=0.003$)，10m障害物歩行(8.4±1.75～7.5±1.77秒，$p<0.001$)，上体起こし(5.2±5.78～8.0±6.72