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General Summary

Basic Research

Our research on bone metabolism has been focused on the relationship between osteoporosis and fracture risk. High levels of pentosidine in urine or blood, or mild hyperhomocysteinemia, that indicate bone collagen abnormalities, might be used as surrogate markers for evaluating bone quality and assessing the risks of bone fracture. Our clinical research focuses on the relationship between systemic disorders, such as life-style related diseases and aging, and bone disease. On the other hand, in basic research, we analyze the hard tissue properties using the mice mucopolysaccharidosis model and focus on the epigenetic modification in giant cell tumors. We found a novel mutation in the H3.3 histone of the giant cell tumor cells.

Our studies on development and application of a new type navigation system with 3D scanner have played a pioneering role. A detailed pre-operative planning of the accurate bone cut is extremely important to achieve satisfactory post-operative outcomes after total knee arthroplasty. Our new type of navigation system incorporates a small 3D scanner located on conventional surgical instruments and allows recognition of relative positions of the knee joint possible in just few seconds. Currently, we are evaluating the operability of the system and examining the accuracy of component position with prototype equipment.

Clinical Research

Our clinical practice has been divided into 10 subspecialties to treat a wide range of musculoskeletal disorders and is managed by different specialist teams: knee joint, hip joint, spine, shoulder joint, foot surgery, trauma, osteoporosis, rheumatic diseases and sports. All teams maintain a high level of expertise and are actively involved in scientific activities. The trauma team has reported on their treatment experience of the intertrochanteric femoral fractures with bone defects using β -TCP, hyaluronic acid, and the FGF-2 complex. They developed and clinically applied an injectable complex that promotes synostosis and repair of cortical bone deficiency in patients with fractures of displaced lesser trochanter and intertrochanteric femoral fractures with AO classification of 31-A2. The foot and ankle joint team focused on pathophysiology of hallux rigidus, a degenerative arthritic disorder of the hallux MTP joint. Their analysis is based on evaluation of CT scans and intraoperative findings. Through this range of clinical research activities, all teams fulfill their important roles at a clinical academic hospital, and their commitment

has been highly evaluated.

Research Activities

Midterm results of arthroscopic Bankart repair for anterior shoulder instability

Outcomes of arthroscopic Bankart repairs in 123 recurrent anterior shoulder instability cases followed for more than 2 years were evaluated. The average patients' age at operation was 30 years. Recurrence ratio was 13% in all patients, however it was 24% in the teenagers. Out of 11 patients with recurrence and age between 10 and 29 years, 8 got instability that occurred during sport activity. Post-surgical recurrence developed in 3 out of 12 patients with bony Bankart lesions, and 2 out of 13 patients with general joint laxity. Midterm results were relatively satisfying, however it seems necessary to improve the surgical procedure for patients with large glenoid defects, general joint laxity, and for teenage athletes practicing collision sports.

The current activities of the hand surgery division

XIAFLEX[®], an injectable collagenase preparation, which digests pathological palmar fascia and can be used in treatment of Dupuytren's contracture has been available in our institution. Many patients received treatment with XIAFLEX[®] and good post-operative results were obtained. Application of the preparation led to lower number of pathological fascia resection for Dupuytren's contracture. The treatment is beneficial because of its low invasiveness compared to conventional surgical approach. Apart from Dupuytren's contractures, we treat many other diseases: from traumatic injuries such as fractures, tendon ruptures and neurovascular injuries to degenerative disorders and tumors. Additionally, we perform highly specialist surgical procedures including tendon suturing and microsurgery. Besides surgical treatments we also provide conservative therapies in our outpatient clinic, when we often cooperate with occupational therapists to facilitate early functional recovery of our patients.

Leg cramps in patients with lumbar spinal canal stenosis: Analysis of prevalence and attempts to reduce invasiveness of surgical procedures in patients with osteoporotic vertebral fractures

Osteoporosis and its complicating disorders of the lumbar spine: osteoporotic vertebral fractures (OVF), lumbar canal stenosis or spinal deformation in adult age are important diseases leading to locomotive syndrome or frailty, particularly in elderly patients. We have recently reported that the lateral approach with insertion of expandable artificial bone cages reduced blood loss during osteoporotic vertebral fracture (OVF) repair and demonstrated that it is an effective procedure with low invasiveness. We also found that leg clamps is not a rare complication that may occur after LCS surgery, result in lower physical activity and worsen frailty or locomotive syndrome. More research addressing this issue seems to be necessary. Among factors that require consideration, especially in surgery for spinal deformity, intraoperative monitoring is very important to avoid post-operative neurological complications. We reported that a properly performed wake-up test could detect motor movements without major complications including psychological

burden in adolescent patients and demonstrated that a combination of MEP monitoring and wake-up test is a safe and useful intraoperative monitoring option.

The two-stage treatment of chronic periprosthetic joint infection with retention of well-fixed and well-functioning cementless stems: Long-term outcomes of 7 cases followed for over 7 years

We evaluated clinical results of two-stage treatment of chronic periprosthetic joint infection (PJI) with retaining well-fixed cementless stems in patients followed for over 7-years. The clinical courses of 7 patients treated for chronic PJI without stem removal were examined. The first-stage surgery involved acetabular cup removal and reconstruction by filling the acetabular defect with antibiotic-loaded acrylic cement and creating a socket-like hemispherical dent. After confirming that the infection had been eradicated, the second-stage acetabular reconstruction was performed. Between two surgeries, patients underwent active range-of-motion and ambulation exercises. One patient died of an unrelated noninfective cause 1 year postoperatively; 6 patients had good functional outcomes and radiographic findings showing no PJI recurrence. Two-stage treatment with stem retention and antibiotic-loaded articulating cement spacers may be beneficial for chronic PJI.

Development of a new type navigation system with a 3D scanner

In total knee arthroplasty, a detailed pre-operative planning of the accurate bone cut is extremely important to achieve satisfactory post-operative outcomes. A CT-based navigation system has been developed as one of computer-assisted surgery techniques aiming to improve the accuracy of surgical planning. However, several problems such as complicated data registration, high operational costs and interference of normal tissue with marker pins limit the widespread use of this navigation system. To address the above issues, we have been developing a new type of navigation system, which is simple, compact, low cost and non-invasive. In our system, a small 3D scanner located on conventional surgical instruments makes recognition of relative positions of the knee joint possible in just few seconds. Currently, we are evaluating the operability of the system and examining the accuracy of component position with prototype equipment.

Pathophysiology of the hallux rigidus

Hallux rigidus is degenerative arthritis of the hallux MTP joint, however its underlying pathology is not yet fully understood. We attempted to establish a plausible explanation based on detailed evaluation of CT images and intraoperative findings. Our findings indicated that erosion of the articular cartilage starts from the dorsal aspect of the metatarsal head and extends more centrally, with the dorsum of proximal phalangeal head impinging at dorsiflexion. Osteophytes were observed not only the dorsum of the metatarsal head but also on the plantar aspect and around the sesamoid bone even in early stages of the disease. We thought that the force of traction is exerted on the plantar aspect at dorsiflexion. This may result in contracture of the plantar structures, drawing the proximal phalanx underneath the metatarsal head and leading to collision of the proximal phalanx and the metatarsal head in dorsiflexion.

The current activities of bone metabolism division

In our outpatient clinic specializing in the bone metabolism, we provide the personalized bone analyses using simultaneous estimation of bone quantity and bone quality. We treat several kinds of refractory bone disorders, such as postmenopausal, glucocorticoid-induced, hormonal disorder-associated, childbirth-associated and vegetarianism-associated osteoporosis, Paget disease and osteomalacia. Among our clinical research activities, we analyze the relationship between a systemic disorder, such as life-style related diseases and aging and/or bone disease. On the other hand, our basic research focuses on analysis of the hard tissue properties using mouse mucopolysaccharidosis model and examine epigenetic modifications in giant cell tumors.

Treatment of intertrochanteric femoral fracture with bone defect using β -TCP, hyaluronic acid and FGF-2 complex

We developed an injectable complex, which promotes synostosis of displaced lesser trochanter fracture and repair of cortical bone defects. The complex was clinically applied for surgical treatment intertrochanteric femoral fractures with the AO classification of 31-A2. Based on 7 operations, the complex (combining 2 g of β -TCP granules with 60% porosities, 2.5 ml of hyaluronic acid, and 1 mg of FGF-2) was injected into the gap between displaced lesser trochanter and diaphysis under fluoroscopy before insertion of an intramedullary nail. In all cases, most of the β -TCP was partially absorbed into the bone, and synostosis of the trochanter region was markedly promoted in all cases at 12 post-operative weeks. Our results indicate that the injectable complex stimulates synostosis of the displaced fracture of the lesser trochanter.

Publications

Funasaki H, Saito M, Mizumura MK¹, Hayashi T, Marumo K (Ochanomizu Univ). Bone quality in female ballet dancers: A possible determinant of bone health. *Open J Orthopedics*. 2017; **7**: 285-94.

Tanaka T, Komaki H, Chazono M, Kitasato S, Kakuta A, Akiyama S, Marumo K. Basic research and clinical application of beta TCP. *Morphologie*. 2017; **334**: 164-72.

Yoshida M, Marumo K. Injections of leukocyte-reduced platelet-rich plasma in partial tears of the Achilles tendinopathy: A report of six cases. *JSM Arthritis*. 2017; **2**: 1021.

Tonotsuka H, Sugaya H, Takahashi N¹, Kawai N¹, Sugiyama H¹, Marumo K (Funabashi Orthopaedic Sports Medicine Center). Target range of motion at 3 months after arthroscopic rotator cuff repair and its effect on the final outcome. *J Orthop Sci*. 2017; **25**: 1-8.

Shinohara K, Watabe AM, Nagase M, Okutsu Y, Takahashi Y, Kurihara H, Kato F. Essential role of endogenous calcitonin gene-related peptide in pain-associated plasticity in the central amygdala. *Eur J Neurosci*. 2017; **46**: 2149-60.

Okutsu Y, Takahashi Y, Nagase M, Shinohara

K, Ikeda R, Kato F. Potentiation of NMDA receptor-mediated synaptic transmission at the parabrachial-central amygdala synapses by CGRP in mice. *Mol Pain*. 2017; **13**: 1744806917709201.

Uehara S¹, Udagawa N¹, Mukai H², Ishihara A³, Maeda K, Yamashita T¹, Murakami K¹, Nishita M², Nakamura T⁴, Kato S⁵, Minami Y², Takahashi N¹, Kobayashi Y¹ (Matsumoto Dental Univ, ²Kobe Univ, ³Tokyo Medical and Dental Univ, ⁴Tokyo Dental College, ⁵Iwaki Meisei Univ). Protein kinase N3 promotes bone resorption by osteoclasts in response to Wnt5a-Ror2 signaling. *Sci Signal*. 2017 Aug 29; **10**. pii: eaan0023.

Nakamura M^{1,2,3}, Kamei M^{1,2}, Bito S¹, Migita K^{1,5}, Miyata S^{1,6}, Kumagai K¹, Abe I¹, Nakagawa Y¹, Nakayama Y¹, Saito M¹, Tanaka T¹, Motokawa S¹ (Jpn Natl Hosp Organ EBM Study Group, ¹Mie Univ, ²Murase Hosp, ³Jpn Natl Hosp Organ Tokyo Med Ctr, ⁵Fukushima Med Univ, ⁶Natl Cerebral Cardiovasc Ctr, Japan). Spinal anesthesia increases the risk of venous thromboembolism in total arthroplasty: Secondary analysis of a J-PSVT cohort study on anesthesia. *Medicine (Baltimore)*. 2017; **96**: e6748.

Kimura T, Kubota M, Suzuki N, Hattori A, Marumo K. Comparison of intercuneiform 1-2 joint mobility between hallux valgus and normal feet using weightbearing computed tomography and 3-Dimensional analysis. *Foot&Ankle International*. 2018; **39**: 355-60.

Okabe H, Aoki K, Yogosawa S, Saito M, Marumo K, Yoshida K. Downregulation of CD24 suppresses bone metastasis of lung cancer. *Cancer Science*. 2018; **109**: 112-20.

Takeda S¹, Saito M, Sakai S¹, Yogo K¹, Marumo K, Endo K¹ (Chugai Pharmaceutical Co., Ltd). Eldecalcitol, an active vitamin D3 derivative, prevents trabecular bone loss and bone fragil-

ity in type I diabetic model rats. *Calcif Tissue Int*. 2017; **101**: 433-44.

Watanabe R¹, Shiraki M¹, Saito M, Okazaki R², Inoue D² (Geriatric clinic Institute, ²Teikyo Univ). Restrictive pulmonary dysfunction is associated with vertebral fractures and bone loss in elderly postmenopausal women. *Osteoporos Int*. 2018; **29**: 625-33.

Reviews and Books

Saito M, Marumo K. The Effects of Homocysteine on the Skeleton. *Curr Osteoporos Rep*. 2018; **16**: 554-60.